a short effective transmission range, e.g., no more than between about 20 and 40 cm, such as about 30 cm. Such a short range reduces the likelihood of accidental communication with a data carrier other than the intended data carrier.

For some applications, a portion of the patient information stored in the data carrier is also printed in human- and/or machine-readable form on the data carrier. For example, a name 172 and identification code 174 of the patient, and/or a barcode 176 may be printed on the data carrier.

Data carrier 24 comprises circuitry 178, which comprises memory and logic. For some applications, data carrier 24 is passive, in which case it is configured to receive energy from communication element 240. For other applications, data carrier 24 comprises a power source (not shown). For some applications in which the data carrier comprises a power source, the data carrier comprises a communication element for communicating and/or energizing another electronic apparatus. Alternatively or additionally, the data carrier comprises a communication element configured for wireless communication.

For some applications, data carrier 24 further comprises a user output 180 for outputting information to the patient or healthcare workers. For example, output 180 may comprise a display screen, light, and/or sound generator, which circuitry 178 drives to communicate information, such as when communications have been established with other elements of system 10, e.g., data carrier 120, administration system 26, imaging system 28, and/or patient management system 160. For some applications, circuitry 178 is configured to additionally function as an alarm clock; for example, the circuitry may drive display 180 to alert the patient prior to a scheduled administration or imaging procedure.

Typically, for safety purposes, upon completion of all the imaging procedures associated with a given patient-specific data carrier 24, system 10 permanently disables the data carrier, in order to ensure that the data carrier is not accidentally reused for another patient.

The patient management system

Reference is made to Fig. 4, which is a schematic illustration of patient management system 160, in accordance with an embodiment of the present invention.

Patient management system 160 manages patient-related administrative and medical information, and typically comprises at least one workstation 200 in communication with one or more servers 202. Typically, workstation 200 and servers 202 comprise standard personal computers and/or computer servers with appropriate memory, communication interfaces and software for carrying out the functions prescribed by relevant embodiments of the present invention. This software may be downloaded to the workstation and servers in electronic form over a network, for example, or it may alternatively be supplied on tangible media, such as CD-ROM.

System 160 performs the following functions:

- receives and registers new patients into system 10, typically into management and control component 150 thereof;
- assigns patient identification codes;
- assigns, issues, and transfers information to patient-specific data carriers 24;
- receives and tracks patient prescriptions for radiopharmaceuticals, and communicates the prescriptions to other elements of system 10, such as dispensing system 20, administration system 26, and/or management and control component 150; and/or
- suggests and assigns imaging protocols based on the patient's imaging needs and patient-specific information.

During reception of a new patient 204, healthcare worker 206 manually enters patient information into workstation 200. Alternatively or additionally, all or a portion of the patient information is provided electronically by another healthcare system or electronic information source. System 160 typically verifies the healthcare worker's identity and access privileges by interrogating a computer-commuticatable identity tag 208 held by the worker, and/or by checking the validity of a password entered into workstation 200 by the healthcare worker.

The patient information provided to system 160 typically includes:

- the patient's general details, such as name, age, gender, address, telephone number, profession, attending and/or treating physician, health insurance plan, and next of

kin;

- the patient's medical profile, such as medical condition, medical history, family medical history, BMI, weight, allergies, sensitivity to one or more chemical compounds, metabolic rate, and other physiological conditions;
- medications prescribed to the patient;
- the patient's imaging history; and/or
- information regarding the desired imaging, including reason for imaging, type of imaging, body structure or organ to be imaged, and known or suspected pathology.

In an embodiment of the present invention, upon entry of such patient information into patient management system 160, the system automatically suggests one or more imaging protocols that may be appropriate for the patient's imaging needs and medical condition. When making such suggestion, the system takes into consideration, in addition to the information regarding the desired imaging, such factors as the patient's general details, medical profile, imaging history, and guidelines for medication interactions. The system typically selects the suggested protocol(s) from a database of preconfigured protocols, which is described hereinbelow with reference to Figs. 6A-E. Healthcare worker 206 selects one of the suggested protocols, or selects another non-suggested protocol directly from the protocol database.

For some applications, the system suggests one or more customizations of the selected protocol, as described hereinbelow with reference to Figs. 6A-E, which the healthcare worker may accept, decline, or modify, in whole or in part. These suggested customizations are typically based on (a) physiological parameters of the patient, such as age, weight, BMI, metabolic rate, and/or hemodynamic state, and/or kinetic parameters of the radiopharmaceutical agent as determined during previous imaging procedures performed on the patient, and/or (b) a medical profile group to which the patient is assigned, such as high, normal, or low BMI, or high BMI - diabetic, or high BMI - normal metabolic rate. (For some applications, such profile groups are stored in a database of management and control component 150.) Alternatively or additionally, the healthcare worker may customize the protocol manually.

Upon selection and customization of the protocol, patient management system 160 schedules, typically automatically:

- a specific imaging system 28 capable of performing the selected imaging procedure;
- a date and time for performing the imaging procedure; and
- a date(s) and time(s) for administration of labeled radiopharmaceutical agent(s).

Patient management system 160 transmits the entered and generated patient-specific information, including the selected protocol, to the patient's patient-specific data carrier 24. The transmitted patient-specific information typically includes:

- the patient's identification code and name;
- an identifier of the selected imaging protocol(s), such as a name and/or an identification code thereof, and/or additional imaging protocol information, such as described hereinbelow with reference to Figs. 6A-E;
- an identifier of the selected administration protocol(s), such as a name and/or an identification code thereof;
- the scheduled imaging system 28;
- the scheduled imaging date and time;
- the scheduled administration date(s) and time(s);
- the patient's personal details;
- the patient's medical profile; and/or
- the patient's imaging history.

The patient management system transmits an order for one or more patient-specific doses of the appropriate labeled radiopharmaceutical agent(s) to dispensing system 20, such as via management and control component 150. Typically, the patient management system additionally transmits at least a portion of the entered and generated patient-specific information to one or more of: (a) management and control component 150, (b) dose calculation system 152, (c) administration system 26, and/or (d) imaging system 28. Typically, a different subset of the information is transmitted to each of these entities.

As described hereinabove with reference to Fig. 3, for some applications, a portion of the patient information stored in data carrier 24 is also printed in human- and/or machine-readable form on the data carrier. For example, a name 172 and identification code 174 of the patient, and/or a barcode 176 may be printed on the data carrier. For such applications, system 160 comprises a printer 210, which is configured to print the information directly on data carrier 24, or to print the information on an adhesive label, which healthcare worker 206 attaches to data carrier 24. For some applications, printer 210 comprises communication element 240, and the printer is configured to both print the information on the data carrier and transmit the information to the data carrier, typically generally at the same time.

In an embodiment of the present invention, system 10 comprises at least one web server, which is configured to accept orders for an imaging procedure over an intranet or the Internet, placed by a physician or other healthcare worker. Such orders can typically be modified up until a deadline, such as midnight before the day of the scheduled imaging procedure.

The management and control component

Reference is again made to Fig. 1. In an embodiment of the present invention, system 10 comprises management and control component 150, which coordinates a portion of the interaction and communication among the elements of system 10. The remainder of the interaction and communication occurs directly between the elements of the system, and/or via other elements of the system. For some applications, component 150 issues a password and/or computer-communicatable identity tags 208 to healthcare workers 206 authorized to interact with one or more elements of system 10. For example, tag 208 may comprise an RFID tag, smart card, disk-on-key (e.g., a USB key), minidisk, or other electronic memory, or a machine-readable code, e.g., a barcode. As appropriate, healthcare workers 206 may be assigned various permission levels, such as permission to view or modify particular system and/or patient data.

Typically, management and control component 150 comprises one or more standard personal computers or servers with appropriate memory, communication interfaces and software for carrying out the functions prescribed by relevant embodiments of the present invention. This software may be downloaded to the management and control component in electronic form over a network, for example, or it may alternatively

be supplied on tangible media, such as CD-ROM.

The dose calculation system

Reference is made to Fig. 5, which is a schematic illustration of radiopharmaceutical dose calculation system 152, in accordance with an embodiment of the present invention. The dose calculation system manages and tracks, typically automatically, radiopharmaceutical inventory, ordering, dose dispensing, and disposal. Typically, the dose calculation system comprises one or more standard personal computers or servers with appropriate memory, communication interfaces and software for carrying out the functions prescribed by relevant embodiments of the present invention. This software may be downloaded to the dose calculation system in electronic form over a network, for example, or it may alternatively be supplied on tangible media, such as CD-ROM. The dose calculation system receives information from dispensing system 20 regarding doses drawn from the inventory.

Dose calculation system 152 typically comprises:

- an ordering sub-system 154, which orders radiopharmaceutical products from radiopharmaceutical manufacturers, distributors, and/or radiopharmacies, typically automatically, such as when the dose calculation system identifies that inventories of a given radiopharmaceutical are lower than needed;
- a receipt and verification sub-system 155, which manages the receipt and registration of radiopharmaceutical products. The receipt and verification sub-system checks the received products against orders placed by the ordering sub-system, and typically performs license management. When a received mother vial 104 includes a mother vial data carrier 106, the sub-system reads information contained in the data carrier to verify that the order has been accurately fulfilled, and, typically, verifies the authenticity of the mother vial;
- a dose calculation sub-system 156, which calculates customized doses of labeled radiopharmaceutical agents for patients based on patient-specific information, protocol information, and/or prescription information, and communicates the customized doses to patient management system 160

and/or dispensing system 20; and/or

- a waste-disposal sub-system 157, which tracks radioactive waste disposal by system 10, such as disposal of radioactive materials contained in waste container 512, described hereinbelow with reference to Fig. 12. For some applications, sub-system 157 additionally tracks radioactive waste disposal of materials in the clinical environment not associated with system 10.

Ordering sub-system 154 and waste-disposal sub-system 157 typically operate in accordance with per country requirements for radiopharmaceutical use. A reporting sub-system reports to relevant nuclear regulatory commissions as required, based on information obtained from the other sub-systems.

In an embodiment of the present invention, dose calculation sub-system 156 designs a cocktail of labeled radiopharmaceutical agents or a series of labeled radiopharmaceutical agents to carry out the desired imaging. When designing such a cocktail or series, the sub-system considers constraints imposed by the physical properties of the agents and by the patient history, and other requirements, such as safety and efficacy requirements. The sub-system determines an appropriate dose for the specific patient having particular physiological parameters (e.g., weight, BMI, and age), and determines the times at which multiple agents are to be administered to the patient in order to achieve optimal imaging.

For some applications, sub-system 156 determines that a plurality of labeled radiopharmaceutical agents are to be administered together and thus must be combined in a single preparation, i.e., a cocktail. For other applications, the sub-system determines that a plurality of labeled radiopharmaceutical agents are to be administered separately at different times and thus must be contained in separate containers 22. As appropriate, sub-system 156 takes into consideration differing half-lives of the plurality of labeled radiopharmaceutical agents, in conjunction with the prescribed time of the imaging procedure. For example, a simultaneous imaging protocol is provided for assessing cardiac perfusion using a cocktail comprising Tc-99m sestamibi injected at rest, and thallium-201 injected at stress, wherein the desired activities at imaging time of the Tc-99m sestamibi and the thallium are 6 mCi and 4 mCi, respectively. When calculating the necessary activity of the dispensed dose, sub-system 156 accounts for the respective half-lives of Tc-99m (6 hours) and thallium-201 (64 hours) in view of the planned time

interval between the dispensing time and administration time. For example, if dispensing is performed 24 hours before administration, sub-system 156 calculates the activities of the Tc-99m and thallium-201 at the time of dispensing to be 96 mCi and 5.5 mCi, respectively.

Protocol information

Reference is made to Figs. 6A-E, which is a table showing exemplary preconfigured SPECT protocols and parameters thereof, in accordance with respective embodiments of the present invention. These protocols are appropriate, for example, for use with the SPECT imaging methods and apparatus described hereinbelow with reference to Fig. 11, and/or in the co-assigned patent applications and/or patent application publications incorporated herein by reference hereinabove. For some applications, the techniques described herein utilize additional protocols described in above-mentioned International Application PCT/IL2005/001173, International Application PCT/IL2005/001215, filed November 16, 2005, above-mentioned US Provisional Patent Application 60/628,105, above-mentioned US Provisional Patent Application 60/675,892, or in one or more of the other co-assigned patent applications and/or patent application publications incorporated herein by reference. Alternatively or additionally, the techniques described herein utilize protocols for non-SPECT imaging modalities, such as PET or CT, or other imaging modalities known in the art. The preconfigured protocols are stored in a database, which is typically used by patient management system 160 for suggesting protocols and/or by dose calculation sub-system 156, as described hereinabove with reference to Figs. 4 and 5, respectively.

For each of the exemplary protocols shown in Fig. 6A, the table indicates general parameters for a rest phase and a stress phase of the protocol. For example, for the "single isotope / low dose / fast imaging" protocol, the table shows that the radiopharmaceutical (RP) for the rest phase of the protocol is less than 0.3 mCi of Thallium, that the waiting time after injection of the radiopharmaceutical is 2 minutes, and that the image acquisition duration is 15 minutes. Parameters for the stress phase are similarly indicated, with the addition of the type of stress (exercise, e.g., treadmill or bicycle, or pharmaceutical, e.g., adenosine). The "thallium stress perfusion" and "simultaneous dual isotope stress perfusion" protocols are optionally dynamic.

For each of the exemplary protocols shown in Figs. 6B-E, the table indicates

administration parameters, detector parameters, scanning parameters, and analysis parameters for the protocol. For example, for Protocol A of Figs. 6B-C ("Cardiac mapping"), the table indicates:

- the labeled radiopharmaceutical agent is Tc-99-sestamibi (MIBI);
- the protocol is a fast protocol, with image acquisition completed prior to substantial uptake of the agent by the liver;
- the injection is by a single bolus;
- image acquisition begins either about 2 minutes after injection, or during or immediately administration, for applications in which the administration is performed while the patient is already placed at camera 452 (Fig. 11);
- the detected photon energy is 140 KeV with an energy resolution of 15%, i.e., the total range of energy levels detected by the detectors 454 of camera 452 (Fig. 11) is set to be 15% of the emitted energy level of the labeled radiopharmaceutical agent (140 Kev). Typically, this range is not centered around the emitted energy level, but instead is shifted towards lower energy levels;
- the total scan time is 120 seconds;
- four detectors 454 of camera 452 are assigned as outer (distal) detectors, and six detectors 454 are assigned as inner (proximal) detectors, as described hereinbelow with reference to Fig. 11;
- each of the inner detectors has an angular range of between 90 and 120 degrees, and each of the outer detectors has an angular range of between 40 and 60 degrees;
- the total number of angular orientations assumed by the detectors in aggregate is 1200, i.e., 10 detectors times 120 orientations each;
- each angular step of the inner detectors is one degree, and each angular step of the outer detectors is 0.3 to 0.5 degrees (corresponding to the range of 40 to 60 degrees described above);
- the dwell time at each step is one second, for both the inner and outer detectors;

- the imaging procedure is gated using 16 to 32 frames;
- the analyses to be performed include intensity image and ejection fraction.

For some applications, the protocol information includes additional information not shown in Figs. 6B-E, such as:

- additional scanning parameters, such as whether the detectors perform multiple scans (in all the protocols shown in the table, the detectors typically perform a single scan); and
- additional analysis parameters, such as:
  - saturation handling (in the first cardiac mapping protocol shown in the table, no saturation handling is performed, while in the second cardiac mapping protocol shown in the table, the analysis is configured to dismiss saturated pixels);
  - whether the analysis handles scatter from multiple sources (in the protocols shown in the table, the analysis does not handle scatter from multiple sources);
  - reconstruction resolution (in all of the protocols shown in the table, the image reconstruction resolution is 2.5 mm in the z-direction, and 5 mm in the x- and y-directions); and
  - parameters that provide the diagnosis system (e.g., expert system) with information regarding how to interpret the results of the imaging study, such as kinetic parameters, predefined pathological values, or patient-specific physiological parameters (e.g., BMI, age, or a group to which the patient is assigned).

Reference is made to Protocol E of Figs. 6B-C. In this cardiac mapping protocol, simultaneous image acquisition is performed using, typically using full conventional doses of both thallium and MIBI-Tc. The detected photon energy of the thallium is 167 KeV, rather than the 72 KeV that is conventionally detected during nuclear imaging procedures. Unlike conventional SPECT cameras, the camera described hereinbelow with reference to Fig. 11 is sufficiently sensitive to detect a clinically-relevant count of the relatively low percentage (8%) of photons emitted at the 167 KeV energy level.

(Detection of 72 KeV energy is generally not practical when a conventional dose of MIBI-Tc is used, because the scatter from the 140 KeV energy level of MIBI-Tc masks the 72 KeV photons emitted by the thallium.)

Reference is made to Protocol I of Figs. 6D-E. In this cardiac dynamic mapping protocol, image acquisition typically begins prior to administration of the radiopharmaceutical agent, such as at one minute prior to administration, as shown in the table. This allows the imaging system to complete one full scan of the region of interest prior to administration of the radiopharmaceutical agent, in order to ensure that the imaging system is able to acquire photons of radiation beginning immediately after the radiopharmaceutical agent is administered.

Typically, a selected preconfigured protocol is customized based on physiological parameters of the specific patient, and/or a medical profile group of the patient, as described hereinabove with reference to Fig. 4. Such customization typically includes customization of the radiopharmaceutical agent, administration parameters, and/or imaging parameters.

For some applications, one or more of the following parameters of the radiopharmaceutical agent are customized:

- the dose, or for multiple radiopharmaceutical agents, the respective doses;
- the radioactivity;
- for cocktails, the ratio of the different radiopharmaceutical agents; and/or
- the volume of the dose, or for multiple radiopharmaceutical agents, the volumes of the respective doses.

For some applications, one or more of the following parameters of the administration are customized:

- the dose administered, or for multiple radiopharmaceutical agents, the respective doses per administration;
- the type of administration, e.g., a single bolus, a plurality of boluses (e.g., two boluses), pulsatile administration, or constant drip administration;
- the labeled radiopharmaceutical agent for each administration, whether a single agent or a cocktail of agents;

- the time of the administration with respect to the time of imaging;
- the timings of multiple administrations with respect to each other and with respect to other activities, such as rest or stress (physical or pharmacological);
- the administration device, e.g., a syringe, a dual-needle syringe, a pump, or an IV line; and/or
- the mode of administration, e.g., manual, automatic, or computer driven.

For some applications, one or more of the following parameters of the imaging procedure are customized. For some applications, such parameters are separately specified for individual components of camera 452 of imaging system 28, or groups of components, such as for individual detectors 454 or groups of detectors of camera 452, described hereinbelow with reference to Fig. 11.

- total acquisition time, and/or acquisition time for a plurality of phases of acquisition;
- detector scanning plan, including detector motions, such as detector angular and translational motions, detector step size (i.e., the density of the step size, typically expressed in degrees), number of detectors utilized for image acquisition, and detector dwell time at each view;
- detector sensitivity;
- detection energy resolution;
- detector calibration plan;
- definition of the region of interest (ROI);
- gating parameters;
- energy bands, i.e., a plurality of non-overlapping energy windows;
- collimator positioning, shape, structure, and orientation;
- multiple/interlaced scans;
- zooming parameters;
- uniformity/non-uniformity of scan;

- Compton scatter map calculation and correction parameters;
- optimal energy window;
- optimal energy resolution, i.e., the range of energy level windows for which detection is enabled; and/or
- adaptivity of scan pattern to acquired counts, e.g., active vision parameters (as described in the above-mentioned International Application PCT/IL2005/001173).

In an embodiment of the present invention, system 10 uses high definition protocols in conjunction with SPECT imaging techniques to enable personalized functional imaging at higher speeds and resolutions than can be achieved using conventional radiopharmaceutical protocols and imaging technology, using imaging techniques described herein and/or incorporated herein by reference. Alternatively or additionally, the system uses low dose protocols that enable personalized functional imaging at higher resolutions but with substantially lower doses than possible using conventional methods.

In an embodiment of the present invention, system 10 uses a protocol pursuant to which a patient undergoes a rest thallium (Tl-201-thallous chloride) and stress Tc-99-sestamibi (MIBI) study having a total study duration of between about 60 and about 90 minutes, and a total image acquisition duration of between about 0.5 and about 6 minutes, e.g., about four minutes. For example, pursuant to the protocol:

- about 3 mCi of thallium may be administered to the patient as a bolus IV injection,
- the patient may rest for between about 10 and about 15 minutes,
- an image acquisition having a duration of about two minutes may be performed,
- the patient may be physically stressed,
- about 20-30 mCi of Tc-99-sestamibi may be administered as a bolus IV injection, and
- a second image acquisition having a duration of about two minutes may be performed.

Such dual-isotope imaging is generally useful for assessing myocardial perfusion of patients with suspected ischemic syndromes and a variety of other conditions. Alternatively, in an embodiment, the rest phase is performed using an approximately 8 to 10 mCi dose of Tc-99-sestamibi, in which case image acquisition typically commences about 30 minutes after injection of the sestamibi. Further alternatively, in an embodiment, image acquisition for the rest phase is performed about two minutes after injection of the thallium, the stress is pharmacological (e.g., using adenosine), and image acquisition for the stress phase is performed essentially immediately after injection of the sestamibi. Still further alternatively, in an embodiment, the rest phase is performed using Tc-99-sestamibi, and image acquisition commences essentially immediately upon injection of a dose of about 8 to 10 mCi.

In accordance with respective embodiments of the present invention, dual-radiopharmaceutical protocols include the administration and simultaneous imaging of the following combinations of labeled radiopharmaceutical agents. Typically, the labeled radiopharmaceutical agents are administered as a mixture (i.e., a cocktail) before or during a simultaneous imaging procedure; alternatively, the labeled radiopharmaceutical agents are administered separately before or during a simultaneous imaging procedure.

- (a) I-123 BMIPP, a fatty acid imaging agent that has been available in Japan for many years, and is currently in Phase III clinical trials in the United States, and (b) a myocardial perfusion agent (e.g., Tc-99m sestamibi, Tc-99m tetrofosmin, or Tl-201-thallous chloride), for simultaneously studying myocardial perfusion and fatty acid metabolism;
- (a) Tl-201-thallous chloride and (b) Tc-99m pertechnetate, for differentiating an organ from its anatomical surroundings, such as differentiating parathyroid glands from the thyroid gland;
- (a) In-111 DTPA, and (b) Tc-99m-MAG3, for differentiating pathological processes in a given organ, such as performing differential diagnosis of a hypo-perfused kidney, e.g., to study true glomerular filtration rate and tubular secretion simultaneously;
- a cocktail of labeled radiopharmaceutical agents, for studying cancer, including simultaneous diagnosis, prediction of therapy response, and

monitoring of therapy, such as simultaneously identifying a tumor, and characterizing tumor perfusion and metabolic activity, e.g., in order to provide a disease signature; and

- the combinations shown in the following table.

TABLE 1

First radiopharmaceutical	First application	Second radiopharmaceutical	Second application
^{201}Tl	Myocardial perfusion	Tc-99m-teboroxime	Myocardial perfusion
		Tc-99m-sestamibi	
		Tc-99m-tetrophosmin	
^{201}Tl	Myocardial perfusion	Tc-99m-PYP	Infarct Imaging
^{201}Tl	Myocardial perfusion	Tc-99m-Annexin	Apoptosis
^{201}Tl	Myocardial perfusion	^{123}I-BMIPP	Hypoxia
Tc-99m-teboroxime	Myocardial perfusion	^{111}In-Annexin	Apoptosis
Tc-99m-teboroxime	Myocardial perfusion	^{123}I-Fatty acid	Metabolism
^{111}In-WBC	Infection	Tc-99m-SC	Bone Marrow
^{111}In-DTPA	Kidney (GFR)	Tc-99m-MAG3	Kidney (tubular secretion)
Tc-99m-RBC	Blood pool	^{111}In-Prostascint	Prostate cancer
Tc-99m-HMPAO	Cerebral blood flow	^{123}I-IBZM	Dopamine D2 receptors

In an embodiment of the present invention, system 10 uses protocols for studying the kinetics of thallium. For some applications, such protocols provide dynamic information regarding myocardial function, such as blood flow, rate of thallium uptake, thallium accumulation/redistribution, thallium metabolism, and/or thallium and/or metabolite secretion and/or wash-out (active or passive). Kinetic perfusion

radiopharmaceutical modeling provides absolute myocardial perfusion measurements, coronary flow reserve, and parametric representation of cellular function.

In accordance with respective embodiments of the present invention, thallium protocols include:

- protocols using a conventional dose of thallium, with a substantially reduced SPECT image acquisition duration, e.g., less than about 6 minutes, such as less than about 2 minutes, e.g., about 0.5 minutes. By way of comparison, conventional thallium SPECT imaging procedures generally have image acquisition durations of between about 10 and about 20 minutes. For some applications, the thallium protocol is customized for a specific patient, as described hereinabove;

- protocols using a conventional dose of thallium and a conventional image acquisition duration, with a substantially increased image resolution. For some applications, acquired photon counts are at least 5 times greater than those acquired using conventional SPECT techniques, e.g., at least 10 times greater, resulting in an image with substantially higher resolution; and

- dynamic protocols for myocardial perfusion studies that provide absolute quantitative measurements. For example, images of the heart may be reconstructed from list mode data, with a temporal resolution of 5-10 seconds. This temporal resolution is typically appropriate for the measurement of the kinetics of uptake and wash-out of thallium from the myocardium, as well as those of an input bolus as it passes through the left ventricle. Such data enables the measurement of absolute myocardial blood flow at rest and during peak stress.

In an embodiment of the present invention, system 10 uses protocols for cardiac stress testing studies, using, for example, Tc99m-sestamibi, Tc-99m tetrofosmin, or thallium. Such protocols differentiate between healthy cardiac tissue and scarred or poorly perfused cardiac tissue. Perfusion defects that appear after exercise or pharmacologic stress suggest either vascular occlusion or myocardial infarction. For some applications, such studies are performed gated to the patient's ECG, in order to study cardiac wall motion. Wall motion studies allow calculation of key cardiac function

parameters, such as ejection fraction and estimated cardiac output.

In accordance with respective embodiments of the present invention, cardiac stress testing protocols, which use, for example, Tc99m-sestamibi, Tc-99m tetrofosmin, or thallium, include:

- protocols using a conventional dose, with a substantially reduced SPECT image acquisition duration, e.g., less than about 6 minutes, such as less than about 2 minutes, e.g., about 0.5 minutes. By way of comparison, conventional cardiac stress testing SPECT imaging procedures generally have image acquisition durations of between about 10 and about 20 minutes. For some applications, the protocol is customized for a specific patient, as described hereinabove. For some applications, such as when the protocol uses Tc99m-sestamibi, image acquisition is performed immediately following administration of the labeled radiopharmaceutical agent, before the agent reaches the liver, thereby reducing interference by the liver on the resulting images.

- protocols using a dose of the labeled radiopharmaceutical agent that is substantially lower than conventional SPECT protocols using the agent. For example, the dose may be between about 50% and about 90% lower than a conventional dose, e.g., about 50% lower than a conventional dose. By using the image acquisition techniques described herein and/or incorporated herein by reference, even at such reduced doses, acquired photon counts are typically at least 5 times greater than those acquired using conventional SPECT techniques at conventional SPECT doses, e.g., at 10 times greater, and image acquisition duration is typically about 50% less than conventional durations, e.g., about 80% less (such as four minutes instead of 20 minutes). Alternatively, the dose may be reduced by about 90%, and the image acquisition duration is approximately the same as conventional image acquisition durations.

In an embodiment of the present invention, system 10 uses Tc-99m teboroxime for performing a SPECT myocardial perfusion study. This radiopharmaceutical is extracted by the myocardium in proportion to myocardial blood flow throughout the entire range of achievable flow rates. When conventional imaging techniques are used, the wash-out rate

of Tc-99m teboroxime from cardiac tissue is so rapid that there is inadequate time for imaging, because the radiopharmaceutical rapidly and avidly accumulates in the liver, which emits gamma rays that blind the imaging of the heart. By using the imaging techniques described herein and/or incorporated herein by reference, sufficient photon counts are obtained in an image acquisition period of no more than approximately two minutes, immediately following administration. The use of such a short period enables the completion of image acquisition prior to substantial uptake of the radiopharmaceutical by the liver, thereby enabling the effective clinical use of Tc-99m teboroxime for cardiac imaging.

In an embodiment of the present invention, a dynamic multiple isotope combination protocol is provided for studying different pathological processes of the same organ, such as studying acute myocardial ischemia. In accordance with this protocol, the following labeled radiopharmaceutical agents are administered as bolus IV injections:

(a) an approximately 2 mCi dose of I-123-BMIPP, followed by a wait of about 48 hours;

(b) an approximately 1 mCi dose of Tl-201-thallous chloride; and

(c) either (i) an approximately 10 mCi dose of Tc-99m-sestamibi or (ii) an approximately 10 mCi dose of Tc-99m-teboroxime.

Agents (b) and (c) are administered as a cocktail, or as separate injections at approximately the same time. Simultaneous image acquisition of all three radiopharmaceutical agents is performed during or soon after administration of agents (b) and (c), typically using an up to about 30 minute acquisition time, such as between about 5 and about 15 minutes, which is faster than that of standard imaging protocols. Typically, camera 452 of imaging system 28, described hereinbelow with reference to Fig. 11, performs image acquisition using an energy window of between about 2% and about 10% of the emitted energy levels of the radiopharmaceutical agents. Typically, detectors 454 of camera 452 sweep the region of interest once every approximately 10 to approximately 15 seconds. The I-123-BMIPP identifies the ischemic/infarcted area of the myocardium, while the other radiopharmaceutical agents identify the perfused area of the myocardium. Simultaneous imaging provides more accurate identification of myocardial perfusion pathologies than is generally possible using conventional imaging techniques

and protocols.

In an embodiment of the present invention, system 10 uses one or more of the protocols described in the above-mentioned US provisional application filed on even date herewith, entitled, "Imaging protocols."

In some embodiments of the present invention, the protocols described herein (including those shown in Figs. 6A-E), and in the co-assigned patent applications incorporated herein by reference, are performed using values that vary from those provided in the protocols by +/- 20%, e.g., +/- 5%, +/- 10%, or +/- 15%. Furthermore, in some embodiments, the protocols are performed with a range of doses from 50%, 75%, 90%, or 100% of the dosage value given for the respective protocol, up to 10 times the dosage value given for the respective protocol (such as up to 2, 4, 6, or 8 times the given dosage value). For example, a dose shown as 3 mCi for a given protocol may, in some embodiments, have a range of 1.5 mCi to 30 mCi, or from 2.7 mCi to 6 mCi. Similarly, in some embodiments, the protocols are performed with a range of acquisition durations (total scan times) from 50%, 75%, 90%, or 100% of the duration value given for the respective protocol, up to 5 times the duration value given for the respective protocol, such as up to 1.5, 2, 3, or 4 times the given duration value. Other protocol values, such as waiting times, energy windows/resolution, angular range, angular step, and dwell time, may also have a range from 50%, 75%, 90%, or 100% of the value given for the respective protocol, up to 5 times the value given for the respective protocol, such up to 1.5, 2, 3, or 4 times the given value.

In respective embodiments of the present invention, all of the protocols described herein and/or in the co-assigned patent applications incorporated herein by reference are enabled to generate clinically-valuable images. A "clinically-valuable image" is an image of an intra-body region of interest (ROI) containing the labeled radiopharmaceutical agent(s), which image fulfills one or more of the following criteria:

- the image is generated according to a protocol, including at the radiopharmaceutical dose specified by the protocol, using a high-definition SPECT camera, for example, camera 452 of imaging system 28, described hereinbelow with reference to Fig. 11, which camera, during the imaging of the ROI, is capable of acquiring at least one of 5000 photons emitted from the ROI during the image acquisition procedure, such as at least one

of 4000, 3000, 2500, 2000, 1500, 1200, 1000, 800, 600, 400, 200, 100, or 50 photons emitted from the ROI. In one particular embodiment, the camera is capable of acquiring at least one of 2000 photons emitted from the ROI during the image acquisition procedure;

- the image is generated according to a protocol, including at the radiopharmaceutical dose and image acquisition duration specified by the protocol, using a high-definition SPECT camera, for example, camera 452, which, during the imaging of the ROI, is capable of acquiring at least 200,000 photons, such as at least 500,000, 1,000,000, 2,000,000, 3,000,000, 4,000,000, 5,000,000, 8,000,000, or 10,000,000 photons, emitted from a portion of the ROI having a volume of no more than 500 cc, such as a volume of no more than 500 cc, 400 cc, 300 cc, 200 cc, 150 cc, 100cc, or 50 cc. In one particular embodiment, the camera is capable of acquiring at least 1,000,000 photons emitted from a volume of the ROI having a volume of no more than 200 cc;

- the image has a resolution of at least 7x7x7 mm, such as at least 6x6x6 mm, 5x5x5 mm, 4x4x4 mm, 4x3x3 mm, or 3x3x3 mm, in at least 50% of the reconstructed volume, wherein the labeled radiopharmaceutical agent as distributed within the ROI has a range of emission-intensities R (which is measured as emitted photons / unit time / volume), and wherein at least 50% of the voxels of the reconstructed three-dimensional emission-intensity image of the ROI have inaccuracies of less than 30% of range R, such as less than 25%, 20%, 15%, 10%, 5%, 2%, 1%, or 0.5% of range R. For example, the agent may emit over a range from 0 photons/second/cc to 10^5 photons/second/cc, such that the range R is 10^5 photons/second/cc, and at least 50% of the voxels of the reconstructed three-dimensional intensity image of the ROI have inaccuracies of less than 15% of range R, i.e., less than 1.5 x 10^4 photons/second/cc. For some applications, the study produce a parametric image related to a physiological process occurring in each voxel. In one particular embodiment, the image has a resolution of at least 5x5x5 mm, and at least 50% of the voxel have inaccuracies of less than 15% of range R;

- the image is generated according to a protocol, including at the radiopharmaceutical dose and image acquisition duration specified by the protocol, the image has a resolution of at least 7x7x7 mm, such as at least 6x6x6 mm, 5x5x5 mm, 4x4x4 mm, 4x3x3 mm, or 3x3x3 mm, wherein the labeled radiopharmaceutical agent has a range of intensities R (photons / unit time / volume), and wherein at least 50% of the voxels of the reconstructed three-dimensional intensity image of the ROI have inaccuracies of less than 30% of range R, such as less than 25%, 20%, 15%, 10%, 5%, 2%, 1%, or 0.5% of range R. For some applications, the study produce a parametric image related to a physiological process occurring in each voxel; and/or

- the image has a resolution of at least 20x20x20 mm, such as at least 15x15x15 mm, 10x10x10 mm, 7x7x7 mm, 5x5x5 mm, 4x4x4 mm, 4x3x3 mm, or 3x3x3 mm, wherein values of parameters of a physiological process modeled by a parametric representation have a range of physiological parameter values R, and wherein at least 50% of the voxels of the reconstructed parametric three-dimensional image have inaccuracies less than 100% of range R, such as less than 70%, 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 2%, 1%, or 0.5% of range R. For example, the physiological process may include blood flow, the values of the parameters of the physiological process may have a range from 0 to 100 cc / minute, such that the range R is 100 cc / minute, and at least 50% of the voxels of the reconstructed parametric three-dimensional image have inaccuracies less than 25% of range R, i.e., less than 25 cc / minute. In one particular embodiment, the image has a resolution of at least 5x5x5 mm, and at least 50% of the voxels have inaccuracies of less than 25% of range R.

The mother vial

Reference is made to Fig. 7, which is a schematic illustration of mother vial 104 and attached data carrier 106, in accordance with an embodiment of the present invention. Data carrier 106 is computer-communicatable, and typically comprises an RFID tag, smart card, disk-on-key (e.g., a USB key), compact disc, minidisk, disposable

computer-readable medium, or other electronic memory, or a machine-readable code, e.g., a barcode. Mother vial 104 is shown contained within shielding 272, to which data carrier 106 is attached. Alternatively, the data carrier is attached directly to the mother vial, or otherwise associated with the mother vial, such as by being stored in proximity to the mother vial, e.g., in a tray that also contains the mother vial.

Data carrier 106 typically contains at least some of the following information:

- a coded signature 256, for authenticating mother vial 104;
- radiopharmaceutical information, a portion of which is typically supplied by the manufacturer, and a portion of which is typically generated by dispensing system 20 in conjunction with dispensing the radiopharmaceutical agent(s). For some applications, a portion of the information is generated by mother vial preparation system 700, described hereinbelow with reference to Fig. 15, in conjunction with preparing the radiopharmaceutical. The information includes, for example:
  - the name of and/or information regarding the manufacturer;
  - the indicated use(s) (e.g., "Formulation for Cardiac Dynamic Studies");
  - the pre-labeled composition;
  - the time of preparation of the labeled radiopharmaceutical agent(s);
  - the radioactivity at the time of preparation;
  - the total solution volume;
  - the pre-labeled-composition expiration date;
  - the appropriate labeling isotope(s);
  - the decay scheme(s) of the appropriate labeling isotope(s);
  - the radiopharmaceutical biodistribution as a function of time;
  - the radiopharmaceutical clearance rate;
  - the percent clearance by the liver;
  - the percent clearance by the kidneys;
  - the breakdown rate;

- the liver uptake as a function of time; and/or
- radiopharmaceutical kinetic parameters, such as described hereinbelow, which parameters may be stored in one or more lookup tables;

- administration protocol information, such as described hereinbelow;
- image acquisition protocol information, such as described hereinbelow;
- image reconstruction protocol information, such as described hereinbelow;
- image analysis protocol information, such as described hereinbelow;
- expert system protocol information, such as described hereinbelow;
- radiolabeling information, which, for some applications, is generated by mother vial preparation system 700, described hereinbelow with reference to Fig. 15. Such information includes, for example:
  - the labeling radioisotope(s), e.g., Tc-99m;
  - time of labeling;
  - activity of the radioisotope(s) per volume at the time of labeling;
  - total solution volume in the mother vial; and/or
  - ratio of radioisotopes (e.g., Tc-99m to Tc-99) at the time of labeling.

If the labeled radiopharmaceutical agent stored in the mother vial is radiolabeled by mother vial preparation system 700, as described hereinbelow with reference to Fig. 15, the labeling information is provided by the mother vial preparation system. Otherwise, the labeling information is provided by the pharmacist and/or conventional labeling system that radiolabels the unlabeled radiopharmaceutical agent.

The radiopharmaceutical kinetic parameters are used by imaging system 28 for performing dynamic imaging studies, for example as described in the above-mentioned International Patent Application PCT/IL2005/001173, and/or in the above-mentioned US provisional application filed on even date herewith, entitled, "Imaging protocols". For some applications, respective sets of these parameters are provided for:

- different patient populations, such as a healthy population and populations which suffer from various pathologies;

- different organs and/or tissue types, for example, brain tissue, cardiac tissue, liver tissue, and tumor tissue;
- different pathologies;
- different patient physiologies;
- different organs, according to the physiology of the specific patient;
- different patient groups, as expected according to the physiology of the specific patient;
- different pathologies, as expected according to the physiology of the specific patient;
- different organs, as measured for the specific patient;
- different patient groups, as measured for the specific patient; and/or
- different pathologies, as measured for the specific patient.

Such kinetic parameters may include, for example:

- volume of blood in a voxel;
- density of blood in a tissue within a voxel;
- labeled radiopharmaceutical agent concentration in the blood within a voxel;
- labeled radiopharmaceutical agent concentration in a tissue within a voxel;
- total labeled radiopharmaceutical agent concentration in a voxel;
- labeled radiopharmaceutical agent concentration in the systemic blood circulation;
- linearity with blood flow;
- receptor binding for molecular radiotracers;
- labeled radiopharmaceutical accumulation/redistribution in tissue;
- labeled radiopharmaceutical metabolic rate;
- diffusion coefficient from the blood to the tissue (i.e., rate of wash-out,

passive or active);

- diffusion coefficient from the tissue to the blood (i.e., rate of uptake, passive or active); and/or
- accumulation rate in a tissue within a voxel.

The administration protocol information is used by administration system 26 to set parameters of administration of the labeled radiopharmaceutical agent(s) contained in container 22. This protocol information may include, for example:

- the dose administered, or for multiple radiopharmaceutical agents, the respective doses per administration;
- the type of administration, e.g., a single bolus, a plurality of boluses (e.g., two boluses), pulsatile administration, or constant drip administration;
- the labeled radiopharmaceutical agent for each administration, whether a single agent or a cocktail of agents;
- the time of the administration with respect to the time of imaging;
- the timings of multiple administrations with respect to each other and with respect to other activities, such as rest or stress (physical or pharmacological);
- the administration device, e.g., a syringe, a dual-needle syringe, a pump, or an IV line;
- the mode of administration, e.g., manual, automatic, or computer driven; and/or
- an algorithm for customizing the administration based on physiological parameters of the specific patient.

The image acquisition protocol information is used by imaging system 28 to set parameters of the image acquisition process. For some applications, such parameters are separately specified for individual components of camera 452 of imaging system 28, or groups of components, such as for individual detectors 454 or groups of detectors. Such acquisition protocol information may include, for example:

- the name(s) and/or identification code(s) of one or more protocols for

which the radiopharmaceutical agent contained in mother vial 104 is suitable;

- total acquisition time, and/or acquisition time for a plurality of phases of acquisition;
- detector scanning plan, including detector motions, such as detector angular and translational motions, detector step size (typically expressed in degrees), and detector dwell time at each view;
- detector sensitivity;
- detector energy resolution;
- detector calibration plan;
- definition of the region of interest (ROI);
- gating parameters;
- energy bands, i.e., a plurality of non-overlapping energy windows;
- collimator positioning, shape, structure, and orientation;
- multiple/interlaced scans;
- zooming parameters;
- uniformity/non-uniformity of scan;
- Compton scatter map calculation and correction parameters;
- optimal energy window;
- optimal energy resolution, i.e., the range of energy window levels detected; and/or
- adaptivity of scan pattern to acquired counts, e.g., active vision parameters (as described in the above-mentioned International Application PCT/IL2005/001173).

For some applications, the optimal energy window is set at least in part responsively to the BMI of the patient. For example, the width of the energy window (i.e., the energy resolution) may be inversely related to the BMI, because the tissue of patients with higher BMIs tends to create more scatter. To compensate for narrower

energy windows, a longer acquisition time and/or a higher dose of radiopharmaceutical agent is typically used. For some applications, the protocol information includes a look-up table of BMIs and associated energy windows. For some applications, the energy window is non-symmetrical around a peak of the energy curve.

The image reconstruction protocol information is used by imaging system 28 to set parameters of the image reconstruction process. Such parameters may include, for example:

- calibration parameters;
- timing of acquisition;
- reconstruction parameters and algorithms;
- priors, i.e., mathematical constants signifying pre-imaging phase knowledge about system behavior;
- multi-resolution reconstruction parameters;
- non-uniform reconstruction grid;
- filters;
- noise modeling and handling;
- mode selection;
- information derived during image acquisition and/or gating;
- protocols for handling interfering organs;
- protocols describing the precise procedure to be followed in radiopharmaceutical administration, time management, patient activity status, imaging process, and other parameters that can affect imaging results;
- optimization parameters per dose and/or cocktail of doses; and/or
- attenuation correction parameters, which are typically based on physiological parameters such as body mass, BMI, and girth.

For some applications, imaging system 28 uses one or more of these parameters to perform the image reconstruction process using techniques described in one or more of

the co-assigned patent applications incorporated herein by reference.

The image analysis protocol information includes analysis algorithms and/or parameters of the image analysis process, which are used by imaging system 28 for performing diagnostic analysis of the reconstructed image. For some applications, such analysis includes tracer kinetics analysis. Such parameters may include, for example:

- information for selection of a model of tracer kinetics;
- information for selection of one or more time scales for tracer kinetics;
- tracer parameters;
- information for analysis of multiple time points;
- information for analysis regarding the clinical meaning of radiation distribution within the patient's body for the purpose of making a clinical diagnosis regarding the patient's health state;
- information for identifying the signatures of multiple labeled radiopharmaceutical agents; and/or
- optimization parameters per dose and/or cocktail of doses.

The expert system protocol information, such as expert system rules, is used by imaging system 28 to set parameters of the expert system used for assisting with diagnosis. For some applications, the expert system is implemented using techniques described in the above-mentioned International Application PCT/IL2005/001173, or in one or more of the other co-assigned patent applications incorporated by reference. Such parameters may include, for example:

- classification of the patient into a patient population;
- multi-parameter vectors of radiopharmaceutical kinetic parameters for different patient populations, such as a healthy population and populations which suffer from various pathologies, and for different tissue types, for example, brain tissue, cardiac tissue, liver tissue, or tumor tissue;
- patient history;
- multi-dimensional thresholds for defining healthy-disease state;
- disease signature classifications per pathology and/or organ (typically per

patient population); and/or

- optimization parameters per dose and/or cocktail of doses.

The portable information-bearing radiopharmaceutical agent container

Fig. 8 is a schematic illustration of data carrier 120, in accordance with an embodiment of the present invention. As mentioned above, data carrier 120 is physically coupled to radiopharmaceutical agent container 22. Data carrier 120 is computer-communicatable, and typically comprises an RFID tag, smart card, disk-on-key (e.g., a USB key), compact disc, minidisk, disposable computer-readable medium, or other electronic memory, or a machine-readable code, e.g., a barcode. One or more communication elements 240 are provided for reading data from and transmitting data to data carrier 24. Respective communication elements 240 are typically in data communication with dispensing system 20 and administration system 26. For some applications, communication elements 240 comprise one or more coils for transmitting and receiving electromagnetic radiation. Typically, the communication elements are configured to have a short effective transmission range, e.g., no more than between about 20 and 40 cm, such as about 30 cm. Such a short range reduces the likelihood of accidental communication with a data carrier other than the intended data carrier.

Data carrier 120 comprises circuitry 250, which comprises memory and logic. For some applications, data carrier 120 is passive, in which case it is configured to receive energy from communication element 240. For other applications, data carrier 120 comprises a power source (not shown). For some applications in which the data carrier comprises a power source, the data carrier comprises a communication element for communicating and/or energizing another electronic apparatus. Alternatively or additionally, the data carrier comprises a communication element 252 configured for wireless communication. For some applications, data carrier 24 further comprises a user output 254 for outputting information to the patient or healthcare workers. For example, output 254 may comprise a display screen, light, and/or sound generator, which the circuitry drives to communicate information, such as when communications have been established with other elements of system 10, e.g., data carrier 120, administration system 26, or imaging system 28. For some applications, data carrier 120 further comprises coded signature 256, which is typically encrypted, color-coded, or both encrypted and color-coded, as described hereinbelow in the section entitled "Signature."

The information contained in data carrier 120 typically includes some or all of the following:

- an administration-device identification code;
- an identifier, such as an identification code and/or name, of the patient for which the specific attached radiopharmaceutical agent container 22 is intended;
- the formulation of the labeled radiopharmaceutical agent(s) contained in attached container 22;
- the time of dispensing of the labeled radiopharmaceutical agent(s) to container 22;
- activity of the labeled radiopharmaceutical agent(s), at the time of dispensing of the labeled radiopharmaceutical agent(s) to container 22;
- the assigned protocol(s) for use with the labeled radiopharmaceutical agent(s) contained in attached container 22;
- the intended time(s) and date(s) of administration of the labeled radiopharmaceutical agent(s) contained in container 22;
- the intended activity(ies) of the labeled radiopharmaceutical agent(s) at the time of administration thereof;
- the intended time profile of administration (single bolus, slow-drip administration, or any other form of administration);
- the identification code of mother vial 104 from which the labeled radiopharmaceutical agent(s) contained in container 22 were dispensed; and/or
- at least a portion of the radiopharmaceutical information stored in data carrier 106 of mother vial 104, as described hereinabove with reference to Fig. 7. This information is typically electronically transferred from data carrier 106 during dispensing of the labeled radiopharmaceutical agent(s) to container 22, as described hereinabove with reference to step 118 of Fig. 2 and hereinbelow with reference to Fig. 12.

As mentioned above, for some applications, all or a portion of the information contained in patient-specific data carrier 24 is alternatively or additionally stored in data carrier 120. Such information is described hereinabove with reference to Fig. 7. For some applications, a portion of the information stored in the data carrier is also printed in human- and/or machine-readable form on the data carrier and/or on the container, for example as a barcode 260, as shown below in Figs. 9A-H.

In an embodiment of the present invention, radiopharmaceutical agent container 22 comprises all or a portion of a drug administration device, such as a syringe or an inhalation device, packaging for an oral dosage form, or radiopharmaceutical packaging.

Reference is made to Figs. 9A-H, which are schematic illustrations of respective embodiments of radiopharmaceutical agent container 22 and data carrier 120, in accordance with respective embodiments of the present invention. In all of these embodiments, data carrier 120 is physically coupled to agent container 22.

Fig. 9A is a schematic illustration of radiopharmaceutical agent container 22 comprising a manual syringe 270, in accordance with an embodiment of the present invention. Syringe 270 is protected by shielding 272, to which data carrier 120 is coupled. Alternatively, the data carrier is coupled directly to an exposed portion of the syringe, such as the end of the plunger of the syringe, as shown in the figure.

Fig. 9B is a schematic illustration of radiopharmaceutical agent container 22 comprising an automatic administration device 280, in accordance with an embodiment of the present invention. Device 280 comprises a chamber 282 for containing the labeled radiopharmaceutical agent(s), a needle 283, a controller 284, a drive 286, and a power source 288. For some applications, controller 284 is preprogrammed with administration instructions, while for other applications, the controller is coupled to administration system 26 and receives an administration signal therefrom prior to administration, or in real time during administration. Administration device 280 typically includes an interlock 290 to prevent administration without verification, for example, of the patient's identity. For some applications, device 180 comprises a flow meter 292, which measures the volume of labeled radiopharmaceutical agent administered. Controller 284 uses this flow information for regulating parameters of the administration, such as rate of administration and total amount of agent administered. Shielding 272 protects medical personnel from the radioactivity of the labeled radiopharmaceutical agent.

Fig. 9C is a schematic illustration of a multi-chamber embodiment of radiopharmaceutical agent container 22, in accordance with an embodiment of the present invention. In this embodiment, container 22 comprises a plurality of chambers in fluid isolation from one another, each of which chambers contains a labeled radiopharmaceutical agent. In the embodiment shown in Fig. 9C, the container comprises two such chambers, a first chamber 282A and a second chamber 282B. Alternatively, the container comprises more than two chambers (configuration not shown). For some multi-chamber applications, container 22 comprises automatic administration device 280, as shown in Fig. 9C, while for other multi-chamber applications, container 22 comprises a plurality of manual syringes 270, as described hereinabove with reference to Fig. 9A (multi-chamber configuration not shown). For some applications, a separate needle 283 is provided for each injection, while for other applications, container 22 is configured to utilize a single needle 283 for the plurality of injections. For example, needle 283 may be configured to slide along a needle mount 294, so as to service the plurality of chambers.

Fig. 9D is a schematic illustration of another configuration of radiopharmaceutical agent container 22, in accordance with an embodiment of the present invention. In this embodiment, container 22 comprises automatic administration device 280, as described hereinabove with reference to Fig. 9B, and controller 284 is configured to perform all or a portion of the functions of data carrier 120. For some applications, one or more of the elements of data carrier 120 are provided separately from the controller. For example, communication element 252 or user output 254 may be provided separately from the controller.

Figs. 9E-G are schematic illustrations of another configuration of radiopharmaceutical agent container 22 comprising manual syringe 270, in accordance with an embodiment of the present invention. In this embodiment, syringe 270 comprises a transmitter 296 fixed with respect to a plunger 298 of the syringe, and shielding 272 is configured so as to modulate effective transmission by transmitter 296. For example, shielding 272 may be shaped so as to define a longitudinal slot 300 along a portion of the shielding. This modulation serves to send, from syringe 270 to administration system 26 and/or imaging system 28, a signal indicative of a time of administration of the labeled radiopharmaceutical agent(s) contained in container 22. The techniques of this embodiment are typically useful when registration of the time of administration with imaging system 28 is important, such as for dynamic studies.

Figs. 9E-G respectively illustrate three steps for administration using these techniques. Fig. 9E shows a first step, during which transmitter 296 is exposed, and therefore effectively transmits a signal. Fig. 9F shows a second step, during which transmitter 296 is shielded by shield 272. Fig. 9G shows a third step, in which transmitter 296 is again exposed. This sequence of exposing, shielding, and again exposing the transmitter serves to signal that administration has occurred. The receiver of the signal (administration system 26 and/or imaging system 28) records the time that this signal is detected. For some applications, other techniques are used to automatically transmit an indication of when the labeled radiopharmaceutical agent(s) are administered. For example, a transmitter may be mounted on shield 272, and may send a signal when electrical contact is established between electrodes (not shown) on plunger 298 and shield 272 at the end of complete motion of the plunger into syringe 270.

Fig. 9H is a schematic illustration of a syringe adaptor 320, in accordance with an embodiment of the present invention. Adaptor 320 comprises shielding 272 and data carrier 120 coupled thereto. The adaptor is configured to placed on a standard administration device, such as a standard syringe. In an embodiment of the present invention, an adaptor similar to adaptor 320 is provided for use with other components of an end-to-end imaging system, such as Tc-99m vials, mother vials, dispensing tools, and dilution containers. Alternatively or additionally, data carrier 120 is configured to be couplable to such other components.

In an embodiment of the present invention, data carrier 120 is configured to be couplable to a standard administration device, such as a syringe. For example, the data carrier may be couplable to the barrel, plunger, or conventional shielding of a conventional syringe, or another syringe known in the art.

The administration system

Reference is made to Fig. 10, which is a schematic illustration of administration system 26, in accordance with an embodiment of the present invention. Administration system 26 comprises a control unit 350, at least one communication element 240, and, for some applications, an automated administration device 352. Typically, control unit 350 comprises a standard personal computer or server with appropriate memory, communication interfaces and software for carrying out the functions prescribed by relevant embodiments of the present invention. This software may be downloaded to the

control unit in electronic form over a network, for example, or it may alternatively be supplied on tangible media, such as CD-ROM. For some applications, administration system 26 comprises a single communication element 240 that communicates with both patient-specific data carrier 24 and data carrier 120 of container 22, while for other applications the administration system comprises separate communication elements 240 for communicating with data carriers 120 and 24 respectively. For example, a communication element for communicating with data carrier 120 may be integrated into or coupled to automated administration device 352.

Upon authenticating container 22, verifying the identity of the patient, and performing additional verifications, as described hereinabove with reference to step 122 of Fig. 2, control unit 350 generates an administration signal that triggers administration to the patient of the labeled radiopharmaceutical agent(s) stored in container 22. For applications in which administration system 26 comprises automated administration device 352, container 22 is operatively coupled to device 352, and the signal drives administration device 352 to administer the labeled radiopharmaceutical agent(s) stored therein to the patient. Automated administration device 352 is configured to perform intravenous (IV) injection, intramuscular (IM) injection, subcutaneous injection, transdermal application, oral administration, nasal administration, inhalation, transcervical application, transrectal administration, or another type of administration known in the art. (It is to be understood that although the administration signal triggers administration of the agent, for some applications automated administration device 352 does not administer the agent until a healthcare worker provides a final authorization to do so, such as to comply with regulatory safety requirements.) For applications in which administration system 26 does not comprise automated administration device 352, the administration signal triggers administration of the agent by instructing a healthcare worker to manually administer the agent to the patient.

For some applications, based on administration protocol information received from data carrier 120 of radiopharmaceutical agent container 22 and/or patient-specific data carrier 24, control unit 350 customizes the administration of the labeled radiopharmaceutical agent(s) contained in agent container 22. Such administration protocol information typically includes all or a portion of the administration protocol information described hereinabove with reference to Fig. 7. For some applications, administration system 26 administers a plurality of labeled radiopharmaceutical agents,

either sequentially or premixed together within a single agent container 22 (i.e., as a cocktail).

For some applications, administration system 26 administers the labeled radiopharmaceutical agent(s) responsively at least in part to acquisition of a signal associated with the agent(s). For example, acquisition of the signal may comprise detection of photons emitted from the agent(s), in order to determine a radioactivity level.

For some applications, administration system 26 monitors uptake and/or clearance of the labeled radiopharmaceutical agent(s) by (a) measuring physiological parameters, e.g., from samples of blood, saliva, or secretions, e.g., urine, breath, feces, or sweat, or (b) by performing an imaging procedure using imaging system 28. For some applications, these measurements are used to estimate pharmacokinetics of the radiopharmaceutical agent(s) in organs, and/or to predict optimal imaging timing (the optimal time to perform the imaging, and/or the optimal timing parameters of the imaging procedure). For some applications, based on these estimates, an expected level of uptake of the radiopharmaceuticals in a target organ is determined, enabling diagnosis of pathologies based on absolute uptake levels in the target organ.

The imaging system

Reference is made to Fig. 11, which is a schematic illustration of imaging system 28, in accordance with an embodiment of the present invention. Imaging system 28 comprises a control unit 450, a communication element 240, a camera 452, and an imaging workstation 453. Typically, control unit 450 and imaging workstation 453 comprise one or more standard personal computers or servers with appropriate memory, communication interfaces and software for carrying out the functions prescribed by relevant embodiments of the present invention. This software may be downloaded to the control unit and imaging workstation in electronic form over a network, for example, or it may alternatively be supplied on tangible media, such as CD-ROM.

Control unit 450 typically comprises: (a) image acquisition functionality, which is configured to drive camera 452 to perform image acquisition of the patient; (b) image reconstruction functionality, which is configured to perform an image reconstruction procedure on the acquired image; (c) image analysis functionality, which is configured to perform an image analysis procedure on the reconstructed image; and (d) diagnosis

functionality, which is configured to perform a diagnostic procedure using the results of the image analysis procedure. It will be appreciated that control unit 450 may comprise a plurality of personal computers or servers, each of which performs one or more of these procedures, and that one or more of these computers or servers may be located remotely from camera 452. Imaging workstation 453 displays the reconstructed images and allows the attending healthcare worker to view and manipulate the images.

As mentioned above with reference to steps 124 through 130 of Fig. 2, imaging system 28 typically customizes one or more of these procedures at least in part responsively to imaging protocol information and/or patient-specific information read by communication element 240 from patient-specific data carrier 24.

For some applications, camera 452 comprises a commercially available diagnostic structural or functional camera, such as a SPECT or PET camera, and/or utilizes imaging techniques described in one or more of the patents and patent applications described hereinabove in the section entitled "Background of the Invention." Alternatively, camera 452 utilizes techniques described in the above-mentioned International Application PCT/IL2005/001173, in above-mentioned PCT Publication WO 05/119025, and/or in the other above-mentioned co-assigned patent applications and/or patent application publications.

In an embodiment of the present invention, camera 452 comprises a plurality of detectors 454, each of which is coupled to a respective angular orientator 456. Each of the detectors comprises a plurality of gamma ray sensors, such as a pixelated CZT array, and a collimator. For example, the array may include 16x64 pixels. Control unit 450 drives, typically separately, each of the orientators to orient its respective detector in a plurality of orientations with respect to a region of interest (ROI). Control unit 450 produces a SPECT image from a plurality of radiation acquisitions acquired with the detectors in different relative orientations.

In an embodiment of the present invention, camera 452 is configured to begin an image acquisition procedure by performing a relatively brief, preliminary scan, and, based on the results of this preliminary scan, to determine one or more parameters of the full image acquisition procedure, such as dwell time per orientation of each detector 454. Typically, this determination further takes into account imaging protocol and/or patient-specific information received by imaging system 28 from patient-specific data

carrier 24, such as the activity of the labeled radiopharmaceutical agent at the time of administration, the time of administration, the patient's BMI (which may be used to estimate a perfusion percentage), and the pharmacokinetics of the labeled radiopharmaceutical agent.

In an embodiment of the present invention, camera 452 is configured to individually set a total angular range of each of detectors 454 responsively to the detector's orientation with respect to the ROI. For example, at least one detector closer to the ROI (a "proximal detector" or an "inner detector") may have a greater total angular range than at least one detector further from the ROI (a "distal detector" or an "outer detector"). The distal detectors are typically located nearer to the ends of a frame holding the detectors, while the proximal detectors are typically located nearer to center of the frame. The use of narrower angular ranges for some of the detectors generally reduces the photon acquisition time spent by these detectors in orientations aimed outside of the ROI. Alternatively, at least one distal detector has a greater total angular range than at least one proximal detector. In order to reduce the total angular range for a given detector, camera 452 typically drives the associated angular orientator 456 to: (a) increase the dwell time of the detector in at least a portion of its orientations, and/or (b) reduce the angle by which the detector is moved during each orienting of the detector. For some applications, camera 452 sets the angular range of the detectors based on protocol information received by imaging system 28 from patient-specific data carrier 24. For example, the number of distal and proximal detectors, and their respective angular ranges, may be specified by the protocol information, as described hereinabove with reference to Figs. 6B-E.

In an embodiment of the present invention, camera 452 comprises a plurality of detectors 454, each of which is coupled to a respective angular orientator 456. Each of the detectors comprises a plurality of gamma ray sensors, such as a pixelated CZT array, and a collimator. Control unit 450 drives, typically separately, each of the orientators to orient its respective detector in a plurality of orientations with respect to a region of interest (ROI). Control unit 450 produces a SPECT image from a plurality of radiation acquisitions acquired with the detectors in different relative orientations.

In an embodiment, camera 452 is configured to drive one of orientators 456 to move its respective detector 454 through a plurality of sequential angular positions, e.g., positions 1, 2, 3, ..., 18, 19, and 20. Typically, a linear relationship relates the sequential

positions, such that, for example, positions 1, 2, 3, ..., 20 represent 1°, 2°, 3°, ..., 20°, or, 2°, 4°, 6°, ..., 40°. Alternatively, a non-linear relationship relates the sequential positions. Higher or lower angular resolutions are typically obtainable, as well.

For some applications, camera 452 steps the orientator in a first pass through a subset of the positions spanning most of the range of positions, and in a second pass the camera steps the orientator through a different subset of the positions. At each position, data are acquired by the detector. For example, during the first pass, the camera may drive the orientator to step through positions 1, 5, 9, 13, and 17, and the detector acquires data at each of these positions. During the second pass, the orientator steps through positions 2, 6, 10, 14, and 18. During two subsequent passes, data are acquired at the remainder of the positions. In this manner, a single-direction interlaced scan of the data is acquired by camera 452.

In an embodiment, a back-and-forth interlaced scan is acquired in which data are sampled when the orientator is moving in both directions. For example, during the first pass, the camera may drive the orientator to step through positions 1, 5, 9, 13, and 17. During the second pass, the orientator steps through positions 18, 14, 10, 6, and 2. During the third pass, the orientator steps through positions 3, 7, 11, 15, and 19, while during the fourth pass, the orientator steps through positions 20, 16, 12, 8, and 4. Fifth and higher passes, if desired, typically repeat the motions used in the earlier passes.

For some applications, the positions in a pass are not ordered from lowest-to-highest or highest-to-lowest. For example the positions of a pass may be 1, 15, 11, 19, and 17. Typically, the positions are, however, distributed generally evenly throughout the range of positions, in order to acquire photon counts representative of the entire region of interest.

As appropriate for a given scanning protocol using interlaced scanning, one or more, or even all of orientators 456 are driven to step through their respective positions in an interlaced fashion.

Typically, execution of an interlaced scan as provided by these embodiments of the present invention allows an operator of camera 452, such as an imaging technician or other healthcare worker, to acquire a high-resolution image of the ROI in about 105% to 115% of the amount of time as would be used if orientator 456 were stepped through the positions sequentially. (Typically, each orientation takes between about 50 and about 200

msec, depending upon the angle of the step.) The high-resolution image is completely acquired after the orientator has stepped through each of its positions. In some cases, additional value is attained by interlacing the scanning, however, as this allows the performance of dynamic studies, in which a plurality of images are acquired during a respective plurality of the time periods, i.e., during each complete pass of the orientator. Although each these images is typically of lower resolution than the high-resolution image acquired using photon counts acquired during all of the passes, the images nevertheless have sufficient resolution to produce clinically-meaningful data for each time period of a dynamic study.

For some applications, interlacing the scanning allows an operator to see an initial, lower-resolution scan of the ROI. If, for example, an adjustment of any form is desired, this can often be seen within the first few seconds of a scan. The present scan is terminated, the adjustment made, and a second scan initiated. In the absence of interlacing, it is typically necessary to wait until a scan has completed until an assessment of the scan's results can be made.

For some applications, it is desirable to know whether the patient has moved during a scan. Patient movement is one reason for lower quality images, and when identified it can typically be corrected by suitable instruction and then a second scanning procedure initiated. Interlaced scanning, as provided by these embodiments of the present invention, allows the operator to immediately assess whether there has been patient movement between one pass and a subsequent pass. In an embodiment, the imaging system displays to an operator the scans obtained from the various passes in rapid succession at the same location on a monitor. As appropriate, the imaging system cycles quickly through the scans repeatedly (e.g., pass 1, pass 2, pass 3, pass 4, pass 1, pass 2, pass 3, pass 4...), e.g., displaying each scan for between about 0.2 and about 2 seconds, allowing an operator to see whether there is jitter between successive scans. If so, patient movement is typically the cause and image acquisition is repeated. For some applications, the scan is acquired in exactly two passes, e.g., the orientator steps through positions 1, 3, 5, ..., 19 during a first pass, and through positions 2, 4, 6, ..., 20 during a second pass, or through positions 20, 18, 16, ..., 2 during the second pass.

Images acquired using these techniques, or other non-interlacing techniques described herein, are generally used to perform one or more of the following image

reconstructions: (a) reconstruction of intensity image, (b) reconstruction of intensity over time, followed by fitting a model of the kinetics (which describe for each voxel a parameter set describing its time curve), and followed by presenting a three-dimensional map of the parameters, and/or (c) direct reconstruction of a three-dimensional parametric representation, without performing a reconstruction of an intensity map, typically by plugging an equation of a kinetic model into a reconstruction algorithm, and generating a result directly in terms of the value of the parameters per voxel (the parameters may include, for example, flow, diffusion coefficients, metabolism rate, or bio-clearance rate).

The radiopharmaceutical dispensing system

Reference is made to Fig. 12, which is a schematic illustration of automated radiopharmaceutical dispensing system 20, in accordance with an embodiment of the present invention. System 20 comprises a control unit 500, at least one robot 502, and at least one communication element 504, which, for some applications, is coupled to robot 502. Control unit 500 typically comprises a conventional personal computer running a conventional operating system, such as Windows XP, with appropriate memory, communication interfaces and software for carrying out the functions described herein. This software may be downloaded to the control unit in electronic form over a network, for example, or it may alternatively be supplied on tangible media, such as CD-ROM. Control unit 500 is in communication with other elements of system 10, for example via management and control component 150. The control unit notifies appropriate elements of the system upon successful completion of dispensing of a dose.

At least one radiolabeled mother vial 104 is placed in a shielded vials complex 505 of dispensing system 20. Control unit 500 authenticates the mother vial, by actuating communication element 504 to read authentication information stored in data carrier 106, and/or by verifying a coded signature 256 coupled to the mother vial, as described hereinbelow in the section entitled "Signature." Upon successful authentication, control unit 500 actuates communication element 504 to read radiopharmaceutical-related information from data carrier 106 of the mother vial, including the radiopharmaceutical agent type, isotope type, batch, lot, radiochemical purity (RCP), preparation time, and half-life information. Dispensing system 20 assays the radioactivity per unit volume of the labeled radiopharmaceutical agent contained in the mother vial. Robot 502 picks up an empty syringe 506 from a syringe tray 508, draws a predetermined amount of solution

from mother vial 104, and brings the syringe to a dose calibrator 510. The syringe used for the assaying is typically discarded into a waste container 512. Typically, robot 502 brings the mother vial to a weighing station 507 for verification that the vial contains the indicated solution volume.

Dispensing system 20 receives a patient-specific dose request for at least one specific labeled radiopharmaceutical agent, having a specific dose, radioactivity, and solution volume. Such a dose is typically calculated by dose calculation sub-system 156 of dose calculation system 152, as described hereinabove with reference to Fig. 5, and/or by patient management system 160, described hereinabove with reference to Fig. 4. Alternatively or additionally, dispensing system 20 is configured to customize, modify, or verify the dose. Further alternatively, dispensing system 20 receives the order from another hospital or radiopharmacy information system, or the order is manually inputted into system 20.

To fill the request, control unit 500 calculates a required volume of the labeled radiopharmaceutical agent and a required volume of saline solution for dilution, if any. To perform this calculation, control unit 500 uses (a) information read from data carrier 106 (such as the half-life of the labeling isotope of the labeled radiopharmaceutical agent), and (b) the assayed radioactivity of the labeled radiopharmaceutical agent. Alternatively, dose calculation sub-system 156 performs all or a portion of this calculation.

For some applications, control unit 500 authenticates mother vial license information read from data carrier 106, in order to verify that a license is available for dispensing the requested dose. Dispensing proceeds only if a license is available and authenticated. The use of such a license generally provides increased quality control of the imaging process, by verifying that only approved manufacturers (or distributors) are able to provide radiopharmaceutical agents for use with system 10. A lack of precision in any aspect of an imaging procedure, which may result from the use of an agent that has not been tested and approved for use with system 10, often causes a deterioration of the resultant image quality and/or ability to make accurate and/or quantitative diagnoses.

Control unit 500 actuates robot 502 to pick up an empty radiopharmaceutical agent container 22 from tray 508. Typically, but not necessarily, container 22 comprises a syringe, such as described hereinabove with reference to Figs. 9A-H. Container 22 has coupled thereto a data carrier 120. For some applications, syringes 506 and containers 22

are stored in a single tray, as shown in Fig. 12, while for other applications, they are stored in separate trays. Robot 502 typically authenticates container 22, by actuating communication element 504 to read authentication information stored in data carrier 120 and/or verifying coded signature 245 coupled to the container, as described hereinbelow in the section entitled "Signature."

Robot 502 removes the needle cap from container 22, turns the container over, and brings container 22 to the appropriate mother vial 104. The robot actuates the container to draw the calculated volume of labeled radiopharmaceutical agent from the mother vial, typically by inserting the needle of container 22 through a membrane of mother vial 104, and withdrawing a plunger of container 22 until the desired volume of agent has been drawn from the mother vial. The robot typically brings the syringe to dose calibrator 510 for quality control assaying of radioactivity. If necessary, robot 502 brings container 22 to a saline vial 514, and actuates the container to draw the required volume of saline solution into the container. Robot 502 replaces the needle cap on the container, and turns the container over. Alternatively, saline solution is drawn prior to drawing the labeled radiopharmaceutical agent from mother vial 104. For some applications, a needle of the container 22 is changed between drawings.

For dispensing a cocktail of labeled radiopharmaceutical agents, each having a respective dose, robot 502 repeats these steps for a plurality of mother vials 104, typically changing the needle of container 22 between drawings. During dispensing of such a cocktail, robot 502 typically draws first from the mother vial containing the lower or lowest radiation labeled radiopharmaceutical agent, such as to reduce any effect the assaying of the first agent may have on the assaying of the subsequent agent(s).

System 20 typically performs a quality control check on the dispensed radiopharmaceutical solution to confirm that the solution contains the desired dose(s) of the radiopharmaceutical agent(s) and radioactivity level.

Control unit 500 activates communication element 504 to write radiopharmaceutical information to data carrier 120 of container 22, as described hereinabove with reference to Fig. 8 and step 118 of Fig. 2. For some applications, the data carrier is coupled to the container prior to placement of the container in dispensing system 20, while for other applications, robot 502 couples a data carrier to each container during or after the dispensing process. Similarly, for some applications in which coded

signature 256 is provided, the coded signature is attached to container 22 prior to placement of the container in dispensing system 20, while for other applications, robot 502 couples a coded signature to each container during or after the dispensing process.

Robot 502 brings the filled container to a shield body tray 530, and inserts the container into a container shield 532. The robot picks up a shield cap 534 from a shield cap tray 536, and secures it to container shield 532. For some applications, data carrier 120 is coupled to shield 532 or cap 534, rather than directly to container 22. Alternatively, separate data carriers 120 are coupled to the container and the shield or cap.

In an embodiment of the present invention, dispensing system 20 comprises a print area 540, at which dispensing system 20 prints and attaches at least one conventional label to container 22, shield 532, and/or cap 534, in order to comply with regulatory labeling requirements. The dispensing system typically prints yet another conventional label for placement on a basket that holds a plurality of containers 22 for transport within or between healthcare facilities.

After the dispensing of container 22 has been completed, robot 502 brings the container to a completed container tray (tray not shown in the figure).

In an embodiment of the present invention, dispensing system 20 comprises at least one diluted mother vial which has a greater volume than a conventional mother vial. For example, the diluted mother vial may have a volume of at least about 10 ml, e.g., at least about 20 ml, such as 21 ml, while a conventional mother vial may have a volume of less than 10 ml, e.g., less than 7 ml, such as 5.8 ml. The labeled radiopharmaceutical agent solution from a conventionally-sized mother vial 104 is transferred to the diluted mother vial, and the balance of the additional volume of the diluted mother vial is filled with saline solution. The resulting diluted solution is used by dispensing system 20 to fill containers 22 with low-dose labeled radiopharmaceutical agents useful for performing low-dose imaging procedures, such as those described in the above-mentioned International Application IL/2005/001173, in above-mentioned PCT Publication WO 05/119025, or in one or more of the other co-assigned patent applications incorporated herein by reference. Alternatively, the resulting lower-dose solution is used for time-dependent administration protocols, pursuant to which a desired total dose is divided into several sub-doses for sequential administration over time. For mechanical handling and administration reasons, each sub-dose must have a minimum volume, e.g., at least 1

ml.

The information contained in data carrier 106 of conventionally-sized mother vial 104 is transferred to a data carrier 106 of the dilution mother vial, with appropriate adjustments to reflect the diluted dose of the labeled radiopharmaceutical agent.

In an embodiment of the present invention, a method for automatically dispensing a labeled radiopharmaceutical agent comprises providing a mother vial having a volume of at least 10 ml, e.g., at least 20 ml; filling the mother vial with at least 5 ml of a non-diluted labeled radiopharmaceutical agent, and with at least 5 ml of saline solution; placing the mother vial in automated radiopharmaceutical dispensing system 20; and dispensing at least one dose from the mother vial to a container. For some applications, dispensing system 20 further dilutes the dose by dispensing saline solution to the container from a saline solution container.

It is noted that dispensing system 20 is theoretically able to dispense similar low doses to containers 22 by drawing a small volume of labeled radiopharmaceutical agent from a conventionally-sized mother vial, and diluting the agent with saline solution drawn from saline vial 512, as described above. However, the drawing of such a small volume may present mechanical challenges for achieving precise volumes within acceptable variations.

Reference is made to Figs. 13A-C, which are schematic illustrations of a system for carrying out a data transfer process, in accordance with an embodiment of the present invention. In this embodiment, information is transferred directly from data carrier 106 of mother vial 104 to data carrier 120 of container 22 while container 22 draws the labeled radiopharmaceutical agent from mother vial 104. As shown in Fig. 13A, container 22 is lowered to mother vial 104 (which is contained within shielding 520 of vials complex 505), as indicated by an arrow 522. As shown in Fig. 13B, as container 22 draws labeled radiopharmaceutical solution from mother vial 104, data carrier 120 of the container is positioned in a vicinity of data carrier 106 of the mother vial. Container 22 is raised from mother vial 104, as indicated by an arrow 524 in Fig. 13C. Information transfer takes place during one or more of the steps illustrated in Figs. 13A-C.

For some applications, information is transferred to data carrier 120 of container 22 during assaying of the contents of the container at dose calibrator 510.

In an embodiment of the present invention, dispensing system 20 is configured to dispense to a plurality of containers 22 for a single patient, or to a plurality of independent chambers within a single container 22 (such as first and second chambers 282A and 282B, described hereinabove with reference to Fig. 9C). For some applications, the plurality of containers are permanently coupled to one another, while for other applications the plurality of containers are removably coupled to one another. Alternatively, the plurality of containers are not coupled to one another, in which case they may be stored in association with one another, e.g., in a single tray.

For some applications, dispensing system 20 utilizes one or more of the dispensing techniques described in the references mentioned hereinabove in the Background of the Invention section, *mutatis mutandis*.

In an embodiment of the present invention, system 10 does not comprise dispensing system 20. System 10 is instead electronically or manually interfaced with a conventional radiopharmacy. Patient management system 160 places orders with the radiopharmacy for a particular dose of a labeled radiopharmaceutical agent for a particular patient. Upon dispensing of the dose into a conventional container, such as a syringe, data carrier 120 is physically coupled to the container, and information is written to the data carrier, such as the identity of the labeled radiopharmaceutical agent, the time of dispensing, the measured radioactivity level, and/or other information described herein as being contained in the data carrier, such as with reference to Fig. 8. For some applications, system 10 comprises a module for automatically measuring the radioactivity level and recording the information in the data carrier. Optionally, the module is in communication with system 10, such as via management control component 150, and receives additional patient-specific or protocol-related information from system 10, and records the information in data carrier 120. For some applications, the radiopharmacy dispenses the labeled radiopharmaceutical agent to one of the novel radiopharmaceutical agent containers 22 described herein.

The radioisotope elution system

Reference is made to Fig. 14, which is a schematic illustration of a radioisotope automatic elution system 600, in accordance with an embodiment of the present invention. System 600 automatically elutes a radioisotope, such as technetium Tc-99m, into radioisotope vials 610. The radioisotope is used for radiolabeling the unlabeled

radiopharmaceutical agent, as described hereinabove with reference to step 110 of Fig. 2. Vials 610 are coupled to radioisotope data carriers 612 containing information about the radioisotope, such as a vial code, the time of preparation, the activity at the time of preparation, and total solution volume. Labels 612 are computer-communicatable, and typically comprise an RFID tag, smart card, disk-on-key (e.g., a USB key), compact disc, minidisk, disposable computer-readable medium, or other electronic memory, or a machine-readable code, e.g., a barcode. For some applications, information contained in data carrier 612 is encrypted for enabling authentication. Alternatively or additionally, data carrier 612 and/or vial 610 comprise coded signature 256, as described hereinabove. The coded signature typically comprises an encrypted signature and/or a color-coded signature, as described hereinbelow in the section entitled "Signature."

The automatic elution process typically begins with a determination by dose calculation system 152 (Fig. 5) of an optimal elution frequency, for example:

- 18 hours, 6 hours, 18 hours, 6 hours, ... ,;
- 23 hours, 1 hour, 23 hours, 1 hour, ... ,;
- 18 hours, 1 hour, 5 hours, 18 hours, 1 hour, 5 hours, ... ,; or
- 18 hours, 6 hours, 23 hours, 1 hour, 18 hours, 6 hours, 23 hours, 1 hour, ... ,.

Dose calculation system 152 electronically notifies a control system 616 of elution system 600 of the desired elution frequency. For applications in which the radioisotope comprises Tc-99m, it will be appreciated that the ratio of Tc-99 to Tc-99m, which is determined by the elution frequency, is important for molecular imaging by an antibody, and there is generally an optimal range of the ratio of Tc-99 to Tc-99m, which should be taken into consideration when preparing Tc-99m with an antibody. Typically, control system 616 comprises one or more standard personal computers or servers with appropriate memory, communication interfaces and software for carrying out the functions prescribed by relevant embodiments of the present invention. This software may be downloaded to the control system in electronic form over a network, for example, or it may alternatively be supplied on tangible media, such as CD-ROM.

Sterile, empty vials 610 of predetermined volumes (e.g., 10 ml or 20 ml), and typically comprising caps 618, are placed on a conveyor belt 620. A first robot 622 places

a shield 624 on each vial 610. Alternatively, the vials 610 are manually shielded. Conveyor belt 620 moves shielded vial 610 into position under a radioisotope generator 626, such as a TC-99m generator. At a required elution time, a second robot 628 lifts the shielded empty vial 610, and, under sterile conditions, removes cap 618 and engages the shielded empty vial 610 with generator 626.

Upon engagement of vial 610 with generator 626, both a first electronic valve 630 of a saline tank 632 and a second electronic valve 634 of generator 626 open, and vial 610 is filled, while a flow meter 636 monitors the amount of saline flow. After flow of a predetermined volume, control system 616 automatically shuts first electronic valve 630 of saline tank 632 and second electronic valve 634 of generator 626.

Filled, shielded vial 610 is automatically disengaged from generator 626, and is automatically sealed under sterile conditions with a shielded seal 638. Filled, shielded vial 610 is lowered back to conveyor belt 620. The conveyor belt moves filled, shielded vial 610 past an assaying and labeling station 640, which assays and labels the vial with data carrier 612, a barcode 642, and/or coded signature 256. For some applications, coded signature 256 is placed on data carrier 612, while for other applications it is placed on vial 610. For still other applications, separate coded signatures 256 are placed on both vial 610 and data carrier 612, and are used to match the vial with the data carrier. For example, a color-coded signature may be printed on vial 610, either prior to the elution or together with the application of data carrier 612, and an encrypted signature may be stored in the data carrier 612. Alternatively, the encrypted signature may be printed.

It will be appreciated that the elution process is subject to modifications and alterations based on communication and information that is received from system 10. For example, a log book of elution system 600 may specify a Tc-99m vial of 1000 mCi, yet a communication request from dose calculation system 152 may modify the order to be a Tc-99m vial of 200 mCi, based on new requirements, e.g., low-dose administration.

The mother vial preparation system

Reference is made to Fig. 15, which is a schematic illustration of a mother vial preparation system 700, in accordance with an embodiment of the present invention. System 700 automatically labels mother vials 104, containing unlabeled radiopharmaceutical agents, with appropriate radioisotopes. System 700 attaches a data

carrier 106 to each mother vial 104, and writes the information to the data carrier that is described hereinabove with reference to Fig. 7. Alternatively, the manufacturer or distributor attaches data carrier 106 to mother vial 104, and writes at least a portion of the information to the carrier.

Prior to beginning the radiolabeling process, a control unit 702 of system 700 authenticates radioisotope vial 610 and mother vial 104, and verifies that radioisotope vial 610 contains the correct radioisotope at the correct radioactivity, and that mother vial 104 contains the correct unlabeled radiopharmaceutical agent. For some applications, such authentication and/or verification is performed by authenticating coded signature 256 of data carrier 612 of radioisotope vial 610. For some applications, such authentication includes authentication of a commercial license associated with the use of mother vial 104. Typically, control unit 702 comprises one or more standard personal computers or servers with appropriate memory, communication interfaces and software for carrying out the functions prescribed by relevant embodiments of the present invention. This software may be downloaded to the control unit in electronic form over a network, for example, or it may alternatively be supplied on tangible media, such as CD-ROM.

Conveyor belt 620 carries shielded radioisotope vial 610 from radioisotope automatic elution system 600 to mother vial preparation system 700. Alternatively, for embodiments in which elution system 600 is not provided, the radioisotope vial is manually placed on conveyor belt 620. The conveyor belt brings vial 610 to a radioisotope filling point 710.

System 700 typically comprises a plurality of dose preparation platforms 712, each of which contains premixed mother vials 104 containing unlabeled radiopharmaceutical agents that require radiolabeling with the radioisotope contained in radioisotope vial 610, e.g., Tc-99m. In the example shown in Fig. 15, preparation platforms 712 comprise a Tc-99m-teboroxime dose preparation platform, a Tc-99m-pertechnetate dose preparation platform, a Tc-99m-sestamibi dose preparation platform, and a Tc-99m-MDP dose preparation platform.

A robot 720 picks up a syringe 722 from a first syringe platform 724, or a micro-syringe 726 from a second syringe platform 728, and travels along a second conveyer belt 730 to filling point 710. It will be appreciated that other types syringes and/or other dispensing tools may also be used. Upon reaching filling point 710, syringe

722 or 726 draws a predetermined amount of radioisotope solution from radioisotope vial 610. The robot typically travels to an assay station 732, which assays the radioisotope solution. Syringe 722 or 726 is then discarded at a discard station 734.

Robot 720 picks up another syringe 722 or 726 from the platform 724 or 728, fills the syringe with a predetermined amount of the radioisotope from vial 610, and travels along second conveyor belt 730 to one of dose preparation platforms 712. At the dose preparation platform, the syringe injects a predetermined amount of radioisotope into mother vial 104 of the dose preparation platform, thereby labeling the unlabeled radiopharmaceutical agent contained in the mother vial.

Robot 720 discards the syringe at discard station 734, picks up a new syringe, draws a predetermined amount of solution from labeled mother vial 104, and assays the solution at assay station 732, in order to determine the radioactivity of the labeled radiopharmaceutical agent contained in mother vial 104. Following the assaying, robot 720 discards the syringe at discard station 734. Typically, system 700 performs one or more quality control procedures on the labeled radiopharmaceutical agent.

System 700 updates data carrier 106 of mother vial 104 with radiolabeling information, such as the time of labeling, and the activity of the radioisotope at the time of labeling, the total solution volume in the mother vial, and the ratio of radioisotopes (e.g., Tc-99m to Tc-99) at the time of labeling, for applications in which the unlabeled radiopharmaceutical agent is labeled with more than one radioisotope.

It is noted that system 700 is configurable to vary a radioactivity of the radioisotope used to label a given radiopharmaceutical agent in order to produce labeled radiopharmaceutical agents of various levels of radioactivity (for example, Tc-99m-teboroxime of 500 mCi and Tc-99m-teboroxime of 50 mCi). For some applications, system 700 comprises at least one cocktail dose preparation platform 736, for labeling a cocktail of radiopharmaceutical agents (for example, Tl-201-thallous chloride, Tc-99m-sestamibi, and I-123-BMIPP).

It will be appreciated that the mother vial preparation process is subject to modifications and alterations based on communication and information that is received from system 10. For example, a log book of system 700 may specify a mother vial of 500 mCi, yet a communication request from dose calculation system 152 may modify the order to be a mother vial of 200 mCi, based on new requirements, e.g., low-dose

administration.

The exercise room

In an embodiment of the present invention, system 10 comprises at least one exercise room, which comprises one or more pieces of exercise equipment, typically including at least one treadmill. The exercise room, and the equipment therein, is typically in communication with one or more elements of system 10, such as patient-specific data carrier 24, management and control component 150, administration system 26, data carrier 120 of radiopharmaceutical agent container 22, and/or imaging system 28. For example, the exercise room may report the duration, time, and type of exercise to imaging system 28, administration system 26, and/or management control component 150, for synchronizing the exercise with administration and imaging. For some applications, the exercise room receives instructions regarding the duration, time, and/or type of exercise to be performed for a given patient, and schedules an appropriate exercise session in a log book. For some applications, the exercise room sends the patient an SMS-like message notifying the patient of the scheduled session, and/or reminding the patient about a scheduled session. For some applications in which data carrier 24 is integrated into watch or bracelet 170, as described hereinabove with reference to Fig. 3, watch or bracelet 170 is configured to receive and display the SMS-like message to the patient.

Signature

In accordance with an embodiment of the present invention, coded signature 256 comprises a signature encrypted using an encryption algorithm, which is either proprietary or known in the art, e.g., Advanced Encryption Standard (AES), Data Encryption Standard (DES), or Triple DES (3DES). Typically, the encryption algorithm utilizes a symmetric key cipher, as is known in the art.

For some applications, coded signature 256 is stored in one of the data carriers described herein. Alternatively or additionally, the coded signature is printed on the apparatus, e.g., as a barcode.

For some applications, coded signature 256 comprises a color-coded signature, which is implemented using techniques described in the above-mentioned US Patent Application Publication 2004/0156081 to Bril et al. Techniques described in the '081

publication include the use of an encrypted image comprising an array of printed positions formed using a group of inks each of which has a predetermined spectrum. The positions are selected to form a predetermined image, either real or virtual, when the image is viewed through an optical processor. The optical processor may further use a distortion, such as a distorted grating or a distorted lens. The correct image is the spectrum, as distorted by the optical processor. An image formed using inks having the same colors as experienced by the human eye, or even by a standard spectrometer, will fail to form the correct predetermined image. Alternatively or additionally, special inks may be used, so that no two ink combinations are exactly alike, and only registered ink combinations provide the correct spectrum. Furthermore, the special inks may be mixtures of 5 or more colors.

Fig. 16A illustrates color spectra 800 of several dyes, for example dyes B, D1, G, D2, and R, each having a well-defined spectral peak, as described in the '081 publication. When dye B and dye G are mixed, the human eye may see a color substantially the same as the color of dye D1. When dye D1 and dye D2 are mixed, the human eye may see a color substantially the same as the color of dye G.

Fig. 16B illustrates a color-coded signature 802, as described in the '081 publication. A color patch 804, which to the human eye may seem a plain orange, for example, may have a first portion 806A, consisting of dye B and dye G, combined to form a hue which is substantially the same as that of dye D1, and a second portion 806B, consisting of dye D1. To the human eye, the color-coded signature 802 appears as a homogeneous patch.

An optical processor 820 comprises an imaging spectrograph, which comprises a grating 822 and, typically, a lens 824. In the example shown in Fig. 16B, the spectrograph produces three structures: a structure 821 formed by diffraction of dye D1 through the grating, a structure 823 formed by diffraction of dye G, and a structure 825 formed by diffraction of dye B. Optical processor 220 thus reveals the authentic spectra of the color-coded signature 802.

For some applications, optical processor 820 comprises two lenses 824 of substantially equal power, one to create a parallel beam at the input to the grating, just before the grating, and one to create an image at the focal point after the grating. Alternatively, a single lens 824, having twice the power of the two lenses, may be placed

just before or just after the grating.

For some applications, a more complex color coding is achieved by using a distorted lens or a distorted grating, such that spectral structure 821, 823, and 825 may be reproduced only when an optical processor having the exact distortion is used. It will be appreciated that a single hue may be produced by mixing several dyes, for example, 3, 5, or 10. It will be appreciated that each printing house may be allocated only a specific mix of dyes, so that no two printing houses may have identical dye combinations, and no two printing houses may reproduce the same color-coded signatures 802.

For some applications, color-coded signature 802 is printed directly on an element of system 10, for example, on radiopharmaceutical agent container 22 (Fig. 1), or on radioisotope vial 610 (Fig. 14). Alternatively or additionally, a label, for example, mother vial data carrier 106 or data carrier 120 (Fig. 1) is color-coded, or includes a color-coded patch or pattern, operative as color-coded signature 802.

For some applications, an encrypted signature 256 and a color-coded signature 802 are combined. The resulting color-coded machine-readable signature 256 is authenticated by optical processor 820. For example, an encrypted signature may be provided on a label colored with a coded color. Alternatively or additionally, encrypted signature 256 is printed on a color-coded background, or with color-coded dyes. Alternatively or additionally, coded signature 256 comprises a color-coded barcode. For some applications, the color-coded barcode may appear black or another color to the eye, but reveal a unique spectrum to optical processor 820. For some applications, the color-coded machine-readable signature further comprises a date, to prevent the recycling or re-use of signatures.

Physical key

Reference is made to Fig. 17, which is a schematic illustration of a computer-readable medium 850, a portion of which is shaped so as to define a physical key 852, in accordance with an embodiment of the present invention. A communication element 854 is shaped so as to define a dedicated slot 856 having a geometry matching that of key 852. Only keys having the particular geometry of slot 856 can be inserted into the slot. Key 852 thus enables authentication of computer-readable medium 850. Computer-readable medium 850 may comprise, for example, a disk-on-key apparatus or a

chip, having, for example, a USB-type connector.

For some applications, patient-specific data carrier 24 comprises computer-readable medium 850, and a communication element of imaging system 28 and/or administration system 26 is shaped so as to define slot 856. Alternatively or additionally, healthcare worker identity tag 208 comprises computer-readable medium 850, and workstation 200, elution system 600, dispensing system 20, administration system 26, and/or imaging system 28 is shaped so as to define slot 856. For some applications, computer-readable medium 850 further comprises coded signature 256, as described hereinabove, while for other applications, key 852 is relied upon in lieu of coded signature 256.

For some applications, authentication, as described herein, is alternatively or additionally based on additional parameters, such as a manufacturer's attribute.

In an embodiment of the present invention, information is transferred from one element of system 10 to another element thereof by physically transferring an electronic information-carrying chip from one element to the other. For example, upon administration of the labeled radiopharmaceutical agent contained in container 22, information may be transferred from data carrier 120 to patient-specific data carrier 24 by physically transferring a memory chip of data carrier 120 to data carrier 24.

Managing Compton residuals

Reference is made to Fig. 18, which is a graph showing particle energy vs. photon count at a detector 454 of camera 452 of imaging system 28 (Fig. 11), in accordance with an embodiment of the present invention. In this embodiment, dose calculation sub-system 156 of radiopharmaceutical dose calculation system 152, described hereinabove with reference to Fig. 5, takes Compton residuals into consideration when calculating doses of a first and a second labeled radiopharmaceutical agent to be mixed together in a cocktail, or to be separately administered for the same image acquisition procedure. If the first agent were to be provided at a relatively high dose and the second agent were to be provided at a lower dose, the first agent would produce a first peak 900A around a first energy level E^1, and the second agent would produce a second peak 902 around a second energy level E^2. A Compton residual 904A produced by the first agent at least partially masks second peak 902. For some applications, in order to prevent such masking, dose

calculation sub-system 156 reduces the dose of the first agent, thereby producing a first peak 900B and a corresponding Compton residual 904B having lower counts than initial first peak 900A and Compton residual 904A, respectively. Compton residual 904B is sufficiently low so as not to mask second peak 902. By using techniques described hereinabove and/or incorporated herein by reference, camera 452 is sufficiently sensitive to acquire sufficient counts emitted from the lower dose of the second agent. For example, the first and second agents may comprise MIBI-Tc and thallium, respectively, which emit energy at 140 KeV and 72 KeV, respectively.

Alternatively, calculation sub-system 156 determines that the dose of the first labeled radiopharmaceutical agent cannot be reduced sufficiently to prevent such Compton masking. To make such a determination, the sub-system typically takes into consideration constraints applied by the physical properties of the first agent, patient-specific information, and/or camera 452. The sub-system may thus determine that the two agents must be prepared as separate doses for non-simultaneous administration. Alternatively, the sub-system determines that the dose of the second agent is to be increased, so as to prevent the masking. To make such a determination, the sub-system typically takes into consideration constraints applied by the physical properties of the first agent, patient-specific information, camera 452, and/or safety and/or regulatory requirements.

Information-bearing radiopharmaceuticals

In an embodiment of the present invention, a portion of the patient, radiopharmaceutical, and/or protocol information described herein is chemically stored together with a labeled radiopharmaceutical agent in a container, such as radiopharmaceutical agent container 22 or mother vial 104. For some applications, such information is chemically stored by providing a chemical indicative of and/or encoding the information, and mixing the chemical with the radiopharmaceutical agent. Alternatively, such information is chemically stored by attaching a chemical marker indicative of the information to the radiopharmaceutical agent, or otherwise chemically modifying the radiopharmaceutical agent to store the information. The information-indicative chemical indicator (i.e., chemical or chemical marker) has properties which are machine-readable, for example, using optical, spectral, fluorescence, or isotope emission techniques.

For some applications, the information is stored by setting a level of a parameter of the chemical indicator, such as concentration or radioactivity, which level is indicative of the information. For example, a plurality of concentrations 0, A_1, A_2, A_3, ..., A_{max} may be defined, each of which represents a respective value. At all of the defined concentrations, the chemical indicator is biologically inert and/or safe in the body, and does not affect the sterility and/or properties of the radiopharmaceutical agent. The plurality of concentrations are sufficiently different from one another so as to be independently measurable and identifiable, such as by measuring a spectral signature of the chemical indicator. For some applications, a plurality of different chemical indicators are used, each of which has defined levels of a parameter representing respective values. The values represented by the plurality of chemical indicators together represent the information.

For some applications, the level of the parameter of the chemical indicator changes over time, e.g., the radioactivity of the chemical indicator declines because of radioactive decay, thereby providing an indication of elapsed time. Such elapsed time may be used, for example, to determine the timing of preparation of the radiopharmaceutical agent and/or subsequent processes, as well as validating whether such timing is within an allowed time window.

For some applications, dispensing system 20 applies the code to the labeled radiopharmaceutical agent and/or container 22 during the dispensing process, and administration system 26 and/or imaging system 28 reads and verifies the stored information. A dedicated reader may be provided for such reading, or a camera of imaging system 28 may be configured to perform such reading.

The scope of the present invention includes embodiments described in the following applications, which are assigned to the assignee of the present application and are incorporated herein by reference. In an embodiment, techniques and apparatus described in one or more of the following applications are combined with techniques and apparatus described herein:

- International Application PCT/IL2005/001173, filed November 9, 2005;
- International Application PCT/IL2005/000572, filed June 1, 2005;
- International Application PCT/IL2005/000575, filed June 1, 2005;

- International Application PCT/IL2005/001215, filed November 16, 2005;
- US Provisional Application 60/625,971, filed November 9, 2004;
- US Provisional Application 60/628,105, filed November 17, 2004;
- US Provisional Application 60/630,561, filed November 26, 2004;
- US Provisional Application 60/632,236, filed December 2, 2004;
- US Provisional Application 60/632,515, filed December 3, 2004;
- US Provisional Application 60/635,630, filed December 14, 2004;
- US Provisional Application 60/636,088, filed December 16, 2004;
- US Provisional Application 60/640,215, filed January 3, 2005;
- US Provisional Application 60/648,385, filed February 1, 2005;
- US Provisional Application 60/648,690, filed February 2, 2005;
- US Provisional Application 60/675,892, filed April 29, 2005;
- US Provisional Application 60/691,780, filed June 20, 2005;
- US Provisional Application 60/700,318, filed July 19, 2005;
- US Provisional Application 60/700,299, filed July 19, 2005;
- US Provisional Application 60/700,317, filed July 19, 2005;
- US Provisional Application 60/700,753, filed July 20, 2005;
- US Provisional Application 60/700,752, filed July 20, 2005;
- US Provisional Application 60/702,979, filed July 28, 2005;
- US Provisional Application 60/720,034, filed September 26, 2005;
- US Provisional Application 60/720,652, filed September 27, 2005;
- US Provisional Application 60/720,541, filed September 27, 2005;
- US Provisional Application 60/750,287, filed December 13, 2005;
- US Provisional Application 60/750,334, filed December 15, 2005; and/or
- US Provisional Application 60/750,597, filed December 15, 2005.

As used in the present application, including in the claims, a "clinical

environment" means any facility or institution in which at least one of radiopharmaceutical preparation, dispensing, and administration occur, including, for example, a radiopharmaceutical manufacturing facility, a pharmacy, a hospital, a doctor's clinic, a day clinic, an out-patient clinic, a laboratory, and a geriatric center.

It will be appreciated by persons skilled in the art that the present invention is not limited to what has been particularly shown and described hereinabove. Rather, the scope of the present invention includes both combinations and subcombinations of the various features described hereinabove, as well as variations and modifications thereof that are not in the prior art, which would occur to persons skilled in the art upon reading the foregoing description.

CLAIMS

1. Apparatus for use with at least one labeled radiopharmaceutical agent, the apparatus comprising:

a container containing the at least one labeled radiopharmaceutical agent; and

a portable computer-communicatable data carrier associated with the container, the data carrier containing imaging protocol information for use with the at least one labeled radiopharmaceutical agent.

2. The apparatus according to claim 1, wherein the apparatus comprises a device configured to write the imaging protocol information to the data carrier.

3. The apparatus according to claim 1, wherein the data carrier additionally contains administration protocol information useful for administering the at least one labeled radiopharmaceutical agent.

4. The apparatus according to claim 1, wherein the imaging protocol information comprises instructions for performing an imaging procedure using the at least one labeled radiopharmaceutical agent.

5. The apparatus according to claim 1, wherein the imaging protocol information comprises an identifier of an imaging protocol.

6. The apparatus according to claim 1, wherein the imaging protocol information comprises a parameter of the at least one labeled radiopharmaceutical agent.

7. The apparatus according to claim 1, wherein the imaging protocol information comprises a parameter useful for configuring at least one aspect of an imaging procedure performed using the at least one labeled radiopharmaceutical agent.

8. The apparatus according to claim 1, wherein the container contains a single dose of the radiopharmaceutical agent, which dose is appropriate for use with the imaging protocol information.

9. The apparatus according to claim 1, wherein the container contains a plurality of labeled radiopharmaceutical agents mixed together.

10. The apparatus according to claim 1, wherein the container is shaped so as to define a plurality of chambers, each of which contains a respective one of a plurality of labeled radiopharmaceutical agents.

11. The apparatus according to any one of claims 1-10,

wherein the data carrier comprises a first data carrier, which contains a first identifier value,

wherein the apparatus further comprises a second computer-communicatable data carrier, which contains a second identifier value, and

wherein the apparatus is configured to operate responsively to a detection of a correspondence between the first and second identifier values.

12. The apparatus according to claim 11, wherein at least one of the first and second data carriers is configured to perform the detection of the correspondence.

13. The apparatus according to claim 11, wherein the apparatus comprises a correspondence-detection element configured to perform the detection of the correspondence.

14. The apparatus according to claim 11, wherein at least one of the first and second data carriers contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

15. The apparatus according to claim 11, wherein at least one of the first and second identifier values comprises an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

16. The apparatus according to claim 11, wherein exactly one of the first and second data carriers comprises a coupling mechanism configured to be coupled to a patient to whom the labeled radiopharmaceutical agent is to be administered.

17. The apparatus according to claim 11, wherein the apparatus comprises an imaging system comprising imaging functionality, the imaging system configured, responsively to the detection of the correspondence, to drive the imaging functionality to perform an imaging procedure using the at least one labeled radiopharmaceutical agent.

18. The apparatus according to any one of claims 1-10, wherein the data carrier is physically coupled to the container.

19. The apparatus according to claim 18, wherein the data carrier contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered, and wherein the imaging protocol information comprises imaging protocol information selected for the patient.

20. The apparatus according to claim 19, wherein the imaging protocol information comprises an identifier of an imaging protocol.

21. The apparatus according to claim 19, wherein the imaging protocol information comprises imaging protocol information customized for the patient.

22. The apparatus according to any one of claims 1-10, wherein the imaging protocol information comprises SPECT imaging protocol information.

23. The apparatus according to claim 22, wherein the SPECT imaging protocol information comprises dynamic SPECT imaging protocol information.

24. The apparatus according to claim 23, wherein the SPECT imaging protocol information comprises at least one kinetic parameter of the at least one labeled radiopharmaceutical agent, the at least one kinetic parameter useful for performing a dynamic SPECT imaging procedure using the at least one labeled radiopharmaceutical agent.

25. The apparatus according to any one of claims 1-10, comprising an imaging system, which comprises:

a communication element, configured to read the imaging protocol information from the data carrier; and

a control unit, comprising imaging functionality, which is configured to perform an imaging procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

26. The apparatus according to claim 25, wherein the imaging system comprises a camera, wherein the imaging functionality comprises image acquisition functionality, and wherein the image acquisition functionality is configured to perform an image acquisition procedure using the camera, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

27. The apparatus according to claim 26, wherein the image acquisition functionality configures a total acquisition time of the image acquisition procedure at least in part responsively to the imaging protocol information.

28. The apparatus according to claim 26, wherein the camera comprises a plurality of detectors, and wherein the image acquisition functionality is configured to configure, at

least in part responsively to the imaging protocol information, at least one motion of at least one of the detectors during the image acquisition procedure.

29. The apparatus according to claim 26, wherein the control unit is configured to configure, at least in part responsively to the imaging protocol information, a waiting time between administration of the labeled radiopharmaceutical agent and commencement of the image acquisition procedure.

30. The apparatus according to claim 26, wherein the image acquisition functionality is configured to perform a gated image acquisition procedure at least in part responsively to the imaging protocol information.

31. The apparatus according to claim 25, wherein the imaging functionality comprises image reconstruction functionality, and wherein the image reconstruction functionality is configured to perform an image reconstruction procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

32. The apparatus according to claim 25, wherein the imaging functionality comprises image analysis functionality, and wherein the image analysis functionality is configured to perform an image analysis procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

33. The apparatus according to claim 25, wherein the imaging functionality comprises diagnosis functionality, and wherein the diagnosis functionality is configured to perform a diagnostic procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

34. The apparatus according to claim 25, wherein the imaging procedure includes a three-dimensional dynamic imaging study, and wherein the imaging functionality is configured to perform the three-dimensional dynamic imaging study, and to configure the study at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

35. The apparatus according to any one of claims 1-10, wherein the data carrier is not physically coupled to the container, and wherein the data carrier contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

36. The apparatus according to claim 35, wherein the data carrier comprises a coupling mechanism configured to be coupled to the patient.

37. The apparatus according to claim 35, wherein the data carrier comprises a first data carrier, and wherein the apparatus further comprises a second computer-communicatable data carrier physically coupled to the container, the second data carrier containing radiopharmaceutical information regarding the at least one labeled radiopharmaceutical agent.

38. Apparatus for use with at least one labeled radiopharmaceutical agent, the apparatus comprising:

a container containing the at least one labeled radiopharmaceutical agent; and

a computer-communicatable data carrier associated with the container, the data carrier containing authenticatable information regarding a commercial license for use of SPECT imaging protocol information with the at least one labeled radiopharmaceutical agent.

39. The apparatus according to claim 38, comprising an imaging system, which comprises:

a communication element, configured to read the authenticatable license information from the data carrier;

a control unit, comprising imaging functionality, the control unit configured to:

authenticate the authenticatable license information, and

only upon authentication, drive the imaging functionality to perform an imaging procedure using the SPECT imaging protocol information.

40. The apparatus according to claim 38, wherein the apparatus comprises a device configured to write the authenticatable license information to the data carrier.

41. The apparatus according to any one of claims 38-40, wherein the data carrier is physically coupled to the container.

42. Apparatus comprising a portable computer-communicatable data carrier containing authenticatable information regarding a commercial license for use of SPECT imaging protocol information.

43. The apparatus according to claim 42, wherein the data carrier additionally contains patient information regarding a patient upon whom an imaging procedure using the

SPECT imaging protocol information is to be performed.

44. The apparatus according to claim 42, wherein the authenticatable license information is encrypted.

45. The apparatus according to claim 42, wherein the apparatus comprises a device configured to write the authenticatable license information to the data carrier.

46. The apparatus according to claim 42, wherein the data carrier comprises a coupling mechanism configured to be coupled to a patient upon whom an imaging procedure using the SPECT imaging protocol information is to be performed.

47. The apparatus according to any one of claims 42-46, comprising an imaging system, which comprises:

a communication element, configured to read the authenticatable license information from the data carrier;

a control unit, comprising imaging functionality, the control unit configured to:

authenticate the authenticatable license information, and

only upon authentication, drive the imaging functionality to perform an imaging procedure using the SPECT imaging protocol information.

48. Apparatus comprising:

a first portable computer-communicatable data carrier containing a first identifier value;

a second portable computer-communicatable data carrier containing a second identifier value; and

an imaging system comprising imaging functionality, the imaging system configured, responsively to a detection of a correspondence between the first and second identifier values, to drive the imaging functionality to perform an imaging procedure on a patient.

49. The apparatus according to claim 48, wherein at least one of the first and second data carriers is configured to perform the detection of the correspondence.

50. The apparatus according to claim 48, wherein the imaging system comprises a correspondence-detection element configured to perform the detection of the correspondence.

51. The apparatus according to claim 48, wherein at least one of the first and second

data carriers contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

52. The apparatus according to claim 48, wherein at least one of the first and second identifier values comprises an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

53. The apparatus according to claim 48, wherein one of the first and second data carriers comprises a coupling mechanism configured to be coupled to a patient to whom the labeled radiopharmaceutical agent is to be administered.

54. The apparatus according to claim 48, wherein the apparatus comprises a device configured to write at least one of the first and second identifier values to the respective first and second data carriers.

55. The apparatus according to any one of claims 48-54,

wherein at least one of the first and second data carriers contains radiopharmaceutical information regarding at least one labeled radiopharmaceutical agent,

wherein the imaging system comprises a communication element, configured to read the radiopharmaceutical information from the at least one of the data carriers, and

wherein the imaging system is configured to configure the imaging procedure at least in part responsively to the read radiopharmaceutical information.

56. The apparatus according to claim 55, wherein the apparatus comprises a container containing the at least one labeled radiopharmaceutical agent.

57. The apparatus according to claim 56, wherein one of the first and second data carriers is physically coupled to the container.

58. The apparatus according to any one of claims 48-54, wherein the imaging functionality comprises a nuclear camera.

59. The apparatus according to claim 58, wherein the nuclear camera comprises a SPECT camera.

60. Apparatus for use with first and second portable computer-communicatable data carriers containing first and second identifier values, respectively, the apparatus comprising an imaging system, which comprises:

imaging functionality; and

a control unit configured to drive the imaging functionality to perform an imaging procedure on a patient, responsively to a detection of a correspondence between the first and second identifier values.

61. The apparatus according to claim 60, wherein the imaging system comprises a correspondence-detection element configured to perform the detection of the correspondence.

62. Apparatus for use with at least one labeled radiopharmaceutical agent for administration to a patient, the apparatus comprising:

a container containing the at least one labeled radiopharmaceutical agent;

a first computer-communicatable data carrier physically coupled to the container, the first data carrier containing radiopharmaceutical information regarding the at least one labeled radiopharmaceutical agent; and

a second portable computer-communicatable data carrier containing patient information regarding the patient, and imaging protocol information for use with the at least one labeled radiopharmaceutical agent.

63. The apparatus according to claim 62, wherein the imaging protocol information comprises SPECT imaging protocol information.

64. The apparatus according to claim 62, wherein the patient information comprises an identifier of the patient.

65. The apparatus according to claim 62, wherein the second data carrier comprises a coupling mechanism configured to be coupled to the patient.

66. The apparatus according to claim 62, wherein the first data carrier contains a first patient identifier, wherein the patient information contained in the second data carrier comprises a second patient identifier, and comprising an administration system, which comprises:

a first communication element, configured to read the first patient identifier from the first data carrier;

a second communication element, configure to read the second patient identifier from the second data carrier; and

a control unit, configured to compare the first patient identifier to the second patient identifier, and, upon detecting a match, generate an administration signal that

triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

67. The apparatus according to claim 62, wherein the first data carrier contains a first protocol identifier, wherein the imaging protocol information contained in the second data carrier comprises a second protocol identifier, and comprising an administration system, which comprises:

a communication element, configured to read the first and second protocol identifiers from the first and second data carriers, respectively; and

a control unit, configured to compare the first protocol identifier to the second protocol identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

68. The apparatus according to claim 62, wherein the first data carrier contains a first protocol identifier, wherein the imaging protocol information contained in the second data carrier comprises a second protocol identifier, and comprising an administration system, which comprises:

a first communication element, configured to read the first protocol identifier from the first data carrier;

a second communication element, configured to read the second protocol identifier from the second data carrier; and

a control unit, configured to compare the first protocol identifier to the second protocol identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

69. The apparatus according to claim 62, comprising an administration system, which comprises:

a communication element; and

a control unit, configured to:

generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container, and

drive the communication element to transmit information regarding the administration to the second data carrier.

70. The apparatus according to claim 62, wherein the apparatus comprises a device configured to write the imaging protocol information to the first data carrier.

71. The apparatus according to claim 62, wherein the apparatus comprises a device configured to write the patient information to the second data carrier.

72. The apparatus according to any one of claims 62-71, wherein the imaging protocol information comprises imaging protocol information selected for the patient.

73. The apparatus according to claim 72, wherein the imaging protocol information comprises an identifier of an imaging protocol.

74. The apparatus according to claim 72, wherein the imaging protocol information comprises imaging protocol information customized for the patient.

75. The apparatus according to any one of claims 62-71, wherein the first data carrier contains a first patient identifier, wherein the patient information contained in the second data carrier includes a second patient identifier, and comprising an administration system, which comprises:

a communication element, configured to read the first and second patient identifiers from the first and second data carriers, respectively; and

a control unit, configured to compare the first patient identifier to the second patient identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

76. The apparatus according to claim 75, wherein the administration system comprises an automated administration device, configured to administer the at least one labeled radiopharmaceutical agent to the patient upon being triggered by the administration signal.

77. The apparatus according to claim 75, wherein the control unit is configured to generate the administration signal to trigger the administration of the at least one labeled radiopharmaceutical agent by instructing a healthcare worker to administer the at least one labeled radiopharmaceutical agent to the patient.

78. Apparatus for use with at least one labeled radiopharmaceutical agent for administration to a patient, the apparatus comprising:

a container containing the at least one labeled radiopharmaceutical agent;

a computer-communicatable data carrier associated with the container, the data carrier containing data regarding at least one of: the labeled radiopharmaceutical agent and the patient; and

a SPECT imaging system comprising:

a communication element, configured to read the data; and

a control unit, configured to utilize the read data to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

79. The apparatus according to claim 78, wherein the data carrier contains the data regarding the labeled radiopharmaceutical agent.

80. The apparatus according to claim 78, wherein the data carrier contains the data regarding the patient.

81. The apparatus according to claim 78, wherein the control unit is configured to utilize the read data to customize the administration of the labeled radiopharmaceutical agent.

82. The apparatus according to claim 78, wherein the control unit is configured to utilize the read data to customize the acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered.

83. The apparatus according to claim 78, wherein the control unit is configured to utilize the read data to customize the reconstruction of the SPECT image.

84. The apparatus according to claim 78, wherein the control unit is configured to utilize the read data to customize the analysis of the SPECT image.

85. The apparatus according to claim 78, wherein the control unit is configured to utilize the read data to customize the diagnosis of a condition of the patient based at least in part on the analysis.

86. The apparatus according to any one of claims 78-85, wherein the apparatus comprises a device configured to write the data to the data carrier.

87. A SPECT imaging system for use with a container containing at least one labeled radiopharmaceutical agent for administration to a patient, and data regarding at least one of: the labeled radiopharmaceutical agent and the patient, the system comprising:

a communication element, configured to read the data; and

a control unit, configured to utilize the read data to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

88. The system according to claim 87, wherein the system comprises a device configured to write the data to the container.

89. An automated radiopharmaceutical dispensing system for use with a container and a computer-communicatable container data carrier associated with the container, the system comprising:

a robot, configured to manipulate the container;

a communication element; and

a control unit, configured to:

receive radiopharmaceutical information regarding at least one labeled radiopharmaceutical agent, the radiopharmaceutical information selected from the group consisting of: imaging protocol information for use with the at least one labeled radiopharmaceutical agent, and authenticatable information regarding a commercial license for use of an imaging protocol with the at least one labeled radiopharmaceutical agent,

receive patient information regarding a patient,

drive the robot to automatically dispense a dose of the labeled radiopharmaceutical agent to the container, and

drive the communication element to transmit to the container data carrier at least a portion of the radiopharmaceutical information and at least a portion of the patient information.

90. The system according to claim 89, wherein the control unit is configured to receive the radiopharmaceutical information regarding a plurality of labeled

radiopharmaceutical agents, and drive the robot to automatically dispense respective doses of the labeled radiopharmaceutical agents to the container.

91. The system according to claim 89, wherein the patient information includes an identifier of an imaging protocol assigned to the patient for performance using the dose, and wherein the control unit is configured to drive the communication element to transmit the imaging protocol identifier to the container data carrier.

92. The system according to claim 89, wherein the control unit is configured to drive the communication element to transmit to the container data carrier at least one of: a time of dispensing of the labeled radiopharmaceutical agent to the container, and information regarding a radioactivity of the dose at the time of dispensing.

93. The system according to claim 89, comprising:

a mother vial that contains the labeled radiopharmaceutical agent prior to dispensing thereof; and

a computer-communicatable mother vial data carrier associated with the mother vial, which mother vial data carrier contains the radiopharmaceutical information,

wherein the control unit is configured to receive the radiopharmaceutical information from the mother vial data carrier.

94. The system according to any one of claims 89-93, wherein the radiopharmaceutical information comprises the imaging protocol information.

95. The system according to claim 94, wherein the imaging protocol information comprises SPECT imaging protocol information.

96. The system according to claim 95, wherein the imaging protocol information comprises at least one kinetic parameter of the at least one labeled radiopharmaceutical agent.

97. The system according to any one of claims 89-93, wherein the radiopharmaceutical information comprises the authenticatable information regarding the commercial license.

98. The system according to claim 97, wherein the information regarding the commercial license comprises information regarding the commercial license for use of a SPECT imaging protocol with the at least one labeled radiopharmaceutical agent.

99. The system according to claim 97, wherein the control unit is configured to

authenticate the authenticatable license information, and to drive the robot to automatically dispense the dose only upon authentication.

100. Apparatus for use with a container, the apparatus comprising:

a mother vial having a volume of at least 10 ml, which contains at least 5 ml of a non-diluted labeled radiopharmaceutical agent, and at least 5 ml of saline solution; and

an automated radiopharmaceutical dispensing system, configured to contain the mother vial, and to dispense at least one dose from the mother vial to the container.

101. A method comprising:

placing at least one labeled radiopharmaceutical agent in a container;

associating a portable computer-communicatable data carrier with the container; and

writing, to the data carrier, imaging protocol information for use with the at least one labeled radiopharmaceutical agent.

102. The method according to claim 101, comprising writing, to the data carrier, administration protocol information useful for administering the at least one labeled radiopharmaceutical agent.

103. The method according to claim 101, wherein writing the imaging protocol information comprises writing instructions for performing an imaging procedure using the at least one labeled radiopharmaceutical agent.

104. The method according to claim 101, wherein writing the imaging protocol information comprises writing an identifier of an imaging protocol.

105. The method according to claim 101, wherein writing the imaging protocol information comprises writing a parameter of the at least one labeled radiopharmaceutical agent.

106. The method according to claim 101, wherein writing the imaging protocol information comprises writing a parameter useful for configuring at least one aspect of an imaging procedure performed using the at least one labeled radiopharmaceutical agent.

107. The method according to claim 101, wherein placing comprises placing a single dose of the radiopharmaceutical agent in the container, which dose is appropriate for use with the imaging protocol information.

108. The method according to claim 101, wherein placing comprises placing, in the container, a plurality of labeled radiopharmaceutical agents mixed together.

109. The method according to claim 101, wherein the container is shaped so as to define a plurality of chambers, and wherein placing the at least one labeled radiopharmaceutical agent in the container comprises placing a plurality of labeled radiopharmaceutical agents in respective chambers.

110. The method according to any one of claims 101-109, wherein associating the data carrier comprises associating a first data carrier with the container, and wherein the method comprises:

writing a first identifier value to the first data carrier;

writing a second identifier to a second computer-communicatable data carrier;

detecting a correspondence between the first and second identifier values; and

performing an operation responsively to the detecting.

111. The method according to claim 110, wherein detecting comprises detecting the correspondence by at least one of the first and second data carriers.

112. The method according to claim 110, wherein detecting comprises detecting by a correspondence-detection element separate from the first and second data carriers.

113. The method according to claim 110, comprising writing, to at least one of the first and second data carriers, an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

114. The method according to claim 110, wherein writing at least one of the first and second identifier values comprises writing an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

115. The method according to claim 110, comprising coupling exactly one of the first and second data carriers to a patient to whom the labeled radiopharmaceutical agent is to be administered.

116. The method according to claim 110, wherein performing the operation comprises, responsively to the detecting of the correspondence, performing an imaging procedure using the at least one labeled radiopharmaceutical agent.

117. The method according to any one of claims 101-109, wherein associating the data carrier with the container comprises physically coupling the data carrier to the container.

118. The method according to claim 117, wherein the data carrier contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered, and wherein writing the imaging protocol information comprises writing imaging protocol information selected for the patient.

119. The method according to claim 118, wherein writing the imaging protocol information comprises writing an identifier of an imaging protocol.

120. The method according to claim 118, wherein writing the imaging protocol information comprises writing imaging protocol information customized for the patient.

121. The method according to any one of claims 101-109, wherein writing the imaging protocol information comprises writing SPECT imaging protocol information.

122. The method according to claim 121, wherein writing the SPECT imaging protocol information comprises writing dynamic SPECT imaging protocol information.

123. The method according to claim 122, wherein writing the SPECT imaging protocol information comprises writing at least one kinetic parameter of the at least one labeled radiopharmaceutical agent, the at least one kinetic parameter useful for performing a dynamic SPECT imaging procedure using the at least one labeled radiopharmaceutical agent.

124. The method according to any one of claims 101-109, comprising:

reading the imaging protocol information from the data carrier; and

performing an imaging procedure, and configuring the procedure at least in part responsively to the imaging protocol information read from the data carrier.

125. The method according to claim 124, wherein performing the imaging procedure comprises performing an image acquisition procedure, and configuring the procedure at least in part responsively to the imaging protocol information read from the data carrier.

126. The method according to claim 125, wherein performing the image acquisition procedure comprises configuring a total acquisition time of the image acquisition procedure at least in part responsively to the imaging protocol information.

127. The method according to claim 125, wherein performing the image acquisition procedure comprises performing the image acquisition procedure using a camera having a plurality of detectors, and configuring, at least in part responsively to the imaging protocol information, at least one motion of at least one of the detectors during the image

acquisition procedure.

128. The method according to claim 125, wherein performing the image acquisition procedure comprises configuring, at least in part responsively to the imaging protocol information, a waiting time between administration of the labeled radiopharmaceutical agent and commencement of the image acquisition procedure.

129. The method according to claim 125, wherein performing the image acquisition procedure comprises performing a gated image acquisition procedure at least in part responsively to the imaging protocol information.

130. The method according to claim 124, wherein performing the imaging procedure comprises performing an image reconstruction procedure, and configuring the procedure at least in part responsively to the imaging protocol information read from the data carrier.

131. The method according to claim 124, wherein performing the imaging procedure comprises performing an image analysis procedure, and configuring the procedure at least in part responsively to the imaging protocol information read from the data carrier.

132. The method according to claim 124, wherein performing the imaging procedure comprises performing a diagnostic procedure, and configuring the procedure at least in part responsively to the imaging protocol information read from the data carrier.

133. The method according to claim 124, wherein performing the imaging procedure comprises performing a three-dimensional dynamic imaging study, and configuring the study at least in part responsively to the imaging protocol information read from the data carrier.

134. The method according to any one of claims 101-109, wherein associating the data carrier with the container does not comprise physically coupling the data carrier to the container, and comprising writing, to the data carrier, an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

135. The method according to claim 134, comprising coupling the data carrier to the patient.

136. The method according to claim 134, wherein associating the data carrier comprises associating a first data carrier with the container, and comprising writing, to a second computer-communicatable data carrier, radiopharmaceutical information regarding the at least one labeled radiopharmaceutical agent, and physically coupling the second data

carrier to the container.

137. A method comprising:

placing at least one labeled radiopharmaceutical agent in a container;

associating a computer-communicatable data carrier with the container; and

writing, to the data carrier, authenticatable information regarding a commercial license for use of SPECT imaging protocol information with the at least one labeled radiopharmaceutical agent.

138. The method according to claim 137, comprising:

reading the authenticatable license information from the data carrier;

authenticating the authenticatable license information; and

only upon authentication, performing an imaging procedure using the SPECT imaging protocol information.

139. The method according to any one of claims 137-138, wherein associating comprises physically coupling the data carrier to the container.

140. A method comprising:

providing a portable computer-communicatable data carrier; and

writing, to the data carrier, authenticatable information regarding a commercial license for use of SPECT imaging protocol information.

141. The method according to claim 140, comprising writing, to the data carrier, patient information regarding a patient upon whom an imaging procedure using the SPECT imaging protocol information is to be performed.

142. The method according to claim 140, wherein writing the authenticatable license information comprises encrypting the authenticatable license information.

143. The method according to claim 140, comprising:

reading the authenticatable license information from the data carrier;

authenticating the authenticatable license information; and

only upon authentication, performing an imaging procedure using the SPECT imaging protocol information.

144. The method according to any one of claims 140-143, comprising coupling the data carrier to a patient upon whom an imaging procedure using the SPECT imaging protocol

information is to be performed.

145. A method comprising:

writing first and second identifier values to first and second computer-communicatable data carriers, respectively;

detecting a correspondence between the first and second identifier values; and

perform an imaging procedure on a patient responsively to the detecting.

146. The method according to claim 145, wherein detecting comprises detecting the correspondence by at least one of the first and second data carriers.

147. The method according to claim 145, wherein detecting comprises detecting by a correspondence-detection element separate from the first and second data carriers.

148. The method according to claim 145, comprising writing, to at least one of the first and second data carriers, an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

149. The method according to claim 145, wherein writing at least one of the first and second identifier values comprises writing an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

150. The method according to claim 145, comprising coupling one of the first and second data carriers to a patient to whom the labeled radiopharmaceutical agent is to be administered.

151. The method according to any one of claims 145-150, comprising:

writing, to at least one of the first and second data carriers, radiopharmaceutical information regarding at least one labeled radiopharmaceutical agent;

reading the radiopharmaceutical information from the at least one of the data carriers; and

configuring the imaging procedure at least in part responsively to the read radiopharmaceutical information.

152. The method according to claim 151, comprising placing the at least one labeled radiopharmaceutical agent in a container.

153. The method according to claim 152, comprising physically coupling one of the first and second data carriers to the container.

154. The method according to any one of claims 145-150, wherein performing the imaging procedure comprises performing a nuclear imaging procedure.

155. The method according to claim 154, wherein performing the nuclear imaging procedure comprises performing a SPECT imaging procedure.

156. A method for use with at least one labeled radiopharmaceutical agent for administration to a patient, the method comprising:

placing at least one labeled radiopharmaceutical agent in a container;

physically coupling a first computer-communicatable data carrier to the container;

writing, to the first data carrier, radiopharmaceutical information regarding the at least one labeled radiopharmaceutical agent; and

writing, to a second portable computer-communicatable data carrier, patient information regarding the patient, and imaging protocol information for use with the at least one labeled radiopharmaceutical agent.

157. The method according to claim 156, wherein writing the imaging protocol information comprises writing SPECT imaging protocol information.

158. The method according to claim 156, wherein writing the patient information comprises writing an identifier of the patient.

159. The method according to claim 156, comprising coupling the second data carrier to the patient.

160. The method according to claim 156, wherein writing the patient information to the second data carrier comprises writing a second patient identifier to the second data carrier, and comprising:

writing a first patient identifier to the first data carrier;

reading the first and second patient identifiers from the first and second data carriers, respectively; and

comparing the first patient identifier to the second patient identifier, and, upon detecting a match, generating an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

161. The method according to claim 156, wherein writing the imaging protocol information to the second data carrier comprises writing a second protocol identifier to the second data carrier, and comprising:

writing a first protocol identifier to the first data carrier;

reading the first and second protocol identifiers from the first and second data carriers, respectively; and

comparing the first protocol identifier to the second protocol identifier, and, upon detecting a match, generating an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

162. The method according to claim 156, comprising:

generating an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container; and

transmitting information regarding the administration to the second data carrier.

163. The method according to any one of claims 156-162, wherein writing the imaging protocol information to the second data carrier comprises writing imaging protocol information selected for the patient.

164. The method according to claim 163, wherein writing the imaging protocol information comprises writing an identifier of an imaging protocol.

165. The method according to claim 163, wherein writing the imaging protocol information comprises writing imaging protocol information customized for the patient.

166. The method according to any one of claims 156-162, wherein writing the patient information to the second data carrier comprises writing a second patient identifier to the second data carrier, and comprising:

writing a first patient identifier to the first data carrier;

reading the first and second patient identifiers from the first and second data carriers, respectively; and

comparing the first patient identifier to the second patient identifier, and, upon detecting a match, generating an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

167. The method according to claim 166, comprising automatically administering the at least one labeled radiopharmaceutical agent to the patient upon triggering by the administration signal.

168. The method according to claim 166, wherein generating the administration signal comprises instructing a healthcare worker to administer the at least one labeled

radiopharmaceutical agent to the patient.

169. A method comprising:

placing, in a container, at least one labeled radiopharmaceutical agent for administration to a patient;

associating a computer-communicatable data carrier with the container;

writing data to the data carrier regarding at least one of: the labeled radiopharmaceutical agent and the patient;

reading the data from the data carrier at a SPECT imaging system;

utilizing the read data to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

170. The method according to claim 169, wherein writing the data comprises writing the data regarding the labeled radiopharmaceutical agent.

171. The method according to claim 169, wherein writing the data comprises writing the data regarding the patient.

172. The method according to claim 169, wherein utilizing the read data comprises utilizing the read data to customize the administration of the labeled radiopharmaceutical agent.

173. The method according to claim 169, wherein utilizing the read data comprises utilizing the read data to customize the acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered.

174. The method according to claim 169, wherein utilizing the read data comprises utilizing the read data to customize the reconstruction of the SPECT image.

175. The method according to claim 169, wherein utilizing the read data comprises utilizing the read data to customize the analysis of the SPECT image.

176. The method according to any one of claims 169-175, wherein utilizing the read data comprises utilizing the read data to customize the diagnosis of a condition of the patient based at least in part on the analysis.

177. A method for use with a container containing at least one labeled radiopharmaceutical agent for administration to a patient, and data regarding at least one of: the labeled radiopharmaceutical agent and the patient, the method comprising:

reading the data at a SPECT imaging system; and

utilizing the read data to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

178. The method according to claim 177, comprising writing the data to the container.

179. A method for use with a container and a computer-communicatable container data carrier associated with the container, the method comprising:

receiving, by an automated radiopharmaceutical dispensing system, radiopharmaceutical information regarding at least one labeled radiopharmaceutical agent, the radiopharmaceutical information selected from the group consisting of: imaging protocol information for use with the at least one labeled radiopharmaceutical agent, and authenticatable information regarding a commercial license for use of an imaging protocol with the at least one labeled radiopharmaceutical agent;

receiving, by the dispensing system, patient information regarding a patient;

automatically robotically dispensing, by the dispensing system, a dose of the labeled radiopharmaceutical agent to the container; and

transmitting to the container data carrier, by the dispensing system, at least a portion of the radiopharmaceutical information and at least a portion of the patient information.

180. The method according to claim 179, wherein receiving the radiopharmaceutical information comprises receiving the radiopharmaceutical information regarding a plurality of labeled radiopharmaceutical agents, and wherein dispensing comprises dispensing respective doses of the labeled radiopharmaceutical agents to the container.

181. The method according to claim 179, wherein the patient information includes an identifier of an imaging protocol assigned to the patient for performance using the dose, and wherein transmitting comprises transmitting the imaging protocol identifier to the container data carrier.

182. The method according to claim 179, wherein transmitting comprises transmitting to the container data carrier at least one of: a time of dispensing of the labeled radiopharmaceutical agent to the container, and information regarding a radioactivity of the dose at the time of dispensing.

183. The method according to claim 179, wherein receiving the radiopharmaceutical information comprises:

providing, to the dispensing system, a mother vial that contains the labeled radiopharmaceutical agent prior to dispensing thereof, and a computer-communicatable mother vial data carrier associated with the mother vial, which mother vial data carrier contains the radiopharmaceutical information; and

receiving the radiopharmaceutical information from the mother vial data carrier.

184. The method according to any one of claims 179-183, wherein receiving the radiopharmaceutical information comprises receiving the imaging protocol information.

185. The method according to claim 184, wherein receiving the imaging protocol information comprises receiving SPECT imaging protocol information.

186. The method according to claim 185, wherein receiving the imaging protocol information comprises receiving at least one kinetic parameter of the at least one labeled radiopharmaceutical agent.

187. The method according to any one of claims 179-183, wherein receiving the radiopharmaceutical information comprises receiving the authenticatable information regarding the commercial license.

188. The method according to claim 187, wherein receiving the information regarding the commercial license comprises receiving information regarding the commercial license for use of a SPECT imaging protocol with the at least one labeled radiopharmaceutical agent.

189. The method according to claim 187, wherein dispensing comprises authenticating the authenticatable license information, and dispensing the dose only upon authentication.

190. A method for automatically dispensing a labeled radiopharmaceutical agent to a container, comprising:

providing a mother vial having a volume of at least 10 ml;

filling the mother vial with at least 5 ml of a non-diluted labeled

radiopharmaceutical agent, and with at least 5 ml of saline solution;

placing the mother vial in an automated radiopharmaceutical dispensing system; and

dispensing at least one dose from the mother vial to the container.

FIG. 1

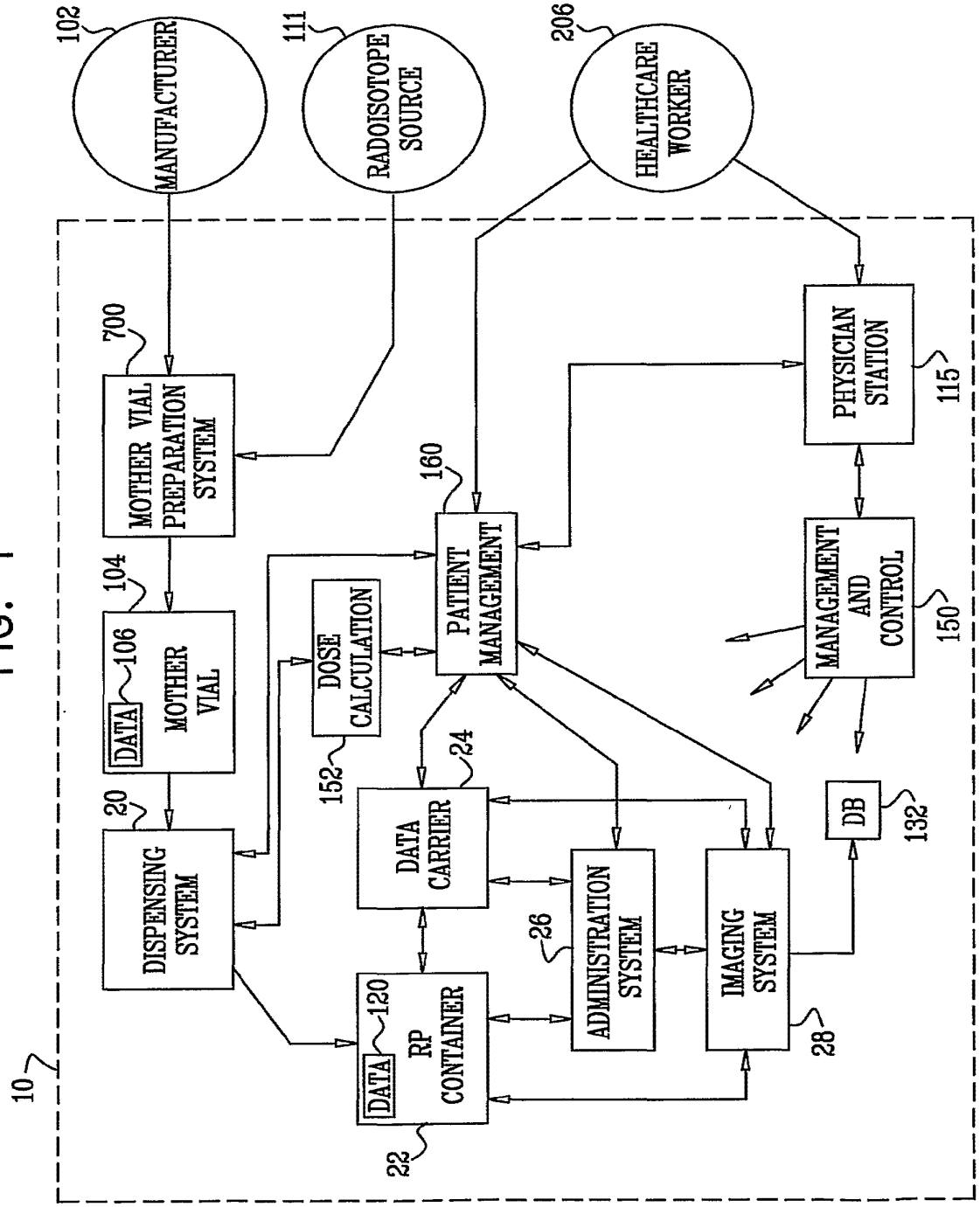

102
MANUFACTURER
111
RADOISOTOPE SOURCE
206
HEALTHCARE WORKER
700
MOTHER VIAL PREPARATION SYSTEM
104
DATA
106
MOTHER VIAL
20
DISPENSING SYSTEM
DOSE CALCULATION
152
160
PATIENT MANAGEMENT
24
DATA CARRIER
120
DATA
RP CONTAINER
22
26
ADMINISTRATION SYSTEM
IMAGING SYSTEM
28
PHYSICIAN STATION
115
MANAGEMENT AND CONTROL
150
DB
132
10

FIG. 2

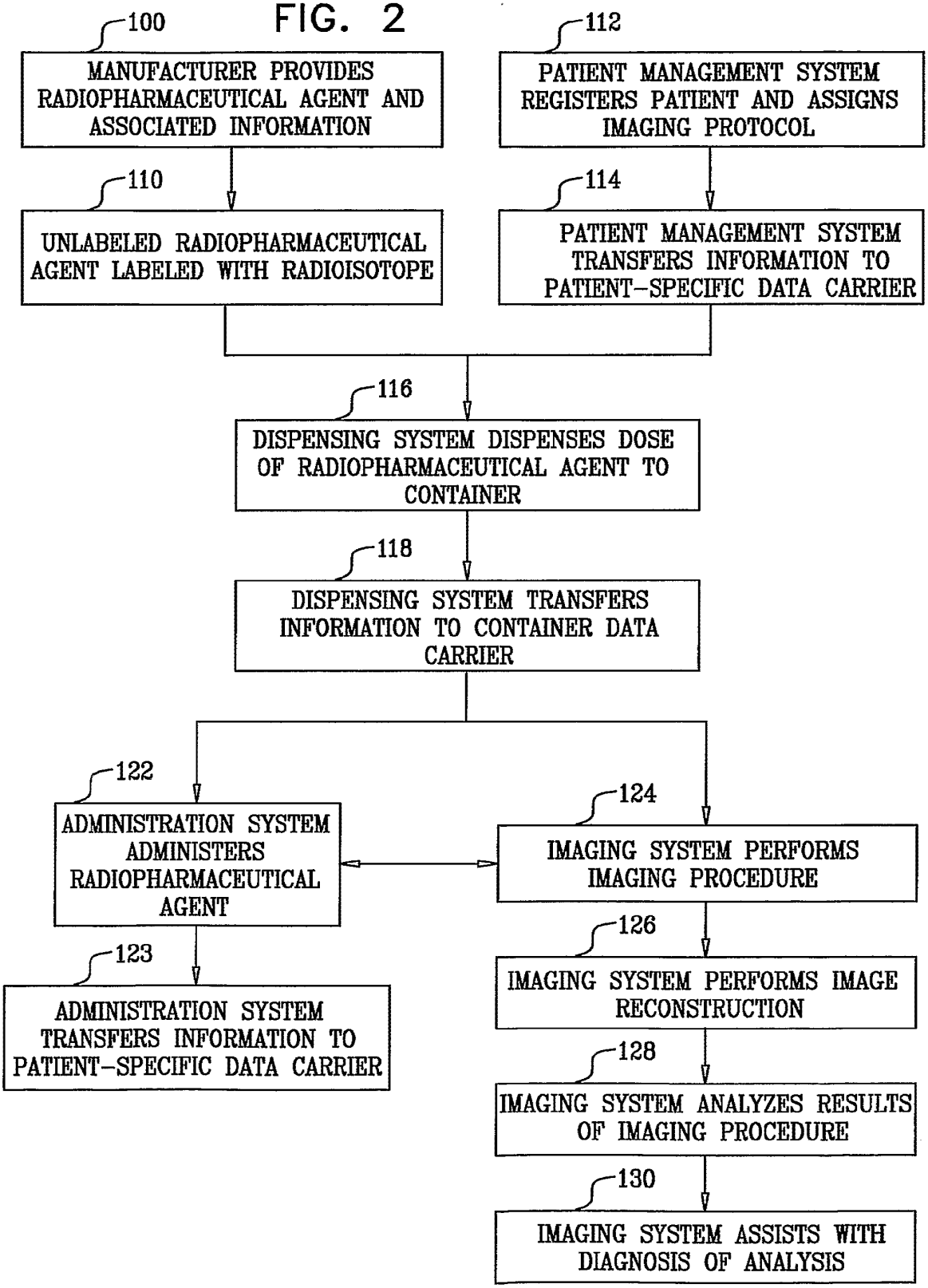

100
MANUFACTURER PROVIDES RADIOPHARMACEUTICAL AGENT AND ASSOCIATED INFORMATION
110
UNLABELED RADIOPHARMACEUTICAL AGENT LABELED WITH RADIOISOTOPE
112
PATIENT MANAGEMENT SYSTEM REGISTERS PATIENT AND ASSIGNS IMAGING PROTOCOL
114
PATIENT MANAGEMENT SYSTEM TRANSFERS INFORMATION TO PATIENT-SPECIFIC DATA CARRIER
116
DISPENSING SYSTEM DISPENSES DOSE OF RADIOPHARMACEUTICAL AGENT TO CONTAINER
118
DISPENSING SYSTEM TRANSFERS INFORMATION TO CONTAINER DATA CARRIER
122
ADMINISTRATION SYSTEM ADMINISTERS RADIOPHARMACEUTICAL AGENT
123
ADMINISTRATION SYSTEM TRANSFERS INFORMATION TO PATIENT-SPECIFIC DATA CARRIER
124
IMAGING SYSTEM PERFORMS IMAGING PROCEDURE
126
IMAGING SYSTEM PERFORMS IMAGE RECONSTRUCTION
128
IMAGING SYSTEM ANALYZES RESULTS OF IMAGING PROCEDURE
130
IMAGING SYSTEM ASSISTS WITH DIAGNOSIS OF ANALYSIS

FIG. 3

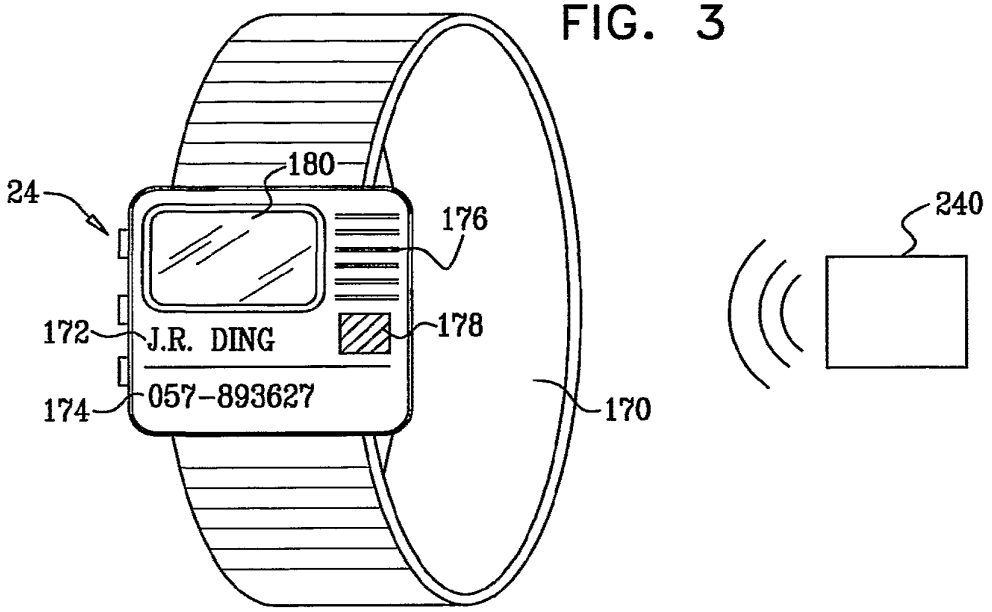

24
180
176
172
J.R. DING
178
174
057-893627
170
240

FIG. 4

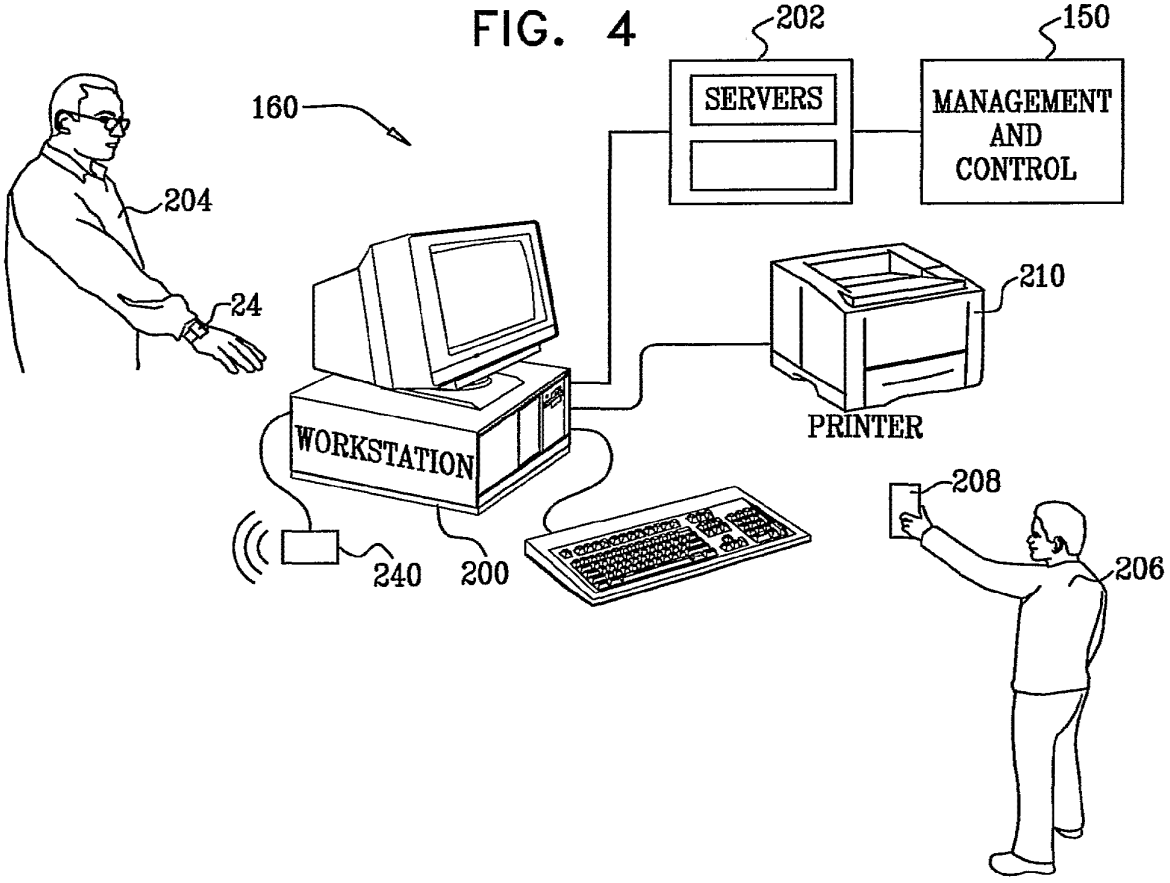

202
150
SERVERS
MANAGEMENT AND CONTROL
160
204
24
210
PRINTER
WORKSTATION
208
206
240
200

FIG. 5

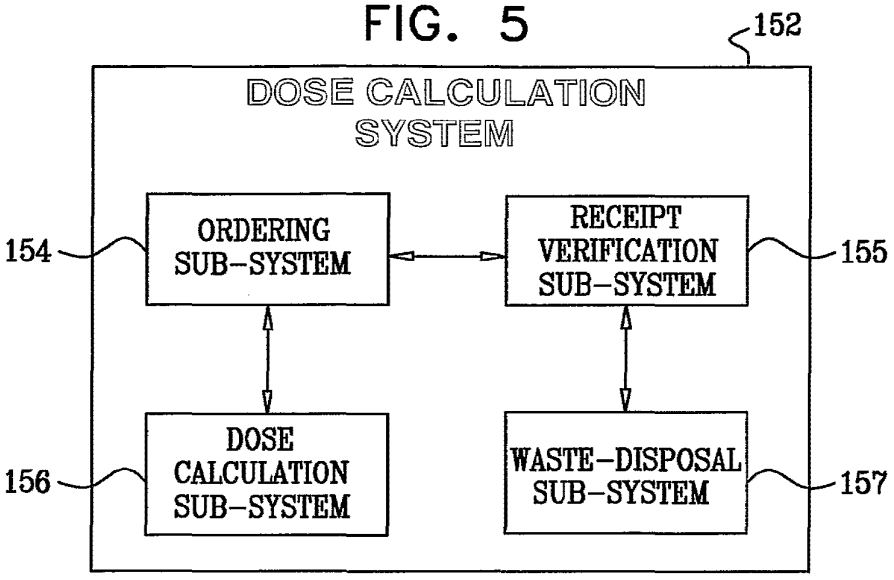

152
DOSE CALCULATION SYSTEM
154
ORDERING SUB-SYSTEM
RECEIPT VERIFICATION SUB-SYSTEM
155
156
DOSE CALCULATION SUB-SYSTEM
WASTE-DISPOSAL SUB-SYSTEM
157

FIG. 6A

	REST PHASE			ACQUISITION DURATION [MIN]	STRESS PHASE				GATED ACQUISITION DURATION [MIN]
	INJECTION		WAITING TIME [MIN]		STRESS	INJECTION		WAITING TIME [MIN]	
	RP	DOSE [mCi]				RP	DOSE [mCi]		
SINGLE ISOTOPE/ LOW DOSE/FAST IMAGING	TL	<0.3	2	15	EXERCISE	TL	<3	10–15	1.5
DUAL ISOTOPE/ LOW DOSE/FAST IMAGING	TL	<0.3	2	15	EXERCISE	Tc–MIBI	30	30–60	1.5
GATED REST THALLIUM (STUNNING)	TL	1.5	2	5 (GATED)	EXERCISE	Tc–MIBI	30	30–60	1.5
THALLIUM STRESS PERFUSION	Tc–MIBI	3	30	1.5	PHARMA	TL	3	0	10 (DYNAMIC)
SIMULTANEOUS DUAL ISOTOPE STRESS PERFUSION	Tc–MIBI	3	20		EXERCISE/PHARMA	TL	3		10 (DYNAMIC)
DYNAMIC IMAGING	TL	0.3			PHARMA (ADENOSINE)	TL	3		10 (DYNAMIC)

FIG. 6B

NO.	PROTOCOL NAME	KEY FEATURES AND PROPERTIES	ADMINISTRATION PARAMETERS			DETECTOR PARAMETERS
			DOSE (mCi)	INJECTION PROFILE	INJECT TO ACQUISITION TIME	DETECTED PHOTON ENERGY / RESOLUTION
A	CARDIAC MAPPING	MIBI-TC, FAST, BEFORE LIVER UPTAKE	20-40	BOLUS	2 MIN, OR ADMIN UNDER THE CAMERA	140 KeV / 15%
B	CARDIAC MAPPING	MIBI-TC AFTER LIVER UPTAKE	20-40	BOLUS	30+ MIN	140 KeV / 15%
C	CARDIAC MAPPING	SIMULTANEOUS FAST DUAL-ISOTOPE TL-201+ LOW DOSE MIBI-TC	TL-201: 3.5-5; MIBI-Tc-99m: 4-8	2 BOLUS (BEFORE AND AT PEAK STRESS)	TL INJECTED PREVIOUSLY AT REST, TC UNDER CAMERA OR 2 MIN	Tc-140 KeV, Tl-72 KeV / 15%
D	CARDIAC MAPPING	SIMULTANEOUS DUAL-ISOTOPE TL-201+ LOW DOSE MIBI-TC	TL-201: 3.5-5; MIBI-Tc-99m: 4-8	2 BOLUS (BEFORE AND AT PEAK STRESS)	SAME AS ONE OF FIRST 2 CARDIAC MAPPING PROTOCOLS	Tc-140 KeV, Tl-72 KeV / 15%
E	CARDIAC MAPPING	SIMULTANEOUS DUAL-ISOTOPE FULL TL-201+ FULL DOSE MIBI-TC	TL-201: 3.5-5; MIBI-Tc-99m: 20-40	2 BOLUS (BEFORE AND AT PEAK STRESS)	SAME AS ONE OF PROTOCOLS A OR B	Tc-140 KeV, Tl-167 KeV / 10%
F	CARDIAC MAPPING - UNDERWEIGHT (**BMI<18.5**)	MIBI-TC-99M AFTER LIVER UPTAKE	15-20	BOLUS	30+ MIN	140 KeV / 15%
G1	CARDIAC MAPPING - NORMAL (**18.6<BMI<24.9**)	MIBI-TC-99M AFTER LIVER UPTAKE	20-30	BOLUS	30+ MIN	140 KeV / 10%
G2	CARDIAC MAPPING - OVERWEIGHT (**25<BMI<29.9**)	MIBI-TC-99M AFTER LIVER UPTAKE	30-35	BOLUS	30+ MIN	140 KeV / 10%

FIG. 6C

NO.	SCANNING PARAMETERS						ANALYSIS PARAMETERS	
	TOTAL SCAN TIME	COLUMNS DIFFERENCES / UNIFORM SCAN	ANGULAR RANGE	TOTAL # ANGULAR ORIENT-TATIONS	ANGULAR STEP / INTERLACE	DWELL TIME	GATED ANALYSIS OF VOLUMES	ANALYSIS ALGORITHM / PARAMETERS
A	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	120X10	a) 0.3-0.5 DEG b) 0.75-1 DEG	1 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
B	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	120X10	a) 0.3-0.5 DEG b) 0.75-1 DEG	1 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
C	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	120X10	a) 0.3-0.5 DEG b) 0.75-1 DEG	1 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
D	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	120X10	a) 0.3-0.5 DEG b) 0.75-1 DEG	1 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
E	UP TO 1200 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	240X10	a) 0.15-0.25 DEG b) 0.375-0.5 DEG	5 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
F	90 SEC	a) 4 X OUTER b) 6 X INNER	a) 20-35 DEG b) 45-60 DEG	60X10	a) .3-.75 DEG b) 0.75-1DEG	1 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
G1	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 30-45 DEG b) 75-90 DEG	120X10	a) 0.5-0.75 DEG b) 0.625-1 DEG	1.5 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
G2	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	120X10	a) 0.3-0.5 DEG b) 0.75-1 DEG	2 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION

FIG. 6D

NO.	PROTOCOL NAME	KEY FEATURES AND PROPERTIES	ADMINISTRATION PARAMETERS			DETECTOR PARAMETERS
			DOSE (mCi)	INJECTION PROFILE	INJECT TO ACQUISITION TIME	DETECTED PHOTON ENERGY / RESOLUTION
H	CARDIAC MAPPING - OBESE (BMI>30)	MIBI-TC AFTER LIVER UPTAKE	35-40	BOLUS	30+ MIN	140 KeV / 6%
I	CARDIAC DYNAMIC MAPPING	TEBOROXIME-TC	20-40	BOLUS	-1 MIN (IMAGE BEFORE INJECT), OR SIMULTANEOUSLY WITH INJECT	140 KeV / 15%
J	CARDIAC DYNAMIC MAPPING (2-STEP)	TEBOROXIME-TC	20-40	(i) INITIAL SMALL BOLUS FOR IDENTIFYING ROI, (ii) FULL BOLUS FOR DYNAMIC STUDY	(i) 5+ MIN (ii) -1 MIN (IMAGE BEFORE INJECT)	140 KeV / 15%
K	TUMOR SCAN (MULTIPLE BODY SEGMENTS - HEAD TO LEGS)	MDP-TC-99M AFTER LIVER UPTAKE	20-40	BOLUS	30+ MIN	140 KeV / 15%
L	TUMOR SCAN (MULTIPLE BODY SEGMENTS - HEAD TO LEGS), FOCUSED SCAN	MDP-TC-99M AFTER LIVER UPTAKE	20-40	BOLUS	30+ MIN	140 KeV / 15%
M	TUMOR SCAN WITH COCKTAIL (MULTIPLE BODY SEGMENTS - HEAD TO LEGS), FOCUSED SCAN	FDG (METABOLISM), MIBI-TC-99M AND TL (PERFUSION)	TL-201: 3.5-5; MIBI-TC-99M: 20-40; 18-F FDG 10-30	BOLUS	30+ MIN	Tc-140 KeV, Tl-72 KeV, FDG 511 KeV / 10%

FIG. 6E

NO.	SCANNING PARAMETERS						ANALYSIS PARAMETERS	
	TOTAL SCAN TIME	COLUMNS DIFFERENCES / UNIFORM SCAN	ANGULAR RANGE	TOTAL # ANGULAR ORIENT-TATIONS	ANGULAR STEP / INTERLACE	DWELL TIME	GATED ANALYSIS OF VOLUMES	ANALYSIS ALGORITHM / PARAMETERS
H	180 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	160X10	a) 0.25-0.375 DEG b) 0.6-0.75 DEG	1.2 SEC	YES, 8-16 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
I	<= 600 SEC	a) 2 X OUTER b) 8 X INNER	a) 40-60 DEG b) 90-120 DEG	600X10	a) continuous b) continuous INTERLACED SCAN	1 SEC	YES, 8 FRAMES	KINETIC PARAMETES, PREDEFINED PATHOLOGICAL VALUES
J	(i) 60 SEC FOR IDENTIFYING ROI (ii) 600 SEC DYNAMIC STUDY	a) 2 X OUTER b) 8 X INNER	a) 40-60 DEG b) 90-120 DEG	(i) 60X10 (ii) 600X10	(i) a) 0.75-1 DEG b) 0.75-0.75-1 DEG (ii) a) continuous b) continuous INTERLACED SCAN	1 SEC	YES, 8 FRAMES	KINETIC PARAMETES, PREDEFINED PATHOLOGICAL VALUES
K	240 SEC PER BODY SEGMENT	16	40-60 DEG	120X16	0.3-0.5 DEG	2 SEC	NO	INTENSITY IMAGE, PREDEFINED PATHOLOGICAL VALUES
L	(i) 120 SEC PER BODY SEGMENT (ii) 60 SEC PER ROI	16	(i) 45-60 DEG (ii) 15-20 DEG	(i) 120X16 (ii) 60x16	(i) 0.375-0.5 DEG (ii) 0.25-0.3	1 SEC	NO	INTENSITY IMAGE, PREDEFINED PATHOLOGICAL VALUES
M	(i) 120 SEC PER BODY SEGMENT (ii) 60 SEC PER ROI	16	(i) 45-60 DEG (ii) 15-20 DEG	(i) 120X16 (ii) 60x16	(i) 0.375-0.5 DEG (ii) 0.25-0.4	1 SEC	NO	INTENSITY IMAGE, PREDEFINED PATHOLOGICAL VALUES

FIG. 7

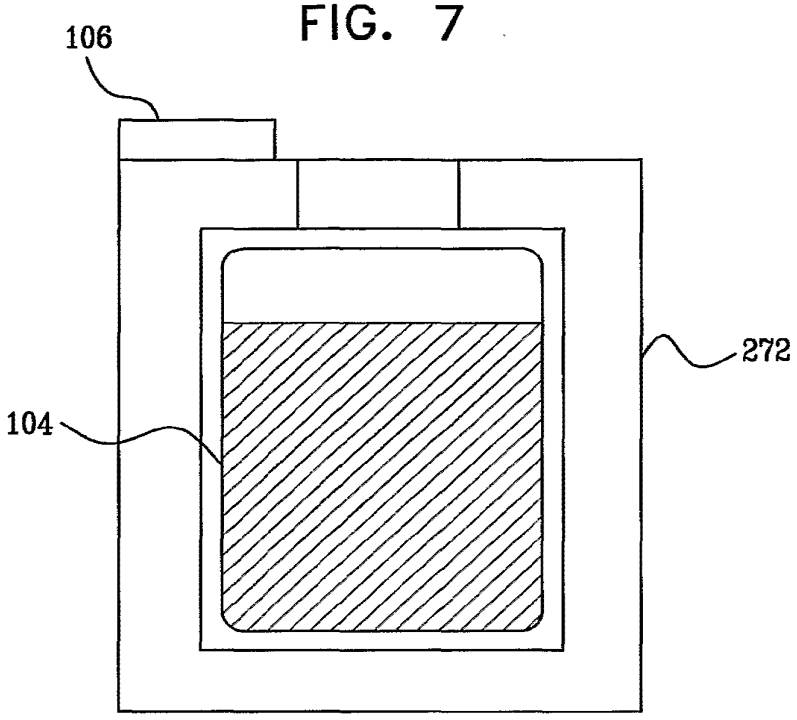


FIG. 8

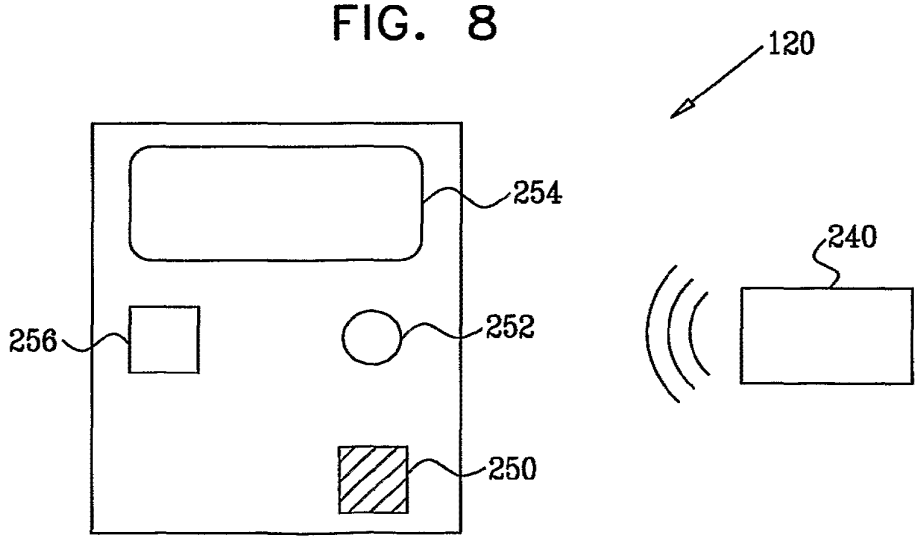


FIG. 9A

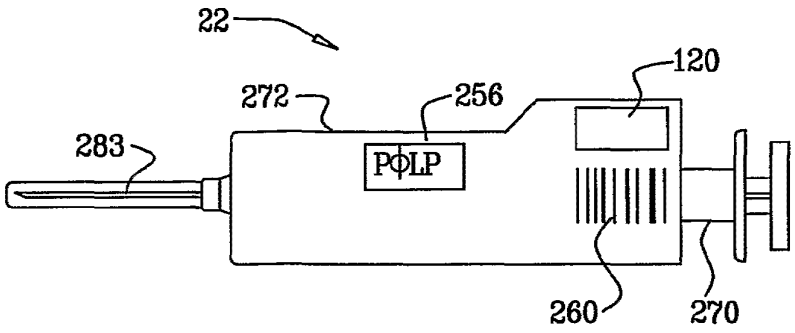


FIG. 9B

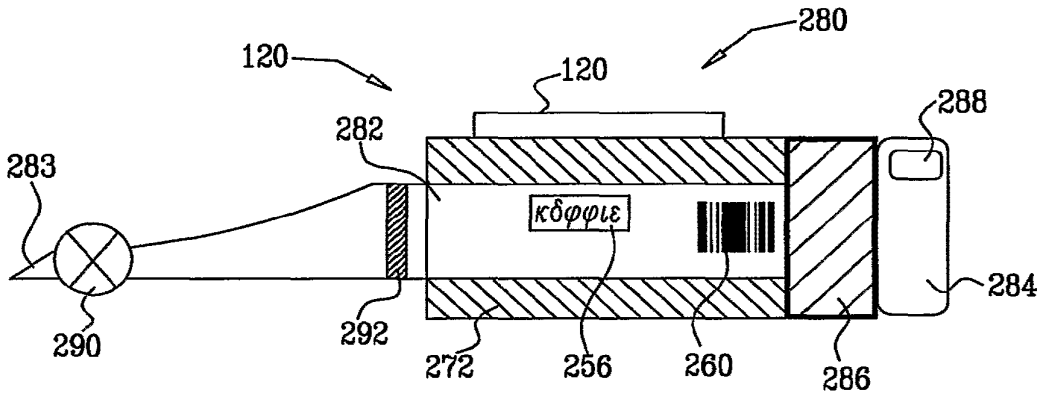


FIG. 9C

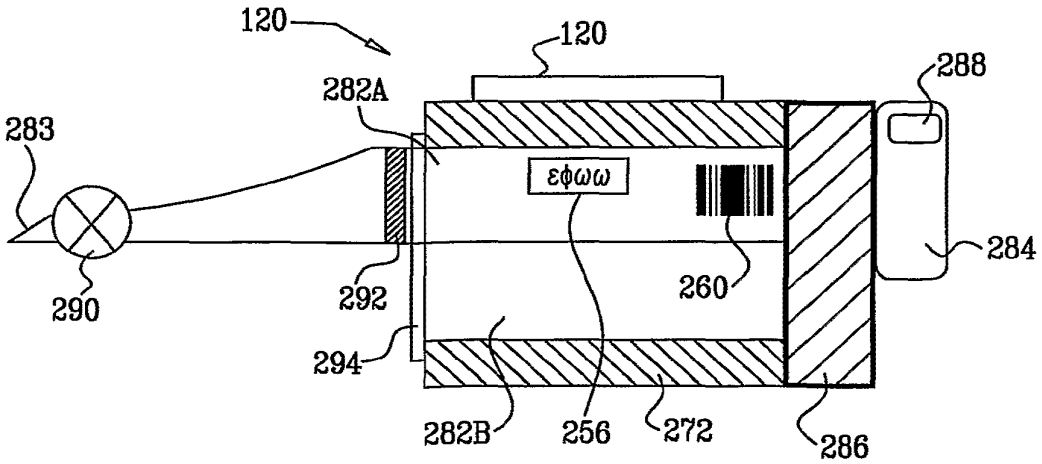


FIG. 9D

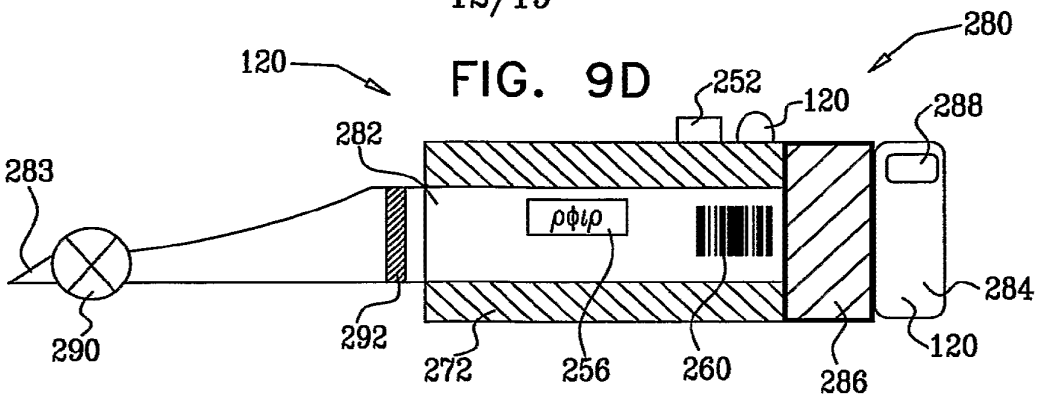


FIG. 9E

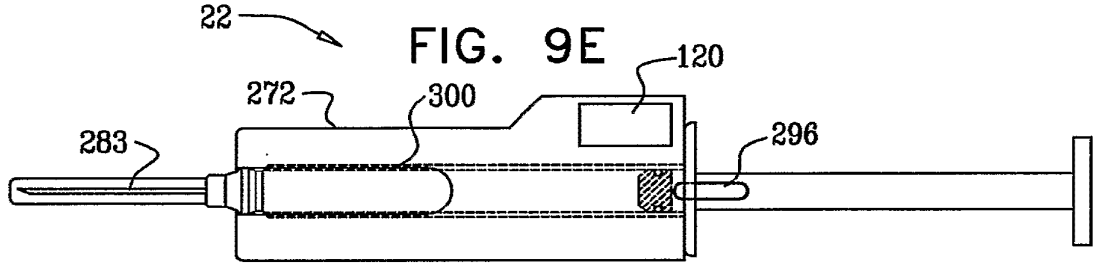


FIG. 9F

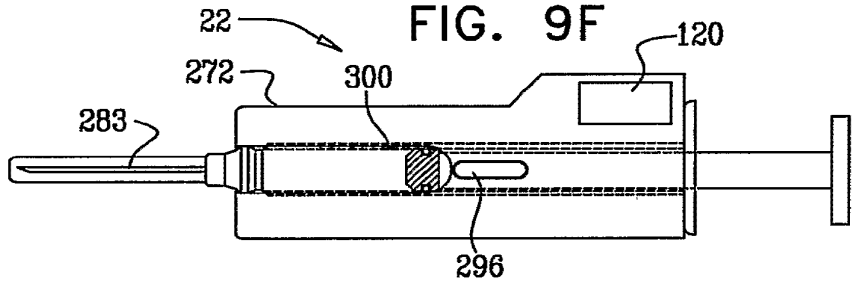


FIG. 9G

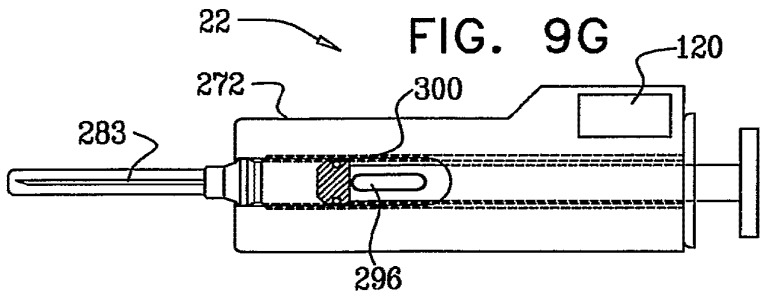


FIG. 9H

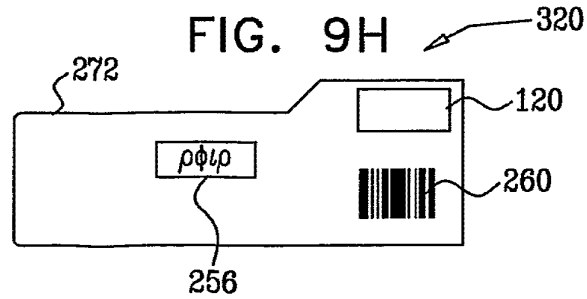


FIG. 10

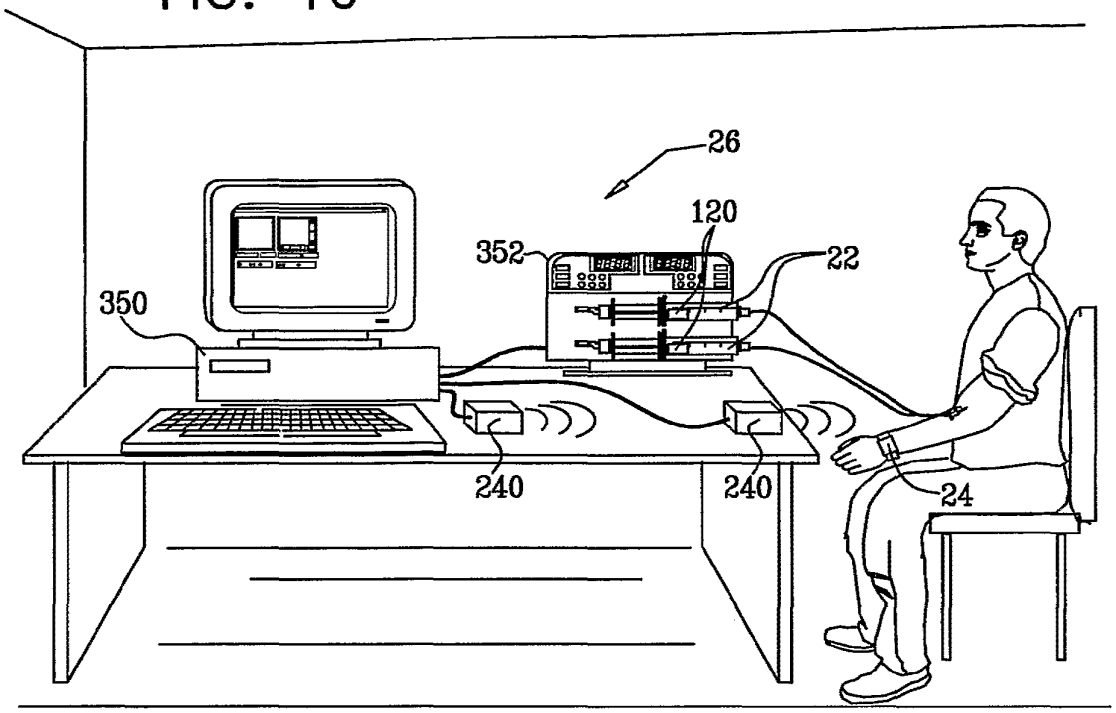
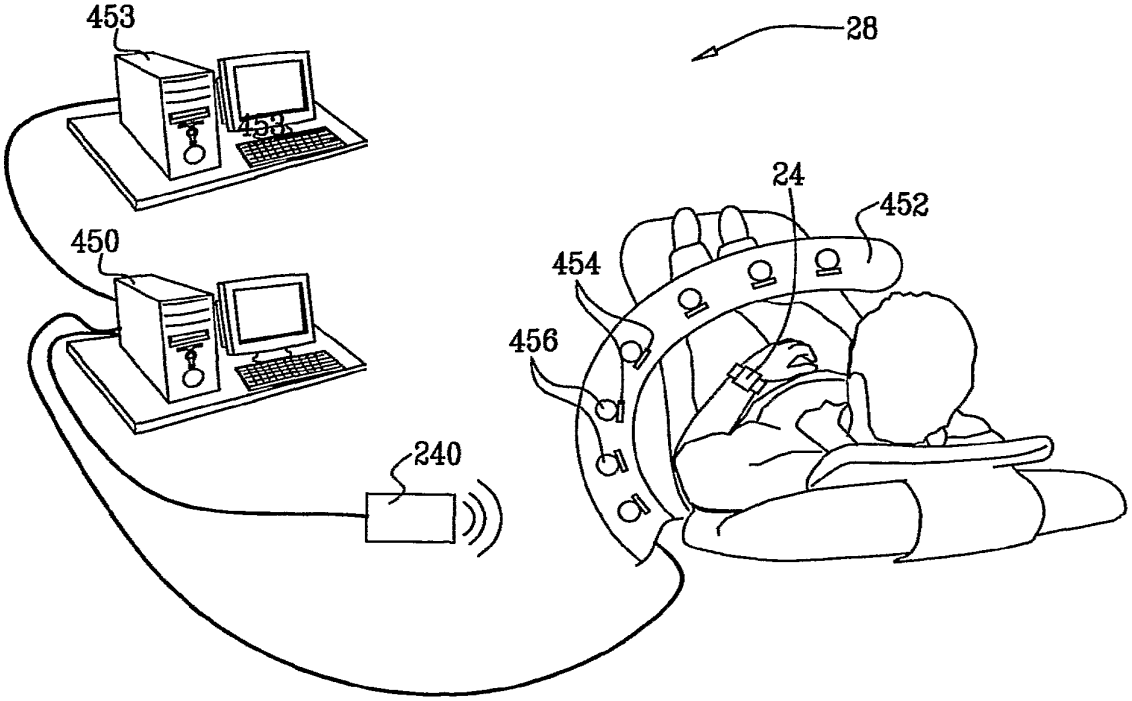


FIG. 11



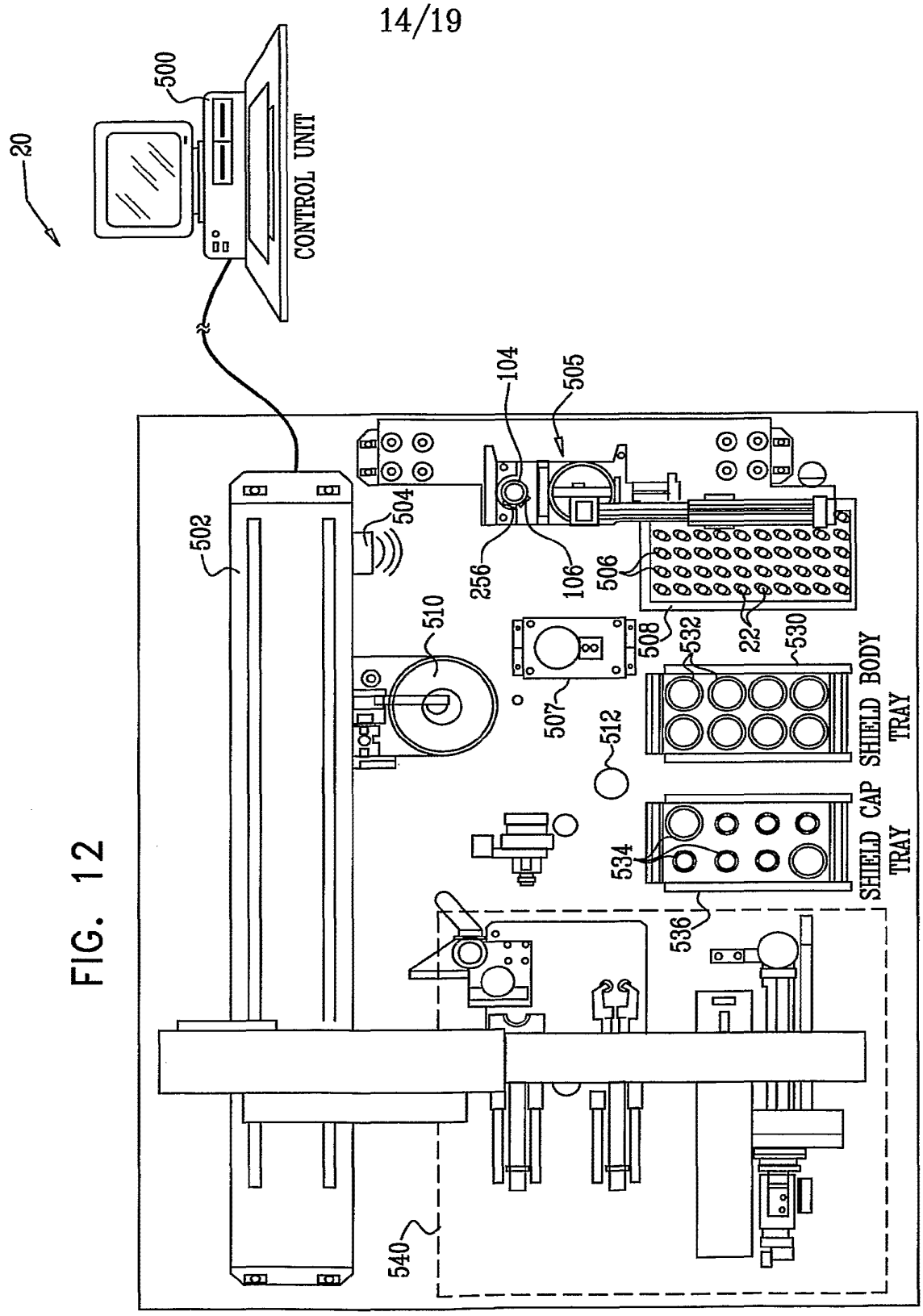

20
500
CONTROL UNIT
104
505
502
504
256
106
506
510
508
532
22
530
507
512
SHIELD BODY TRAY
534
SHIELD CAP TRAY
536
540

FIG. 12

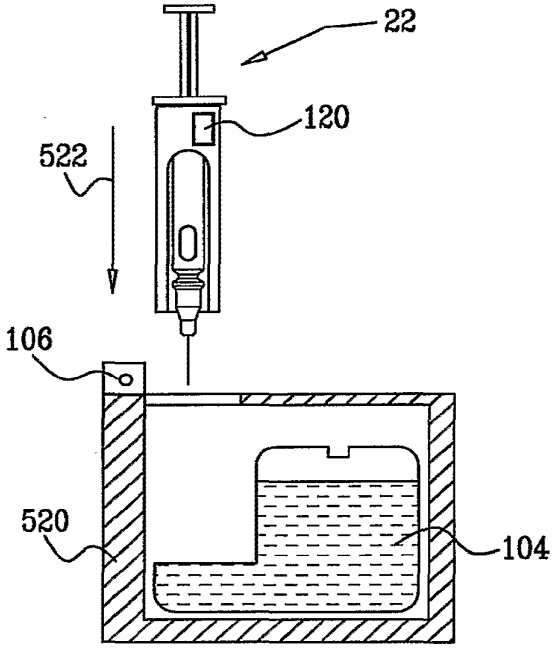


FIG. 13A

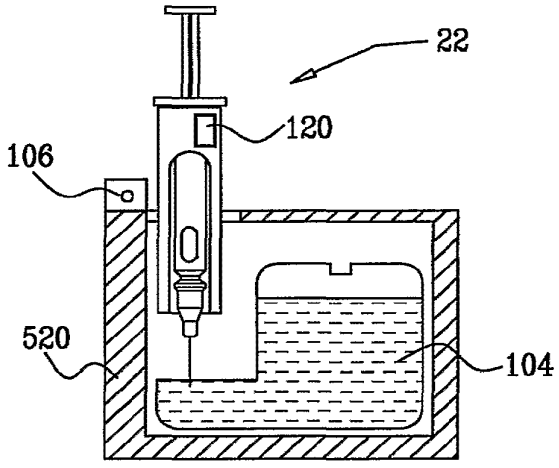


FIG. 13B

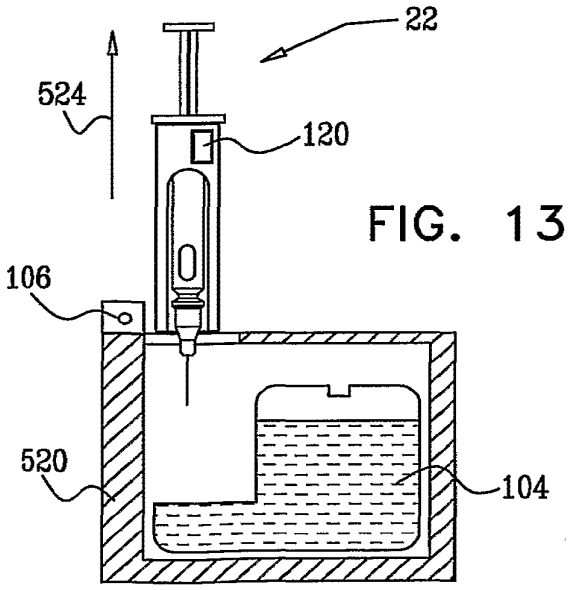


FIG. 13C

FIG. 14

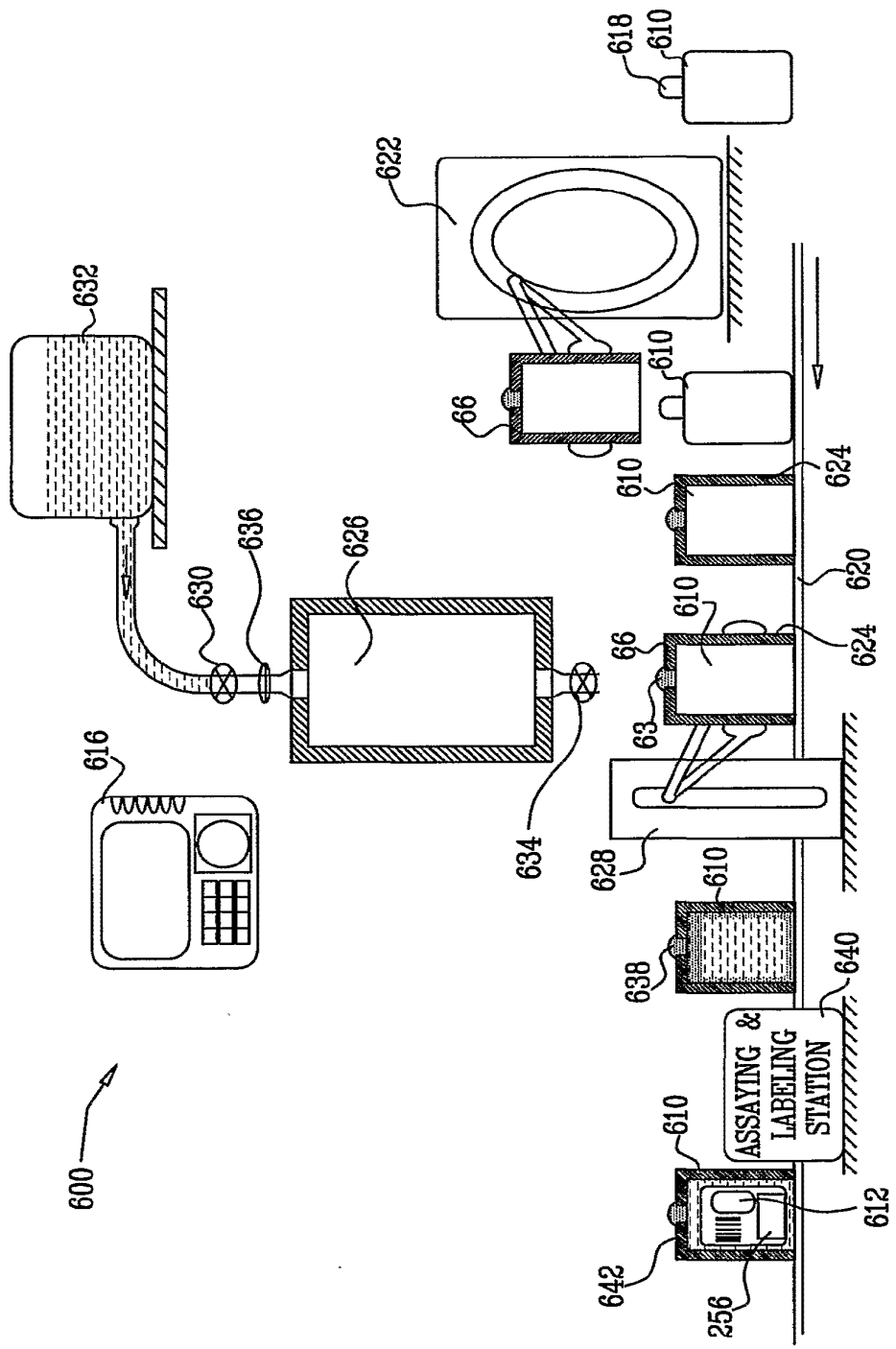

600
616
632
630
636
626
634
622
618
610
66
624
620
63
628
638
640
ASSAYING & LABELING STATION
612
642
256

FIG. 15

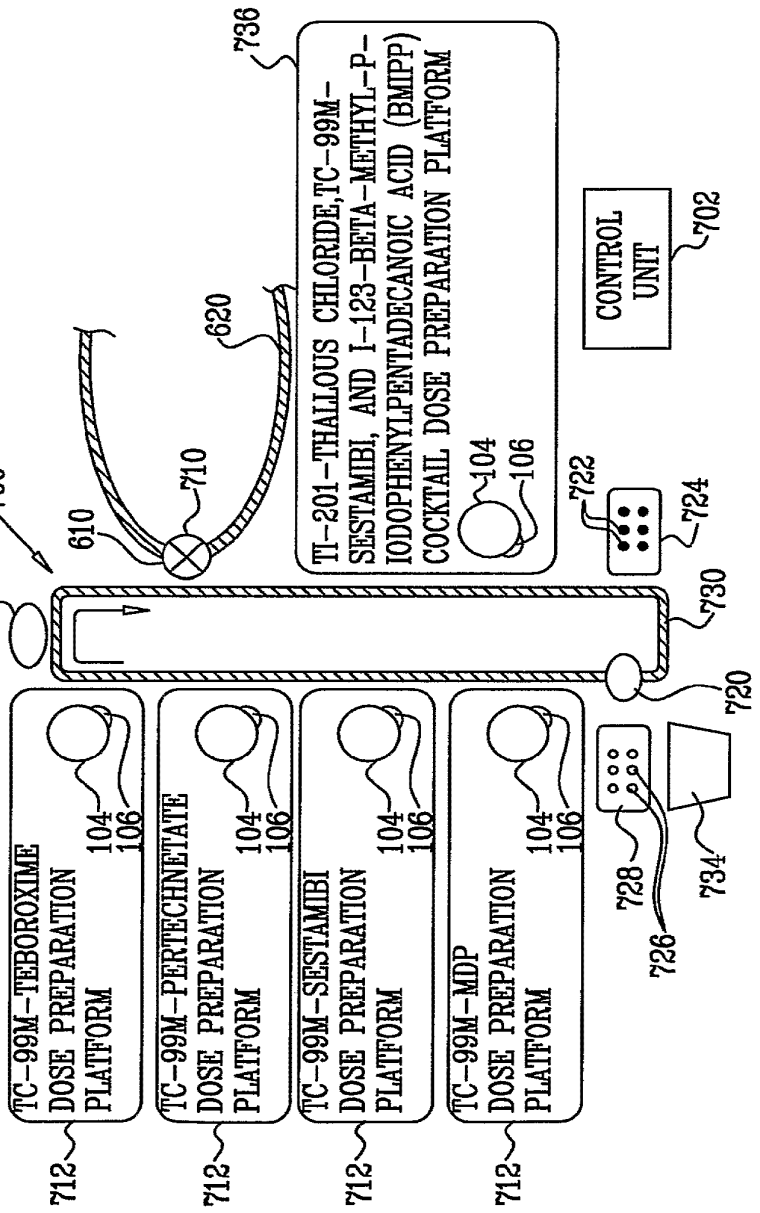

700
732
610
710
620
736
TI-201-THALLOUS CHLORIDE,TC-99M-SESTAMIBI, AND I-123-BETA-METHYL-P-IODOPHENYLPENTADECANOIC ACID (BMIPP) COCKTAIL DOSE PREPARATION PLATFORM
104
106
722
724
730
720
CONTROL UNIT
702
TC-99M-TEBOROXIME DOSE PREPARATION PLATFORM
TC-99M-PERTECHNETATE DOSE PREPARATION PLATFORM
TC-99M-SESTAMIBI DOSE PREPARATION PLATFORM
TC-99M-MDP DOSE PREPARATION PLATFORM
712
728
726
734

FIG. 16A

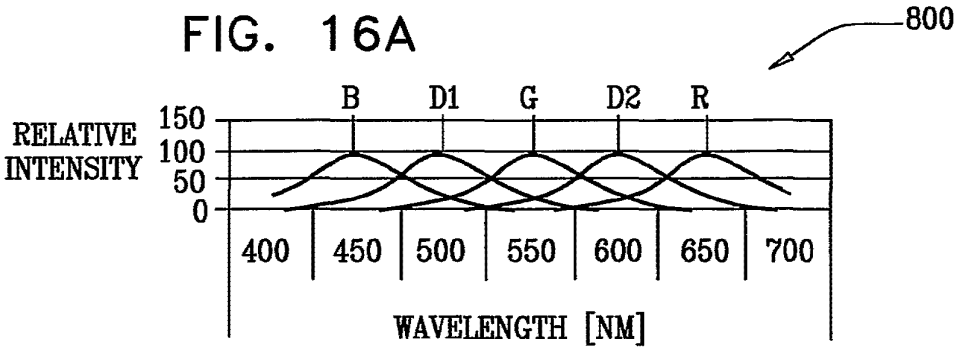


FIG. 16B

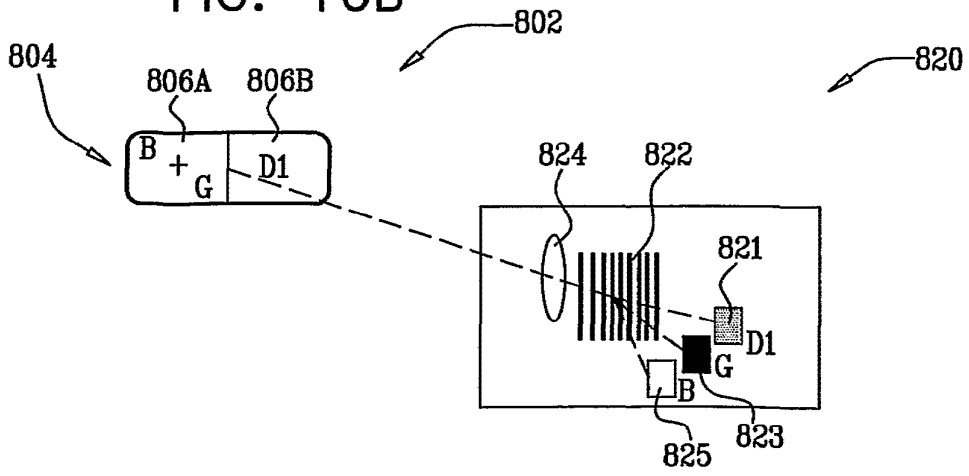


FIG. 17

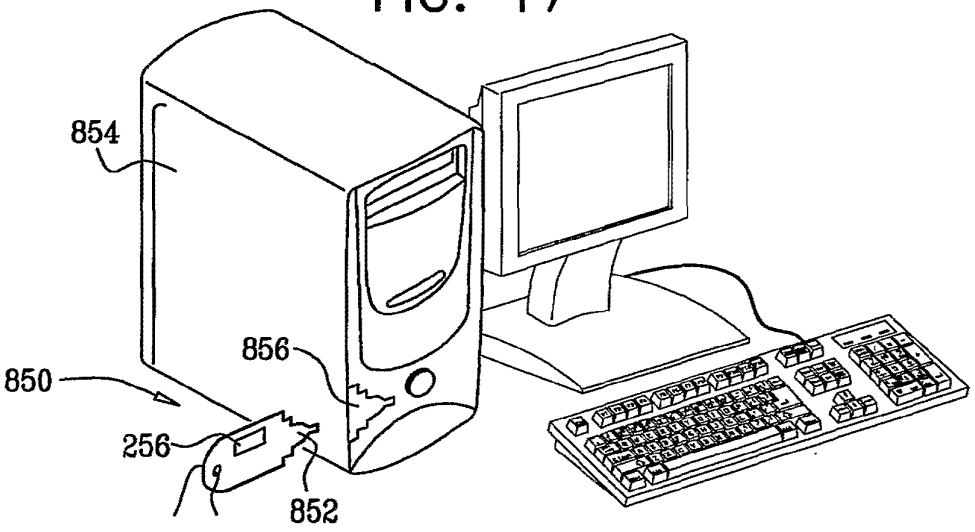
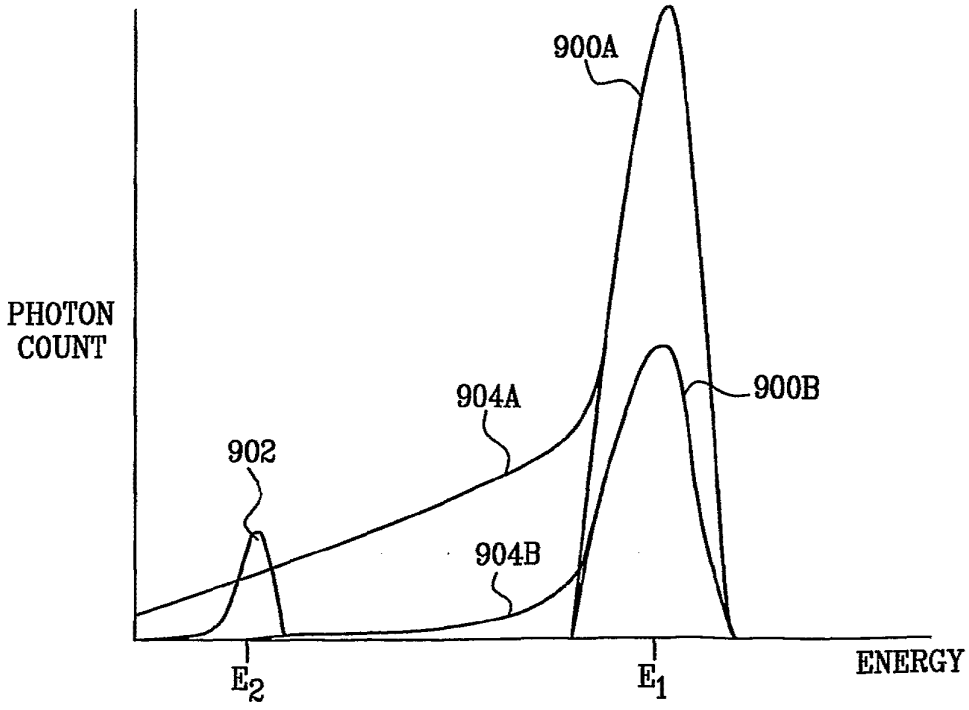

854
856
850
256
852

FIG. 18


900A
PHOTON COUNT
904A
900B
902
904B
E_2
E_1
ENERGY

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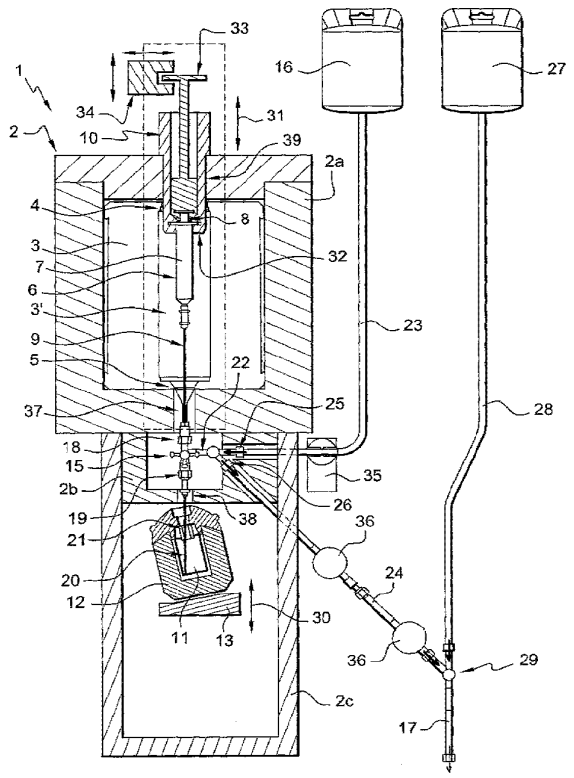
(81) États désignés *(sauf indication contraire, pour tout titre de protection nationale disponible)* : AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

[Suite sur la page suivante]

(54) Title: MEDICAL UNIT FOR THE COLLECTION, CALIBRATION, DILUTION AND/OR INJECTION OF AN INJECTABLE RADIOACTIVE PRODUCT

(54) Titre : UNITE MEDICALE POUR LE PRELEVEMENT, LE CALIBRAGE, LA DILUTION ET/OU L'INJECTION D'UN PRODUIT RADIOACTIF INJECTABLE



(57) Abstract: The medical unit according to the invention comprises a shielded enclosure (2) that accommodates means (13) for supporting a container (12) comprising a source or a generator of radioactive product (11), means (10) for supporting a syringe (6), a device of the activity meter type (3), and a system of conduits (9, 23, 24) joined to at least one valve (15). The syringe support (10), the valve (15) and the radioactive source support (13) are arranged vertically relative to one another, each facing downwards, said syringe support (10) being designed to support said syringe (6) with its plunger (8) oriented upwards. The valve (15) and the syringe plunger (8) can be manoeuvred for performing the operations of collection, dilution and injection.

(57) Abrégé : L'unité médicale selon l'invention comporte une enceinte blindée (2) dans laquelle sont logés : des moyens (13) support d'un conteneur (12) comprenant une source ou un générateur de produit radioactif (11); des moyens (10) pour le support d'une seringue (6); un dispositif de type activimètre (3); et un système de conduites (9, 23, 24) associé à au moins une vanne (15). Le support de seringue (10), la vanne (15) et le support de source radioactive (13) sont agencés verticalement les uns par rapport aux autres, respectivement du haut vers le bas, ledit support de seringue (10) étant agencé pour supporter ladite seringue (6) avec son piston (8) orienté vers le haut. La vanne (15) et le piston de seringue (8) sont manoeuvrables pour assurer les opérations de prélèvement, de dilution et d'injection.

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(84) États désignés *(sauf indication contraire, pour tout titre de protection régionale disponible)* : ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), eurasien (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), européen (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Déclaration en vertu de la règle 4.17 :

— *relative à la qualité d'inventeur (règle 4.17.iv))*

Publiée :

— *sans rapport de recherche internationale, sera republiée dès réception de ce rapport*

UNITE MEDICALE POUR LE PRELEVEMENT, LE CALIBRAGE, LA DILUTION ET/OU L'INJECTION D'UN PRODUIT RADIOACTIF INJECTABLE

La présente invention concerne le domaine général de la médecine nucléaire. Elle concerne plus particulièrement une unité médicale employée pour le prélèvement, le calibrage, la dilution et/ou l'injection d'une substance radioactive destinée à être injectée à un patient.

Certaines substances radioactives sont particulièrement utiles dans le domaine médical, par exemple dans les procédures d'imagerie, à titre d'agents de contraste, ou comme agents thérapeutiques.

Pour limiter les doses de radiations reçues par le patient et par le personnel chargé des manipulations, on utilise des radioéléments de courtes demi-vies à usage médical, c'est-à-dire que le niveau de radiation émis par ces produits radioactifs décroît rapidement avec le temps.

Mais de tels produits radioactifs à courte demi-vie rendent problématique l'administration d'une dose appropriée au patient. Le dosage correspondant doit en effet être très précis ; il doit tenir compte du temps nécessaire pour la préparation de la dose à injecter, et aussi du temps susceptible de séparer le moment de la préparation de la dose de produit et le moment de l'injection proprement dite de cette dose au patient.

En outre, malgré le type de produits mis en œuvre (courte demi-vie), une autre contrainte à prendre en compte concerne la radioprotection du personnel médical chargé de préparer la dose radioactive et de l'injecter au patient. Cette radioprotection doit aussi être effective pour le patient.

De manière classique, les doses à injecter sont prélevées dans une seringue munie d'un blindage approprié, placée elle-même dans une enceinte blindée équipée de moyens de mesure et de contrôle appropriés, permettant de prélever dans la seringue la dose de produit radioactif recherchée. Ensuite, un opérateur récupère la seringue blindée et il se rend auprès du patient pour réaliser l'injection.

Cependant, cette manière d'opérer n'offre pas une sécurité optimale, tant sur le plan de la radioprotection pour l'opérateur que sur le plan de la précision de la dose injectée au patient.

Le document US-6 767 319 décrit un matériel de calibrage et d'injection de produit radioactif visant à limiter l'exposition du personnel à la substance radioactive et aussi optimiser la sécurité du patient.

L'installation correspondante comprend trois enceintes radioprotectrices indépendantes, contenant respectivement :

- des moyens pour le support d'une source en produit radioactif injectable,
- des moyens pour le support d'une seringue, qui sont équipés de moyens pour la manœuvre automatique de son piston, et qui sont associés à un dispositif de type activimètre pour la mesure en temps réel de l'activité radio-isotopique émise par le produit contenu dans la seringue, et
- un système de vannes.

Ce système de vannes est raccordé hydrauliquement, par le biais de tubulures, à l'enceinte contenant la source mère radioactive, à l'enceinte contenant la seringue, à une source de sérum physiologique et à un cathéter d'injection destiné à être connecté au patient.

Ce matériel comprend encore des moyens destinés à piloter le système de vannes et les moyens de manœuvre du piston de seringue, cela de manière adaptée pour assurer, dans un premier temps, le prélèvement d'une dose de produit radioactif et/ou de sérum physiologique au sein de la seringue, et dans un second temps l'éjection au travers du cathéter d'injection, du produit radioactif et/ou du sérum physiologique préalablement prélevés. La dose de produit radioactif est mesurée par le dispositif activimètre au cours du prélèvement dans la seringue.

Dans ce matériel, les tubulures reliant l'enceinte contenant le système de vannes et celles contenant la seringue ou la source radioactive, ne sont pas protégées et sont source d'émissions radioactives dans l'environnement.

De plus, du fait de sa structure, le matériel correspondant est encombrant. En outre, la complexité du réseau de tubulures entraîne la présence de volumes morts importants.

La présente invention propose une unité médicale originale de calibration et d'injection de produits radioactifs, très compacte, permettant le prélèvement, la mesure et l'injection des produits avec une grande précision, en toute sécurité, et avec des volumes morts réduits.

Cette unité médicale est du type comprenant :

- des moyens pour le support d'un conteneur en matériau radioprotecteur dans lequel est logée une source ou un générateur de produit radioactif injectable,
- des moyens pour le support d'une seringue équipée d'un piston,
- un dispositif de type activimètre pour la mesure en temps réel de l'activité radio-isotopique émise par le contenu de ladite seringue, et

- un système de conduites associé à au moins une vanne pour le raccordement hydraulique de ladite source radioactive, de ladite seringue, d'une source de sérum physiologique et d'un cathéter d'injection destiné à être connecté au patient,

ladite vanne et ledit piston de seringue étant manœuvrables pour assurer, d'une part, une aspiration dudit produit radioactif ou dudit sérum physiologique au sein de ladite seringue, et d'autre part, une éjection dudit produit radioactif, dudit sérum physiologique ou d'un mélange de ces deux produits, préalablement aspirés au sein de ladite seringue, cela au travers dudit cathéter d'injection, la dose de produit radioactif prélevée et injectée par ladite seringue étant mesurée par ledit activimètre.

Conformément à l'invention, l'unité médicale comporte encore une enceinte blindée réalisée en au moins un matériau radioprotecteur, dans laquelle sont logés le support de source radioactive, au moins une partie des moyens support de la seringue, l'activimètre, la vanne, et au moins une partie du système de conduites.

De plus, le support de seringue, la vanne et le support de source radioactive sont agencés verticalement les uns par rapport aux autres, respectivement du haut vers le bas, le support de seringue étant agencé pour porter la seringue verticalement avec son piston orienté vers le haut.

Cet agencement particulier permet à la seringue de prélèvement/injection et à la source de produit radioactif d'être très proches de la vanne, pour obtenir un ensemble très compact, avec des volumes morts minimisés.

Selon une caractéristique de réalisation, la vanne consiste en une vanne trois voies comprenant :

- une voie supérieure, destinée à être raccordée à la seringue de prélèvement et d'injection,
- une voie inférieure, destinée à être raccordée à la source de produit radioactif injectable, et
- une voie latérale, destinée à être raccordée à une première conduite connectée à la source de sérum physiologique et à une seconde conduite connectée au cathéter d'injection, lesdites conduites étant équipées chacune d'un clapet anti-retour convenablement orienté.

Dans ce cas, l'activimètre a avantageusement une forme générale tubulaire délimitant un puits central, d'axe vertical, destiné à contenir la seringue, ledit activimètre étant muni de deux ouvertures, l'une supérieure et l'autre inférieure, cette dernière étant orientée en regard de la vanne trois voies et du support de la source radioactive.

Pour réduire les volumes morts dans les conduits de ce matériel, la voie supérieure de la vanne, destinée à être raccordée à la seringue, comporte avantageusement un opercule hermétique destiné à être percé par l'aiguille équipant ladite seringue montée sur son support ; de même, la voie inférieure de la vanne, destinée à être raccordée à la source de produit radioactif est avantageusement prolongée par une aiguille destinée à percer un opercule obturant le flacon contenant ladite source radioactive.

Encore selon une caractéristique de réalisation de l'invention, les supports de source radioactive et de seringue sont portés chacun par des moyens assurant leur(s) déplacement(s) selon un axe vertical ou sensiblement vertical, cela entre deux positions :

- une première position, dans laquelle un opérateur peut charger la source radioactive et la seringue sur leurs supports respectifs, ou à l'inverse les décharger, et
- une seconde position dans laquelle la source radioactive et la seringue sont raccordées à la vanne.

Selon cette caractéristique, les moyens de déplacement du support de seringue permettent avantageusement son cheminement verticalement au travers d'un orifice ménagé dans l'enceinte blindée, entre :

- une position supérieure de chargement/déchargement, dans laquelle ledit support se situe au moins partiellement hors de ladite enceinte, et
- une position inférieure de raccordement, dans laquelle la seringue se positionne au sein du logement central de l'activimètre et est raccordée à la vanne.

De plus, le support de source radioactive chemine avantageusement au sein de l'enceinte blindée entre ses positions de chargement/déchargement et de raccordement ; cette enceinte est encore munie d'une trappe frontale pour permettre l'accès d'un opérateur au support de source radioactive au moins dans sa position de chargement/déchargement.

Encore selon une autre caractéristique, l'unité médicale comprend des moyens de commande informatiques et/ou électroniques aptes à piloter la vanne et les moyens de manœuvre du piston de seringue, cela de manière à mettre en œuvre les opérations de prélèvement et d'éjection par la seringue. De même, les moyens de commande informatiques/électroniques pilotent également éventuellement les moyens de déplacement du support de seringue et du support de source radioactive.

Dans ce cas, les moyens de manœuvre du piston de la seringue sont avantageusement de type motoréducteur débrayable, contrôlés par les moyens

informatiques/électroniques, pour assurer, d'une part, le prélèvement automatique d'une dose déterminée de produit radioactif au sein de la seringue et, d'autre part, pour assurer l'injection de cette dose au patient, soit automatiquement, soit manuellement. L'opérateur peut en effet, s'il le souhaite, débrayer les moyens motoréducteurs et contrôler manuellement l'injection de la dose radioactive au patient.

Selon toujours une forme de réalisation intéressante, l'enceinte se compose de trois sous-enceintes alignées verticalement les unes par rapport aux autres, à savoir :

- une sous-enceinte supérieure contenant la seringue et l'activimètre,
- une sous-enceinte intermédiaire contenant la vanne, et
- une sous-enceinte inférieure contenant la source de produit radioactif.

Ces sous-enceintes sont raccordées deux à deux par des ouvertures traversantes au travers desquelles passent certaines des conduites de raccordement hydraulique.

Pour optimiser encore le traitement des données des médicales, les moyens de commande informatiques/électroniques sont pourvus d'une connectique pour l'envoi et/ou la réception de données, en particulier pour les échanges avec un serveur informatique.

L'unité médicale selon l'invention peut être rendue mobile. Pour cela, elle est montée sur des roues avantageusement motorisées ; elle intègre éventuellement un système de géolocalisation, par exemple de type GPS.

L'invention sera encore illustrée, sans être aucunement limitée, par la description suivante d'un mode de réalisation particulier, donné uniquement à titre d'exemple et représenté sur les dessins annexés dans lesquels :

- la figure 1 est une représentation schématique, en coupe, d'une unité médicale conforme à l'invention ;
- la figure 2 est une vue en perspective de la structure externe d'une forme de réalisation possible de l'unité médicale illustrée figure 1.

Tel que représenté sur la figure 1, l'unité médicale 1 conforme à l'invention comprend une enceinte blindée 2 réalisée en matériau radioprotecteur dans laquelle on trouve un dispositif 3 pour la mesure en temps réel de l'activité radio-isotopique (activimètre de type ACAD (marque déposée)), de forme générale cylindrique d'axe vertical, muni d'une ouverture supérieure 4 et d'une ouverture inférieure 5.

Une seringue classique 6, comprenant un corps 7, un piston 8 et une aiguille 9, est installée dans le puits de mesure 3' de l'activimètre 3 (connectée à une unité de traitement appropriée) ; cette seringue 6 est montée verticalement sur un support

supérieur 10, son piston 8 étant orienté vers le haut, et donc son aiguille 9 étant orientée vers le bas.

Une source ou générateur 11 de produit radioactif est placé sous l'activimètre 3, en regard de son ouverture inférieure 5. Cette source de produit radioactif 11 est contenue dans un flacon conditionné dans un conteneur blindé 12 réalisé en matériau radioprotecteur. Le conteneur blindé 12 est logé dans l'enceinte blindée 2, posé sur un support 13.

Une vanne trois voies motorisée 15, logée dans l'enceinte blindée 2 entre la seringue 6 et le flacon de source radioactive 11, assure une connexion hydraulique appropriée entre ladite seringue 6, ledit flacon de source radioactive 11, une poche de sérum physiologique 16 (extérieure à l'enceinte blindée 2) et un cathéter 17 d'injection au patient (également extérieur à l'enceinte blindée 2). Cette vanne 15 est localisée en regard de l'ouverture inférieure 5 de l'activimètre 3, et en regard de la source radioactive 11.

La voie supérieure 18 de cette vanne trois voies 15 comporte un opercule hermétique destiné à être percé par l'aiguille 9 de la seringue 6. La voie inférieure 19 de la vanne 15 se prolonge par une aiguille 20 destinée à percer l'opercule hermétique 21 qui obture le flacon de source radioactive 11. La voie latérale 22 de la vanne 15 est connectée, par un raccordement en Y, à une tubulure 23 aboutissant à la poche de sérum physiologique 16, et à une tubulure 24 aboutissant au cathéter d'injection 17.
La tubulure 23 est équipée d'un clapet anti-retour 25 empêchant un retour de liquide en direction de la poche de sérum physiologique 16. La tubulure 24 est également équipée d'un clapet anti-retour 26 imposant le passage de liquide en direction du patient.

Sur la figure 1, on remarque que le cathéter 17 est également en communication avec une seconde poche 27 de sérum physiologique, par le biais d'une tubulure 28 et d'un raccordement en Y 29.

La vanne trois voies 15 a deux positions principales : - une première mettant en communication ses voies supérieure 18 et inférieure 19 (permettant la mise en communication de la seringue 6 avec la source de produit radioactif 11 pour assurer le prélèvement d'une dose de produit radioactif dans le corps de seringue 7), et - une seconde position, mettant en communication la voie supérieure 18 et la voie latérale 22 (soit pour aspirer du sérum physiologique venant de la poche 16 dans le corps de seringue 7, lors d'une opération d'aspiration par la seringue 6, soit pour éjecter le

liquide contenu dans le corps de seringue 7 dans le cathéter d'injection 17, par une manœuvre de vidange du corps de seringue 7).

Une troisième position possible de la vanne 15 consiste à mettre en communication la source de radioéléments 11 et les tubulures 23 et 24, cela pour casser la dépression du flacon de source radioactive 11 en autorisant l'aspiration du sérum physiologique provenant de la poche 16.

La vanne trois voies 15 est montée fixe à l'intérieur de l'enceinte 2 sur l'axe vertical ou sensiblement sur l'axe vertical passant par la seringue 6 et la source 11 de produit radioactif.

Le support 13 de la source de produit radioactif 11 est mobile verticalement, conformément à la flèche d'orientation 30, sous l'action de moyens mécaniques appropriés (non représentés) actionnés manuellement (ou au pied), ou par des moyens moteurs (également non représentés) de manière à permettre l'intégration de l'aiguille 20 dans le flacon de source radioactive 11, ou le retrait de cette aiguille 20 dudit flacon.

L'opérateur manœuvre le support mobile 13 dans cette dernière position « extraite » lorsqu'il souhaite changer la source de produit radioactif.

D'autre part, le support 10 de la seringue 6 est également mobile verticalement, conformément à la flèche d'orientation 31, sous l'action de moyens mécaniques appropriés (non représentés) actionnés manuellement ou par des moyens moteurs (également non représentés), de manière à permettre l'intégration de l'aiguille 9 de la seringue 6 dans la vanne trois voies 15, ou l'extraction de la seringue 6 au-dessus de l'activimètre 3 et hors du conteneur blindé 2, pour réaliser les opérations de mise en place et de retrait de la seringue 6.

Le support 10 de la seringue 6 est également structuré pour permettre une manœuvre du piston 8 de la seringue depuis l'extérieur du conteneur blindé 2, alors que ladite seringue 6 est centrée dans le puits de mesure 3' de l'activimètre 3.

Pour cela, le support 10 comporte une partie cylindrique 32 en prise avec la partie arrière du corps de seringue 7, et une partie centrale 33, en forme de piston coulissant dans la partie cylindrique 32, en prise avec la partie arrière du piston de seringue 8.

Lorsque le corps de seringue 7 est en position dans le puits de mesure 3' de l'activimètre 3, l'extrémité supérieure du piston coulissant 33 est accessible depuis l'extérieur de l'enceinte blindée 2. Cette extrémité supérieure de piston 33 est associée à une motorisation débrayable 34 qui, une fois embrayée, permet l'actionnement

automatique du piston de seringue 8 et qui, lorsqu'elle est débrayée, permet l'actionnement manuel de ce piston 8.

Cette particularité offre à l'opérateur un choix de gestion, automatique ou manuelle, du prélèvement de produit radioactif par la seringue 6 et/ou de l'éjection du produit dans le cathéter 17.

Sur la figure 1, on remarque encore la présence d'une électrovanne à pincement 35, positionnée sur la tubulure 23 de la poche de sérum physiologique 16. Cette électrovanne 35 a pour fonction d'empêcher la circulation intempestive de sérum physiologique au travers de la tubulure 23, avant la connexion du cathéter d'injection 17 au patient.

Sur la tubulure 24 d'alimentation du cathéter 17, on remarque aussi la présence de deux moyens anti-bulles/antibactérien 36 qui se présentent, par exemple, sous la forme de filtres, garantissant la stérilité du processus d'injection.

Toujours sur la figure 1, on remarque que l'enceinte blindée 2 se présente sous la forme de trois sous-ensembles blindés :

- un premier ensemble 2a intègre l'activimètre 3 et une partie du support de seringue 10,
- un second ensemble 2b cloisonne la vanne trois voies motorisée 15, et
- un troisième ensemble 2c cloisonne le support mobile 13 avec son conteneur blindé 12.

Les trois sous-enceintes 2a, 2b et 2c sont superposées ; la connexion entre la seringue 6 et la vanne 15 s'effectue au travers d'une ouverture 37 ménagée entre lesdits sous-ensembles 2a et 2b. La connexion entre la vanne 15 et la source de produit radioactif 11 est réalisée au travers d'une ouverture 38 ménagée entre les sous-ensembles 2b et 2c.

Le support 10 de la seringue 6 est réalisé en matériau radioprotecteur. Ses dimensions sont ajustées au mieux dans une ouverture 39 ménagée dans la partie supérieure du sous-ensemble 2a, pour obtenir une continuité de blindage en position abaissée (c'est-à-dire lorsque la seringue 6 est centrée dans le puits de mesure 3' de l'activimètre 3).

L'enceinte blindée 2 comporte encore des ouvertures appropriées pour le passage des tubulures 23 et 24 reliées, respectivement, à la poche de sérum physiologique 16 et au cathéter 17.

Les principales étapes mises en œuvre au sein de l'unité médicale 1, pour la préparation d'une dose déterminée de produit radioactif, puis son injection au patient, sont détaillées ci-dessous.

Tout d'abord, la dose de produit radioactif à injecter au patient est préparée au sein de la seringue 6.

Pour cela, la seringue 6 (avec son piston 8 en position basse) et la source de produit radioactif 11 sont connectées à la vanne trois voies 15 ; ensuite, cette vanne 15 est pilotée de sorte que ses voies supérieure 18 et inférieure 19 soient raccordées hydrauliquement, permettant la mise en communication respectivement de l'aiguille de seringue 9 avec la source 11 de produit radioactif.

Le piston de seringue 8 est ensuite manœuvré, vers le haut, pour aspirer la dose voulue de produit radioactif dans le corps de seringue 7, qui est mesurée en temps réel par l'activimètre 3. Cette dose est notamment fonction du poids du patient.

La dose préparée au sein de la seringue peut ensuite être administrée au patient.

A cet effet, la vanne 15 est à nouveau pilotée, cela de sorte que ses voies supérieure 18 et latérale 22 soient respectivement en communication avec l'aiguille de seringue 9, et avec les tubulures 23 et 24 (connectées à la poche 16 de sérum physiologique et au cathéter d'injection 17).

Avant la phase d'injection proprement dite, le piston de seringue 8 peut, si nécessaire, être piloté (vers le haut) pour aspirer un volume complémentaire de sérum physiologique provenant de la poche 16 ; ce volume de sérum permet de diluer le produit radioactif, et aussi d'obtenir un volume d'injection suffisant.

La seringue 6 est ensuite vidangée par le déplacement adapté du piston de seringue 8 (vers le bas). Le produit radioactif, éventuellement dilué par le volume complémentaire de sérum physiologique, chemine alors au travers de la tubulure 24 où il est filtré par les dispositifs 36, puis le long du cathéter d'injection 17 jusqu'au patient.

Suite à cette phase d'injection, l'opérateur peut éventuellement mettre en œuvre une phase complémentaire de rinçage du corps de seringue 7, de la vanne 15, et des conduites aval 17 et 24, avec un volume adapté de sérum physiologique pour assurer l'administration au patient de la totalité de la dose radioactive souhaitée.

A cet effet, le piston de seringue 8 est manœuvré successivement en aspiration (vers le haut) pour prélever un volume déterminé de sérum physiologique en provenance de la poche 16, puis manœuvré en éjection (vers le bas) pour éjecter ce volume au travers de la conduite 24 et du cathéter d'éjection 17.

Lorsque l'opérateur souhaite remplacer la seringue 6 ou la source de produit radioactif 11, il lui suffit de manœuvrer leurs structures supports respectives 10 et 13.
A titre indicatif, la seringue 6 et la vanne 15 avec ses différentes conduites peuvent être remplacées suite à chaque injection. La seringue 6, d'une part, et la vanne 15 avec son aiguille 20, ses tubulures 23, 24, la poche de sérum physiologique 16 et le cathéter 17, d'autre part, constituent un ensemble stérile à usage unique, remplaçable très facilement après chaque utilisation.

Les différents cycles précités de prélèvement, de dilution et d'injection de ce matériel sont gérés par des moyens de commande électroniques/informatiques de type automate programmable, aptes à piloter automatiquement les moyens de manœuvre 34 du piston de seringue 8 et la vanne trois voies 15, de manière appropriée.
L'ensemble de ces cycles peut être totalement automatisé. En fonction des besoins, ou des souhaits de l'utilisateur, l'injection de la dose radioactive au patient peut aussi être réalisée manuellement grâce aux moyens débrayables du motoréducteur 34.

Une forme particulièrement intéressante de l'unité médicale illustrée schématiquement sur la figure 1, est représentée sur la figure 2.

Sur cette figure 2, l'enceinte blindée 2 qui intègre l'ensemble du matériel fonctionnel décrit ci-dessus, est montée sur un châssis équipé de quatre roues 40. De préférence, certaines au moins des roues 40 sont associées à une motorisation, constituant une simple assistance aux déplacements, ou assurant elle-même le déplacement autonome de l'unité mobile, pilotée à distance par un boîtier à manette adapté.

L'unité mobile 1 peut aussi intégrer un système de géolocalisation, par exemple de type GPS, pour connaître en permanence son positionnement à distance dans un bâtiment.

Dans la partie inférieure de l'enceinte 2, on remarque la présence d'une trappe blindée 41 donnant accès à l'intérieur de la sous-enceinte 2c, pour le chargement ou le déchargement sur son support 13 du conteneur blindé 12 renfermant la source de produit radioactif 11 (en particulier lorsque ce support 13 est en position basse de chargement/déchargement).

Dans la partie supérieure, on remarque le support de seringue 10, la poche de sérum physiologique 16 accrochée à un support 42, ainsi qu'un tableau 43 de commande et de visualisation, à écran tactile, intégrant l'automate programmable de gestion des cycles, ou en relation directe avec celui-ci (par exemple déporté au sein du châssis de l'unité). Ce tableau de commande, de dialogue et de visualisation 43

permet d'effectuer les opérations de calibration (mesure d'activité), et la visualisation en temps réel des diverses phases de préparation du transfert (dilution ...) et d'injection du produit radioactif.

Les moyens de commande électroniques/informatiques correspondants sont équipés d'une connectique 44 pour l'envoi et/ou la réception de données, en particulier pour réaliser certains échanges avec un serveur informatique situé à proximité ou à distance (par exemple par l'intermédiaire d'un réseau intranet ou du réseau internet), notamment pour réaliser une télémaintenance à distance et collecter certaines données concernant le patient (nécessaires notamment à la détermination de la dose de radioéléments qui doit lui être administrée).

Le châssis de l'unité 1 porte également des moyens propres d'énergie, par exemple de type batteries rechargeables, assurant l'alimentation électrique notamment des roues motorisées 40 et des moyens de commande électroniques/informatiques.

Cette unité mobile blindée 1 constitue une unité autonome permettant la calibration et l'injection de tous produits radioactifs (en particulier de FDG). Elle est très compacte du fait de la superposition de l'activimètre, de la vanne trois voies et de la source de produit radioactif sur le même axe vertical ou sensiblement sur le même axe vertical, et du fait de la superposition des sous-enceintes 2a, 2b et 2c. Cette unité permet un prélèvement, une mesure et une injection en toute sécurité.

- REVENDICATIONS -

1.- Unité médicale pour le prélèvement, le calibrage, la dilution et/ou l'injection d'un produit radioactif, injectable à un patient, laquelle unité (1) comprend au moins :

- des moyens (13) pour le support d'un conteneur (12) en matériau radioprotecteur dans lequel est logée une source ou un générateur de produit radioactif injectable (11),
- des moyens (10) pour le support d'une seringue (6) équipée d'un piston (8),
- un dispositif (3) de type activimètre pour la mesure en temps réel de l'activité radio-isotopique émise par le contenu de ladite seringue (6), et
- un système de conduites (9, 20, 23, 24) associé à au moins une vanne (15) pour le raccordement hydraulique de ladite source radioactive (11), de ladite seringue (6), d'une source de sérum physiologique (16) et d'un cathéter d'injection (17) destiné à être connecté au patient,

ladite vanne (15) et ledit piston de seringue (8) étant manœuvrables pour assurer, d'une part, une aspiration dudit produit radioactif (11) ou dudit sérum physiologique (16) au sein de ladite seringue (6), et d'autre part, une éjection dudit produit radioactif (11), dudit sérum physiologique ou d'un mélange de ces deux produits, préalablement aspiré(s) au sein de ladite seringue (6), cela au travers dudit cathéter d'injection (17), la dose de produit radioactif prélevée et injectée par ladite seringue (6) étant mesurée par ledit activimètre (3),

caractérisée en ce qu'elle comporte une enceinte blindée (2) réalisée en au moins un matériau radioprotecteur, dans laquelle sont logés ledit support (13) de source radioactive (11), au moins une partie des moyens supports (10) de la seringue (6), ledit activimètre (3), ladite vanne (15) et au moins une partie dudit système de conduites (9, 20, 23, 24), et en ce que ledit support de seringue (10), ladite vanne (15) et ledit support (13) de source radioactive (11) sont agencés verticalement les uns par rapport aux autres, respectivement du haut vers le bas, ledit support de seringue (10) étant agencé pour porter ladite seringue (6) avec son piston (8) orienté vers le haut.

2.- Unité médicale selon la revendication 1, caractérisée en ce que la vanne (15) consiste en une vanne trois voies comprenant :

- une voie supérieure (18), destinée à être raccordée à la seringue (6) de prélèvement et d'injection,
- une voie inférieure (19), destinée à être raccordée à la source de produit radioactif injectable (11), et
- une voie latérale (22), destinée à être raccordée à une première conduite (23) connectée à la source de sérum physiologique (16) et à une seconde conduite (24)

connectée au cathéter d'injection (17), lesdites conduites (23, 24) étant équipées chacune d'un clapet anti-retour (25, 26) convenablement orienté.

3.- Unité médicale selon la revendication 2, caractérisée en ce que l'activimètre (3) a une forme générale tubulaire délimitant un puits central (3') d'axe vertical, destiné à contenir la seringue (6), ledit activimètre (3) étant muni de deux ouvertures, l'une supérieure (4) et l'autre inférieure (5), cette dernière étant orientée en regard de la vanne trois voies (15) et du support (13) de la source radioactive (11).

4.- Unité médicale selon l'une quelconque des revendications 2 ou 3, caractérisée en ce que la voie supérieure (18) de la vanne (15), destinée à être raccordée à la seringue (6), comporte un opercule hermétique destiné à être percé par l'aiguille (9) équipant ladite seringue (6).

5.- Unité médicale selon l'une quelconque des revendications 2 à 4, caractérisée en ce que la voie inférieure (19) de la vanne (15), destinée à être raccordée à la source de produit radioactif injectable (11), est prolongée par une aiguille (20) destinée à percer un opercule (21) obturant le flacon contenant ladite source radioactive (11).

6.- Unité médicale selon l'une quelconque des revendications 1 à 5, caractérisée en ce que les supports (13, 10) de source radioactive (11) et de seringue (6) sont portés chacun par des moyens assurant leur(s) déplacement(s) selon un axe vertical ou sensiblement vertical, cela entre deux positions :

- une première position, dans laquelle un opérateur peut charger la source radioactive (11) et la seringue (6) sur leurs supports respectifs (13, 10), ou à l'inverse les décharger, et
- une seconde position dans laquelle la source radioactive (11) et la seringue (6) sont raccordées à la vanne (15).

7.- Unité médicale selon la revendication 6, caractérisée en ce que les moyens de déplacement du support de seringue (10) permettent son cheminement verticalement au travers d'un orifice (39) ménagé dans l'enceinte blindée (2), entre :

- une position supérieure de chargement/déchargement, dans laquelle ledit support (10) se situe au moins partiellement hors de ladite enceinte (2), et
- une position inférieure de raccordement, dans laquelle la seringue (6) se positionne au sein du puits central (3') de l'activimètre (3) et est raccordée à la vanne (15).

8.- Unité médicale selon l'une quelconque des revendications 6 ou 7, caractérisée en ce que le support (13) de source radioactive (11) chemine au sein de l'enceinte blindée (2) entre ses positions de chargement/déchargement et de

raccordement, ladite enceinte (2) étant encore munie d'une trappe (41) frontale pour permettre l'accès d'un opérateur audit support (13) de source radioactive (11) au moins dans sa position de chargement/déchargement.

9.- Unité médicale selon l'une quelconque des revendications 1 à 8, caractérisée en ce qu'elle comprend encore des moyens de commande informatiques et/ou électroniques aptes à piloter la vanne (15) et les moyens (33, 34) de manœuvre du piston de seringue (8), cela de manière à mettre en œuvre les opérations de prélèvement et d'éjection par ladite seringue (6), lesquels moyens de commande informatiques/électroniques pilotent également éventuellement les moyens de déplacement du support de seringue (10) et du support de source radioactive (13).

10.- Unité médicale selon la revendication 9, caractérisée en ce que les moyens de manœuvre du piston (8) de la seringue (6) sont de type motoréducteurs débrayables (34), contrôlés par les moyens de commande informatiques/électroniques, pour assurer, d'une part, le prélèvement automatique d'une dose déterminée de produit radioactif au sein de ladite seringue (6), et d'autre part, pour assurer l'injection de cette dose au patient, soit automatiquement, soit manuellement.

11.- Unité médicale selon l'une quelconque des revendications 1 à 10, caractérisée en ce que l'enceinte (2) se compose de trois sous-enceintes (2a, 2b, 2c) alignées verticalement les unes par rapport aux autres, à savoir - une sous-enceinte supérieure (2a) contenant la seringue (6) et l'activimètre (3), - une sous-enceinte intermédiaire (2b) contenant la vanne (15), et - une sous-enceinte inférieure (2c) contenant la source de produit radioactif (11), lesquelles sous-enceintes (2a, 2b, 2c) sont raccordées deux à deux par des ouvertures traversantes (37, 38) au travers desquelles passent certaines des conduites (9, 20) de raccordement hydraulique.

12.- Unité médicale selon l'une quelconque des revendications 1 à 11, caractérisée en ce que les moyens de commande informatiques/électroniques sont pourvus d'une connectique (44) pour l'envoi et/ou la réception de données, en particulier pour les échanges avec un serveur informatique.

13.- Unité médicale selon l'une quelconque des revendications 1 à 12, caractérisée en ce qu'elle est montée sur des roues (40) pour la rendre mobile, et en ce qu'elle intègre éventuellement un système de géolocalisation, par exemple de type GPS.

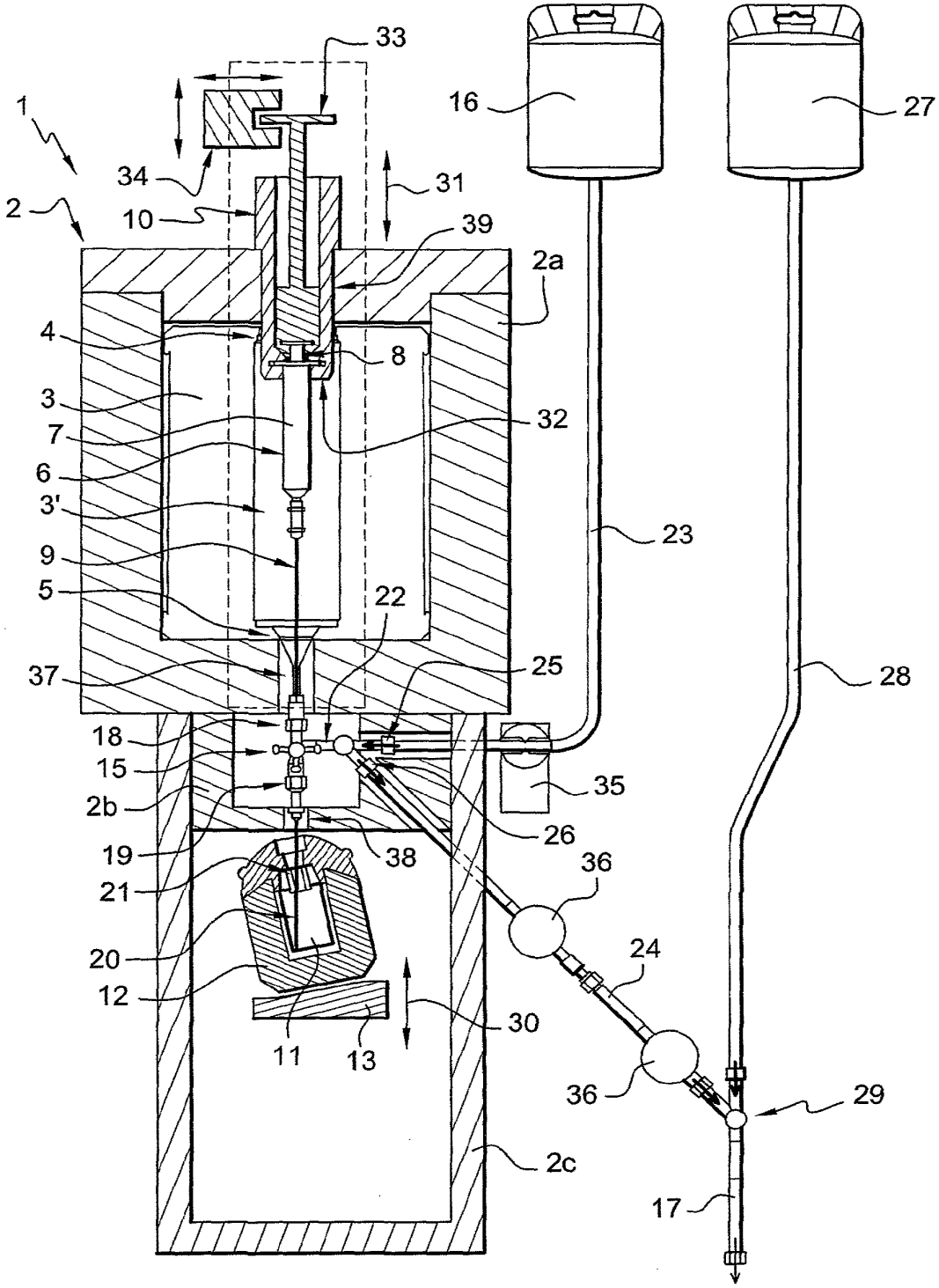
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Fig. 1

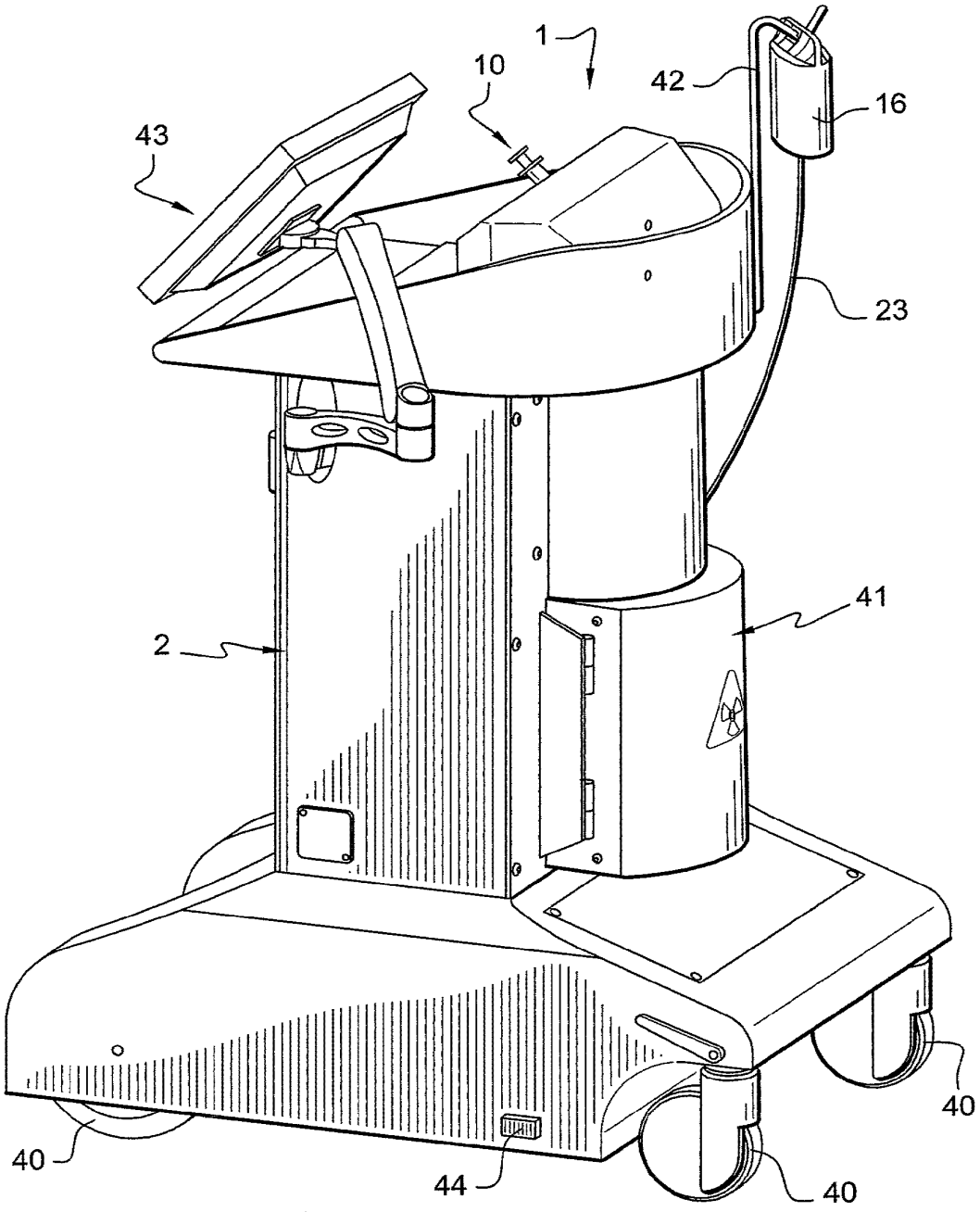

Fig. 2

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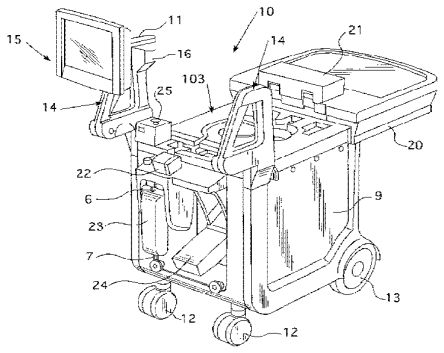

(57) Abstract: A fluid path set for a fluid delivery system includes a tube coil that is designed to optimally position one or more volumes of a pharmaceutical within an ionization chamber to optimally measure and prepare a pharmaceutical dose for administration to a patient. The tube coil may be maintained in a desired dimensional geometry by means of a core structure around which the tube coil is positioned. Novel developments in radiopharmaceutical administration methods and systems include, but are not limited to, the configuration and layout of a fluid path set for use in a fluid delivery system, arrangements for piercing and drawing fluid from a pharmaceutical container (such as a vial), arrangements for optimizing the positioning of a tube coil within an ionization chamber, a handling system for transporting vial shields that maintain an operator's hand and fingers at a safe distance from a pharmaceutical vial, a method for calibrating a radiopharmaceutical delivery system in which the difference between the expected and measured activities of two radioisotopes are used to calculate an estimated error in the measured activity of a third radioisotope and a vial access system that ensures an optimal draw of fluid from a radiopharmaceutical container.

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RADIOPHARMACEUTICAL ADMINISTRATION METHODS, FLUID DELIVERY SYSTEMS AND COMPONENTS THEREOF

BACKGROUND OF THE INVENTION

[1] The present invention relates to methods, systems and components thereof for delivering pharmaceutical substances to patients for imaging procedures and, more particularly, for delivering radiopharmaceuticals to patients for positron emission tomography (PET) or single-photon emission computerized tomography (SPECT) procedures.

[2] PET and SPECT are noninvasive, three-dimensional, imaging procedures that provide information regarding physiological and biochemical processes in patients. PET and SPECT images of, for example, the brain or another organ, are produced by injecting the patient with a dose of a radiopharmaceutical (using, for example, fluid delivery systems such as those disclosed in U.S. Patent No. 6,767,319, JP Publication Nos. 2000-350783 and 2002-306609 and PCT Publication Nos. WO 2004/091688, WO 2006/007750 and 2004/004787, the disclosures of which are incorporated herein by reference) and then creating an image based on the radiation emitted by the radiopharmaceutical. The radiopharmaceutical generally includes a radioactive substance, such as a radioisotope, that can be absorbed by certain cells in the brain or other organs, concentrating it there.

[3] Radioisotopes, especially those with short half-lives, can be relatively safely administered to patients in the form of a labeled substrate, ligand, drug, antibody, neurotransmitter or other compound or molecule that is normally processed or used by the body (for example, glucose). The radioisotope acts as a tracer of specific physiological or biological processes. For example, fluorodeoxyglucose (FDG) is a normal molecule of glucose, the basic energy fuel of cells, to which is attached a radioisotope or radioactive fluor (i.e., F-18). The F-18 radioisotope is produced in a cyclotron equipped with a unit to synthesize the FDG molecule.

[4] Cells (for example, in the brain) that are more active in a given period of time after an injection of FDG will absorb more FDG because they have a higher metabolism and require more energy. The F-18 radioisotope in the FDG molecule experiences a radioactive decay, emitting a positron. When a positron collides with an electron, annihilation occurs, liberating a burst of energy in the form of two beams of gamma rays in opposite directions. The PET scanner detects the emitted gamma rays to compile a three dimensional image.

[5] To allow for cell uptake of the radiopharmaceutical, the patient typically rests for a period of time (45-90 minutes for FDG) after the radiopharmaceutical is injected. After sufficient time for cell uptake has elapsed, the patient is typically placed on a movable bed that slides into the PET (or SPECT or other suitable) scanner. The PET scanner includes several rings of radiation detectors. Each detector emits a brief pulse of light every time it is struck with a gamma ray coming from the radioisotope within the patient's body. The pulse of light is amplified, by for example a photomultiplier, and the information is sent to the computer for forming images of the patient.

[6] To minimize the radiation dose to patients, radiopharmaceuticals containing radioisotopes, such as Flourine-18, Technetium-99, Carbon-11, Copper-64, Gallium-67, Iodine-123, Nitrogen-13, Oxygen-15, Rubidium-82, Thallium-201, Chromium-51, Iodine-131, Iodine-151, Iridium-192, Phosphorus-32, Samarium-153, and Yttrium-90, having relatively short half-lives are typically used for PET and SPECT imaging procedures and other radio-therapies. F-18, for example, has a half-life of 109.7 minutes.

[7] Because of its short half-life, the radioactivity level of the radioisotope will quickly decrease after it is manufactured in a cyclotron or a reactor. Consequently, the elapsed time (and corresponding decrease in radioactivity level of the radioisotope) after synthesis of the radiopharmaceutical must be factored into calculating the volume of radiopharmaceutical required to be injected into the patient to deliver the desired radioactivity dose. If the time delay after synthesis is long in relation to the radioisotope's half-life or if the calculated volume of radiopharmaceutical to be injected into the patient is insufficient to deliver the desired radioactivity dose, the delivered radioactivity dose may be too low to provide diagnostic-quality images, resulting in wasted time and effort and exposing the patient and medical personnel to unnecessary radiation.

[8] Further, long-term radiation exposure to technologists and other personnel working in the scanner room can pose a significant health risk. Although the half-life of the radiopharmaceutical is rather short and the applied dosages are considered an acceptable risk to the patient, under current procedures administering personnel are exposed each time they work with the radiopharmaceuticals and other contaminated materials, such as tubing and syringes, used to inject the radiopharmaceuticals into patients. Constant and repeated exposure over an extended period of time can be harmful.

[9] A number of techniques are used to reduce radiation exposure to medical personnel, including minimizing the time of exposure of personnel, maintaining distance between personnel and the source of radiation and shielding personnel from the source of radiation. In general, the radiopharmaceuticals are typically delivered to a nuclear medicine hospital suite or other medical facility from a radiopharmaceutical synthesis facility (within or outside the hospital or medical facility) equipped with a cyclotron in, for example, a lead-shielded container (often called a "PIG"). Often, the radiopharmaceutical is manually drawn from such containers into a shielded syringe. See, for example, U.S. Pat. No. 5,927,351, disclosing a drawing station for handling radiopharmaceuticals for use in syringes. Remote injection mechanisms can also be used to maintain distance between the operator and the radiopharmaceutical. See, for example, U.S. Pat. No. 5,514,071, disclosing an apparatus for remotely administering radioactive material from a lead encapsulated syringe. Nevertheless, these current procedures and systems still result in unnecessary and repeated exposure of technicians and other medical personnel to radiation.

[10] It has long been recognized as very desirable to develop devices, systems, components and methods for calculating and delivering accurate and effective doses of radiopharmaceuticals to patients, while reducing the exposure of administering or other medical personnel to such hazardous pharmaceuticals.

SUMMARY OF THE INVENTION

[11] The present invention broadly contemplates and provides devices, systems, components and methods for accurately calculating or delivering effective doses of pharmaceuticals to patients.

[12] In a first aspect, the invention provides a fluid path set including a tube coil that is designed to optimally position one or more volumes of a pharmaceutical within an ionization chamber to optimally measure and prepare a pharmaceutical dose for administration to a patient. The tube coil may be maintained in a desired dimensional geometry by means of a core structure around which the tube coil is positioned or coiled.

[13] The fluid path set includes a medical fluid component comprising a first tubing section for connection to a source of a medical fluid, a pharmaceutical component comprising a second tubing section for connection to a source of a pharmaceutical, a coil assembly component comprising a tube coil having a height of approximately 1.53 inches, a diameter of approximately 1.95 inches and a volume capacity of

approximately 12.5 ml, and a connector comprising a first port for connecting the first tubing section of the medical fluid component, a second port for connecting the second tubing section of the pharmaceutical component and a third port for connecting the tube coil of the coil assembly component.

[14] In a second aspect, the present invention provides a vial access system for inserting a cannula into a pharmaceutical container, such as a vial. The vial access system includes structures that shields the operator from exposure to hazardous pharmaceuticals, such as radiopharmaceuticals, and is designed with an inclined bottom surface to tilt the pharmaceutical container from the horizontal and thereby allow the cannula to optimally extract the pharmaceutical from the container.

[15] The vial access system includes a base portion comprising a substantially horizontal lower surface and a sloped upper surface adapted to support a vial comprising a bottom wall and a substantially cylindrical wall connected thereto. The sloped upper surface is adapted to ensure that a residual volume of fluid in the vial gathers in an area defined at least partially by a portion of the junction between the bottom wall and the cylindrical wall of the vial.

[16] In a third aspect, the present invention provides a vented cannula for insertion into a pharmaceutical container, such as a vial. The vented cannula may be used in the vial access system of the present invention or may be fluidly connected to a shielded syringe to provide an alternate fluid delivery system.

[17] The vented cannula includes a main hub comprising two opposed lateral sides and defining a fluid port and a vent, a fluid draw needle in connection with the fluid port and adapted to be placed within the container, a vent needle in connection with the vent and adapted to be placed within the container; and two resilient arms connected to the opposed lateral sides of the main hub. Each of the two arms includes a top edge and a hook member formed thereon and extending outwardly therefrom.

[18] In a fourth aspect, the present invention provides a fluid delivery system having a retractable shielded cover to shield operators of the system from the fluid path components and the pharmaceutical contained therein. In another aspect, the fluid path components and the pharmaceutical may be disposed in a slidable drawer that may be removed from the shielded system to allow access thereto.

[19] The fluid delivery system includes a housing having an upper surface defining a plurality of recessed portions for accommodating one or more components of a fluid path set, a cover movably connected to the housing and a locking mechanism

associated with the cover. The cover is adapted to move between a first position that exposes the upper surface and a second position that overlies the upper surface, and the locking mechanism is adapted to lock the cover in the second position.

[20] In another aspect, the fluid delivery system includes a syringe comprising a body defining a discharge outlet and a plunger movably disposed within the body, a connector comprising a valve member and defining first, second and third ports, a first tubing segment connected between the discharge outlet of the syringe and the first port of the connector, a cannula defining a fluid port, a second tubing segment connected between the fluid port of the cannula and the second port of the connector, a third tubing segment comprising a first end connected to the third port of the connector and a second end comprising a second connector, and a per-patient tubing set comprising a first end that is adapted to be connected to the second connector on the second end of the third tubing segment and a patient end that is adapted to be connected to venous access device in a patient.

[21] In a fifth aspect, the present invention provides a method of priming the fluid path components of the fluid delivery system to remove air therefrom and to prepare the system to administer a pharmaceutical dose to a patient.

[22] A method of priming at least a portion of a fluid path set in a fluid delivery system includes: (1) placing a tubing section of the fluid path set in fluid connection with a source of a radiopharmaceutical; (2) placing a portion of the tubing section within a dose calibrator of the fluid delivery system; (3) pumping a volume of the radiopharmaceutical through the tubing section; (4) monitoring the dose calibrator to determine if a measured activity level is substantially equal to or above a predetermined activity level; and (5) if the measured activity level is substantially equal to or above the predetermined activity level, then concluding that the tubing section of the fluid path set has been primed.

[23] In a sixth aspect, the present invention provides a carrying system for connecting to and transporting a vial shield (containing a pharmaceutical vial). The carrying system may be used to transport the vial shield to and place the vial shield within the fluid delivery system of the present invention. In another aspect, the carrying system may be used to position the vial shield within the vial access device of the present invention.

[24] The vial shield carrying system includes a collar unit adapted to removably engage a flange on the vial shield and a handle unit adapted to engage the collar unit. The collar unit defines two elongated slots formed in a top surface thereof, each of the

slots including a pin disposed therein and extending between two opposing walls thereof. The handle unit includes a handle connected to a U-shaped cross piece that defines two, downwardly extending arms having hook members formed therein. The open ends of the hook members are formed on opposite ends of the arms and are adapted to engage the pins in the slots of the collar unit through rotation of the handle.

[25] In a seventh aspect, the present invention provides a system and a method for calibrating a radiopharmaceutical delivery system in which the difference between the expected (based on decay from the initial activity) and measured activities of two radioisotopes are used to calculate an estimated error in the measured activity of a third radioisotope. In response to a difference between the expected and measured activity of the first or the second radioisotope, the gain of the ionization chamber is adjusted to eliminate or reduce the error for that radioisotope. When the estimated error of the third radioisotope falls within an acceptable range, the activity of the third radioisotope is measured to check that the actual error between the expected and measured activity of the third radioisotope is substantially similar to the estimated error.

[26] Preferably, the energy levels of the first, second and third radioisotopes are less than, greater than, and relatively close to, respectively, the energy level of the radioisotope to be delivered by the system to the patient. In addition, the operator may take consecutive measurements of the first and second radioisotopes (i.e., in an iterative fashion) and adjust the gain of the ionization chamber in response thereto, before measuring the activity of the third radioisotope and comparing it against the estimated error of the third radioisotope.

[27] A method of calibrating includes (1) measuring an activity level of a first radioisotope in an ionization chamber of the fluid delivery system, the first radioisotope having an energy level less than that of the radioisotope to be delivered to the patient; (2) comparing the measured activity level of the first radioisotope to an expected activity level of the first radioisotope; (3) adjusting the gain of the ionization chamber to compensate for the difference, if any, between the measured activity and the expected activity of the first radioisotope; (4) measuring an activity level of a second radioisotope in the ionization chamber of the fluid delivery system, the second radioisotope having an energy level similar to or greater than that of the radioisotope to be delivered to the patient; (5) comparing the measured activity level of the second radioisotope to an expected activity level of the second radioisotope; (6) adjusting the gain of the ionization chamber to compensate for the difference, if

any, between the measured activity and the expected activity of the second radioisotope; and (7) calculating an estimated error in a measured activity of a third radioisotope based on the differences, if any, between the measured activity and the expected activity of the first radioisotope and the measured activity and the expected activity of the second radioisotope.

[28] Broadly contemplated herein are improvements in radiopharmaceutical administration methods and systems. These inventions include, but are not limited to, the configuration and layout of a fluid path set for use in a fluid delivery system, arrangements for piercing and drawing fluid from a radiopharmaceutical container (such as a vial), arrangements for optimizing the positioning of a tube coil within an ionization chamber, a handle / carrying system for transporting vial shields or "pigs" that keeps an operator's hand and fingers at a safe distance from a vial access cap, and a vial access system that ensures an optimal draw of fluid from a radiopharmaceutical container.

[29] The novel features which are considered characteristic of the present invention are set forth herebelow. The invention itself, however, both as to its construction and its method of operation, together with additional objects and advantages thereof, will be best understood from the following description of the specific embodiments when read in connection with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[30] For the present invention to be clearly understood and readily practiced, the present invention will be described in conjunction with the following figures, wherein like reference characters designate the same or similar elements, which figures are incorporated into and constitute a part of the specification.

[31] Fig. 1A is a perspective view of a fluid delivery system of the present invention.

[32] Fig. 1B is another perspective view of the fluid delivery system of Fig. 1A with the shielded cover thereof in a retracted position.

[33] Fig. 1C is a top plan view of the fluid delivery system shown in Figs. 1A and 1B with various fluid path components positioned therein.

[34] Fig. 1D is a cross-sectional view taken along line 1D-1D of Fig. 1A.

[35] Fig. 1E is a cross-sectional view taken along line 1E-1E of Fig. 1A.

[36] Fig. 2A is a schematic illustration of the multi-patient fluid path set and components thereof of the present invention.

[37] Fig. 2B is an exploded view showing the multi-patient fluid path set shown in Fig. 2A connected to a fluid source and disposed above the fluid delivery system shown in Figs. 1A-1E.

[38] Fig. 2C is a perspective view of an alternate embodiment of the multi-patient fluid path set of the present invention.

[39] Fig. 3A is an elevational view of a preferred embodiment of a coil assembly of the present invention.

[40] Fig. 3B is a partial cross-sectional view of Fig. 3A.

[41] Fig. 3C is a plan view (in partial cross-section) taken along line 3C-3C of Fig. 3A.

[42] Fig. 3D is a cross-sectional view taken along line 3D-3D of Fig. 3A.

[43] Fig. 3E is a perspective view of the core element of the coil assembly shown in Fig. 3A.

[44] Fig. 3F is an enlarged view of Fig. 1D showing the coil assembly in the ionization chamber of the fluid delivery system.

[45] Fig. 4A is an elevational view of preferred embodiments of a vial shield carrying system and a vial access system of the present invention.

[46] Fig. 4B is a perspective view showing the vial shield, the vial shield carrying system and the vial access system of Fig. 4A.

[47] Fig. 4C is an elevational view of a pharmaceutical vial that may be used in the fluid delivery system of the present invention.

[48] Figs. 5A-5D are various views of an alternate embodiment of a vial shield carrying system of the present invention.

[49] Fig. 6A is a bottom perspective view of a preferred embodiment of a vial access system of the present invention.

[50] Fig. 6B is a top perspective view of the vial access system shown in Fig. 6A.

[51] Fig. 6C is an exploded, perspective view of a preferred embodiment of the vented cannula of the multi-patient fluid path set of the present invention oriented to be connected to the cap of the vial access system shown in Figs. 6A-6B.

[52] Fig. 6D is a perspective view (similar to Fig. 4B) showing the vial access system and the vial-carrying shield disposed in a well of the fluid delivery system, and the vented cannula connected to the cap of the vial access system and in position to be lowered and inserted through the septum cap of the vial shield into the radiopharmaceutical vial.

[53] Fig. 6E is another perspective view (similar to Fig. 6D) showing the cap of the vial access system lowered into position and the vented cannula thereby inserted into the pharmaceutical vial.

[54] Fig. 6F is an enlarged view of Fig. 1E showing the vial access system and the vented cannula of the present invention.

[55] Fig. 6G is a perspective view of the vented cannula shown in Fig. 6C.

[56] Fig. 6H is an elevational view of the vented cannula shown in Fig. 6G.

[57] Fig. 6I is a left-side view of the vented cannula shown in Fig. 6H.

[58] Fig. 6J is a right-side view of the vented cannula shown in Fig. 6H.

[59] Fig. 7 shows a main screen of a graphical user interface of the present invention.

[60] Figs. 8, 9, 10, 11, 12A, 12B, 13, 14, 15, 16A, 16B, 17, 18, 19, 20, 21 and 22 are various depictions of a graphical user interface for use in system preparation tasks.

[61] Figs. 23, 24A-F, 25A, 25B, 26A, 26B, 27A, 27B, 28A, 28B, 29, 30A, 30B, 31, 32A and 32B are various depictions of a graphical user interface for use in patient treatment tasks.

[62] Figs. 33A-C, 34A and 34B are various depictions of a graphical user interface for use in injection history/recall operations or tasks.

[63] Figs. 35, 36, 37, 38, 39A, 39B, 40, 41, 42, 43, 44A-D, 45A-D and 46 are various depictions of a graphical user interface for use in system configuration tasks.

[64] Fig. 47A is a perspective view of the vented cannula shown in Figs. 6C and 6G-6J being utilized as part of a first alternate fluid delivery system.

[65] Fig. 47B is another perspective view showing the first alternate fluid delivery system of Fig. 47A.

[66] Fig. 47C is an elevational view of the first alternate fluid delivery system of Figs. 47A and 47B.

[67] Fig. 48 is a perspective view of the vented cannula shown in Figs. 6C and 6G-6J being utilized as part of a second alternate fluid delivery system.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[68] As used herein, the term "pharmaceutical" refers to any substance or drug to be injected or otherwise delivered into the body (either human or animal) in a medical procedure and includes, but is not limited to, substances used in imaging procedures (for example, contrast media) and therapeutic substances. A number of such pharmaceutical substances pose a danger to both the patient and the personnel administering the substance if not handled and/or injected properly. Examples of hazardous pharmaceuticals include, but are not limited to, radiopharmaceuticals, biological pharmaceuticals, chemotherapeutic pharmaceuticals and gene therapeutic pharmaceuticals.

[69] Turning now to the drawings, Figs. 1A-1E show a preferred embodiment of the administration, injector or fluid delivery system 10 of the present invention. The fluid delivery 10 is preferably a cart-like apparatus 9 having wheels 13 and/or casters 12 for allowing the system to be movable. One or more of the wheels 13 may be lockable to prevent the system 10 from moving once it is in position. The system 10 also preferably includes one or more handles 14 for allowing an operator to move or position the system 10. Alternately, the fluid delivery system 10 may be a stand-alone or fixed-position apparatus.

[70] The fluid delivery system 10 includes a display or graphical user interface (GUI) 15 for programming and operating the system 10. The GUI display 15 is preferably attached to one of the handles 14 (as shown) of the system 10. The display 15 may be a color display and incorporate touch-screen capability, as known in the art, for ease of use. The display 15 may be fixed, but is preferably pivotally connected to the fluid delivery system 10 (as shown), by means of a movable arm 11 that is pivotally connected to a joint 16. Further, the display 15 may be tilted or swiveled with respect to the arm 11 to allow for optimal positioning of the display 15 by an operator.

[71] The fluid delivery system 10 preferably includes a retractable lid or cover 20 having a primary handle including a latch release 1 (see Figs. 1D and 1E) and a secondary handle 21. The lid 20 preferably covers an upper surface 103 that defines a number of recessed portions, such as wells and troughs, into which a vial or container (see 902 in Fig. 4C) of a pharmaceutical or a radiopharmaceutical (discussed in more detail below) and various components of a multi-patient fluid path set (hereinafter MPDS; discussed in more detail below) may be positioned during an injection procedure. A locking mechanism, such as a combination or a key lock (not shown), may be used to lock the lid 20 in a closed position to, for example, prevent use or access of the system 10 by unauthorized personnel. In another embodiment, the locking mechanism may be a software-implemented lock, such as a password-protected access point, that is accessible through the display 15 and is adapted to lock the cover in a closed position and/or to prevent unauthorized personnel from accessing or operating the system 10.

[72] The lid 20 is slidable or retractable (by, for example, using primary handle and latch release 1) with respect to the cart 9 to allow for insertion and removal of the vial or container 902 and MPDS from the fluid delivery system 10. The lid 20, upper surface 103 and various other portions of the cart 9 preferably include suitable radioactive shielding (such as lead) for minimizing potential radiation exposure from the radiopharmaceutical to the operator. In this manner, the radiopharmaceutical vial 902 and the components of the MPDS can lie below the plane of surface 103, whereupon the surface 103 or one or more portions thereof can be covered by the lid 20 during use to limit radiation exposure to the operator or other medical personnel. Further, instead of a retractable lid 20, surface 103 itself could be disposed on a portion of the injector apparatus 10 (e.g., a drawer-type mechanism) that slidably displaces with respect to a remainder of the injector apparatus 10.

[73] As further shown in Figs. 1A, 1B and 1D, the fluid delivery system 10 includes a pumping mechanism, such as a peristaltic pump 22, a removable/replaceable source of medical fluid 23 (such as saline), a printer 24 and an interrupt button 25. The peristaltic pump 22 is shown in a closed position in Fig. 1A, but may be opened (see Figs. 1B, 1C and 2B) to receive a length of tubing 27(see Figs. 1C and 2) in fluid connection with the source of medical fluid 23 to inject the fluid into a patient (discussed in more detail below). While a peristaltic pump 22 is currently preferred, any suitable type of pumping mechanism, such as a piston-driven syringe pump, gear pump, rotary pump or in-line pump, may be used.

[74] The printer 24 may be used to generate records of the injection and/or imaging procedures performed on patients, for inclusion in patients' medical records or for billing or inventory purposes. The printer 24 may be pivotally connected to the system 10 (see Fig. 1B) to allow an operator to load paper or labels into the printer 24.

[75] The interrupt button 25 allows an operator to quickly and easily pause or abort an injection procedure in the event of, for example, patient discomfort or an emergency, without having to resort to the GUI display 15 (which also can be manipulated to pause or abort an injection procedure). The interrupt button 25 may be connected to LEDs and/or a printed circuit board to provide visual and/or auditory alarms when the interrupt button 25 has been activated.

[76] Turning to Figs. 1C-1E, 2A and 2B, additional features and components of the fluid delivery system 10, including the upper surface 103, the MPDS 200, a vial access device 600 and a single-patient fluid path set 700 (hereinafter SPDS), will be discussed.

[77] As shown in Fig. 1C, the upper surface 103 generally defines wells and recesses or troughs into which various components of the MPDS are situated. Specifically, a first recess or trough 107 accommodates a first tubing section 204 of the MPDS 200 and a tubing holder 150 for holding the tubing section 204 and preventing it from getting kinked or tangled with, for example, the SPDS 700. The first tubing section 204 may also include the tubing length 27 that is placed within the peristaltic pump 22 and is in fluid connection with the medical fluid source 23.

[78] The first trough 107 leads into a second recess or trough 113 that accommodates a second pumping mechanism 180, such as a peristaltic pump, and a T-connector 205 (preferably including check valves 214, 215) of the MPDS 200. As shown in Fig. 1C, the second trough 113 also leads to a first well 111 that accommodates a vial access device 600 and a radiopharmaceutical vial or container 902 disposed in a vial shield or PIG 554 (discussed in more detail below) and to a second well 121 that accommodates a dose calibrator or ionization chamber 160 for the fluid delivery system 10. As shown in Figs. 1D and 3F, the ionization chamber 160 preferably accommodates a coil assembly 400 of the MPDS 200 (discussed in more detail below).

[79] A third recess or trough 125 extends from the second well 121 to a third well 127 and further along the surface 103 of the fluid delivery system 10. The trough 125 accommodates a T-connector 222 of the MPDS 200, two pinch valves 170, 172, an

air detector 174 and a mount or retainer 176 for holding the connector end 228 of the MPDS 200. The pinch valves are preferably powered and controlled by the fluid delivery system 10, but alternately could be manually-operated. In another alternate embodiment, the pinch valves 170, 172 and the T-connector 222 of the MPDS 200 may be replaced with a manual or automated 3-way stopcock.

[80] The third well 127 accommodates a waste receptacle or bag 224 for receiving medical fluid and/or pharmaceutical that is discarded during, for example, a priming procedure (discussed in more detail below) to prepare the system 10 for an injection procedure.

[81] As shown in Fig. 1C, the SPDS 700 includes a length of tubing (preferably coiled, as shown) having a first end 702 that is attachable to the connector end 228 of the MPDS 200 and a patient end 704 having a luer connector that is attachable to, for example, a catheter (not shown) placed in a venous structure of a patient. As discussed in more detail below, the MPDS 200 may be used for multiple patients but the SPDS 700 is intended to be used on a per-patient basis and discarded after use with a single patient to prevent, for example, cross-contamination between patients.

[82] As can be appreciated after reviewing Fig. 1A-1E, the secondary handle 21 of lid 20 overlies the tubing holder 150 and the mount 176 when the lid 20 and handle 21 are closed to cover the MPDS 200. The secondary handle 21 may be flipped open (from the closed position shown in Fig. 1A) without retracting the cover 20 to allow an operator to connect the SPDS 700 to the MPDS 200(as discussed in more detail below). As best shown in Fig. 1C, the SPDS 700 may be placed under the secondary handle 21 when it is closed.

[83] The fluid delivery system 10 further includes a system controller 5 (see Figs. 1D and 1E) in communication with the various components thereof, including the GUI 15, the pumps 22, 180, the dose calibrator or ionization chamber 160, the stop button 25, the air detector 176, the printer 24 and the motors 30, 31 (see Fig. 3F) for pinch valves 170, 172, respectively, for controlling the operation of the system 10. The system controller 5 is preferably a single-board computer, including a CPU having a main memory.

[84] As can be appreciated, the wells and troughs formed in the upper surface 103 can be sized, configured or arranged as suitable for the length, design or configuration of the MPDS 200 or other components thereof, including the radiopharmaceutical vial 902, vial shield 554, vial access device 600, ionization chamber 160, waste receptacle 224, etc.

[85] It should be understood that Fig. 1C in no way is intended to convey dimensions or relative dimensions of the aforementioned recessed portions or MPDS components; instead, Fig. 1C conveys general positional relationships of such recessed portions with respect to one another.

[86] It should further be understood and appreciated that the recessed portions shown and described with respect to Fig. 1C are preferably encased throughout with suitable radioactive shielding to further minimize exposure to an operator.

[87] Turning now to Figs. 2A and 2B, a preferred embodiment of the MPDS 200 and components thereof will be discussed. In addition, specific details of the coil assembly 400 employed in the MPDS 200 are shown and described with respect to Figs. 3A-3F and Fig. 1D.

[88] By way of a general overview, the MPDS 200 in accordance with at least one presently preferred embodiment of the present invention allows for FDG (or other radiopharmaceutical) to be drawn from a bulk radiopharmaceutical vial 902 and placed into a coil assembly 400 that allows an ionization chamber 160 to measure the amount of activity in the coil assembly 400. Once the system prepares a dose having the desired activity level, the fluid delivery system 10 will deliver the FDG dose to the patient (through the SPDS 700).

[89] Generally, the MPDS 200 can be considered in terms of four components: (1) a medical fluid or saline component; (2) an FDG or pharmaceutical component; (3) a coil assembly component; and (4) a waste component. The saline component preferably draws saline out of a bulk source 23 (e.g., via peristaltic pump 22). This is then used to prime the MPDS (i.e., remove air therefrom), position FDG in the coil assembly 400 in the ionization chamber 160, and then deliver the dose to the patient.

[90] The FDG component preferably serves to draw FDG out of a bulk radiopharmaceutical vial 902 (e.g., via peristaltic pump 180) and place the same into the fluid path to the ionization chamber 160.

[91] The coil assembly component preferably is employed to position the radiopharmaceutical to allow its radioactivity level to be optimally measured by the ionization chamber 160. Through the arrangement of the coil assembly 400 (as discussed in more detail below), the radiopharmaceutical can be optimally oriented and located within the "linear region" of the ionization chamber 160 to more accurately measure its activity level and prepare an optimal dose for injection into a patient.

[92] The waste component preferably holds the saline fluid and/or radiopharmaceutical that are discarded during the prime and dose preparation procedures, which are conducted to prepare the fluid path and the pharmaceutical dose for injection into a patient.

[93] Fig. 2A schematically illustrates the MPDS 200 in accordance with a preferred embodiment of the present invention. The MPDS shown in Fig. 2A may preferably be pre-connected as shown and may originally be stored in a sterile packet or container for use in an injector apparatus, such as fluid delivery system 10, when desired. For a non-restrictive and illustrative appreciation of a manner in which MPDS 200 can be incorporated in an injector apparatus, simultaneous reference may be made to Figs. 1A-1E and 2B (and the discussion thereof hereinabove).

[94] Primary components of MPDS 200 include, as shown, a spike 202 for connecting the MPDS to the medical fluid or saline source 23, a vented cannula 208 for connecting with a source of FDG or other radiopharmaceutical, a coil assembly 400, a T-connector 205 with check valves 214, 215 for fluidly connecting the saline source 23, the radiopharmaceutical source and the coil assembly 400, a waste bag 224, a connector end 228, and a T-connector 222 for fluidly connecting the coil assembly 400, the waste bag 224 and the connector end 228.

[95] In general, MPDS 200 and fluid delivery system 10 are configured for priming (i.e., purging air from) the MPDS 200, delivering pharmaceutical (e.g., FDG) to a patient, and providing a saline flush, while minimizing or eliminating exposure of administering or operating personnel to the detrimental effects of the pharmaceutical and minimizing or eliminating creation of contaminated waste. Moreover, MPDS 200 and other elements of the present invention also facilitate safe delivery of the pharmaceutical to multiple destinations (for example, dose delivery to a series of patients).

[96] A T-connector 205 and check valves 214, 215 preferably accommodate a first tubing section 204 that is in fluid connection with spike 202 and a second tubing section 210 in fluid connection with cannula 208. The check valves 214, 215 may be integrally formed with the T-connector 205 or may be separate components, or they could be combined into a single dual check valve. The check valves 214, 215 prevent saline from being pumped by peristaltic pump 22 into second tubing section 210 and the pharmaceutical from being pumped by peristaltic pump 180 into the first tubing section 204.

[97] A third tubing section 216 thence preferably leads to coil assembly 400 (including tube coil 444), and a fourth tubing section 220 preferably leads from the coil assembly 400 to the T-connector 222. As described below, in a preferred embodiment the tube coil 444 is formed from a tubing section 217 that has dimensions different from those of the third tubing section 216 and the fourth tubing section 220. In an alternate embodiment, the third tubing section 216, the tube coil 444 and the fourth tubing section 220 are formed from the same length of tubing.

[98] A fifth tubing section 226 leads from the T-connector 222 to the waste receptacle 224 and a sixth tubing section 230 leads from the T-connector 222 to the connector end 228. As shown above in Fig. 1C, the connector end 228 mates with the first end 702 of the SPDS 700 for delivery of a pharmaceutical to a patient.

[99] In a preferred embodiment, the connector end 228 is a swabable luer valve (Part No. 245204024 provided by Halkey-Roberts Corporation of St. Petersburg, FL) that is biased to close or seal off the connector end 228 of the MPDS 200 when the SPDS 700 is not connected thereto. The swabable luer valve prevents the MPDS 200 from being contaminated and allows an operator to swab or clean (by, for example, an alcohol wipe) the connector end 228 prior to connecting an SPDS 7000 thereto. Alternately, however, the connector end 228 may be a standard luer connector as known in the art.

[100] As schematically shown in Fig. 2A, the tubing length 27 of the first tubing section 204 can be placed within pump 22 (indicated by dotted lines) to pump saline or other medical fluid from source 23 and a portion of the second tubing section 210 can be placed within pump 180 (indicated by dotted lines) to pump a radiopharmaceutical from a radiopharmaceutical source.

[101] Absolute and relative dimensions of the components shown in Fig. 2A, including tubing, may be chosen to best suit the applications at hand. Preferably, the first tubing section 204 is approximately 56.75 inches in length, has an outer diameter (OD) of approximately 0.188 inches and an inner diameter (ID) of approximately 0.062 inches and has a 45 durometer, the third tubing section 216 is approximately 15 inches in length, has an OD of approximately 0.163 inches and an ID of approximately 0.062 inches and has a 60 durometer, the fourth tubing section 220 is approximately 12 inches in length, has an OD of approximately 0.163 inches and an ID of approximately 0.062 inches and has a 60 durometer, and the fifth tubing section 226 and the sixth tubing section 230 are each approximately 5 inches in length, have an OD of approximately 0.163 inches and an ID of approximately 0.062 inches and have a 60 durometer. The second tubing section 210 is approximately

8.75 inches in length and is formed of microbore tubing having an OD of about 0.094 inches and an ID of about 0.032 inches and a 45 durometer. The tubing in tube coil 444 preferably is approximately 41 inches in length, has an OD of about 0.218 inches and an ID of about 0.156 inches and an 80 durometer.

[102] Preferably, the microbore tubing of second tubing section 210 is formed of, for example, silicone, C-Flex, or silicone-like PVC material. Essentially, the use of microbore tubing in second tubing section 210 improves volume accuracy and thereby improves measured activity accuracy (i.e., of pharmaceutical delivered to the patient) and reduces radiopharmaceutical waste.

[103] By way of tubing material for the other tubing sections 204, 216, 220, 226, 230 and tube coil 444, essentially any suitable polymeric material, including standard PVC or pump tubing, may be employed.

[104] In an alternate embodiment of the MPDS 200' shown in Fig. 2C, a conventional manifold 228' or stopcock may be substituted for the connector end 228 of the MPDS 200 (all other components of the MPDS 200' may be identical or similar to those shown in Fig. 2A and are denoted in Fig. 2C by prime notations). As shown in Fig. 2C, the manifold 228' includes three outlet ports (preferably including swabable valves) to which respective first ends 702' of the SPDSs 700' are connected. By connecting the respective patient ends 704 of the SPDSs 700' to, for example, catheters placed in patients, pharmaceutical doses can be delivered sequentially or concurrently to three separate patients. While the manifold 228' shown in Fig. 2C includes three ports for connection to three SPDSs 700', two, four, five or any suitable number of ports may be included in manifold 228' for connection with a like number of SPDSs 700'.

[105] Referring again to Figs. 1A-2B, the placement of the MPDS 200 in the fluid delivery system 10 and the connection of the SPDS will now be discussed. To set up the system 10 at, for example, the beginning of the day, the operator lifts the secondary handle 21, grasps the primary handle and latch release 1 and retracts the lid 20 to reveal the upper surface 103 of the system 10. If a used MPDS 200 is present in the system 10, the operator will remove and discard it.

[106] A new MPDS 200 may be removed from its (typically sterile) packaging and placed in the system 10 as shown in Fig. 1C. This includes placing the waste receptacle 224 into well 127, placing coil assembly 400 into ionization chamber 160, placing second tubing section 210 into operative connection with pump 180, placing the tubing length 27 of the first tubing section 204 into operative connection with pump

22 and tubing holder 150, placing vented cannula 208 into fluid connection with radiopharmaceutical source or vial 902 located in well 111, placing fifth tubing section 226 in operative connection with pinch valve 170, and placing sixth tubing section 230 in operative connection with pinch valve 172, air detector 174 and mount 176. A saline source 23 may be hung on hook 6 (see Figs. 1A, 1B and 2B) or otherwise mounted on fluid delivery system 10, and spike 202 is inserted into port 7 (see Figs. 1A, 1B and 2B) of source 23 to fluidly connect the MPDS 200 to the source 23. Of course, this installation procedure does not need to completed in the order described above, but may be completed in any suitable order consistent with the description or drawings hereof.

[107] After the MPDS 200 is installed and preferably primed (as discussed below), the first end 702 of the SPDS 700 is connected to the connector end 228 of the MPDS 200 and the SPDS 700 is preferably primed to provide a wet connection at the patient end 704 of the SPDS 700, which is then connected to a catheter (not shown) located in a patient. The SPDS 700 is preferably a coiled tubing formed of standard PVC, approximately 60 inches in length and having an OD of approximately 0.100 inches and an ID of approximately 0.060 inches and a 90 durometer.

[108] As shown in Figs. 2A and 2B, the MPDS 200 includes a coil assembly 400. In the broadest sense, coil assembly 400 may include a section of tubing (including portions of third and fourth tubing sections 216, 220) that is simply gathered (in a coiled or an uncoiled, amorphous fashion) and placed inside ionization chamber 160.

[109] As shown in Figs. 3A-3F, however, a preferred embodiment of coil assembly 400 includes a (preferably thermoformed) core element or structure 446 that is preferably configured for allowing a tubing section 217 to be wrapped thereupon and to assume the coiled tube section indicated at 444. As such, the coiled tube section or tube coil 444 is preferably formed on the core element 446 to facilitate optimal positioning of the tube coil 444 within the ionization chamber 160.

[110] To facilitate positioning of the tube coil 444, the core element 446 preferably includes a tube channel 410 defined by shoulders 412, 414 (see Fig. 3B) that retain tube coil 444 therebetween to hold the tube coil 444 in position and to prevent tube kinking. Further, the upper surface 420 of core element 446 defines an inlet channel or groove 422 and an outlet channel or groove 424 to accommodate third tubing section 216 and fourth tubing section 220, respectively.

[111] In an alternate embodiment, the core element 446 could include a coiled tube channel (not shown) formed therealong to further guide and retain the tubing segments or turns that form tube coil 444 between shoulders 412, 414.

[112] The core element 446 preferably is self-centering when inserted into the sleeve 162 of the ionization chamber 160 of the fluid delivery system 10 to thereby facilitate optimal performance (see Fig. 3F). This may be achieved either through structural features of the coil assembly 400, the structure of core element 446 itself, or a combination thereof when used with the sleeve 162 of the ionization chamber 160.

[113] As best shown in Fig. 3E, the core element 446 is preferably formed by folding two elements (450, 452) together along an integral hinge 455. Suitable form-locking mechanisms can be molded onto the core element 446 to facilitate clasping of the elements 450, 452 together.

[114] Figs. 1C, 1D and 3F show coil assembly 400 positioned concentrically in the sleeve 162 of the ionization chamber 160. The core element 446 and the tube coil 444 are sized and dimensioned so that the coil assembly 400 is optimally positioned within the "linear region" of the ionization chamber 160 so that the ionization chamber 160 can accurately determine the activity level of one or more volumes of radiopharmaceutical that is located within the tube coil 444. The "linear region" of an ionization chamber is the region in which activity level measurements are repeatable and predictable. For the preferred ionization chamber (Model IK-102 Short Ionization Chamber provided by Veenstra Instruments) used in system 10, the "linear region" is located within a window of 5 mm to 65 mm measured from the base or bottom wall 160a of the ionization chamber 160 (see Fig. 3F).

[115] In a preferred embodiment, the tube coil 444 is comprised of approximately 7 turns (see Figs. 3A and 3B) formed from a length of tubing that is approximately 41.0 inches. As shown in Fig. 3B, the height H of the tube coil 444 is approximately 1.53 inches and the diameter D of the tube coil 444 is approximately 1.95 inches. The tube coil 444 is preferably formed from a tube having an OD of 0.218 inches and an ID of 0.156 inches. Further, based on the length and ID of the tubing, the tube coil 444 preferably has a volume capacity of approximately 12.5 ml.

[116] As discussed heretofore, a source, container or vial 902 (see Fig. 4C) of a pharmaceutical or radiopharmaceutical is placed into the fluid delivery system 10 (e.g., in well 111 formed in upper surface 103) to prepare and perform an injection procedure. A radiopharmaceutical container or vial 902 is typically placed in a conventional vial shield or PIG 554 for transport by personnel.

[117] Turning now to Figs. 4A and 4B, preferred embodiments of a vial shield carrying device or system 500 and a vial access system 600 of the present invention are shown. Vial access system 600 is removably disposed within well 111 of fluid delivery system 10 and operates to hold vial shield 554 and to access the contents of the vial 902 contained therein. (Vial access system 600 will be described in more detail below with reference to Figs. 6A-6J.

[118] As best shown in Fig. 4A, the vial shield 544 (containing a radiopharmaceutical vial 902) includes a flange 504 formed along a top end thereof and a removable septum cap 562 that is securely and removably engaged with the vial shield 544 (e.g., via threading) to allow insertion and removal of the vial 902 therefrom.

[119] As shown in Figs. 4A and 4B, the carrying system 500 includes a collar unit 502 that removably engages the flange 504 formed on the vial shield 554. The collar 502 may be formed in two pieces 506, 508 that are pivotally connected together (e.g., at one end thereof) to allow the collar 502 to engage and disengage the flange 504.

[120] The collar 502 includes two elongated slots 510 formed in a top surface therein. As best shown in Fig. 4B, the slots 510 each include a pin 512 disposed therein and extending between two opposing walls 514 thereof.

[121] The carrying system 500 further includes a handle unit 520 that engages with the collar unit 502 and the septum cap 562 to allow the vial shield 554 (and vial 902) to be carried and installed in the fluid delivery system 10. The handle unit 520 includes a handle 556 that is rigidly connected to a generally U-shaped cross piece 564a. The cross-piece 564a defines two, downwardly extending arms 530 having slots 532 formed thereon.

[122] The slots 523 each form a slight hook on the ends thereof and are adapted to engage and retain a second cross piece 564b that supports a plunger 566 having a generally frustoconical shape that mates with a generally frustoconical recess of the septum cap 562 (see Fig. 4B).

[123] The second cross piece 564b is also generally U-shaped and defines two downwardly extending arms 534 having hooks 536 formed therein. The open ends of the hooks 536 are formed on opposite ends of the arms 534 and are adapted to accept and retain the pins 512 in slots 510 of collar 502. The slots 510 are sized to provide sufficient clearance for the arms 534 to be inserted thereinto (in a downward direction) and for the hooks 536 to engage pins 512 (through rotation of handle 556).

[124] The plunger 566 is connected to the second cross piece 564b by means of a connector (such as a screw 540) and a spring 538. The plunger 566 is biased by spring 538 to ensure a tight fit between the plunger 566 and the septum cap 562.

[125] To engage and carry the vial shield 554, the collar 502 is connected to the flange 504 of the vial shield 554 as described above. The handle unit 520 is then moved into proximity to the vial shield 554 (by an operator grasping the handle 556 and moving the unit 520 into position) and the arms 534 are lowered into the slots 510 of the collar 502. At substantially the same time, the plunger 566 is engaged with the septum cap 562, with the spring 538 insuring a tight fit between the two. The operator then turns the handle unit 520 in a clockwise direction (see Arrow A in Fig. 4A) to seat the pins 512 in slots 510 into the hooks 536 of arms 534.

[126] The operator then lifts the combined vial shield 554 and vial carrying system 500 (by moving the handle unit 520 in an upward direction) and transports it to, for example, the fluid delivery system 10. The operator then lowers the vial shield 554 into the vial access system 600 disposed in well 111 (see Fig. 4A) and rotates the handle unit 520 in a counter-clockwise direction to disengage the hooks 536 from the pins 512. The operator then lifts the handle 556 in an upward direction to remove the arms 534 from the slots 510 and the plunger 566 from the septum cap 562, thereby leaving the vial shield 554 (with septum cap 562 and collar 502) in vial access device 600 in well 111 (see Fig. 4B).

[127] In a preferred embodiment, the plunger 566 includes radioactive shielding (such as lead) to shield the operator from radiation that would otherwise leak through or be emitted from the septum of the septum cap 562. Together with the vial shield 554 and the septum cap 562, the plunger 556 of the vial carrying system 500 shields the operator from the radiation emitted by the radiopharmaceutical and prevents unnecessary radiation exposure. Further by extending the handle 556 from the vial shield 554, the distance between the two functions to also lessen any possible radiation exposure to the operator.

[128] An alternate embodiment of the carrying system is shown in Figs. 5A-5D. As with the preferred embodiment described above with respect to Figs. 4A and 4B, the carrying system 1500 helps minimize operator exposure to radiation. Dimensions shown in Fig. 5A are for illustrative and non-restrictive purposes; here they are given in inches. As with Figs. 4A and 4B, generally contemplated here is an integral carrying system 1500 that enables the vial shield 1554 to be carried and placed in the fluid delivery system 10 with minimal operator finger/hand radiation exposure

because the design of the carrying system 1500 increases the distance from the vial 902 contained within the vial shield 1554.

[129] Shown in Figs. 5A and 5C is a vial shield 1554 with a plunger 1566 of the carrying/installation handle system 1500 engaged with the septum cap 1562 of the vial shield 1544. The septum cap 1562 engages securely with the vial shield 1554 (e.g., via threading) to provide suitable radioactive shielding.

[130] As shown in Figs. 5A-5D, a crosspiece 1564a with a central aperture is rigidly connected to handle 1556 and is preferably configured to slidably accommodate an extension tube 1558. At a free end of extension tube 1558, the plunger 1566 is preferably disposed to engage with septum cap 1562. Though this engagement may be embodied in essentially any suitable way, here plunger 1566 has a generally frustoconical shape that engages with a generally frustoconical recess of septum cap 1562.

[131] As further shown in Figs. 5A and 5B (and as can be better appreciated by the perspective views in Figs. 5C and 5D), handle 1556 preferably terminates in a ring 1564b that is configured for engaging with structural features of cap 1562 (to be described more fully below).

[132] As shown in Fig. 5B, plunger 1566 may be hingedly or pivotably connected to extension tube 1558 via a hinge or pivot connection 1568, which provides freedom of motion to allow the plunger 1566 to mate with the septum cap 1562 without the operator having to otherwise place her hand and fingers directly above the septum cap 1562 before it is covered by the plunger 1566 (thereby reducing the possibility of radiation exposure to the operator).

[133] While Figs. 5A-5C show handle 1556 in a retracted position, i.e., maximally displaced away from plunger 1566, Fig. 5D shows in perspective view a different stage of the engagement of handle 1556 with vial shield 1554. As such, Figs. 5A-5C shows handle 1556 maximally retracted from plunger 1566 (and, by extension, cap 1562), while Fig. 5D shows handle 1556 in a "fully engaged" configuration with respect to cap 1562.

[134] Preferably, plunger 1566 will initially mate with cap 1562. Thence, handle 1556 is preferably moved towards cap 1562 (conceptually progressing from Fig. 5B to 5D) such that slots 1570 on ring 1564b fit over and capture posts 1572 (through clockwise rotation of handle 1556) on cap 1562. The handle 1556 may then be lifted to carry and deposit the vial shield 1554 in the well 111, as described above.

The carrying system 1500 is disengaged from the vial shield 1554 through counter-clockwise rotation of the handle 1556 to disengage the capture posts 1572 from the slots 1570 on the ring 1564b. Of course, after the contents of the vial 902 are depleted, the carrying system 1500 can be attached to the vial shield 1554 as described above to remove the vial shield 1554 and the vial 902 from the fluid delivery system 10.

[135] As discussed above with respect to Figs. 4A-4B, the fluid delivery system 10 includes a vial access system 600 that is removably disposed within well 111 of fluid delivery system 10 and is adapted to hold vial shield 554, 1554 and to provide access to the contents of the vial 902 within vial shield 554, 1554.

[136] Because vials (such as vial 902 described herein) typically come in various sizes, such as 10 ml, 15 ml, 20 ml and 30 ml, the fluid delivery system 10 of the present invention is intended to accommodate various vial sizes. To do so, the fluid delivery system 10 may include one or more vial shields and vial access systems (varying primarily in size in relation to the preferred embodiment of the vial shields 554, 1554 and vial access system 600 disclosed and described herein) that are specifically sized to accommodate known vial sizes. In a preferred embodiment, three vial shields and vial access systems 600 are provided with the fluid delivery system 10, and the well 111 is configured and designed to accept each of the vial access systems 600. However, the fluid delivery system 10 can be provided with one, four, five or any suitable number of vial shields and vial access systems depending on evolving needs or changes in the size or shape of the vials. Thus, depending on the size of the vial used at a clinical site or for a particular procedure, an operator of the fluid delivery system 10 can select the appropriate vial shield and vial access system and place it in the well 111 of the fluid delivery system to enable a fluid injection procedure.

[137] Preferred embodiments of the vial access system 600 and the vented cannula 208 of the MPDS 200 are described below in relation to Figs. 6A-6J (and with reference to Figs. 4A and 4B). Generally, as best shown in Figs. 6A, 6B and 6F, the vial access system 600 includes a base portion 670 that preferably includes a sloped surface 672, the function of which will be more fully appreciated herebelow. Two (preferably removable and extendable) support members or pins 674 are provided to support and retain a vial shield 554 (i.e., enclosing a vial 902; see Fig. 4C) when it is placed on the sloped surface 672 (e.g., after being carried and disposed there using the vial shield carrying systems 500, 1500 discussed above).

[138] As shown, the vial access system 600 further includes a vertical support arm 676 that is disposed within a housing 678. A cap member 684 and a handle member 682 are connected to an upper end of the vertical support arm 676. The vertical support arm 676 is preferably slidably and rotationally displaceable with respect to the housing 678. That is, the arm 676 may slide and rotate with respect to the housing 678 (see e.g., Figs. 4B and 6D) to allow the vial shield 554 to be readily inserted and removed therefrom and to lower the vented cannula 208 into the vial 902 contained within the vial shield 554 (as discussed in more detail below).

[139] The handle 682 is used by an operator or technician to insert and remove the vial access system 600 from the well 111 of the fluid delivery system 10. The handle 682 is preferably connected to the vertical support arm 676 via a suitable pivot connection (such as a hinge or bolt connection) 680 to permit movement of the handle 682 between an extended, carrying position (see Fig. 6D) for carrying the vial access system 600 and a horizontal or operating position (see Figs. 6B and 6E) in which the handle 682 rests on top of the cap 684 (e.g., when the vial access system 600 is disposed in the well 111), thereby allowing the cover 20 of the fluid delivery system 10 to be closed.

[140] The cap 684 is preferably rigidly connected to the vertical support arm 676 via an arm 650 (see Figs. 6A and 6D), but it may be pivotally connected to the vertical support arm 676 via, for example, a pivot connection (not shown) or adjustably connected to the vertical support arm 676 via, for example, a slot (not shown) formed in the arm 650. As best shown in Figs. 6E and 6F, when the cap 684 is lowered (by sliding the vertical support arm 676 within the housing 678) to insert the cannula 208 into the vial 902 within the vial shield 554, and the handle 682 is pivoted to a horizontal position atop the cap 684, the cap 684 and the handle 682 (and thus the remainder of the vial access system 600) lies below or flush with the upper surface 103 of the fluid delivery system 10, thereby allowing the cover 20 to close over the upper surface 103 of the fluid delivery system 10 and the MPDS 200 installed therein. The cap 684 preferably includes or is formed with radioactive shielding material (e.g., lead) to minimize radiation exposure to personnel from the FDG or other radioactive solution contained within the vial 902 in the vial shield 554.

[141] As best shown in Figs. 6A and 6C, the underside of cap 684 includes a mounting mechanism 686 for accepting the cannula 208 (or other suitable type of spike, cannula or needle) for piercing the septum of a vial 902 or other pharmaceutical container in the vial shield 554. The mounting mechanism 686 preferably includes

two arms 687 that define a groove or slot 688 therebetween. Each of the arms 687 includes a tab member 690 extending downwardly therefrom.

[142] The vented cannula 208, in accordance with a preferred embodiment of the present invention, may be employed for spiking a pharmaceutical source (such as the radiopharmaceutical vial 902 discussed above) and preferably includes a main hub 332 to which are connected (or integrally formed) two, resilient spring arms 350. The spring arms 350 and the main hub 332 cooperate to define two U-shaped channels 352 on lateral sides of the main hub 332.

[143] As shown in Figs. 6C and 6G-6J, each of the spring arms 350 includes a flange or hook member 370 formed thereon and extending outwardly therefrom. The hook members 370 each defines an inclined surface or edge 372 formed thereon.

[144] The vented cannula 208 further includes a ledge or flange 338 that is connected to or integrally formed with the main hub 332 and is disposed in a horizontal plane above the two spring arms 350. The ledge 338 and the top edges of the spring arms 350 cooperate to define horizontal grooves or slots 360 therebetween for accommodating the arms 687 of the mounting mechanism 686 on the cap 684 of the vial access system 600.

[145] To connect the cannula 208 to the mounting mechanism 686 on the cap 684, the main hub 332 of the cannula 208 is aligned with the slot 688 of the mounting mechanism 686 and the arms 687 of the mounting mechanism 686 are aligned with the grooves 360 defined between the spring arms 350 and the top ledge 338 of the main hub 332. Once the structural elements of the cannula 208 and the mounting mechanism 686 are aligned, the cannula 208 is inserted into the mounting mechanism 686 until the hook members 370 of the spring arms 350 engage the front edges 691 of the tab members 690. Upon further insertion of the cannula 208, the front edges 691 of the tab members 690 engage and ride along the inclined surfaces 372 of the hook members 370, thereby moving the spring arms 350 in an inward direction (i.e., toward the vertical axis of cannula 208). This inward movement of the hook members 370 allows them to clear the front edges 691 of the tab members 690 and ride along the inner sides 693 thereof until the hook members 370 clear the tab members 690 and move or snap back into their original position to engage the rear edges 692 of the tab members 690. At this point, the cannula 208 is fully inserted into and retained by the mounting mechanism 686. To remove the cannula 208 from the mounting mechanism 686 (e.g., when the MPDS 200 is removed from the fluid delivery system 10), the operator pinches the hook members 370 together (i.e., moves them toward the vertical axis of the cannula 208) until they clear the

rear edges 692 of the tab members 690, and then slides the cannula 208 out of engagement with the mounting mechanism 686.

[146] Referring again to Figs. 6C and 6G-6J, the vented cannula 208 includes a longer, fluid draw needle 340 in fluid connection with the second tubing section 210 of the MPDS 200 via a fluid port 384 and a shorter, vent needle 342 in fluid connection with a vent 334. As known in the art, the vent 334 may include a suitable filter for filtering the ambient air that is drawn into the vial 902 to allow fluid to be drawn therefrom.

[147] The description now turns to the preferred operation and use of the vial access system 600 and the vented cannula 208 of the present invention. When a vial shield 554 (holding a pharmaceutical vial 902) is to be placed in the vial access system 600, the vertical support arm 676 is raised to an extended position and rotated (see Figs. 2B and 4A) to move the cap 684 out of its normal position above the sloped surface 672. The vial shield 554 is then inserted into the well 111 and placed on the sloped surface 672 (see Fig. 6F). The support pins 674 engage the vial shield 554 to hold it in position on the sloped surface 672.

[148] After the vial shield 554 is inserted into the vial access system 600 (see Fig. 4B), the vented cannula 208 of the MPDS 200 is inserted into the mounting mechanism 686 on the cap 684 and the cap 684 is rotated back into position (e.g., by turning the handle 682) above the septum cap 562 of the vial shield 554 (see Fig. 6D). Then the cap 684 is lowered (e.g., by using the handle 682 to urge the vertical support arm 676 into the housing 678) to insert the fluid draw needle 340 and the vent needle 342 of the cannula 208 through the septum of the septum cap 562 and into the pharmaceutical vial 902 (see Fig. 6F). The handle 682 is then rotated to lie in a substantially horizontal orientation on or above the cap 684 (see Figs. 1C and 6E), thereby allowing the cover 20 of the fluid delivery system 10 to be closed. While the preferred method of operating the vial access system 600 and the vented cannula 208 is provided above, the method and steps can be conducted in any suitable order or arrangement to achieve the desired results.

[149] As best shown in Fig. 6F, the support surface 672 is preferably configured such that when a vial is pierced by the fluid draw and vent needles 340, 342 of the cannula 208, the bottom end of the fluid draw needle 340 will be placed at or near the location where the cylindrical wall of the vial meets the bottom (floor) of the vial. Thus, to the extent that some vials may not have a completely flat bottom or floor (e.g., may have a rounded bump with a maximum height at the central longitudinal axis of the vial), the fluid draw needle 340 will be in a position to maximally draw

fluid from the vial as it collects at the junction of the vial's bottom and cylindrical wall (i.e., to avoid waste of the pharmaceutical). Or, even in a flat-bottomed vial, such an orientation of the vial will help ensure that fluid maximally gathers and is drawn in a closely defined area.

[150] As discussed above, the dimensions of the vial access system(s) 600 provided with the fluid delivery system 10 can preferably be chosen in accordance with dimensions of the vial shields and vials to be employed, to ensure that as much fluid from the vial is drawn as possible. By way of a non-restrictive example, the sloped surface 672 could be sloped at an angle of about 10-13 degrees with respect to the horizontal.

[151] Instead of being incorporated into and as part of the MPDS 200 for use with the fluid delivery system 10, the vented cannula 208 of the present invention may be used in other fluid delivery systems, including ones that use shielded syringes (see e.g., U.S. Patent Nos. 5,927,351 and 5,514,071, the contents of which are incorporated herein by reference), for injecting pharmaceuticals or other medical fluids into patients.

[152] As shown in Figs. 47A-C, the vented cannula 208 may be used with a hand-held syringe 380 (preferably held within a conventional lead-shielded container (not shown for ease of illustration)) having a discharge outlet 386 and a plunger 381 slidably disposed therein. The fluid draw needle 340 of the cannula 208 is in fluid connection with the shielded syringe 380 by means of a tube 383 connected between the discharge outlet 386 of the syringe 380 and the fluid port 384 of the cannula 208. The tube 383 preferably includes a connector 387, such as a standard luer connector, for removably connecting the tube 383 to the shielded syringe 380. The other end of the tube 383 may be non-removably attached to the fluid port 384 of the cannula 208 by use of, for example, an adhesive. Alternately, the tube 383 may include a connector (not shown) for removable connection to the fluid port 384 or may be press fit and held by friction forces onto the fluid port 384.

[153] The tube 383 may be fashioned in any length or diameter suitable for the application. In use, the fluid draw and vent needles 340, 342 of the cannula 208 are inserted into a vial (not shown) containing a pharmaceutical or other fluid. The plunger 381 is retracted (moved away from the discharge outlet 386 of the syringe 380) to aspirate fluid from the vial into the syringe 380. The connector 387 is disconnected from the shielded syringe 380 and the syringe 380 is then connected, generally via an intermediate tubing (not shown), to a catheter disposed in a patient.

The plunger 381 is then advanced (moved toward the discharge outlet 386) to inject fluid into the patient.

[154] As shown in Fig. 48, the vented cannula 208 may also be utilized as part of a second alternate fluid delivery system 399 including a shielded (not shown for ease of illustration), hand-held syringe 380' having a discharge outlet 386' and a plunger 381' slidably disposed therein. In addition to like elements shown in Figs 47A-C, the system 399 includes first, second and third tubing segments 390, 391, 392 that are connected via a T-connector 393 having an integral stopcock 394. The third tubing segment 392 also preferably includes a swabable valve 395 to which the first end 702 of the SPDS 700 described above could be connected. Instead of a swabable valve 395, it is contemplated that a conventional luer connector could be used for suitable applications.

[155] After the vented cannula 208 is placed in a pharmaceutical source (not shown), the stopcock 394 is actuated to open the fluid path between the vented cannula 208 and the syringe 380' and to close the path to the third tubing segment 392. The plunger is then retracted to aspirate fluid into the syringe 380' from the pharmaceutical source. The stopcock 394 is then actuated to open the fluid path between the syringe 380' and the third tubing segment 392 and to close the path to the second tubing segment 391. The first end 702 of the SPDS 700 is then preferably connected to the swabable valve or luer connector 395, and the plunger 381' is advanced to pump fluid to the patient end 704 of the SPDS 700 (e.g., to purge air from the tubing and to thereby provide a wet connection between the patient end 704 of the SPDS 700 and the catheter (not shown) in a patient). The patient end 704 is then connected to the catheter and the plunger 381' is advanced again to pump or deliver fluid through the SPDS 700 to the patient.

[156] After the fluid is delivered to the patient, the SPDS 700 is disconnected from the patient and the valve or luer connector 395 and is discarded. If another injection is to be performed, a new SPDS 700 can be connected to the valve or connector 395 and the system 399 can be primed to again provide a wet connection at the patient end 704 of the SPDS 700.

[157] The disclosure now turns to the operation of the fluid delivery system 10 and its various components. As known in the art, in injection procedures and other fluid delivery operations in which pharmaceuticals are delivered to a patient, air is purged from the fluid path by pumping an amount of the pharmaceutical and/or a diluent, such as saline, through the fluid path to the end of a tubing set (e.g., MPDS 200 or SPDS 700) before connecting the tubing set to a catheter in the patient. Such an air

purging or "priming" procedure is standard practice to prevent the occurrence of an air embolism in a patient, which can cause serious injury or death. Further, the dimensions (e.g., length and ID) of the SPDS 700 and the various tubing sections of the MPDS 200 (provided above) are necessary for accurate priming, activity measurement and delivery of the pharmaceutical to the patient because the system 10 relies on those dimensions to accurately determine and monitor the volume of pharmaceutical and saline that is required for those various operations.

[158] Referring again to Figs. 1C and 2A, once the MPDS 200 is installed in the fluid delivery system 10, the spike 202 is placed in fluid connection with the saline source 23 and the cannula 208 is inserted into the vial 902 and placed in fluid connection with the pharmaceutical therein, the MPDS 200 is primed to remove air therefrom.

[159] In a preferred method of priming the MPDS 200, the pump 22 is activated to draw saline out of source 23 and to move the saline through first tubing section 204, check valve 215, T-connector 205 and into third tubing section 216. The pump 180 is then activated to draw a small amount of pharmaceutical out of vial 902 and to move the pharmaceutical through second tubing section 210, check valve 214, T-connector 205 and into third tubing section 216. The pump 23 is then activated again to draw additional saline from saline source 23 to thereby move the volume of pharmaceutical present in third tubing section 216 into the tube coil 444 of coil assembly 400 located in the dose calibrator 160.

[160] To ensure that the second tubing section 210 is primed, the dose calibrator 160 is monitored to measure the level of radioactivity in the coil 444. If the dose calibrator measures no activity (or an activity level below a predetermined, baseline activity level), then the second tubing section 210 has not been appropriately primed and the priming process described above needs to be reinitiated by the operator. If the dose calibrator measures any activity level (or an activity level above the predetermined, baseline activity level), then the system 10 concludes that the second tubing section 210 has been correctly primed.

[161] After the second tubing section 210 is primed, the motor 30 is activated to open the pinch valve 170 and thereby open the fluid path from the fourth tubing section 220 through the T-connector 222 and the fifth tubing section 226 to the waste receptacle 224, the motor 31 is activated to close the pinch valve 172 and thereby close the fluid path along the sixth tubing section 230, and pump 22 is activated again to move the saline and the pharmaceutical in tube coil 444 through fourth tubing section 220, T-connector 222, fifth tubing section 226 and into waste receptacle 224.

[162] Subsequently, the first end 702 of the SPDS 700 is connected to the connector end 228 of the MPDS 200. The motor 30 is activated to close the pinch valve 170 (and thereby close the fluid path from the fourth tubing section 220 through the T-connector 222 and the fifth tubing section 226 to the waste receptacle 224), the motor 31 is activated to open the pinch valve 172 (and thereby open the fluid path along the sixth tubing section 230), and the pump 22 is activated again to move the saline through the T-connector 222 and the sixth tubing section 230 to the patient end 704 of the SPDS 700. At this point, the entire length of the MPDS 200 and the SPDS 700 is primed and the patient end 704 of the SPDS 700 can be connected to the catheter or other venous access device placed in a patient.

[163] In an alternate embodiment, after the pharmaceutical is moved into the waste receptacle 224, the remainder of the MPDS 200 is primed prior to the SPDS 700 being connected to connector end 228 of the MPDS 200. (This alternate priming method may be accomplished if the connector end 228 of the MPDS 200 is not the preferred swabable luer valve but rather is, for example, a standard luer connector or another connector that is not biased to a closed position when disconnected from the first end 702 of the SPDS 700.) Then, the first end 702 of the SPDS 700 is connected to the connector end 228 of the MPDS 200 and the SPDS 200 is primed to provide a wet connection at the patient end 704 of the SPDS 700.

[164] To accomplish this alternate priming method, the motor 30 is activated to close the pinch valve 170 (and thereby close the fluid path from the fourth tubing section 220 through the T-connector 222 and the fifth tubing section 226 to the waste receptacle 224), the motor 31 is activated to open the pinch valve 172 (and thereby open the fluid path along the sixth tubing section 230), and the pump 22 is activated again to move the saline through the T-connector 222 and the sixth tubing section 230 to the connector end 228 of the MPDS 200. Then, after the first end 702 of the SPDS 700 is connected to the connector end 228 of the MPDS 200, the pump 22 is activated again to move saline through the SPDS 700 to the patient end 704 thereof.

[165] After the MPDS 200 and the SPDS 700 are primed and the patient end 704 of the SPDS 700 is connected to the patient, the system 10 is ready for an injection procedure. While preferred and alternate methods of priming the MPDS 200 and the SPDS 200 are described above, other methods or steps may be employed or the steps above may be rearranged in any suitable manner to purge air from the MPDS 200 and the SPDS 700.

[166] In an alternate embodiment of the MPDS 200, the T-connector 205 and the check valves 214, 215 can be replaced with an automated, motor-driven stopcock. T-connector 222 also can be replaced with an automated stopcock as well.

[167] The disclosure now turns to embodiments of the present invention, as illustrated in Figures 7-46, that could conceivably be employed in programming and operating a fluid delivery system as broadly contemplated herein.

[168] Shown schematically in Figures 7-46 are various incarnations of a touch screen arrangement 1000 displayed on a graphical user interface, such as GUI 15, that could be employed with the fluid delivery system 10. As a non-restrictive example, such a touch screen arrangement could be utilized in conjunction with a system controller 5 and/or computer of any of a variety of fluid delivery systems as broadly contemplated herein.

[169] In order to clearly and unambiguously communicate to an operator the current status of the system 10, a graphical user interface with easily legible symbols and icons, including exceedingly user-friendly data entry mechanisms, is broadly contemplated. An operator will thus be able to intuitively understand and undertake various tasks for operating system 10.

[170] While a touch screen arrangement is contemplated in connection with Figures 7-46, it is to be understood that other types of data entry arrangements are conceivable that would achieve an equivalent purpose. For example, soft or hard key entry could be used, as well as trackball arrangements, mouse arrangements, or a cursor control touch pad (remote from the screen).

[171] The touch screen arrangement 1000 shown in Figures 7-46 can preferably be employed for four categories of tasks, namely: (1) system preparation, (2) patient treatment, (3) injection history (i.e., obtaining information regarding previous treatments) and (4) system configuration. Preferably, a touch screen arrangement 1000 will be flexibly and selectably manipulable to accommodate and undertake any and all of these tasks as desired.

System Preparation

[172] The "system preparation" category includes a number of tasks that are preferably performed in the following order to prepare the system 10 for a fluid injection or delivery procedure: (1) disposing of a used MPDS 200 and vial 902 from, for example, the previous day or previous use of the system 10 (if still present in the system 10); (2) conducting a quality control check or "daily QC" of the system 10;

(3) installing a new pharmaceutical vial 902 and a new MPDS 200 in the system 10; and (4) priming the MPDS 200 to remove air therefrom. While the above order is the preferred one for preparing the system 10, the tasks may be performed in any suitable manner and order for the intended application.

[173] Fig. 7 conveys a "main" screen visible on touch screen arrangement 1000, which may be an initial screen presented to an operator when the system 10 is initially activated.

[174] As such, and as shown in Fig. 7, touch screen arrangement 1000 preferably generally depicts at a very high level the fluid path (e.g., MPDS 200 and SPDS 700) of the fluid delivery system 10. It can be appreciated that touch screen 1000 can easily be "mapped" (i.e., provide a one-to-one correspondence) to major components of the MPDS 200, the SPDS 700 and other components of the system 10 such as that discussed and illustrated herein with respect to Figs. 1A-6J, but that level of detail is generally not required for programming and use of the system 10.

[175] As shown in Fig. 7, the touch screen shows a saline field 1002 (here in the stylized shape of an IV bag), a pharmaceutical or FDG field 1004 (here in the stylized shape of a vial) and an ionization chamber graphic 1010. A tubing graphic 1008, as shown, encompasses a three-way junction with branches leading, respectively, to saline field 1002, FDG field 1004 and ionization chamber graphic 1010. As shown, the tubing graphic 1008 is coiled inside the ionization chamber graphic 1010 to indicate the tube coil 444 described above.

[176] Touch screen arrangement 1000 in Fig. 7 shows the system 10 as being in an "idle" state. As such, no fluid is shown as being disposed in or moving through tubing graphic 1008 and ionization chamber graphic 1010. Further, saline and FDG fields 1002, 1004 in Fig. 7 both convey an "empty" status, to indicate that the system 10 has not yet been provided with information regarding the presence and/or amount of fluid in the saline source 23 and the vial 902.

[177] Indicated at 1006 is a touch field showing desired activity (currently displayed as 15.0 mCi) for an injection procedure to be performed. When the system 10 is activated, the desired activity field 1006 preferably displays a default activity value that can be pre-programmed into the system 10 or pre-set by the operator. Alternately, the desired activity field 1006 can default to the last activity level that was programmed into the system 10. Further, a display (read-only) system preparation field 1020 includes an associated "setup" button 1022a that, when activated, permits system preparation tasks to be performed.

[178] Indicated at 1012, 1014, 1016 and 1018, respectively, in Fig. 7 are circular status icons that provide quick and easy reference to different aspects of system status and, as such, will highlight when an aspect of system status is "on" or "active" or provide status information on the system 10. Thus, icons 1012-1018 from left to right, respectively, convey information on the following system aspects: activity present 1012, fluid motion / injection status 1014, check for air / priming status 1016, and system battery status 1018.

[179] The system battery (not shown) provides power to the system controller 5 and to the ionization chamber 160 (to maintain the ionization chamber at its normal operating state) in the event that the system 10 is disconnected from an AC power source. The system battery is charged while the system 10 is connected to an AC power source.

[180] Fig. 7 also shows four rectangular touch fields 1020-1023 along the bottom thereof. Reset button 1020 is activated to reset or clear information, such as case identification information, desired activity level, etc., from the treatment screens (as described in more detail below). Configuration button 1021 is activated to access the configuration screens for the system 10 (as described in more detail below). Records or Injection History button 1022 is activated to access information regarding prior injection procedures (as described in more detail below). Help button 1023 is activated to access searchable text, FAQs or other information that might be provided about the use and operation of the system 10.

[181] When the setup button 1022a is activated, the touch screen changes to that shown in Fig. 8. and "summary" 1030, "setup guide" 1032 and "daily QC" (quality control) 1034 touch fields preferably appear and the "summary" touch field 1030 is activated, prompting the appearance of a summary display 1038. As shown, summary display 1038 provides FDG and saline fields 1040, 1044, respectively, as well as MPDS tubing field 1048 and waste field 1050.

[182] In the saline field 1044, a "replace" button 1046 can be activated by the user to inform the system 10 that the saline source 23 has been replaced and to allow the user to input the volume of the saline source into the system 10 (see Fig. 13). After the saline volume is input via pop-up screen 1110 including keypad 1114 in Fig. 13, the saline volume is displayed as shown in Fig. 11. In a preferred embodiment, the saline source 23 is replaced at the same time that a new vial 902 is placed into the system 10.

[183] As part of the FDG field 1040 in Fig. 8, there are shown a number of informational displays (shown here as blank) regarding assay information that can be input by a

user into the system 10. An edit button 1042 can be activated by the user to facilitate the entry of such information. When the edit button 1042 is activated, the display shown in Fig. 10 appears. The user can then input the noted assay information (typically provided on the pharmaceutical vial 902) into the system 10. Specifically, a lot number can be entered into field 1072, while the activity and volume of, for example, FDG or other radiopharmaceutical in the vial can be entered into touch fields 1080 and 1082, respectively. In a manner well known to those of ordinary skill in the art, the activation of any of these fields can prompt a numerical keypad pop-up to assist in data entry, or data can be entered in essentially any other suitable manner (e.g., directly via a physical keyboard).

[184] Further, the assay date of the radiopharmaceutical in the vial is entered in field 1074 via a calendar button 1074a (which prompts the appearance of a pop-up calendar in known manner), or a simplified entry touch field 1074 which selectively permits the entry of a day such as "today" or "yesterday" (which is useful for radiopharmaceuticals, such as FDG, that have very short half-lives).

[185] The assay time is entered into touch field 1076 (via a pop-up time field or keyboard/keypad entry) and an AM/PM toggle field 1076a. Other functional buttons are present, such as "clear all" 1078, "cancel" 1084 and "OK" 1086 buttons, to facilitate entry, deletion and/or acceptance of inputted values of the requested assay information. When the OK button 1086 is activated to accept the assay information shown in Fig. 10, the display shown in Fig. 11 appears.

[186] Finally, as shown in both Figs. 8 and 11, information regarding the amount of radioactivity present in the MPDS tubing 200 is displayed at area 1048, while a waste field 1050 is preferably provided to graphically display the quantity of fluid and the activity level in the waste receptacle 224. Further, an "OK" button 1036 is activated to notify the system 10 that the system preparation tasks have been completed.

[187] Fig. 9 illustrates the display screen that is shown when the "setup guide" touch field 1032 shown in Fig. 8 is activated. As shown, setup guide 1032 prompts the appearance of a setup screen 1053 to assist an operator in physically preparing the system 10 for a procedure. Setup screen 1053 preferably includes four tabs 1054, 1056, 1058, 1060), which each, respectively, assist an operator in a different aspect of system setup (here, FDG removal, saline source installation, FDG installation, and MPDS installation, respectively).

[188] Fig. 9 also shows that FDG tab 1058 has been activated, prompting the appearance of display 1062. Up and down arrows 1066, 1068 preferably permit an operator to go through numbered procedure steps 1-4 as shown to install FDG vial 902 into the system 10, and a graphical image 1064 of the fluid delivery system 10 preferably graphically relates each of the numbered procedure steps. Here, for instance, "step 1" is shown graphically for the unlocking and opening of the cart. After the FDG vial 902 is installed in the system 10, status icon 1012a is highlighted (see Fig. 11) because activity is now present in the system 10.

[189] After the FDG vial 902, the saline source 23 and the MPDS 200 have been installed using, for example, the display shown in Fig. 9, and the FDG assay information and the saline volume information have been provided to the system (as shown in Fig. 11), the "purge air" button 1052 shown in Fig. 11 can be activated to prime the MPDS 200. When purge air button 1052 is activated, the "Prime MPDS" query prompt 1100 shown in Fig. 12A is displayed. When the "Yes" button 1101 in Fig. 12A is activated, the MPDS priming operation described in detail above is performed by the system 10 and a "Priming MPDS" status display 1102 is shown (see Fig. 12B) to indicate the status and completion of the MPDS priming operation to the user.

[190] After the MPDS 200 is primed by the system 10, a volume of fluid (i.e., a mixture of saline and a pharmaceutical (e.g., FDG)) is present in the waste receptacle 224 (as described in detail above). The outcome of the MPDS priming operation and the current status of the system 10 is displayed to the user, as shown in Fig. 14.

[191] As Fig. 14 shows, and as compared to the pre-MPDS priming system status shown in Fig. 11, the waste receptacle 224 contains 20 ml of waste (i.e., saline and pharmaceutical) and has an activity level of 15 mCi, the MPDS tubing has an activity level of 2 mCi, the saline source 23 contains 485 ml of saline (compared to 500 ml in Fig. 11) and the vial 902 contains 15 ml of FDG and has an activity level of 374 mCi (compared to 30 ml and an activity level of 700 mCi in Fig. 11).

[192] As shown in Fig. 14, the "Activity" (i.e., 700.0 mCi) listed in the Assay Information section of display 1038 is the amount of radioactivity provided by the radiopharmaceutical at the time it was assayed. The "Total Activity" (i.e., 415 mCi) shown next to the FDG display 1040 is the amount of radioactivity currently provided by the radiopharmaceutical present in the vial 902. The difference (i.e., 285 mCi) between the "Activity" and the "Total Activity" is calculated from the decay rate of the radioisotope and the elapsed time since the radiopharmaceutical was assayed. The activity level (i.e., 374 mCi) displayed within the FDG display

1040 is the 'extractable activity'; that is, the amount of activity that can be extracted from the vial 902. The "extractable activity" is less than the "total activity" because there is a small volume of radiopharmaceutical (e.g., approximately 1-2 ml) that cannot be extracted from pharmaceutical vials or containers and becomes discarded waste.

[193] Preferably prior to installing and priming the MPDS 200, the operator or other personnel should perform a quality control check on the fluid delivery system 10. In a preferred embodiment, the quality control check is performed daily, for example at the beginning of a work day, to ensure that the fluid delivery system 10 is in good working order. The quality control check is initiated by activating the "Daily QC" field or button 1034, as shown in Fig. 15. When activated, the "daily QC" touch field 1034 prompts the appearance of a QC display 1120 to assist an operator in performing a quality control check. A menu of checks to be performed preferably appears via the following touch fields: zero check (1122), bias adjustment (1124), background check (1126), constancy/accuracy test (1128) and ionization chamber battery (i.e., high voltage) measurement check (1130). In addition, the QC display 1120 provides a warning prompt 1121 to the operator that no activity (i.e., no radiopharmaceutical) should be inside the ionization chamber 160 when the quality control check is conducted.

[194] To the left of each touch field, preferably, is a "check box" or "pass/fail" indicator that preferably indicates one of the following four states, as appropriate: highlighted (if the corresponding touch field 1122-1130 is activated) to indicate an active test or check; not highlighted and blank to indicate an unexecuted test or check; checked with a checkmark to indicate a successful test or check; and an "X" to indicate a failed test or check.

[195] The QC display 1120 also includes a "Previous Test" button 1132 and a "Start" button 1134. The Previous Test button 1132 is activated to display the results of the previous quality control check of the system 10. When the Start button 1134 is activated, the tests or checks displayed in the QC display 1120 are initiated. Preferably, the checks are conducted in the order presented (i.e., from top to bottom) but they may be performed in any suitable order.

[196] Upon activating the Start button 1134, the "Zero Check" test 1122 is initiated. As shown in Fig. 16A, when the Zero Check test is initiated, the system 10 creates a pop-up 1136 that queries the operator as to whether there is activity (i.e., a radiopharmaceutical) inside of the ionization chamber 160 of the fluid delivery system 10. If the operator activates the "No" touch button 1137 in pop-up 1136,

system 10 "zeros out" the ionization chamber by automatically adjusting internal parameters so that the output from the ionization chamber indicates no activity. This check primarily accounts for environmental background radiation. When the check is completed, the system 10 displays a checkmark (see Fig. 16B) in the Zero Check display 1122.

[197] As shown in Fig. 17, the quality control check continues on to the Bias Adjustment check, which is similar to the Zero Check above but makes finer adjustments to internal biasing parameters to offset the effects of minor current fluctuations due to noise within the circuitry of the ionization chamber. The fine adjustments are made to ensure consistent activity readings from one measurement to the next. Fig. 17 shows a checkmark in the Bias Adjustment display 1124, thereby indicating that the system 10 has successfully adjusted the bias setting.

[198] Fig. 17 further shows that the Background Check is in progress. As such, field 1126 is highlighted and a progress bar 1126a indicates the degree of progress (here, 20%). The Background Check basically completes the ionization chamber "zeroing" steps conducted during the Zero and Bias Adjustment checks. The system 10 takes several readings (e.g., 10) from the ionization chamber and captures the average of those readings for display to the user. This allows the user to determine whether the ionization chamber has been sufficiently zeroed out.

[199] The next system check is the "Constancy/Accuracy" test, which is used to monitor the performance of the ionization chamber by measuring the same check source at intervals over a long period of time. The check source (e.g., Cs-137) is placed in the ionization chamber and the measured activity is compared to the expected activity based on the original assay information (decayed for time) of the check source. This ensures that the ionization chamber is providing accurate readings. The measured activity is also compared to previous readings of the same check source (decayed for time) by the ionization chamber. This ensures that the readings provided by the ionization chamber are consistent over time.

[200] When the system 10 initiates the "Constancy / Accuracy" test, a pop-up 1140 is generated (see Fig. 18) to prompt the operator to place a suitable pharmaceutical (in this example, Cs-137) in the ionization chamber 160 and to input information about the radiopharmaceutical (see data fields in pop-up 1140) into the system 10. In a preferred embodiment, the pop-up 1140 automatically includes the radiopharmaceutical information from the most recent "Constancy/Accuracy" test, and the operator activates the "Edit" button 1144 to input new and accurate

information when necessary. In an alternate embodiment the data fields in pop-up 1140 could be left blank for filling by the operator.

[201] After the pharmaceutical is placed in the ionization chamber 160 and the data fields in pop-up 1140 are complete and accurate, the operator activates the "OK" button 1146 to initiate the "Constancy/Accuracy" test. The "Constancy/Accuracy" display bar 1128 preferably includes a test progress bar (not shown) similar to bar 1126a in Fig. 17 that indicates the degree of progress to the operator. If the operator wishes to bypass the Constancy/Accuracy" test, she may activate the "Skip" button 1142 to bypass the test and proceed to the "Battery Measurement" test (discussed below with respect to Fig. 20). Once the "Constancy/Accuracy" test is completed, another pop-up 1148 is generated by the system 10 (see Fig. 19) to prompt the operator to remove the pharmaceutical from the ionization chamber 160. After the operator activates the "OK" button 1149 in pop-up 1148 to inform the system 10 that the radiopharmaceutical has been removed from the ionization chamber 160, the system 10 then initiates the ionization chamber "Battery Measurement" check.

[202] As shown in Fig. 20, the four previous system checks (see displays 1122-1128) are indicated by checkmarks as having been successfully completed. The ionization chamber "Battery Measurement" check measures the voltage output provided by a battery pack internal to the ionization chamber to ensure that the voltage output is sufficient to produce accurate readings from the ionization chamber. The ionization chamber "Battery Measurement" check is shown as being 84% completed by progress bar 1130a.

[203] After the "Battery Measurement" check is completed, the system 10 generates a "Summary" display screen 1150, as shown in Fig. 21, with specific results for all of the checks. If the "Constancy/Accuracy" test was bypassed by the operator (by activating Skip button 1142 in Fig. 18), the system 10 generates "Summary" display 1150a shown in Fig. 22, which indicates that the "Constancy/Accuracy" test was skipped.

[204] Screen 1150 also includes a print button 1152 that is activated to, for example, print out the test results (via printer 24 of system 10) for the system's maintenance file. In addition, the Summary display 1150 includes a New Test button 1154, which is activated by the operator to initiate a new series of quality control checks. When the New Test button is activated, the display 1120 shown in Fig. 15 is generated and the quality control check is conducted again by the system 10.

Patient Treatment

[205] The "Patient Treatment" category of tasks is described below in relation to Figs. 23-32B. The "Patient Treatment" category includes a number of tasks that are preferably performed in the following order to administer or inject a radiopharmaceutical into a patient: (1) setting the desired activity level to be delivered to the patient; (2) inputting patient and/or case identification information into the system 10; (3) connecting the first end 702 of the SPDS 700 to the connector end 228 of the MPDS 200; (4) priming the SPDS 700 to remove air therefrom; (5) connecting the patient end 704 of the SPDS 700 to the patient; (6) conducting a test injection to ensure the integrity of the fluid path to the patient; (7) preparing the radiopharmaceutical dose to be administered or injected into the patient; (8) measuring the activity level of the radiopharmaceutical dose in the dose calibrator 160 to ensure that it is equal or substantially equal to the desired activity level to be delivered to the patient; (9) discarding the radiopharmaceutical dose if, for example, the patient is experiencing discomfort or the measured activity level is not equal or substantially equal to the desired activity level; and (10) administering or injecting the radiopharmaceutical dose to the patient if the measured activity level is equal or substantially equal to the desired activity level. While the above order is the preferred one for the "Patient Treatment" tasks, the tasks may be performed in any suitable manner and order for the intended application.

[206] After the operator prepares the system 10 for a fluid delivery procedure by, for example, completing the steps set forth above in the "System Preparation" tasks, the system 10 generates the display 1000 shown in Fig. 23 which indicates in the upper left hand side thereof that the "System is ready." The saline field 1002 indicates that 500 ml of saline is available and the FDG field 1004 indicates that 700 mCi of FDG are available, as shown.

[207] As further shown in Fig. 23, the Desired Activity field 1006 indicates that 15.0 mCi is the current desired activity level. This 15.0 mCi activity level is preferably an operator-defined, default setting in the system 10, but also could be the desired activity level that was programmed for the last injection procedure.

[208] The desired activity level is preferably set by the operator in one of two ways: (1) manual input; or (2) a calculation based on patient weight. If the operator wants to set the desired activity level by manual input rather than by patient weight, the operator activates the "No" button 1202a in display 1006. In response thereto, the system 10 generates the display and keypad 1204 shown in Fig. 24A. The operator uses the keypad 1204 to input the desired activity level.

[209] If instead the operator wants to set the desired activity level based on patient weight, the operator activates the "Yes" button 1202b in Fig. 23. Upon activation of the "Yes" button 1202b, the system 10 generates the display 1000 and pop-up 1205 shown in Fig. 24B, which prompts the operator to "Enter patient weight" (displayed in pounds or kilograms in data field 1003) using pop-up 1205. Further, the operator can select the formula to be used in calculating the weight-based activity level by activating formula touch field 1011. When formula touch field 1011 is activated, the pop-up table 1013 shown in Fig. 24C is displayed and the operator is prompted to "Select formula." In a preferred embodiment the operator can select up to five operator-defined formulas. For example, as shown in Fig. 24C, the operator can select among three predefined formulas: (1) Standard (0.1 mCi/lb.); (2) Melanoma (0.13 mCi/lb.); and (3) Pediatric (0.07 mCi/lb.). However, the system 10 can include more than pre-set or predefined weight-based formulas. For example, the system 10 can also include formulas based on other patient parameters, such as glucose-level or cardiac output, or scanner parameters, such as acquisition time or crystal type.

[210] Once the formula is selected, the desired activity level is calculated using the formula and the patient's weight. The desired activity level (e.g., 13.5 mCi), the patient's weight (e.g., 135 lb.) and the formula (e.g., 0.1 mCi/lb.) are displayed in field 1006 and the screen display 100 indicates that the "System is ready", as shown in Fig. 24D.

[211] In addition, as displayed in display and keypad 1204 shown in Fig. 24A, in a preferred embodiment the system 10 includes pre-defined minimum and maximum activity levels that define the operating range (i.e., 5-25 mCi) of the system 10. The operating range of the system 10 cannot be altered by the operator, and the system 10 preferably will not accept a desired activity level (whether manually input or calculated based on patient weight or other patient or scanner parameter) that falls outside of the system's operating range. In a preferred embodiment, the system will default to the maximum or the minimum activity level (i.e., 25 mCi or 5 mCi) if the operator attempts to input or the system calculates a desired activity level that is greater than the maximum activity level or less than the minimum activity level, respectively.

[212] Furthermore, if desired for safety or medical practice or preference reasons, the operator preferably can define her own minimum and maximum desired activity levels for the system, as long as they fall within the operating range of the system 10. For example, the operator can define a minimum desired activity level of 10.0

mCi and a maximum desired activity level of 17.5 mCi for the system 10 because those two parameters fall within the 5-25 mCi operating range of the system 10. In such a case, as shown in Fig 24E, even though the operator inputted a patient weight of 5 lb. and chose a formula of 0.1 mCi/lb. (which would result in a calculated desired activity level of 0.5 mCi), the system 10 sets the desired activity level to the minimum desired activity level of 10.0 mCi. When the system 10 uses the minimum desired activity level instead of a manually input activity level or a calculated weight-based activity level, the system 10 indicates that to the operator by using, for example, the downward arrow icon 1006a shown in display field 1006 of Fig. 24E.

[213] Likewise, as shown in Fig. 24F, even though the operator inputted a patient weight of 999 lb. and chose a formula of 0.1 mCi/lb. (which would result in a calculated desired activity level of 99.9 mCi), the system 10 set the desired activity level to the maximum desired activity level of 17.5 mCi. When the system 10 uses the maximum desired activity level instead of a manually input activity level or a calculated weight-based activity level, the system 10 indicates that to the operator by using, for example, the upward arrow icon 1006b shown in display field 1006 of Fig. 24F.

[214] After the desired activity level is programmed or set by the system 10, preferably the operator inputs case information including patient identification and injection site information into the system 10, as shown in Figs. 25A and 25B. When the operator activates the Edit button 1208 in the Case ID field 1206 (see e.g., Fig. 23), the "Case Information" pop-up display 1217 shown in Fig. 25A appears. The display 1217 includes an "Identification" field 1217a and a keypad 1217j for inputting a patent or other identification number in field 1217a. In addition, the display 1217 includes a number of "Injection Site" touch buttons 1217b-1217i for identifying and recording in the system 10 the site on the patient at which the radiopharmaceutical will be administered or injected, including 'Left Antecubital' 1217b, 'Right Antecubital' 1217c, 'Left Hand' 1217d, 'Right Hand' 1217e, 'Left Foot' 1217f, 'Right Foot' 1217g, 'Access Port' 1217h and 'Other' 1217i.

[215] Once the Identification and Injection Site information is input into the system 10, the information is displayed in the Case ID field 1206, as shown in Fig. 25B. Further, as shown in Fig. 25B, after the requisite information is input into the system 10 and displayed in the Case ID field 1206, a Patient Preparation field 1210 including a Prime touch button 1212 is generated and displayed for the operator.

[216] Before the Prime button is 1212 is activated, the first end 702 of the SPDS 700 should be attached to the connector end 228 of the MPDS 200, as discussed in detail

above. When the SPDS 700 is connected to the MPDS 700, the operator can activate the prime button 1212 to cause the system 10 to prime the SPDS 700 to remove air therefrom.

[217] As shown in Fig. 26A, after the Prime button 1212 is activated the system 10 indicates that the system is "Priming" the SPDS 700 and generates a progress bar 1213 (which indicates in Fig. 26A that the priming operation is 17% completed). Further, the system 10 highlights the fluid path field 1008 and the coil field 1010 in display 1000 to indicate that saline is being pumped from saline source 23 (indicated by saline field 1002) through the MPDS 200 and the SPDS 700 to prime the SPDS 700. After the SPDS priming operation is completed, the system 10 generates a prompt display 1215, as shown in Fig. 26B, that queries the operator as to whether all air has been expelled or purged from the SPDS 700. If the "Yes" button 1215a is activated, the SPDS priming operation is completed and the system 10 is ready to conduct a test injection and/or to prepare the pharmaceutical dose for injection into the patient, as discussed in more detail below. If, on the other hand, the "No" button 1215b is activated, the SPDS priming operation is preferably conducted again.

[218] After the SPDS priming operation is completed, the patient end 704 of the SDPS 700 is connected to the patient (as described above) and the Patient Preparation display field 1210 on the touch screen 1000 includes a "Test Inject" button 1212a, as shown in Fig. 28A. If the operator desires to conduct a test injection to, for example, ensure the integrity of the fluid path along the MPDS 700, the SPDS 200 and the patient's vasculature, the operator activates the "Test Injection" button 1212a and the system 10 pumps saline from the saline source 23 through the MPDS 200 and the SPDS 700 to the patient. Concurrently, the system 10 generates the display shown in Fig. 27A to inform the operator that the system 10 is "Test Injecting" and highlights the fluid path display 1008 from the saline source icon 1002 to the ionization chamber display 1010. The display 1000 also includes a progress bar 1213a to indicate the degree of progress made (here 45%) in completing the test injection procedure.

[219] If the operator needs to pause the test injection due to, for example, patient discomfort or incorrect positioning of the catheter in the patient, she can activate the "Pause" button 1212d in the Patient Preparation" display 1210 (see Fig. 27A) to pause the procedure. When the test injection procedure is paused, the system 10 generates the display shown in Fig. 27B, indicating that the test injection is "Paused" and providing a "Resume" button 1212b and a "Stop" button 1212c in the Patient Preparation display 1210. To resume or stop the test injection, the operator

can activate the corresponding "Resume" and "Stop" buttons, 1212b, 1212c, respectively.

[220] In addition to using the various "Pause" and "Stop" buttons provided by the GUI display 15, an operator can also depress the interrupt button 25 on the cabinet 9 of the system 10 to at any time pause or stop a procedure or operation being conducted by the system.

[221] After the test injection is completed or terminated the system 10 generates the display 1000 shown in Fig. 28A, which includes an FDG Dose display 1216 and a corresponding "Prepare" button 1218. After the operator activates the "Prepare" button 1218, the system 10 generates the display shown in Fig. 28B and begins to pump a volume of FDG (or other suitable pharmaceutical or radiopharmaceutical) from the vial 902 through the MPDS 200 to the tube coil 444 thereof disposed in the ionization chamber 160. As shown in Fig. 28B, to reflect this operation the display 1000 informs the operator that the system 10 is "Measuring Dose" and highlights the fluid path display 1008 from the FDG source display 1004 to the ionization chamber display 1010. The display also includes a progress bar 1214a that shows the system's progress (here 78%) in measuring the pharmaceutical dose.

[222] In a preferred embodiment, the system 10 prepares the pharmaceutical dose in accord with the methodology described in PCT Publication No. WO 2006/007750, in which the activity level of a first amount of a radioactive liquid is measured and used to calculate a second amount of the radioactive liquid that is required for the combined amounts to have a pre-determined level of radioactivity to be delivered to a patient. The contents of PCT Publication No. 2006/007750 are incorporated herein by reference. The dimensions of the coil assembly 400 and the core structure 446, including the height, diameter and volume of the tube coil 444, the length, number of turns, OD and ID of the tubing that forms the tube coil 444, and the dimensional location of the "linear region" of the Veenstra IK-102 ionization chamber, provided above are necessary to optimally and accurately prepare the pharmaceutical dose, whether in accord with the preferred methodology described in PCT Publication No. WO 2006/007750 or using another suitable dose preparation methodology.

[223] The stated tube coil 444 dimensions are necessary to optimally position within the "linear region" of ionization chamber: (1) the volume(s) of pharmaceutical required to deliver the desired activity level to the patient; and (2) the volume of saline necessary to position the total volume of pharmaceutical in the tube coil. The tube coil 444 could be formed from tubing having a larger ID than that stated above (i.e.,

0.156 inches), but larger IDs tend to allow the radiopharmaceutical to be diffused with the saline (which is used to 'place' or 'position' the radiopharmaceutical within the tube coil 444), which may result in the radiopharmaceutical volume or a portion thereof being positioned outside of the tube coil 444 and thus outside of the "linear region" of the ionization chamber (resulting in inaccurate activity level measurements and delivery). Likewise, the tube coil 44 could be formed from tubing having a smaller ID than 0.156 inches (which would possibly further decrease or prevent the diffusion of the radiopharmaceutical with the saline), but the dimensions of the tube coil 444 (e.g., length of tubing, coil tube height, number of turns) required to maintain a tube coil volume of 12.5 ml would result in the tube coil 444 extending beyond the "linear region" of the ionization chamber (resulting in inaccurate activity level measurements and delivery).

[224] Further, the core structure 446 operates to maintain the desired tube coil geometry (e.g., tube coil diameter and height) and to properly position the tube coil 444 axially and vertically within the sleeve 162 so that the tube coil 444 thereby resides within the "linear region" of the ionization chamber 160 (see e.g., Fig. 3F).

[225] With specific reference to the dose preparation methodology described in PCT Publication No. WO 2006/007750, the 12.5 ml volume of the tube coil 444 is designed to accommodate two volumes of a radiopharmaceutical from vial 902 separated by a volume of saline from source 23, regardless of whether the dose is prepared shortly after the radiopharmaceutical was assayed (when a small volume of the radiopharmaceutical is required to deliver a desired activity level) or after a significant amount of time has passed (e.g., in relation to the radioisotope's half-life) since the radiopharmaceutical was assayed (when a greater volume of the radiopharmaceutical is required to deliver the same desired activity level). As a specific example of the above, the 12.5 ml tube coil 444 is designed to accommodate: (1) two 1/16 ml volumes or "slugs" of a pharmaceutical (for a total volume of 1/8 ml) at a concentration of 40 mCi/ml (i.e., highest concentration that the system 10 is designed to handle), separated by a calculated volume of saline necessary to fill or substantially fill the remaining tube coil volume; and (2) two 1.5 ml "slugs" of a pharmaceutical (for a total volume of 3 ml) at a concentration of 1.67 mCi/ml (i.e., lowest concentration that the system 10 is designed to handle), separated by a calculated volume of saline necessary to fill or substantially fill the remaining tube coil volume.

[226] After the dose is pumped by the system 10 into the tube coil 444 disposed within the ionization chamber 160, the activity level of the dose is measured by the system 10.

The measured activity level is then displayed to the operator and the ionization chamber display 1010 is highlighted, as shown in Fig. 29. A new display field 1006a is generated by the system, showing the measured "Calibrated Activity" (here 13.5 mCi) of the prepared dose. Just below field 1006a is a "plus/minus" range indicator 1224. Range indicator 1224, as shown, includes a center circle 1224a, flanked on each side by 10 rectangles. Left and right arrows are also included, respectively, at the far left and far right of indicator 1224. Preferably, as shown in Fig. 29, center circle highlights when the measured "Calibrated Activity" level is the same as the previously programmed, desired activity level (which is the case in Fig. 29). Otherwise, if the measured activity level is greater or lesser than the desired activity level, corresponding rectangles or, in some cases, arrows will highlight to the right of the center circle 1224a (for measured activity > desired activity) or to the left of the center circle 1224a (for measured activity < desired activity) to visually indicate to the operator the difference between the measured and desired activity levels.

[227] In a preferred embodiment, each of the rectangles represents a default value of a 1% discrepancy in the desired to measured activity level, such that three rectangles to the right of the center circle 1224a would be highlighted if the measured activity level was 3% greater than the desired activity level of 13.5 mCi. If the measured activity exceeds the desired activity by more than 10%, then all the rectangles to the right of the center circle 1224a and the right arrow would highlight. Preferably, the extent of the rectangles in indicator 1224 will convey an acceptable range within which the measured activity may fall. Thus, such an acceptable range could be plus or minus ten percent or could be another range as deemed appropriate, with each rectangle representing one tenth of the positive or negative extent of that range. Alternately, however, the default value of each rectangular could be pre-set to another value (such as 0.1 mCi) or could be changed by the operator to another value more suitable for the intended application.

[228] In addition to displaying the measured activity level, as shown in Fig. 29 the display 1000 also generates a "Discard" button 1222 and an "Inject" button 1220 in the FDG Dose display 1216. If for example the measured activity is outside of a clinically acceptable range for the intended procedure, the operator can activate the "Discard" button 1222 to have the system 10 discard the measured dose (i.e., by pumping the dose to the waste receptacle 224, as discussed in detail above) and to prepare another dose for delivery to the patient. Specifically, when the "Discard" button 1222 is activated the system generates the dialog box 1231 shown in Fig. 30A, which queries the operator to confirm that the measured dose is to be discarded. If the

operator confirms that the measured dose is to be discarded by activating the "Yes" button 1231a, the system 10 generates the display shown in Fig. 30B, which indicates to the operator that the system is "Discarding" and creates a progress bar 1233 that indicates the status of the "discarding" operation (here 86% completed). The display 1000 also highlights the fluid path display 1008 from the saline source display 1002 to the ionization chamber display 1010 to indicate that the system 10 is pumping saline through the MPDS 200 to push the dose from the tube coil 444 to the waste receptacle 224 (as described above).

[229] If, on the other hand, the operator activates the "No" button 1231b in Fig. 30A to inform the system 10 that she does not want to discard the measured dose, the system 10 reverts to the display shown in Fig. 29 and the "Discard" button 1222 and the "Inject" button 1220 are again made available to prompt the operator to decide whether to discard or to inject the measured pharmaceutical dose.

[230] If the operator desires to inject the measured dose and thus activates the "Inject" button 1220 shown in Fig. 29, the system 10 generates the display shown in Fig. 31 which indicates to the operator that the system 10 is "Injecting" and, via progress bar 1223, that the injection operation (in Fig. 31) is 27% completed. The fluid path display 1008 between the saline source display 1002 and through the ionization chamber display 1010 to the arrow at the end of the fluid path display 1008 is highlighted to indicate that the system 10 is pumping saline from the saline source 23 to push the dose in the ionization chamber 160 through the remainder of the MPDS 200 and the SPDS 700 to the patient (as described above). Further, the system 10 generates a "Pause" button 1230 in FDG Dose display 1216. As with the test injection operation discussed above (see Fig. 27A), the operator can activate the "Pause" button 1230 or the interrupt button 25 to pause the injection procedure.

[231] After the "Pause" button 1221 is activated, the display shown in Fig. 32A is generated and displayed to the operator. The display shown in Fig. 32A informs the operator that the system 10 is "Paused" and includes a "Discard" button 1222a and a "Resume" button 1230a in the FDG Dose display 1216.

[232] If the injection needs to be terminated, the operator activates the "Discard" button 1222a and the system reverts to that shown and described above with respect to Figs. 30A and 30B to discard the dose into the waste receptacle 224. However, if the procedure can be resumed, the operator activates the "Resume" button 1230a in Fig. 32A and the injection procedure continues to deliver the measured dose to the patient.

[233] When the injection procedure is completed, a pop-up 1240 preferably appears as shown in Fig. 32B. This pop-up 1240, as shown, preferably contains information about the activity and volume of the dose (e.g., FDG) just delivered to the patient, the total fluid delivered (which would include saline) and other identifying information including, for example, the patient identification number, radiopharmaceutical lot number and patient injection site (as shown on the right of pop-up 1240). Activating the "OK" button 1242 causes pop-up 1240 to disappear and the system to revert to an "Idle" state (as shown in Fig. 7) or a "Ready" state (as shown in Fig. 23), while activating the "print" button 1244 prompts the injection information to be printed out by the printer 24 for patient, billing, inventory or other suitable records.

[234] Other capabilities and functions not expressly discussed hereinabove or shown in the drawings are of course conceivable in accordance with the embodiments of the present invention. For instance, if the extraction of a pharmaceutical dose (e.g., FDG) from a vial is interrupted for an unforeseeable reason and is not prompted by a desired "pause", the system could alert the operator to discard the dose (and in that connection present a button for the purpose).

Injection History

[235] The disclosure now turns to a discussion of the injection history operations or tasks that can be performed using the display 1000, as depicted in Figs. 33A-C, 34A and 34B.

[236] The injection history operations or tasks may be prompted by activating the Records / Injection History button 1022, which is displayed when the system 10 is in an "Idle" state (see e.g., Fig. 7) or a "Ready" state (see e.g., Figs. 23, 24D and 28A). Activation of Records button 1022 preferably prompts the appearance of the calendar display 1302 shown in Fig. 33A (here 'October 2006'). Highlighted touch fields within the calendar display 1302 preferably correspond to those dates of the displayed month (here 'October 2006' in field 1309) on which the system 10 was used to perform an injection procedure, while those other days of the displayed month in which the system 10 was not used are not highlighted. Arrow buttons to the left 1309a and right (not shown), respectively, of field 1309 preferably permit the operator to scroll through different months to access and retrieve injection history information.

[237] The calendar display 1302 also includes a "Print Summary" button 1304, a "Print Days" button 1306 and a "Done" button 1308. Activation of the "Print Summary"

button 1304 provides a high-level summary of the injection procedures conducted for the specified month (here 'October 2006'), similar to the injection procedure information displayed in Fig. 34A. The "Print Days" button 1306 preferably prompts the appearance of the display 1302a shown in Fig. 33B. The "Done" button 1308 can be activated once the operator has completed the necessary injection history retrieval operation or task, and the display 1000 then preferably reverts to the "Idle" state display (see e.g., Fig. 7) or the "Ready" state display (see e.g., Figs. 23, 24D and 28A) as appropriate.

[238] Referring now to Fig. 33B (prompted by activation of "Print Days" button 1306), the display 1302a includes an "All Days" touch field 1330 (which is activated in Fig. 33B) including a "Print" button 1334, and a "Range" touch field 1332. If the operator mistakenly activated the "Print Days" button 1309 on display 1302 (see Fig. 33A), she can activate the "Cancel" button 1336 to return to the display 1302 shown in Fig. 33A. If the operator wishes to print the injection history information for all the days in the selected month (here 'October 2006'), "Print" button 1334 can be activated and the printer 24 will print the injection history records for the days in which the system 10 performed injection procedures. If the operator instead wants to access injection history information for a range of days in the selected month, the operator can activate the "Range" touch field 1332, which prompts the appearance of the display 1302b shown in Fig. 33C.

[239] As shown in Fig. 33C, the display 1302b includes a "From" touch field 1332a and a "To" touch field 1332b which the operator activates to select the "From" and "To" dates in the selected month to establish the range of dates for which injection history information is to be accessed. Once the date range is selected, the "Print" button 1334 is activated to prompt the printer 24 to print the injection history information.

[240] Referring back to Fig. 33A, in addition to activating the "Print Summary" button 1304 or the "Print Days" button 1306, the operator is also able to activate any of the highlighted calendar buttons to access injection history information for that day of the selected month. For example, if the operator wanted to retrieve injection history information for 10 October 2006, the operator would activate the "10" button 1340 shown in Fig. 33A and the system 10 would generate the display 1310 (including selected date field 1310a) shown in Fig. 34A.

[241] As shown in Fig. 34A, a series of display fields 1312 includes information on the lot number, case ID, delivery time and delivered activity of a given injection procedure conducted on the selected day (here '10 October 2006 (Tuesday)'). Page up 1316 and page down 1318 arrow buttons are provided to allow the operator to scroll

through the procedures conducted on the selected day. Page left 1350 and page right 1351 arrow buttons are also provided to allow the operator to scroll through and select dates prior to or subsequent to the selected '10 October 2006' date displayed in date field 1310a. A "Month View" button 1320 can be activated to revert to a "month view" as shown in Fig. 33A, while the "Print Day" button 1306a can be activated to print the injection history details of all injection procedures on the day in question (i.e., the day currently being displayed). Further, "magnifying glass" touch fields 1314 are provided for each procedure and, upon activation, preferably prompts a detailed injection history display 1360 (see Fig. 34B) for the selected procedure.

[242] As shown in Fig. 34B, the detailed injection history display 1360 provides details on the specific pharmaceutical injected (here "FDG"), the date (10 October 2006) and time (09:15) of injection and the activity level (15.1 mCi) and volume (5 ml) of the injected pharmaceutical. Further, the display 1360 indicates the total volume (35.0 ml) of injected fluid (pharmaceutical and saline), the Patient Identification number, the Lot number of the pharmaceutical and the IV Injection Site on the patient. The "Print" button 1363 is activated to print the injection details and the "OK" button 1362 is activated to revert to the display 1310 shown in Fig. 34A.

System Configuration

[243] The disclosure now turns to a discussion of system configuration tasks, as depicted in Figures 35-46. The configuration tasks are undertaken to permit an operator to set various system preferences, including but not limited to preferences related to the following: (1) Language; (2) Date / Time display; (3) Units; (4) Audio; (5) FDG / Pharmaceutical dose preparation formulas; (6) Saline volumes; (7) Case Information display; (8) Printing; (9) Daily QC isotope reference information; (10) Linearity measurement tests; (11) Calibration tests; and (12) Field Service reminders.

[244] The system configuration tasks may be prompted by activating the Configuration button 1021, which is displayed when the system 10 is in an "Idle" state (see e.g., Fig. 7) or a "Ready" state (see e.g., Figs. 23, 24D and 28A). Activation of Configuration button 1021 preferably prompts the appearance of the "System", "Treatment" and "Maintenance" touch fields (1402, 1404 and 1406, respectively) shown in Fig. 35, each of which when activated prompts the appearance of a distinct tabbed menu display 1400a-c (as explained in more detail below). An "OK" button 1418 may be activated when the system configuration tasks are completed, while a "default" button" 1416 may be activated to reset the system 10 to the default configuration settings.

[245] As shown in Fig. 35, the "System" touch field 1402 is activated and the tabbed menu display 1400a is provided. On menu display 1400a, tabs for language, date/time, units and audio are provided (1408, 1410, 1412, and 1414, respectively), and language tab 1408 is activated to prompt a language menu 1420. Preferably, language menu 1420 will permit the selection of any of a number of languages to be used with the system 10 in accordance with operator or local preferences.

[246] Fig. 36 shows date/time tab 1410 activated to prompt a date/time display 1422. Via a calendar button 1422a, a current date can be set, while date format preferences (e.g., European vs. American, etc.) can be set via touch field 1422b. A time display field 1422c preferably shows the current time and a time edit button 1422d may be activated to set the time as well as to select a 12- or 24-hour time format.

[247] Fig. 37 shows units tab 1412 activated to prompt a display 1424. Display 1424 preferably permits, via buttons 1426a, 1426b, 1428a, 1428b, a choice of units for weight (lbs. vs. kg) and activity (Curies vs. Becquerels), respectively.

[248] Fig. 38 shows audio tab 1414 activated to prompt a display 1444. "High", "normal" and "low" audio volumes (e.g., for prompts or alarms) can be selected via buttons 1444a, 1444b and 1444c, respectively.

[249] Fig. 39A shows the treatment touch field 1404 activated, which generates a second tabbed menu display 1400b. On menu display 1400b, tabs for "FDG", "saline", "case" and "printing" are provided (1450, 1452, 1454, and 1456, respectively). In Fig. 39A, FDG tab 1450 is activated to prompt a display 1460. Preferably, display 1460 includes an entry field 1462 for entering a default desired activity level (which may then automatically appear in field 1006 of Fig. 7).

[250] The display 1460 further includes a weight-based dosing sub-menu 1460a that includes on/off buttons 1464a, 1464b and an "Edit Formulas" button 1466. If the operator would like the system 10 to default to a weight-based calculation for desired activity level, the operator activates the "On" button 1464a. If a default, weight-based calculation for desired activity level is not desired, the operator can select the "Off" button 1464b (as shown in Fig. 39A). Further, upon activation of the "Edit Formulas" button 1466, the system 10 generates the pop-up edit display 1470 shown in Fig. 39B to allow the operator to edit existing or add new formulas for calculating desired activity level based on, for example, patient weight.

[251] As shown in Fig. 39B, the edit display 1470 may include a column of five buttons 1476, each preferably corresponding to a predetermined formula for a procedure

type that, for instance, may commonly be repeated. Here, a "Melanoma" button 1476a is activated to then present a sub-display 1478 which can afford an editing of any or all of the following: name of the formula (via button 1478a), multiplier to be used in calculating weight-based desired activity level (via touch field 1478b), and minimum and maximum desired activity levels (via touch fields 1478c and 1478d, respectively). Also, the entire formula can be deleted (via button 1478e) from the set 1476, if desired. Further, the operator may enter new formulas into the system 10 by activating the "New Formula" buttons 1476b

[252] Fig. 40 shows Saline tab 1452 activated to prompt a display 1480. Display 1480 preferably contains touch fields 1482, 1484 and 1486, respectively, for pre-selecting a default saline bulk size (here 500 ml) for the saline source 23 (if, for example, the facility generally uses or will use the same bulk size of saline), an additional saline flush volume (e.g., to account for the additional tubing length if the SPDS 700 is connected to an IV instead of directly to a catheter in a patient) and a test inject volume (here 30 ml). The Default Bulk Size volume entered in 1482, for example, can be a quantity that initially appears to an operator at a time when saline is installed in the system 10, which can be changed or left alone as appropriate. Any data entry in touch fields 1482, 1484, 1486 can be accomplished, e.g., via a keypad 1488.

[253] Fig. 41 shows case tab 1454 activated to prompt a display 1490. Display 1490 preferably permits the operator to set a default preference (via on/off buttons 1492) as to whether Case ID information (i.e., for a given patient) can be edited as appropriate. Further, the display 1490 allows the operator to set a default injection site for the system 10 by activating one of the injection site buttons 1494 provided in display 1490. Of course, the default injection site location can be changed by the operator during the preparation steps for the fluid delivery procedure if the actual injection site is different from the default injection site.

[254] Fig. 42 shows printing tab 1456 activated to prompt a display 1502 which allows an operator to establish an automatic printing of record labels (e.g., as may be printed at the end of an injection procedure) and the quantity of record labels to be printed.

[255] Finally, Fig. 43A shows maintenance touch field 1406 activated, which generates a third tabbed menu display 1400c. On menu display 1400c, tabs for "Daily QC", "Linearity", "Calibration" and "Field Service" (1510, 1512, 1514, 1516, respectively) are provided. The maintenance tabs relate to general maintenance and calibration of the system 10.

[256] As shown in Fig. 43, Daily QC tab 1510 is activated to prompt a display 1518. Display 1518 allows the operator to input information related to the radioisotope to be used to conduct daily QC tests (described above) of the system 10. Specifically, Isotope touch field 1520 and Lot Number touch field 1522 permit the operator to input the specific radioisotope to be used (here Cs-137) and the lot number thereof, respectively. Further, the operator can input the time and date that the radioisotope was created (e.g., in a cyclotron or a reactor), as well as the activity level of the radioisotope when it was created, in the Time and Activity touch fields 1526, 1524, respectively. The Edit button 1526a can be activated to edit the previously entered time and date information.

[257] Fig. 44A shows linearity tab 1512 activated to prompt a display 1530. Display 1530 prompts the operator for information and assists in conducting a linearity measurement for the system 10, which should be conducted every quarter (as noted in display 1530). Linearity measurements are based on the known decay of radioisotopes and are conducted to ensure that the ionization chamber 160 in the system 10 is reliably measuring the activity level of a radioisotope placed therein. Specifically, during a linearity measurement the measured activity level of a radioisotope is compared to the known activity level of the radioisotope (based on its half-life decay) at selected intervals (e.g., every 15 minutes) over a period of time (e.g., 24 hours) to determine whether the measured activity level falls within an acceptable error range.

[258] When the linearity tab 1512 is activated, details from the most recent linearity measurement are shown in sub-display 1532, while a button 1534 can be activated to prompt the appearance of a related graph (of, for example, measured vs. known activity level over the measurement period). To conduct a new linearity measurement, button 1536 is activated, which preferably generates the display 1540 shown in Fig. 44B.

[259] As shown in Fig. 44B, isotope field 1542 may be activated to identify the radioisotope to be used for the linearity measurement (here F-18). While isotope field 1542 preferably conveys the reference isotope, the activity level of the radioisotope (e.g., at the time it was drawn) can be input into activity level field 1544. In addition, the reference date and time for the activity level (e.g., the date and time that the radioisotope was drawn) is input into touch fields 1546 and 1548, respectively, by using, for example, a calendar button 1546a and a AM/PM time button 1548a. Once the requisite radioisotope information is inputted into display 1540, the operator can activate the "Begin Measurement" button 1543 to start the

linearity measurement. Of course, the operator can activate the "Cancel" button 1541 to cancel the linearity measurement and return to the display 1530 shown in Fig. 44A

[260] After the "Begin Measurement" button 1543 is activated, the pop-up display 1545 shown in Fig. 44C is generated to prompt the operator to confirm that the reference radioisotope has been placed in the ionization chamber 160. If the operator activates the "Yes" button 1545a (as shown in Fig. 44C) to confirm that the F-18 radioisotope has been placed in the ionization chamber 160, the system 10 will begin the linearity measurement.

[261] If the operator activates the "No" button 1545b, the display reverts to the display 1540 shown in Fig. 44B, and the operator can then load the reference radioisotope source into the ionization chamber and once again activate the "Begin Measurement" button 1543 to start the linearity measurement.

[262] After the operator activates the "Yes" button 1545a, the display 1547 shown in Fig. 44D is generated. In addition to displaying the radioisotope in field 1542 and the maximum allowable error for the linearity measurement in field 1552, the display 1547 also shows the estimated time for completion of the linearity measurement (here "23:15:03" hours) and the measured activity (in field 1554), the calculated activity (in field 1558) and the current error (in percentage format) (in field 1556). The linearity measurement may be aborted via an "Abort" button 1560 and the results of the linearity measurement, including a graph of the results, may be printed by selecting a "Print" button (not shown).

[263] As shown in Fig. 45A, activation of calibration tab 1514 prompts the system 10 to generate a calibration display 1570, which shows the results of a previous ionization chamber calibration routine. Ionization chamber calibration routines are preferably conducted upon installation of the system 10 (at, for example, a medical facility) and approximately once a year thereafter to ensure that the ionization chamber 160 of the system 10 is properly calibrated to operate over the range of energies and activity levels of the radiopharmaceuticals for which the ionization chamber 160 is intended to be used. In a preferred calibration routine, the gain of the ionization chamber is increased or decreased to best fit or adjust the measured activity levels of two or three radioisotopes (preferably having energy levels different from (e.g., lower than and greater than) the energy levels of the radiopharmaceuticals to be used with the system 10) against their known activity levels.

[264] By way of a specific example, the system 10 is currently intended to be used to administer FDG (which contains the radioisotope F-18) to patients. The energy level of F-18 is 511 KeV. In a first preferred embodiment, three radioisotopes are used to calibrate the ionization chamber 160: (1) Co-57 (energy level of 122 KeV; less than that of F-18); (2) Co-60 (energy level of 1333 KeV; greater than that of F-18); and (3) Cs-137 (energy level of 662 KeV; relatively close to that of F-18). In a second preferred embodiment, two radioisotopes are used for the calibration routine: (1) Co-57; and (2) Cs-137.

[265] Returning to Fig. 45A, the calibration display 1570 includes a sub-display 1571 conveying previous calibration results for Co-57 (field 1571a), Co-60 (field 1571b) and Cs-137 (field 1571c), while a button 1574 can be activated to begin a new calibration routine. Previous results can also be printed, e.g., via a button 1572.

[266] Upon activating button 1574, a display 1573 is generated (see Fig. 45B) that prompts the operator to place the radioisotope source (here Co-57) in the ionization chamber 160. The display 1573 includes a sub-display 1573a that lists various information about the isotope, including the isotope's name, the lot number, the date and time that the isotope was drawn and the activity level of the isotope when it was drawn. Further, the display 1573 includes "Cancel" button 1573b, "Edit" button 1573c and "OK" button 1573d. The cancel button 1573b is activated to cancel the calibration routine, the edit button 1573c is activated to edit the isotope information provided in sub-display 1573a and the OK button 1573d is activated (as shown in Fig. 45B) to commence the calibration routine with respect to the noted radioisotope (here Co-57), as discussed in more detail below.

[267] If the edit button 1573c in display 1573 is activated, the edit source display 1576 shown in Fig. 45C appears. The operator can edit the isotope information in display 1576 by entering the isotope name in field 1580, the lot number in field 1582, the activity level (at isotope creation) in field 1584 and the reference time and date (of isotope creation) in field 1586 via edit button 1586a. After the isotope information is entered, the operator activates the OK button 1578 and the display 1000 reverts to the display 1573 shown in Fig. 45B. If the isotope information is now correct, the operator can activate the OK button 1573d in display 1573 to commence the calibration routine for the noted radioisotope (here Co-57).

[268] After the OK button 1573d is activated, a tabbed calibration display 1590, including touch tabs for Co-57 (tab 1592), Co-60 (tab 1594) and Cs-137 (tab 1596), appears (as shown in Fig. 45D) and shows the results of the calibration routine for the noted radioisotope (here Co-57). Specifically, the display 1590a for Co-57 tab 1592

shows the target or expected activity for Co-57 (in field 1598), the actual measured activity for the Co-57 placed in the ionization chamber 160 (in field 1600) and the error between the target and measured activity (in field 1602). To thereafter compensate for the error (here 1%), the low gain of the ionization chamber (displayed in field 1604) is adjusted by using the 'plus' and 'minus' buttons 1606, respectively. Further, as shown in Fig. 45D, based on the error for Co-57 the system 10 calculates an estimated error (here 1%) for Cs-137 and displays it in field 1612. Based on the target or expected activity for Cs-137 (entered by the operator and displayed in field 1608) and the estimated error, the estimated measured activity is calculated by the system 10 and displayed in field 1610.

[269] The calibration routine is continued by thereafter activating the tab 1594 for the Co-60 isotope and repeating the steps described above with respect to Figs. 45B-45D. To compensate for the error (not shown) between the expected activity and the measured activity for Co-60, the high gain of the ionization chamber is adjusted (in the same way as shown in Fig. 45D for Co-57). The system 10 then uses the error for Co-60 to revise the estimated error for Cs-137, which is then displayed in field 1612 for the operator.

[270] The operator may continue the process above (i.e., iteratively conducting Co-57 and Co-60 activity measurements and adjusting the low and high gain of the ionization chamber) until the estimated error for Cs-137 (whose energy level of 662 KeV is relatively close to the 511 KeV energy level of F-18) is within an acceptable range (e.g., 1%). At that time, the operator activates the tab 1596 for the Cs-137 isotope and places the Cs-137 source in the ionization chamber to confirm that the difference between the expected and measured activity of the Cs-137 isotope is substantially similar to or within an acceptable range from the estimated error displayed in field 1612. At this point the calibration routine is completed, and the results may be printed and/or stored for later accessing by system maintenance personnel. As shown, an "abort" button 1614 for terminating the calibration procedure is provided for the operator.

[271] Finally, Fig. 46 shows field service tab 1516 activated to prompt a display 1620 which can be used to pre-set one or more future reminder dates to undertake preventative maintenance for the system 10.

[272] It is to be appreciated that the systems, devices and methods of the present invention can be used in a very wide variety of drug delivery and therapeutic procedures. In general, the systems, devices and methods of the present invention are particularly suited for use in connection with any hazardous pharmaceutical or substance to be

injected into a patient (human or animal). Even pharmaceuticals, such as contrast agents or thrombolytic agents, that are not considered to be especially hazardous can be beneficially administered via systems broadly contemplated herein and provide hospital personnel additional protection against adverse effects.

[273] To the extent that systems of the present invention can be applicable to radiotherapy drugs or pharmaceuticals wherein the drug or pharmaceutical itself is radioactive, it is to be appreciated that, as clear to one skilled in the art, maintaining containment of radiotherapy pharmaceuticals promotes safety. If the drug or pharmaceutical is radioactive, the use of radiation absorbing or leaded shielding will help protect the operator and patient from unnecessary radiation. Containment of radiotherapy pharmaceutical is discussed in U.S. Patent Application Publication No. 2003-0004463, the contents of which are incorporated herein by reference.

[274] While procedures discussed herein in accordance with embodiments of the present invention have generally been described with respect to liquid drugs, it is to be understood that they can also apply to powdered drugs with either a liquid or gaseous vehicle, or gaseous drugs that are to be delivered to a recipient.

[275] If not otherwise stated herein, it may be assumed that all components and/or processes described heretofore may, if appropriate, be considered to be interchangeable with similar components and/or processes disclosed elsewhere in the specification, unless an express indication is made to the contrary.

[276] If not otherwise stated herein, any and all patents, patent publications, articles and other printed publications discussed or mentioned herein are hereby incorporated by reference as if set forth in their entirety herein.

[277] It should be appreciated that the apparatus, systems, components and methods of the present invention may be configured and conducted as appropriate for any context at hand. The embodiments described above are to be considered in all respects only as illustrative and not restrictive.

WHAT IS CLAIMED IS:

1. A fluid path set for use in a fluid delivery system, the fluid path set comprising:

a medical fluid component comprising a first tubing section for connection to a source of a medical fluid;

a pharmaceutical component comprising a second tubing section for connection to a source of a pharmaceutical;

a coil assembly component comprising a tube coil having a height of approximately 1.53 inches, a diameter of approximately 1.95 inches and a volume capacity of approximately 12.5 ml; and

a connector comprising a first port for connecting the first tubing section of the medical fluid component, a second port for connecting the second tubing section of the pharmaceutical component and a third port for connecting the tube coil of the coil assembly component.

2. The fluid path set of Claim 1 wherein the tube coil comprises a tubing section having an outer diameter of approximately 0.218 inches, an inner diameter of approximately 0.156 inches and a length of approximately 41 inches.

3. The fluid path set of Claim 2 wherein the tube coil is formed in a helical coil of approximately 7 turns of the tubing section.

4. The fluid path set of Claim 3 wherein the coil assembly further comprises a core structure around which the tube coil is formed, the core structure comprising an upper shoulder and a lower shoulder that define a tube channel therebetween, the upper and lower shoulders adapted to retain the tube coil therebetween within the tube channel.

5. The fluid path set of Claim 4 wherein the core structure further comprises an upper surface defining an inlet for accommodating a first end of the tubing section and an outlet for accommodating a second end of the tubing section.

6. The fluid path set of Claim 5 wherein the coil assembly component further comprises a third tubing section connected to the third port of the connector and the first end of the tubing section and a fourth tubing section connected to the second end of the tubing section.

7. The fluid path set of Claim 6, further comprising:

a waste component comprising a fifth tubing section in connection with a waste receptacle;

a sixth tubing section having a connector end that is adapted to be connected to a single-patient tubing set; and

a second connector comprising a first port for connecting the fourth tubing section of the coil assembly component, a second port for connecting the fifth tubing section of the waste component and a third port for connecting the sixth tubing section.

8. The fluid path set of Claim 7 wherein the connector end comprises a swabable luer valve that is biased to a closed position when the single-patient tubing set is not connected thereto.

9. The fluid path set of Claim 7 wherein the connector end comprises a manifold or a stopcock each having two or more outlet ports for connection to respective single-patient tubing sets.

10. The fluid path set of Claim 7 wherein the first tubing section is approximately 56.75 inches in length and has an outer diameter of approximately 0.188 inches, an inner diameter of approximately 0.062 inches and a durometer of 45, the second tubing section is approximately 8.75 inches in length and has an outer diameter of approximately 0.094 inches, an inner diameter of approximately 0.032 inches and a durometer of 45, the third tubing section is approximately 15 inches in length and has an outer diameter of approximately 0.163 inches, an inner diameter of approximately 0.062 inches and a durometer of 60, the fourth tubing section is approximately 12 inches in length and has an outer diameter of approximately 0.163 inches, an inner diameter of approximately 0.062 inches and a durometer of 60, and the fifth tubing section and the sixth tubing section are each approximately 5 inches in length and have an outer diameter of approximately 0.163 inches, an inner diameter of approximately 0.062 inches and a durometer of 60.

11. The fluid path set of Claim 1 wherein the first tubing section comprises a first check valve and a spike for connecting to the source of a medical fluid and the second tubing

section comprises a second check valve and a vented cannula for connecting to the source of a pharmaceutical.

12. The fluid path set of Claim 1 wherein the second tubing section comprises a vented cannula comprising:

a main hub comprising two opposed lateral sides and defining a fluid port and a vent;

a fluid draw needle in connection with the second tubing section through the fluid port and adapted to be placed within the source of a pharmaceutical;

a vent needle in connection with the vent and adapted to be placed within the source of a pharmaceutical; and

two resilient arms connected to the opposed lateral sides of the main hub, each of the two arms comprising a top edge and a hook member formed thereon and extending outwardly therefrom.

13. The fluid path set of Claim 12 wherein the fluid draw needle is longer than the vent needle.

14. The fluid path set of Claim 12 wherein the vent comprises a filter.

15. The fluid path set of Claim 12 wherein the main hub of the vented cannula further comprises a ledge extending therefrom in a horizontal plane above the two arms, the ledge and the top edges of the two arms cooperating to define horizontal slots therebetween.

16. The fluid path set of Claim 15 wherein the hook members extend outwardly from the arms in a plane substantially normal to the horizontal plane of the ledge.

17. The fluid path set of Claim 12 wherein the main hub and each of the arms cooperate to define substantially U-shaped grooves extending along the lateral sides of the main hub.

18. A vented cannula for drawing fluid from a container, the vented cannula comprising:

a main hub comprising two opposed lateral sides and defining a fluid port and a vent;

a fluid draw needle in connection with the fluid port and adapted to be placed within the container;

a vent needle in connection with the vent and adapted to be placed within the container; and

two resilient arms connected to the opposed lateral sides of the main hub, each of the two arms comprising a top edge and a hook member formed thereon and extending outwardly therefrom.

19. The vented cannula of Claim 18 wherein the fluid draw needle is longer than the vent needle.

20. The vented cannula of Claim 18 wherein the vent comprises a filter.

21. The vented cannula of Claim 18 wherein the main hub of the vented cannula further comprises a ledge extending therefrom in a horizontal plane above the two arms, the ledge and the top edges of the two arms cooperating to define horizontal slots therebetween.

22. The vented cannula of Claim 21 wherein the hook members extend outwardly from the arms in a plane substantially normal to the horizontal plane of the ledge.

23. The vented cannula of Claim 18 wherein the main hub and each of the arms cooperate to define substantially U-shaped grooves extending along the lateral sides of the main hub.

24. A method of calibrating a fluid delivery system for delivering a pharmaceutical containing a radioisotope to a patient, the method comprising:

measuring an activity level of a first radioisotope in an ionization chamber of the fluid delivery system, the first radioisotope having an energy level less than that of the radioisotope to be delivered to the patient;

comparing the measured activity level of the first radioisotope to an expected activity level of the first radioisotope;

adjusting the gain of the ionization chamber to compensate for the difference, if any, between the measured activity and the expected activity of the first radioisotope;

measuring an activity level of a second radioisotope in the ionization chamber of the fluid delivery system, the second radioisotope having an energy level similar to or greater than that of the radioisotope to be delivered to the patient;

comparing the measured activity level of the second radioisotope to an expected activity level of the second radioisotope;

adjusting the gain of the ionization chamber to compensate for the difference, if any, between the measured activity and the expected activity of the second radioisotope; and

calculating an estimated error in a measured activity of a third radioisotope based on the differences, if any, between the measured activity and the expected activity of the first radioisotope and the measured activity and the expected activity of the second radioisotope.

25. The method of Claim 24, further comprising:

comparing the estimated error in a measured activity of the third radioisotope to a predetermined acceptable error or error range;

if the estimated error is the same as or similar to the predetermined acceptable error or is within the predetermined acceptable error range, then measuring an activity level of the third radioisotope in the ionization chamber of the fluid delivery system;

calculating the difference, if any, between the measured activity level of the third radioisotope and an expected activity level of the third radioisotope to derive an actual error; and

determining whether the actual error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range.

26. The method of Claim 24 wherein the calculating step comprises:

calculating an initial estimated error in a measured activity of a third radioisotope based on the difference, if any, between the measured activity and the expected activity of the first radioisotope; and

calculating a revised estimated error in a measured activity of the third radioisotope based on the difference, if any, between the measured activity and the expected activity of the second radioisotope.

27. The method of Claim 26, further comprising:

comparing the revised estimated error in a measured activity of the third radioisotope to a predetermined acceptable error or error range;

if the revised estimated error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range, then measuring an activity level of the third radioisotope in the ionization chamber of the fluid delivery system;

calculating the difference, if any, between the measured activity level of the third radioisotope and an expected activity level of the third radioisotope to derive an actual error; and

determining whether the actual error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range.

28. The method of Claim 27, further comprising:

if the revised estimated error is not the same or similar to the predetermined acceptable error or is not within the predetermined acceptable error range, then remeasuring the activity level of the first radioisotope in the ionization chamber of the fluid delivery system;

comparing the remeasured activity level of the first radioisotope to the expected activity level of the first radioisotope;

adjusting the gain of the ionization chamber to compensate for the difference, if any, between the remeasured activity and the expected activity of the first radioisotope;

calculating a second revised estimated error in a measured activity of the third radioisotope based on the difference, if any, between the remeasured activity and the expected activity of the first radioisotope;

remeasuring the activity level of the second radioisotope in the ionization chamber of the fluid delivery system;

comparing the remeasured activity level of the second radioisotope to the expected activity level of the second radioisotope;

adjusting the gain of the ionization chamber to compensate for the difference, if any, between the remeasured activity and the expected activity of the second radioisotope; and

calculating a third revised estimated error in a measured activity of the third radioisotope based on the difference, if any, between the remeasured activity and the expected activity of the second radioisotope.

29. The method of Claim 28, further comprising:

comparing the third revised estimated error in a measured activity of the third radioisotope to a predetermined acceptable error or error range;

if the third revised estimated error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range, then measuring an activity level of the third radioisotope in the ionization chamber of the fluid delivery system;

calculating the difference, if any, between the measured activity level of the third radioisotope and an expected activity level of the third radioisotope to derive an actual error; and

determining whether the actual error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range.

30. The method of Claim 27, further comprising:

if the revised estimated error is not the same or similar to the predetermined acceptable error or is not within the predetermined acceptable error range, then remeasuring the activity level of the first radioisotope in the ionization chamber of the fluid delivery system;

comparing the remeasured activity level of the first radioisotope to the expected activity level of the first radioisotope;

adjusting the gain of the ionization chamber to compensate for the difference, if any, between the remeasured activity and the expected activity of the first radioisotope;

calculating a second revised estimated error in a measured activity of the third radioisotope based on the difference, if any, between the remeasured activity and the expected activity of the first radioisotope;

comparing the second revised estimated error in a measured activity of the third radioisotope to a predetermined acceptable error or error range;

if the second revised estimated error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range, then measuring an activity level of the third radioisotope in the ionization chamber of the fluid delivery system;

calculating the difference, if any, between the measured activity level of the third radioisotope and an expected activity level of the third radioisotope to derive an actual error;

determining whether the actual error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range;

if the second revised estimated error is not the same or similar to the predetermined acceptable error or is not within the predetermined acceptable error range, then remeasuring the activity level of the second radioisotope in the ionization chamber of the fluid delivery system;

comparing the remeasured activity level of the second radioisotope to the expected activity level of the second radioisotope;

adjusting the gain of the ionization chamber to compensate for the difference, if any, between the remeasured activity and the expected activity of the second radioisotope; and

calculating a third revised estimated error in a measured activity of the third radioisotope based on the difference, if any, between the remeasured activity and the expected activity of the second radioisotope.

31. The method of Claim 30, further comprising:

comparing the third revised estimated error in a measured activity of the third radioisotope to a predetermined acceptable error or error range;

if the third revised estimated error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range, then measuring an activity level of the third radioisotope in the ionization chamber of the fluid delivery system;

calculating the difference, if any, between the measured activity level of the third radioisotope and an expected activity level of the third radioisotope to derive an actual error; and

determining whether the actual error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range.

32. The method of Claim 24 wherein the radioisotope to be delivered to the patient is F-18.

33. The method of Claim 32 wherein the first radioisotope is Co-57, the second radioisotope is Co-60 and the third radioisotope is Cs-137.

34. The method of Claim 24 wherein the low gain of the ionization chamber is adjusted to compensate for the difference, if any, between the measured activity and the expected activity of the first radioisotope and the high gain of the ionization chamber is adjusted to compensate for the difference, if any, between the measured activity and the expected activity of the second radioisotope.

35. A vial access system comprising:

a base portion comprising a substantially horizontal lower surface and a sloped upper surface adapted to support a vial comprising a bottom wall and a substantially cylindrical wall connected thereto, the sloped upper surface adapted to ensure that a residual volume of fluid in the vial gathers in an area defined at least partially by a portion of the junction between the bottom wall and the cylindrical wall of the vial.

36. The vial access system of Claim 35, further comprising:

a housing extending vertically from the base portion;

a vertical support arm comprising an upper end, the vertical support arm movably disposed within the housing; and

a cap member connected to the upper end of the vertical support arm and adapted to overlie a septum of the vial.

37. The vial access system of Claim 36 wherein the cap member comprises a mounting mechanism disposed on an underside thereof, the mounting mechanism adapted to retain a cannula therein for insertion through the septum of the vial.

38. The vial access system of Claim 37 wherein the vertical support arm is slidably disposed within the housing to allow the cannula to be inserted into and removed from the vial.

39. The vial access system of Claim 38 wherein the vertical support arm is rotatably disposed within the housing to allow the cap member to be rotated into and out of a position that overlies the septum of the vial.

40. The vial access system of Claim 37 wherein the mounting mechanism comprises two arms that cooperate to define a slot therebetween, each of the two arms comprising a tab member extending downwardly therefrom, each of the tab members comprising a front edge and a rear edge.

41. The vial access system of Claim 36, further comprising a handle member pivotally connected to the upper end of the vertical support arm.

42. The vial access system of Claim 36 wherein the cap member includes or is formed from radioactive shielding material.

43. The vial access system of Claim 35, further comprising at least one support member connected to the base portion for retaining the vial on the sloped upper surface of the base portion.

44. The vial access system of Claim 43 wherein the at least one support member comprises two support pins that are connected to the sloped upper surface of the base portion.

45. The vial access system of Claim 35 wherein the vial is contained within a vial shield and the fluid is a radiopharmaceutical.

46. The vial access system of Claim 35 wherein the sloped upper surface is sloped at an angle of approximately 10-13 degrees with respect to a horizontal plane.

47. A method of priming at least a portion of a fluid path set in a fluid delivery system, the method comprising:

placing a tubing section of the fluid path set in fluid connection with a source of a radiopharmaceutical;

placing a portion of the tubing section within a dose calibrator of the fluid delivery system;

pumping a volume of the radiopharmaceutical through the tubing section;

monitoring the dose calibrator to determine if a measured activity level is substantially equal to or above a predetermined activity level; and

if the measured activity level is substantially equal to or above the predetermined activity level, then concluding that the tubing section of the fluid path set has been primed.

48. The method of Claim 47, further comprising:

if the measured activity level is zero or below the predetermined activity level, then concluding that the tubing section of the fluid path has not been primed; and

pumping a second volume of the radiopharmaceutical through the tubing section.

49. The method of Claim 47, further comprising:

placing a second tubing section in fluid connection with a source of medical fluid and the tubing section;

pumping a volume of the medical fluid through the second tubing section and at least a portion of the tubing section to move the volume of the radiopharmaceutical to the portion of the tubing section that is positioned within the dose calibrator.

50. The method of Claim 49, further comprising:

placing the tubing section in fluid connection with a waste receptacle;

pumping a second volume of the medical fluid through the second tubing section and at least a portion of the tubing section to move the volume of the radiopharmaceutical into the waste receptacle.

51. A fluid delivery system, comprising:

a housing having an upper surface defining a plurality of recessed portions for accommodating one or more components of a fluid path set;

a cover movably connected to the housing and adapted to move between a first position that exposes the upper surface and a second position that overlies the upper surface; and.

a locking mechanism associated with the cover and adapted to lock the cover in the second position.

52. The fluid delivery system of Claim 51 wherein the cover is slidably connected to the housing.

53. The fluid delivery system of Claim 51 wherein the first position allows an operator to insert or remove the one or more components of the fluid path set.

54. The fluid delivery system of Claim 51 wherein the plurality of recessed portions includes wells and troughs.

55. The fluid delivery system of Claim 51, further comprising:

one or more handles connected to the housing;

a plurality of wheels or casters connected to the housing; and

a display connected to the housing.

56. The fluid delivery system of Claim 51 wherein the cover and the upper surface comprises or is formed from a radioactive shielding material.

57. The fluid delivery system of Claim 51, further comprising:

a dose calibrator for measuring the radioactivity level of a radiopharmaceutical;

a pumping mechanism for pumping the radiopharmaceutical; and

a controller in communication with the dose calibrator and the pumping mechanism.

58. The fluid delivery system of Claim 51 wherein the locking mechanism comprises a mechanical lock that locks the cover to the housing in the second position.

59. The fluid delivery system of Claim 57 wherein the locking mechanism is a software-implemented lock that is in communication with the controller, the software implemented lock adapted to lock the cover to the housing in the second position.

60. The fluid delivery system of Claim 51, further comprising a printer associated with the housing.

61. A vial shield carrying system for carrying a vial shield containing a pharmaceutical vial, the vial shield carrying system comprising in combination:

a collar unit adapted to removably engage a flange on the vial shield, the collar unit defining two elongated slots formed in a top surface thereof, each of the slots including a pin disposed therein and extending between two opposing walls thereof; and

a handle unit adapted to engage the collar unit, the handle unit comprising a handle connected to a U-shaped cross piece defining two, downwardly extending arms having hook members formed therein, the open ends of the hook members formed on opposite ends of the arms and adapted to engage the pins in the slots of the collar unit through rotation of the handle.

62. The vial shield carrying system of Claim 61, further comprising a plunger connected to the U-shaped cross piece and adapted to mate with a septum cap of the vial shield when the handle unit engages the collar unit on the vial shield.

63. The vial shield carrying system of Claim 62, further comprising a spring disposed between the plunger and the U-shaped cross piece, the spring adapted to bias the plunger into engagement with the septum cap of the vial shield.

64. The vial shield carrying system of Claim 63 wherein the arms are lowered into the slots of the collar unit, the plunger is engaged with the septum cap of the vial shield and the handle is rotated in a clockwise direction to seat the pins of the collar unit in the hook members of the handle unit.

65. The vial shield carrying system of Claim 64 wherein the handle is rotated in a counter-clockwise direction to disengage the hook members of the handle unit from the pins of the collar unit.

66. The vial shield carrying system of Claim 62 wherein the plunger comprises or is formed from a radioactive shielding material.

67. The vial shield carrying system of Claim 61 wherein the collar unit comprises two members that are pivotally connected to allow the collar unit to engage and disengage the flange of the vial shield.

68. A fluid delivery system, comprising:

a syringe comprising a body defining a discharge outlet and a plunger movably disposed within the body;

a connector comprising a valve member and defining first, second and third ports;

a first tubing segment connected between the discharge outlet of the syringe and the first port of the connector;

a cannula defining a fluid port;

a second tubing segment connected between the fluid port of the cannula and the second port of the connector;

a third tubing segment comprising a first end connected to the third port of the connector and a second end comprising a second connector; and

a per-patient tubing set comprising a first end that is adapted to be connected to the second connector on the second end of the third tubing segment and a patient end that is adapted to be connected to venous access device in a patient.

69. The fluid delivery system of Claim 68 wherein the connector comprises a T-connector and the valve member comprises a stopcock.

70. The fluid delivery system of Claim 68 wherein the second connector comprises a swabable valve or a luer connector.

71. The fluid delivery system of Claim 68 wherein the syringe contains a radiopharmaceutical and is disposed within a lead-shielded container.

72. The fluid delivery system of Claim 68 wherein the syringe is a hand-held syringe.

73. The fluid delivery system of Claim 68 wherein the cannula further comprises:

a main hub comprising two opposed lateral sides and defining a vent;

a fluid draw needle in connection with the fluid port and adapted to be placed within a fluid container;

a vent needle in connection with the vent and adapted to be placed within the fluid container; and

two resilient arms connected to the opposed lateral sides of the main hub, each of the two arms comprising a top edge and a hook member formed thereon and extending outwardly therefrom.

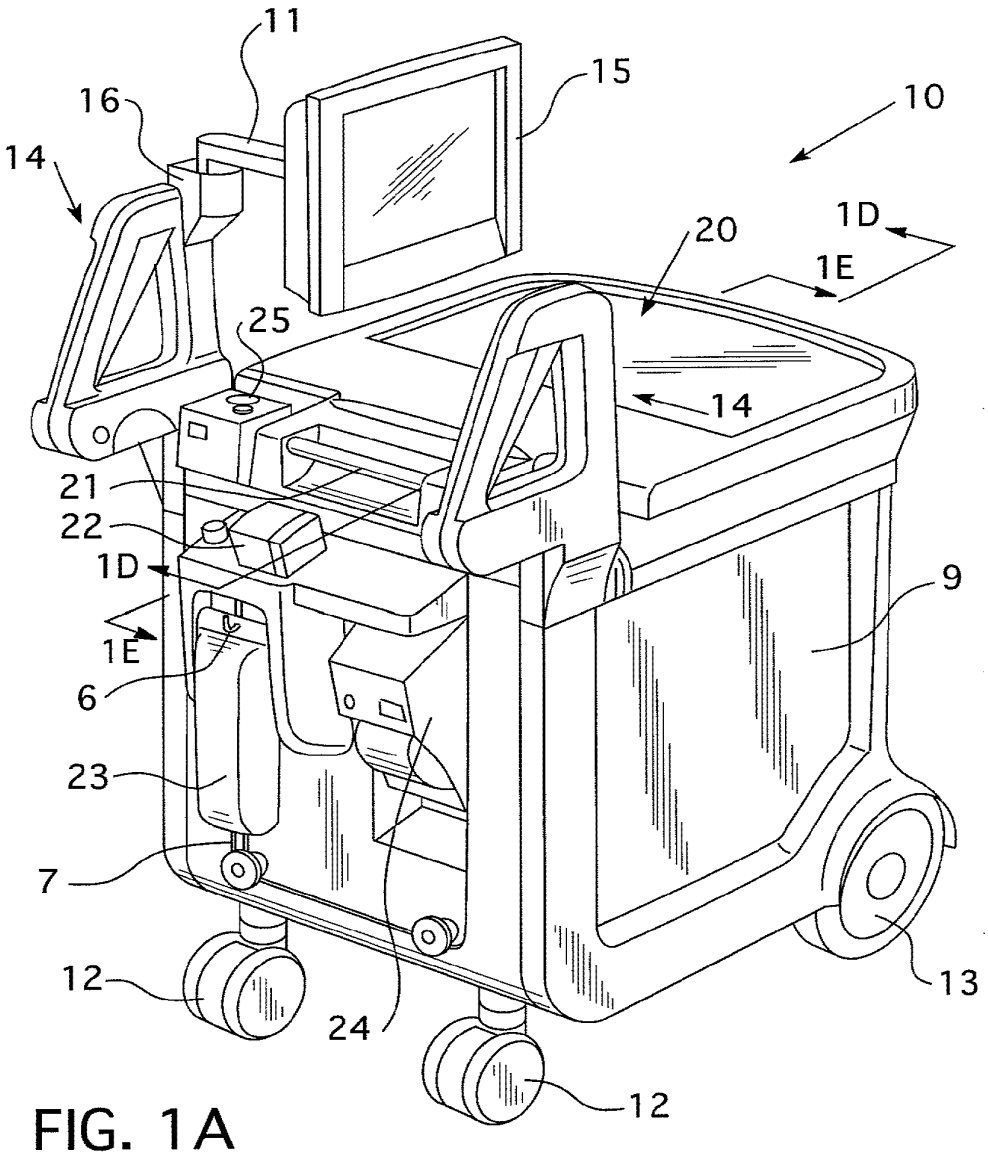

FIG. 1A

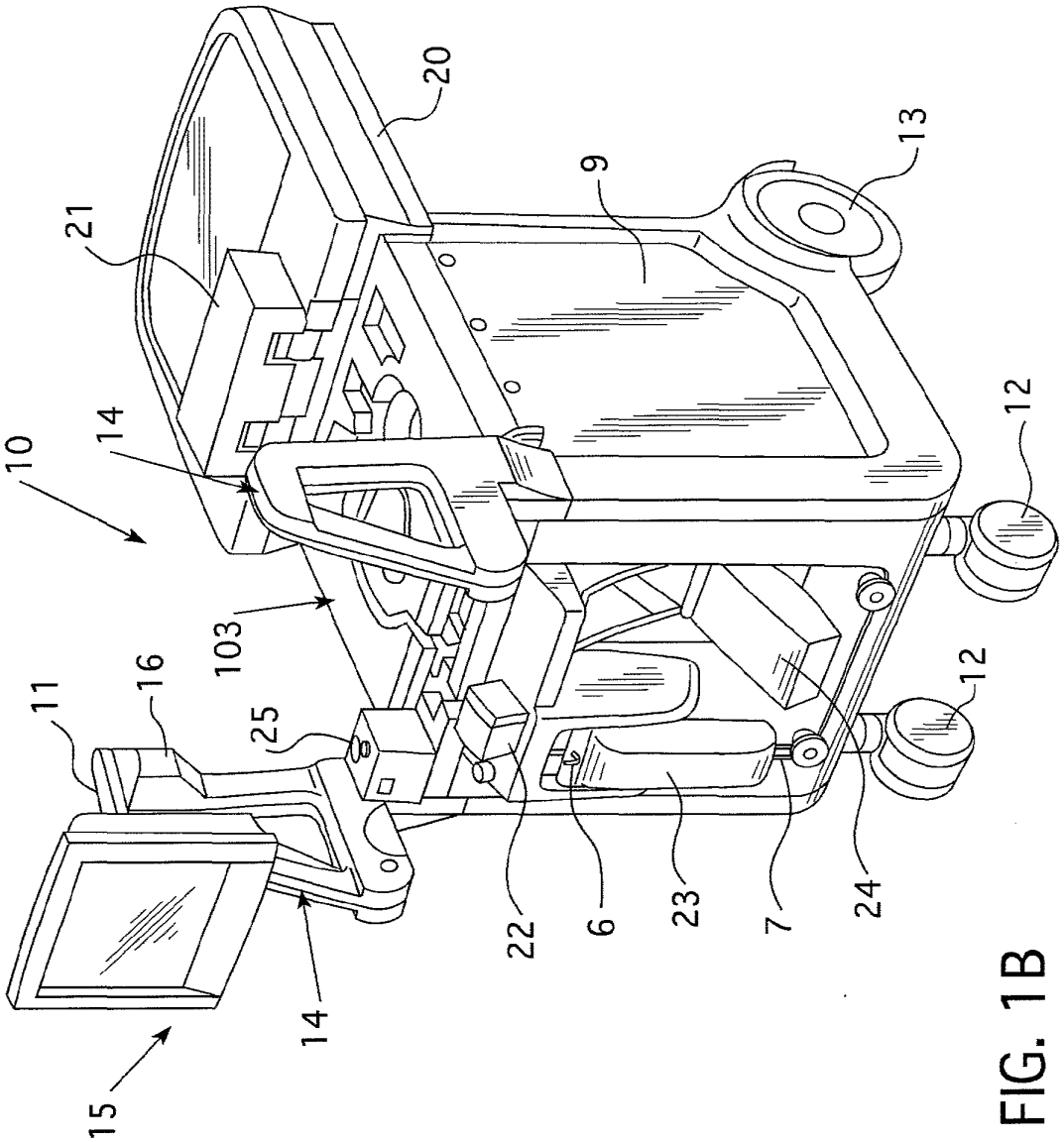

FIG. 1B

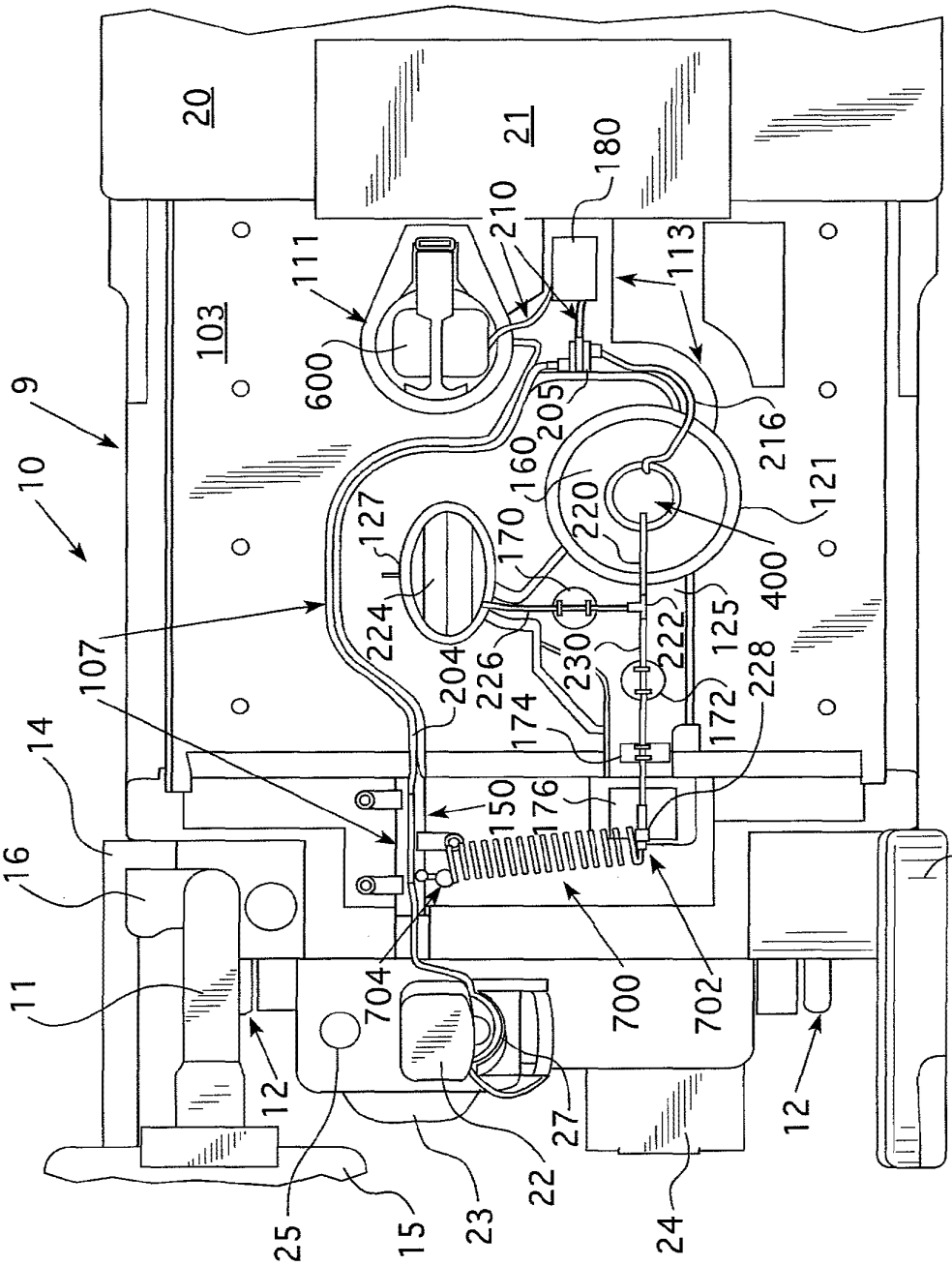
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FIG. 1C

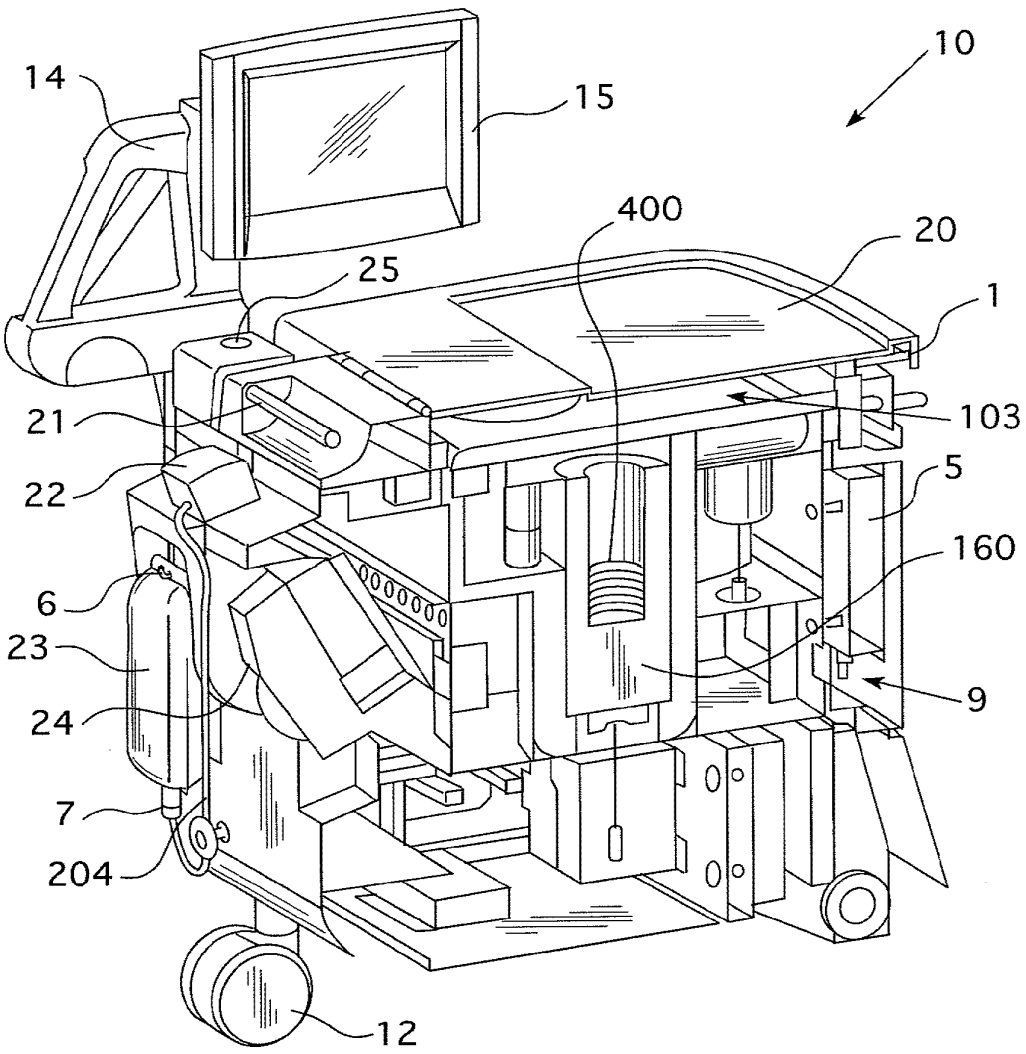

FIG. 1D

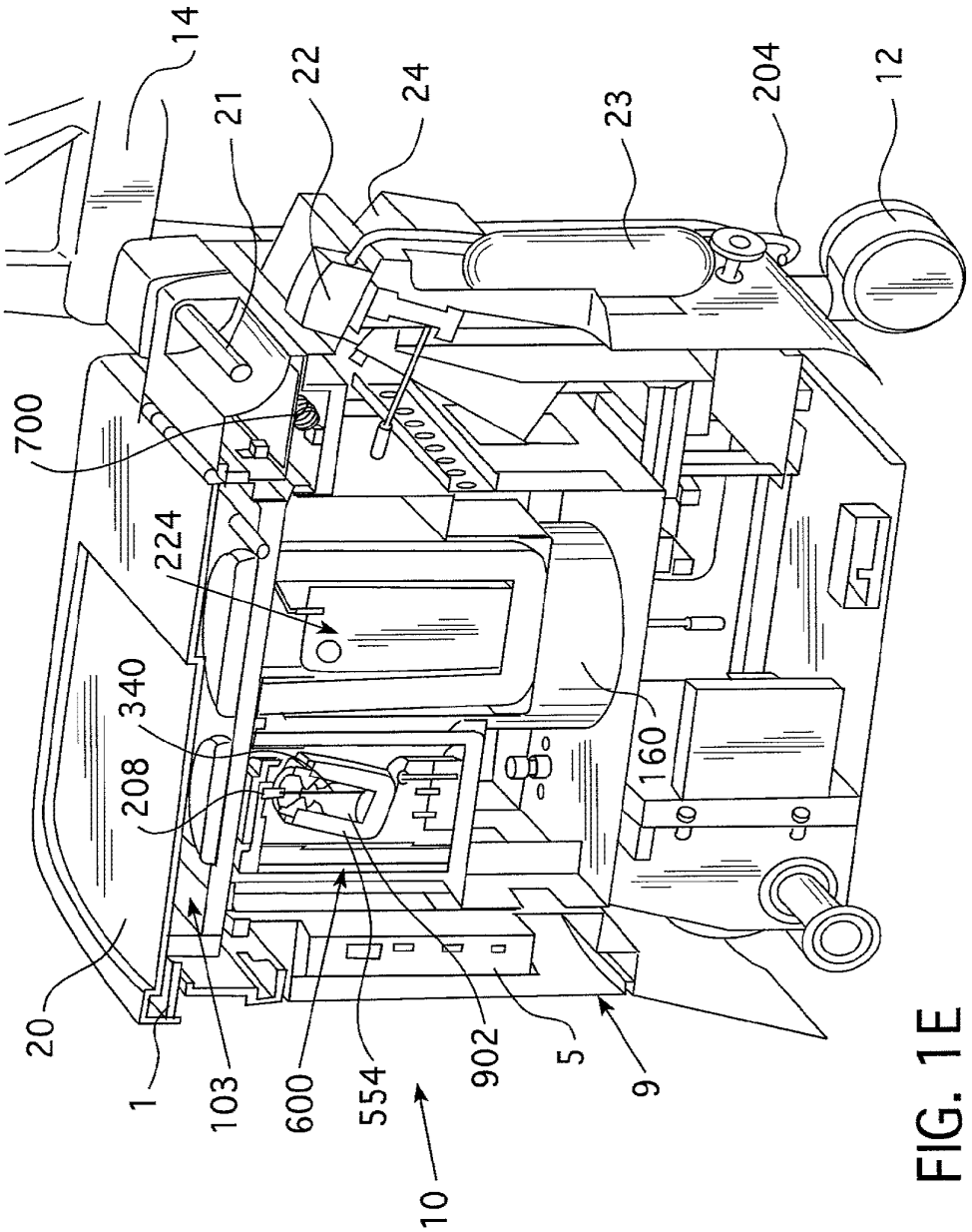

FIG. 1E

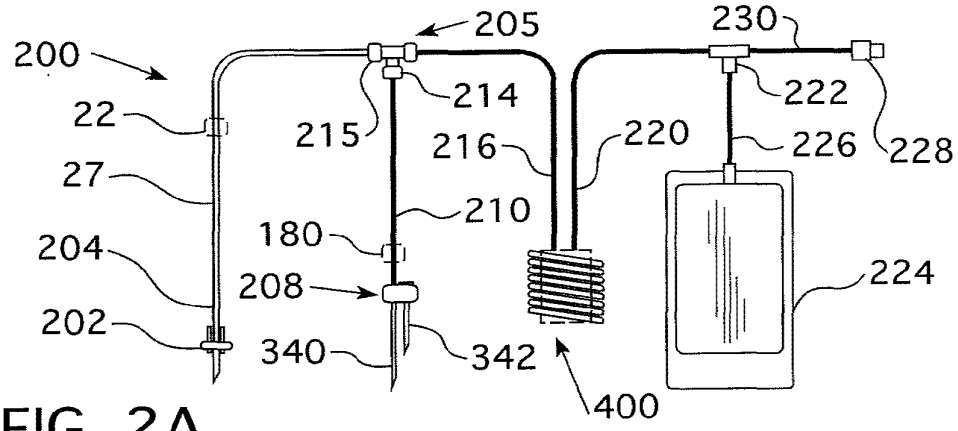
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FIG. 2A

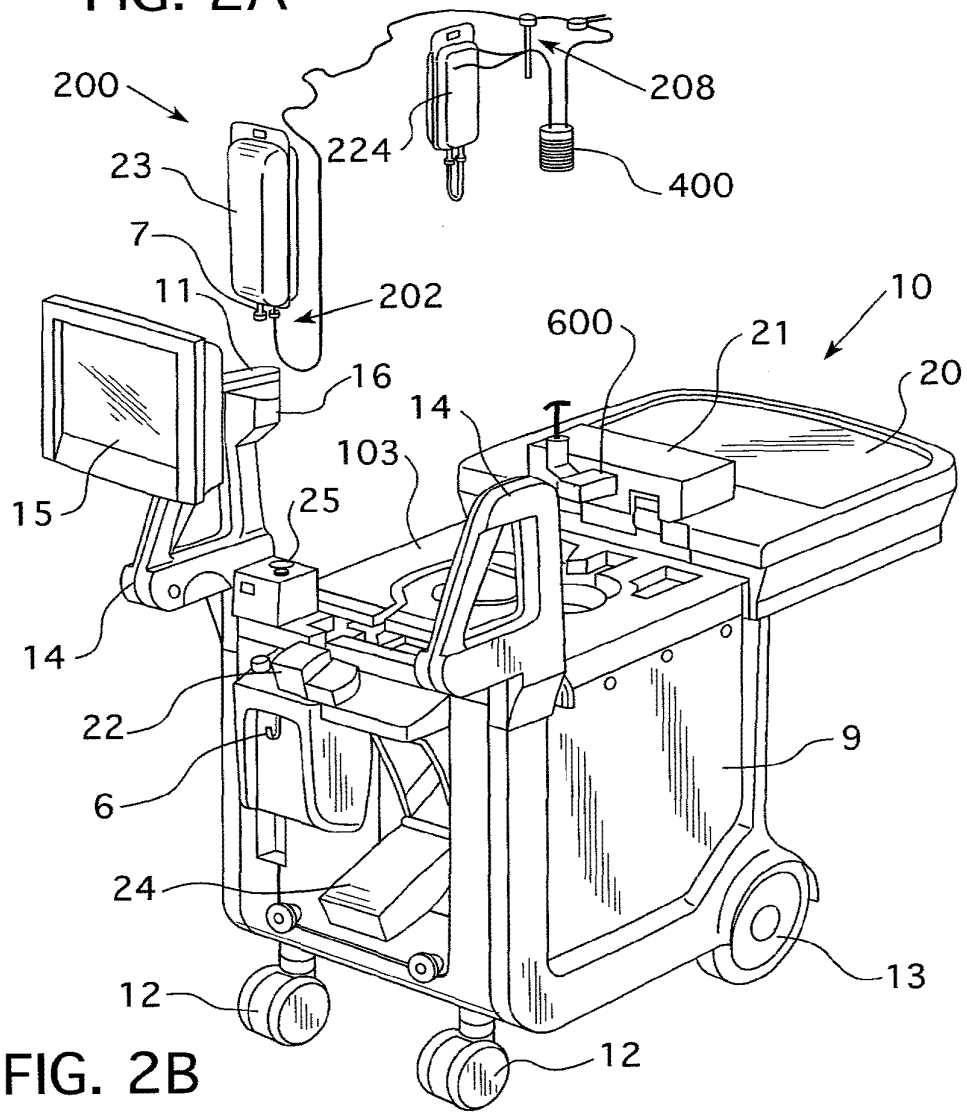
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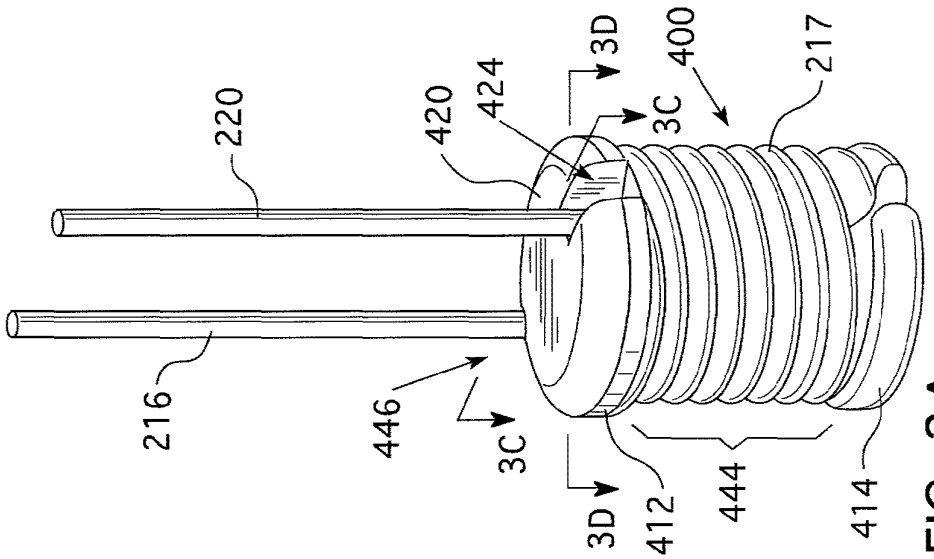
FIG. 2B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3C
3D
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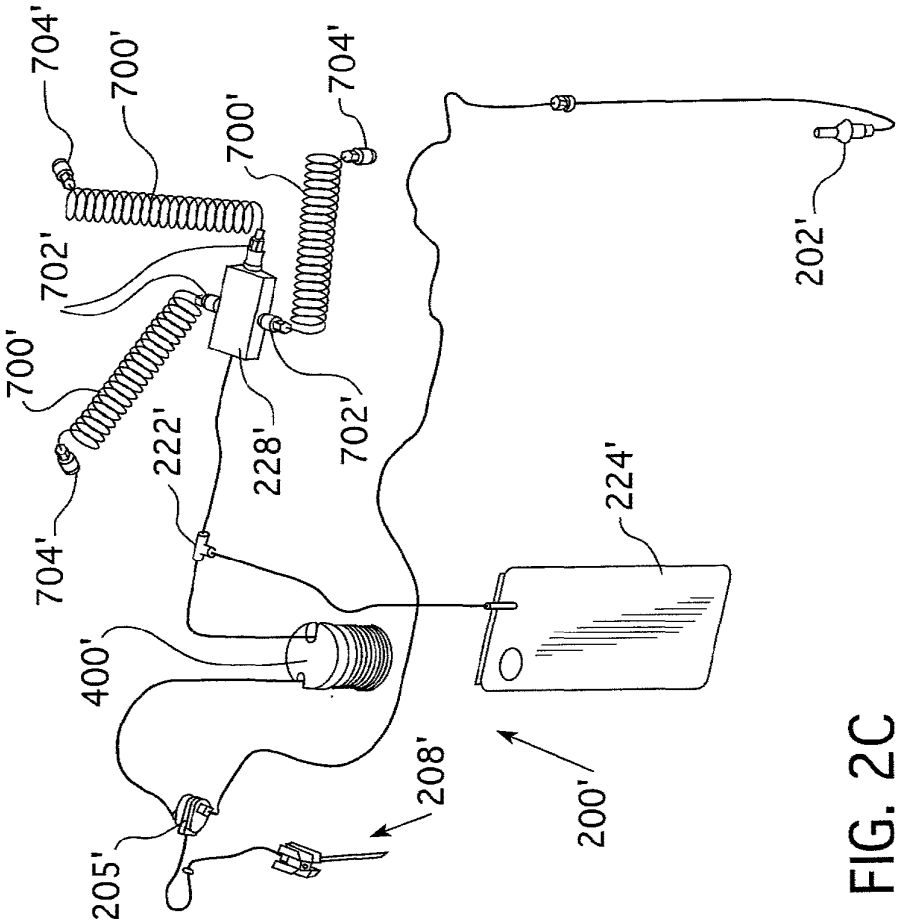
FIG. 3A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200'

FIG. 2C

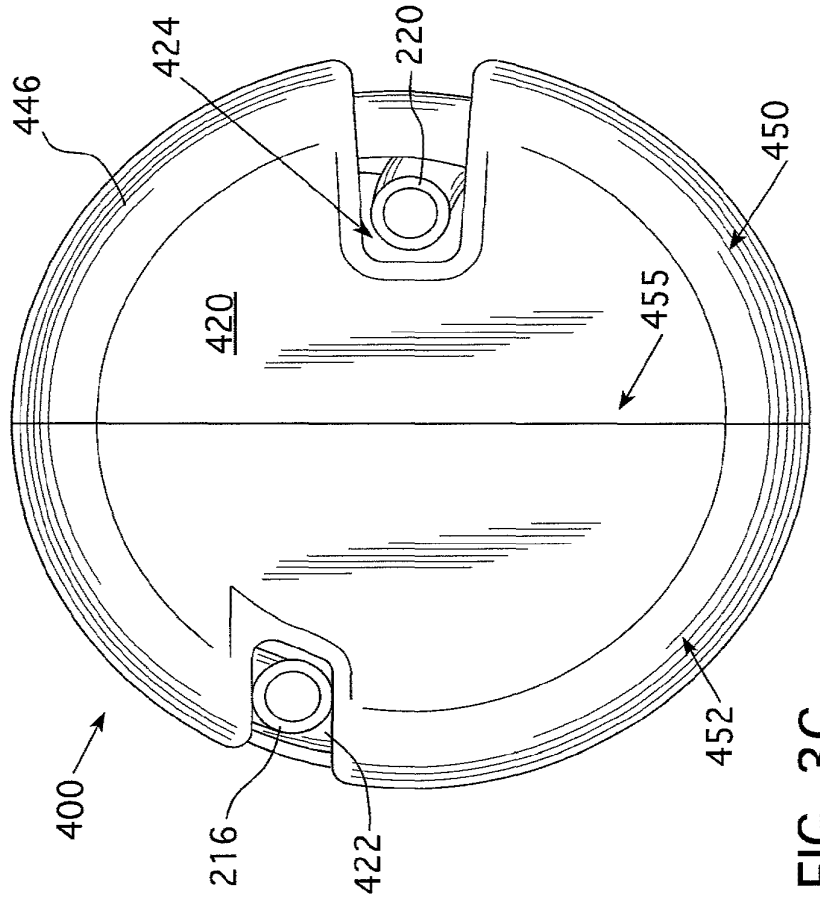
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FIG. 3C

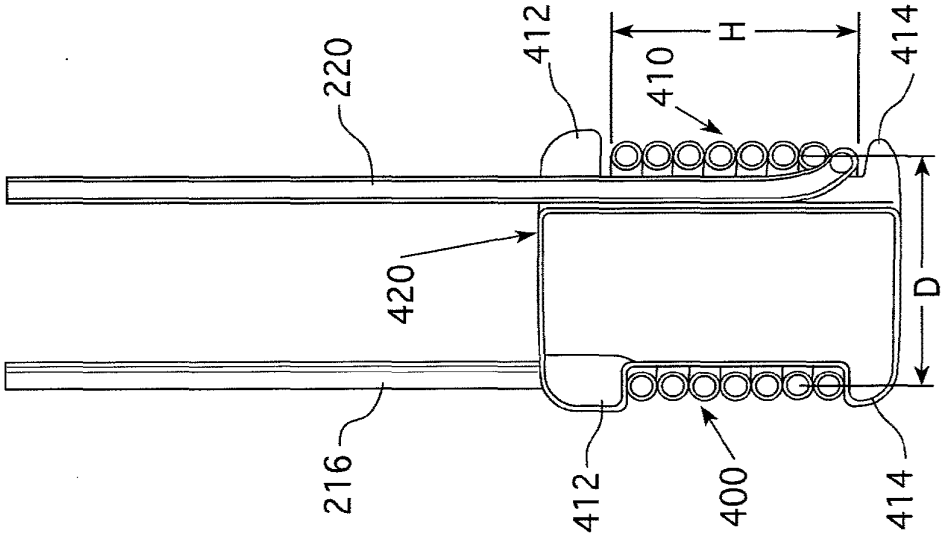
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FIG. 3B

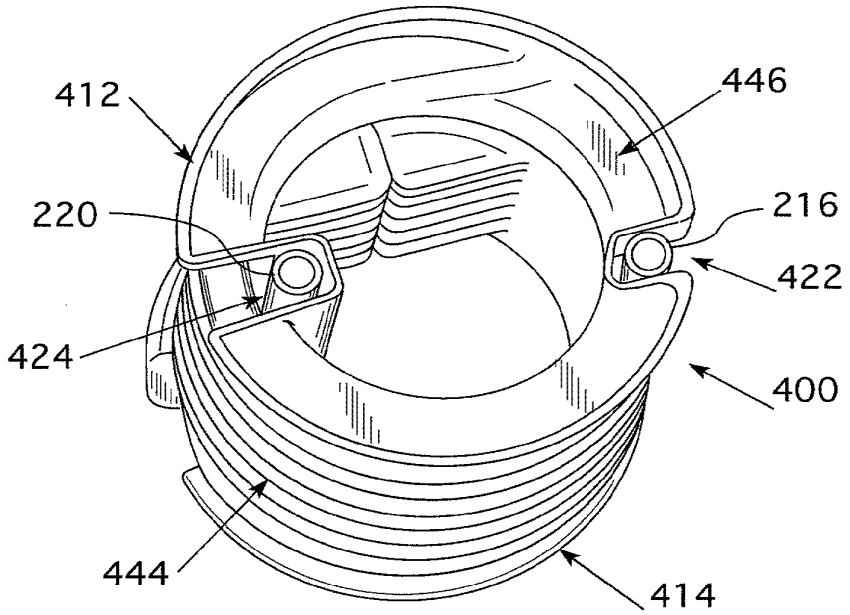
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FIG. 3D

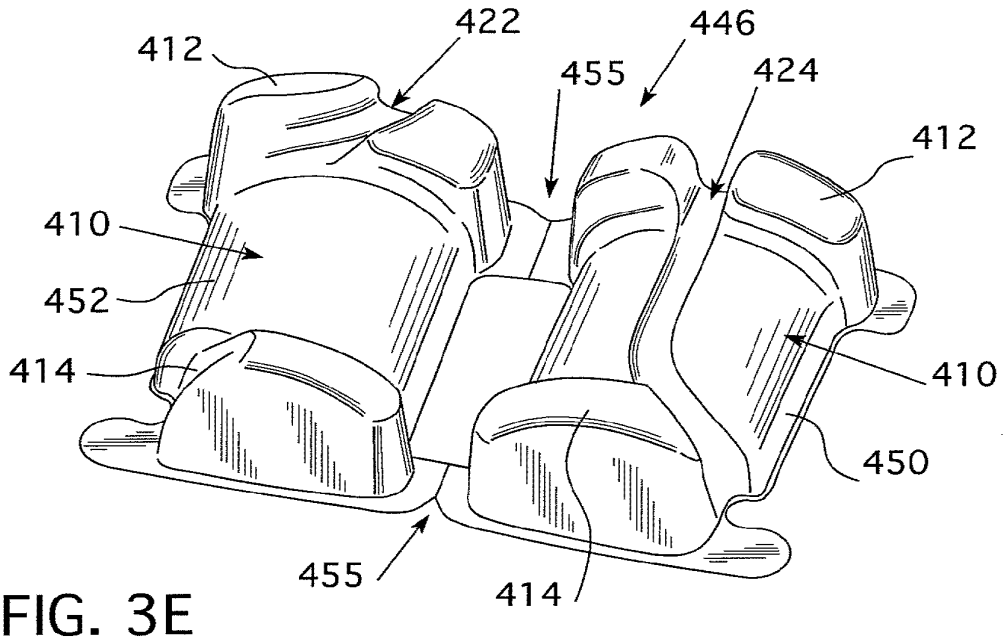
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FIG. 3E

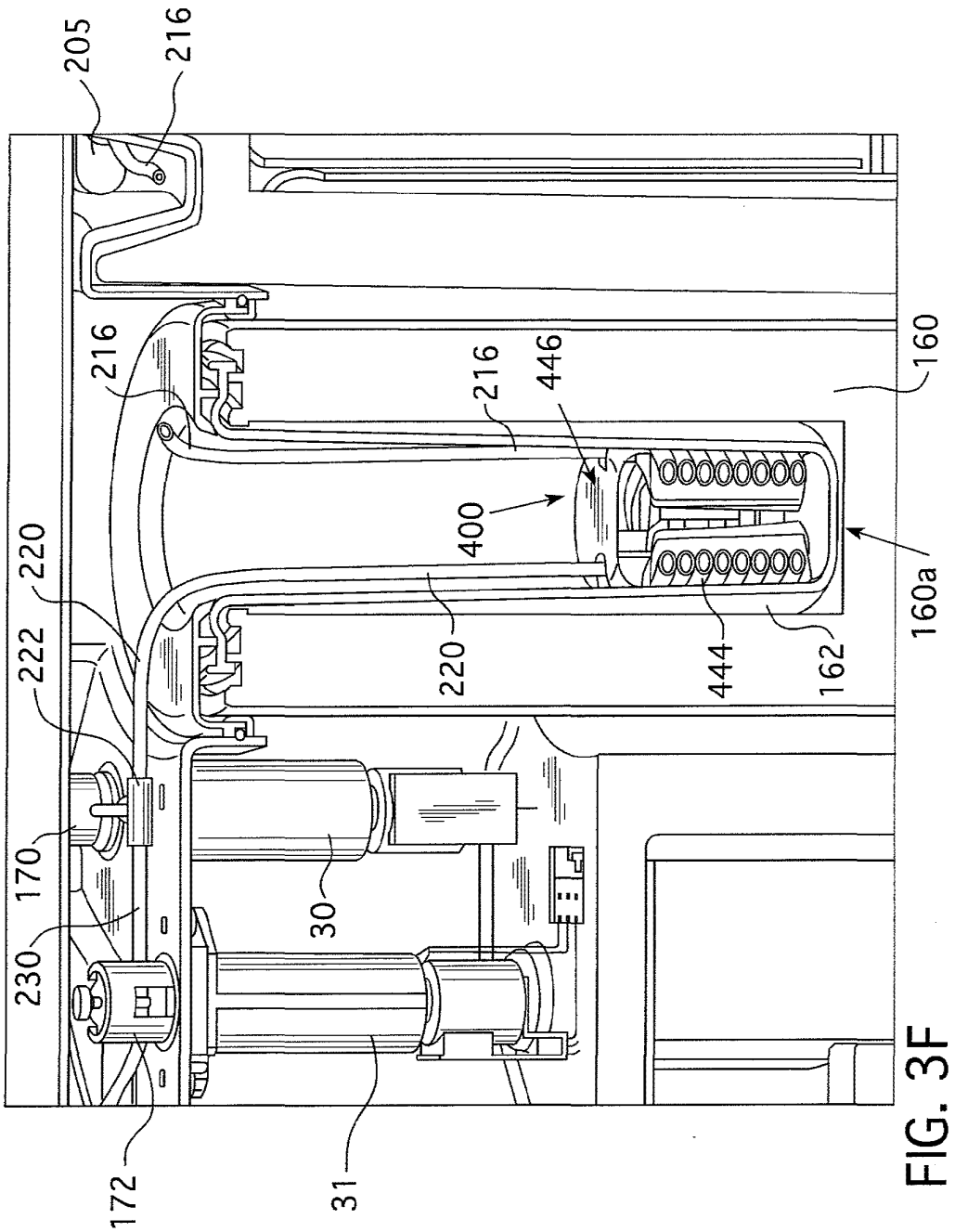
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FIG. 3F

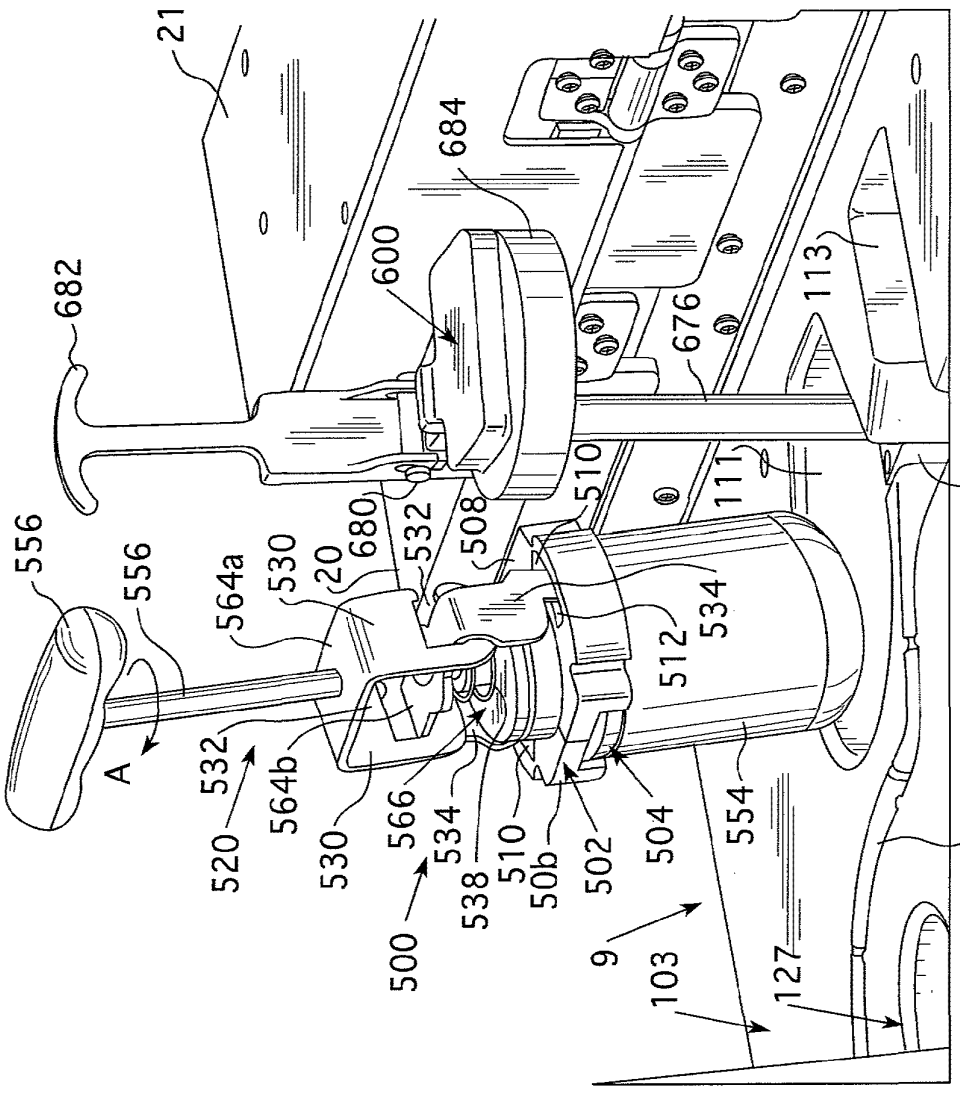
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FIG. 4A

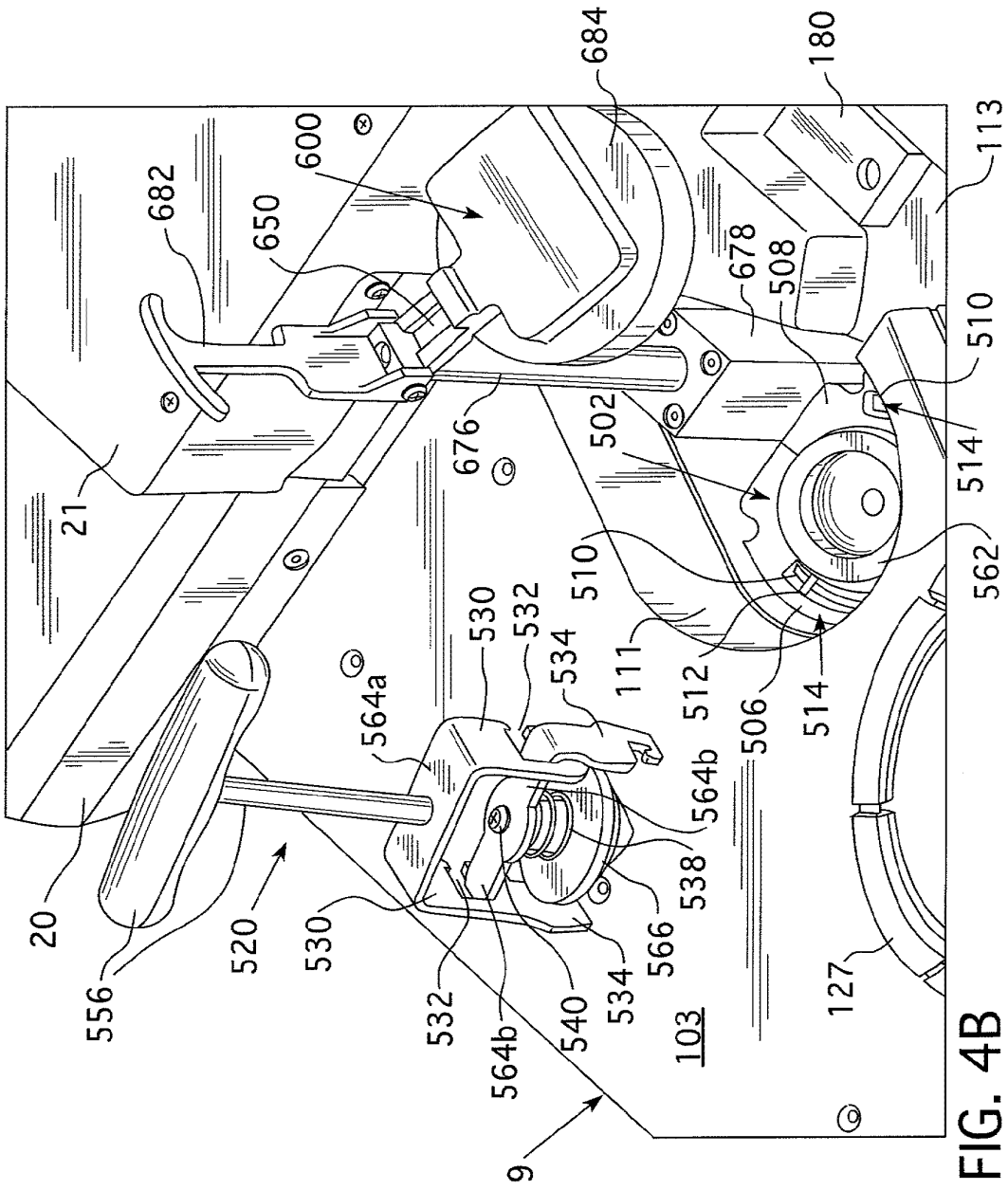
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FIG. 4B

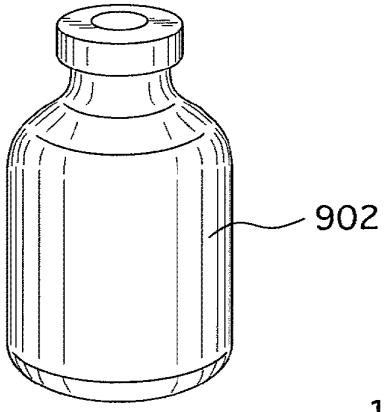

FIG. 4C

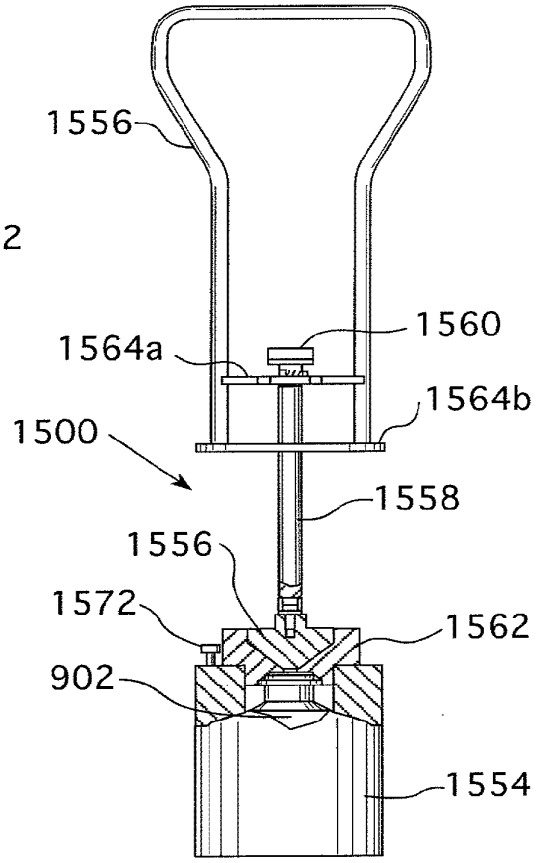

FIG. 5A

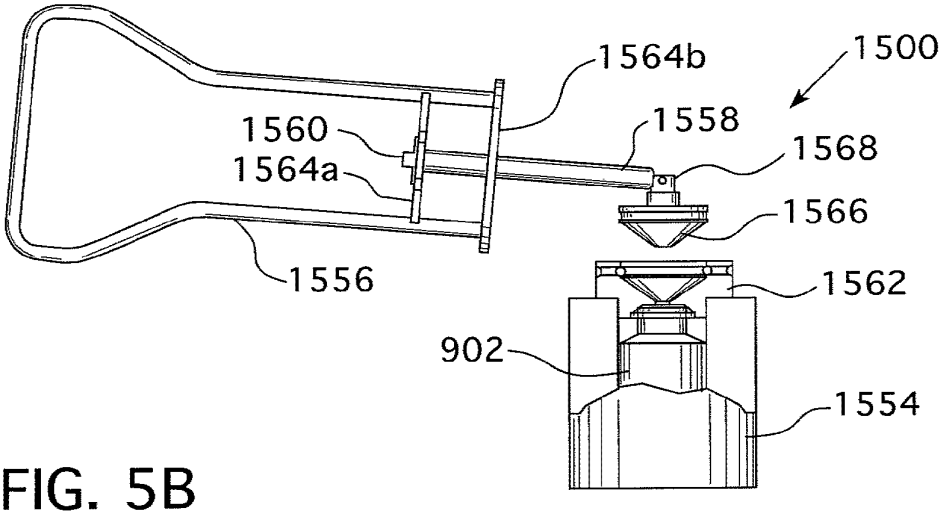

FIG. 5B

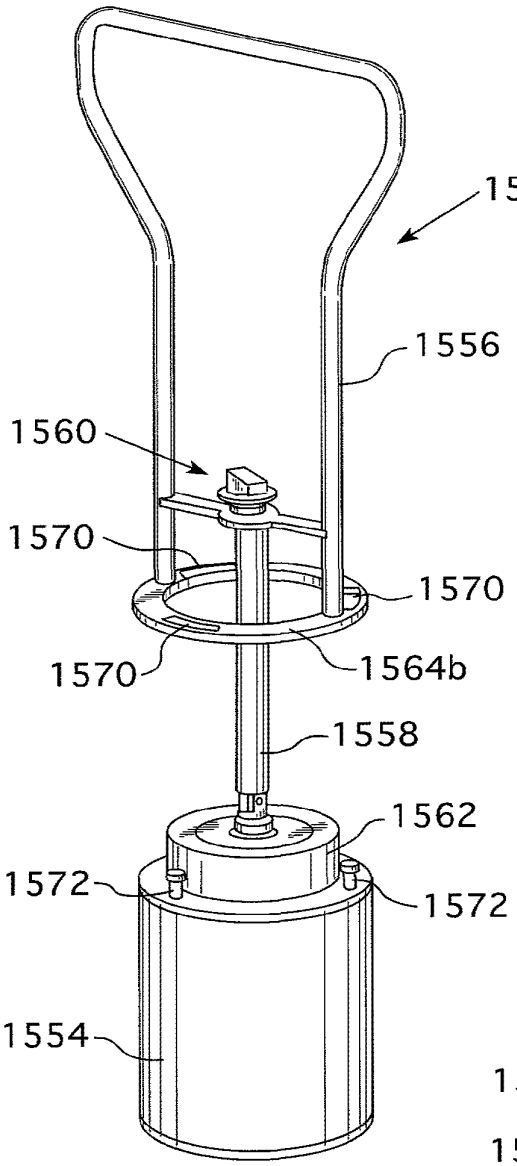
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FIG. 5C

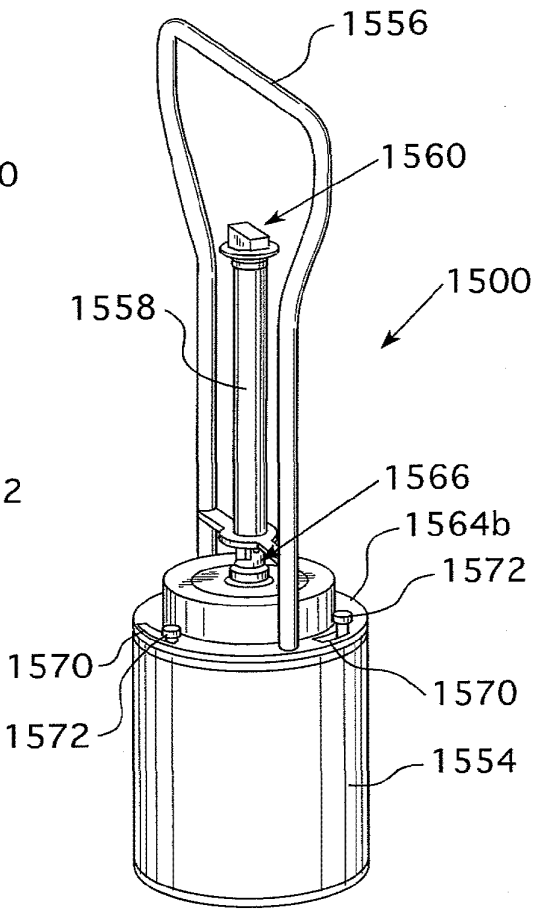
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FIG. 5D

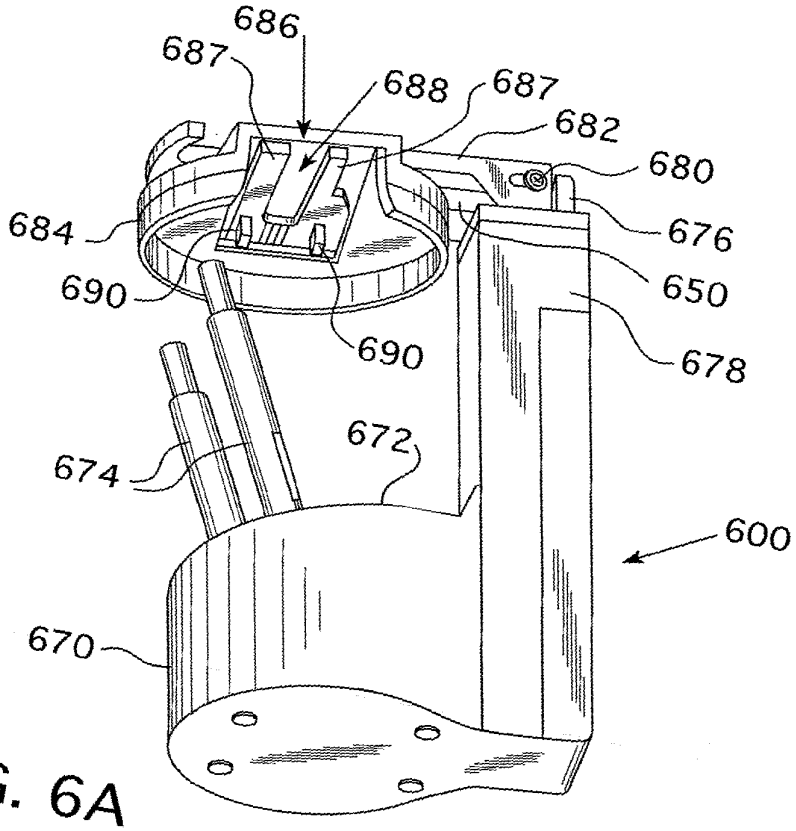
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FIG. 6A

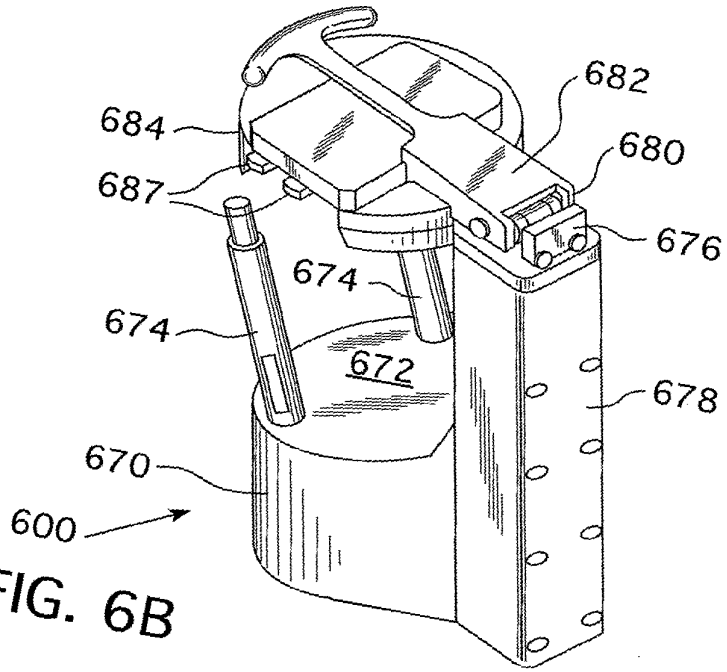
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FIG. 6B

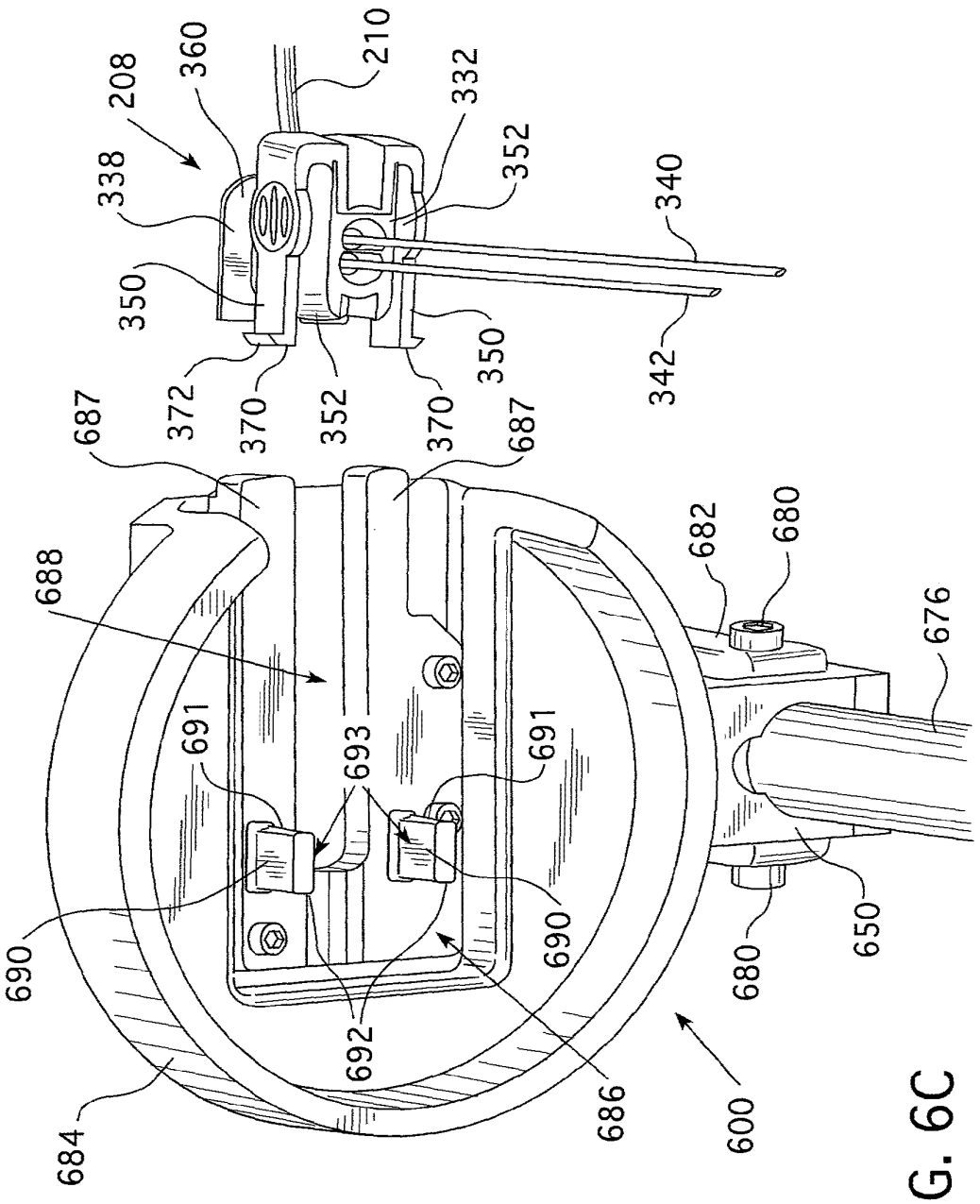
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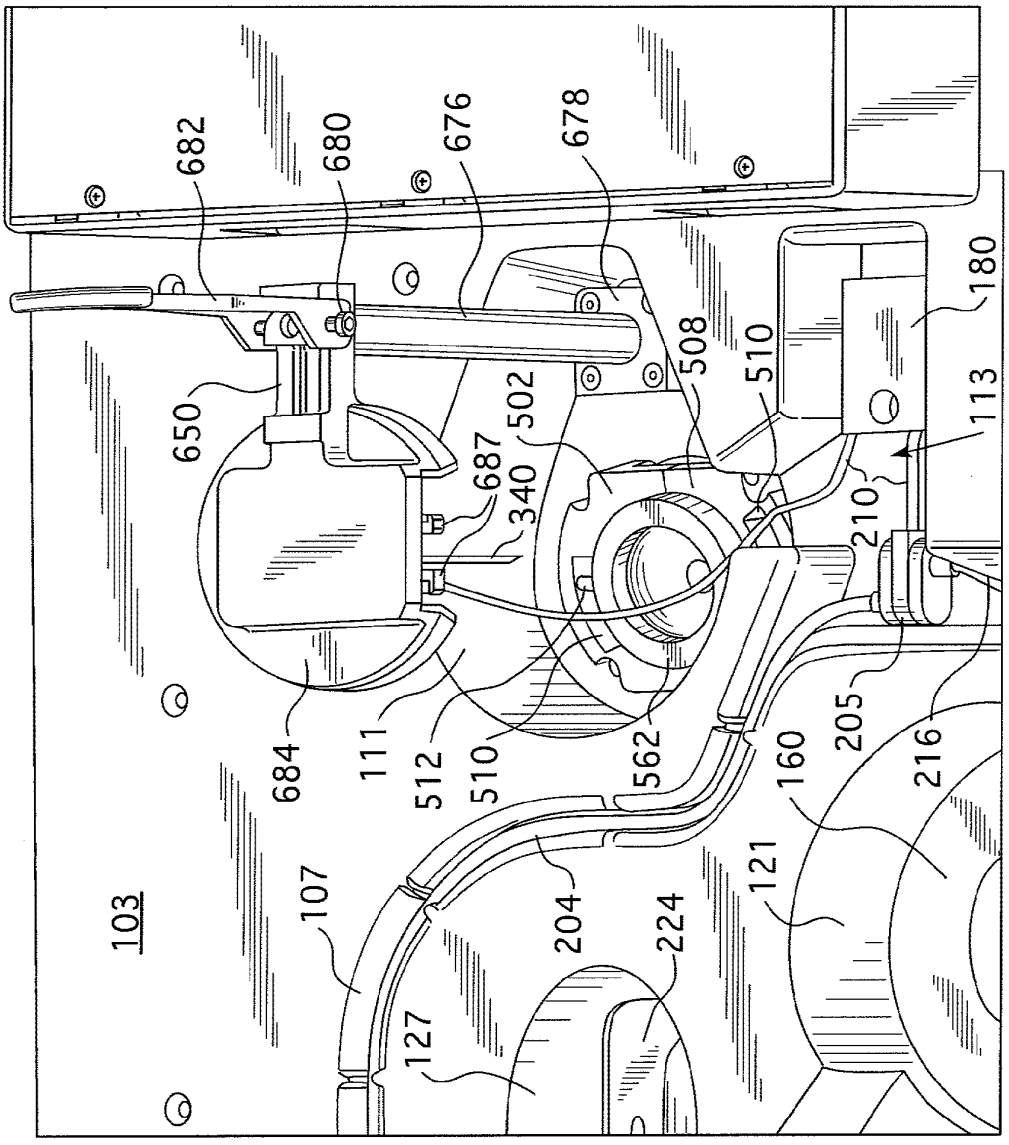
FIG. 6C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127

FIG. 6D

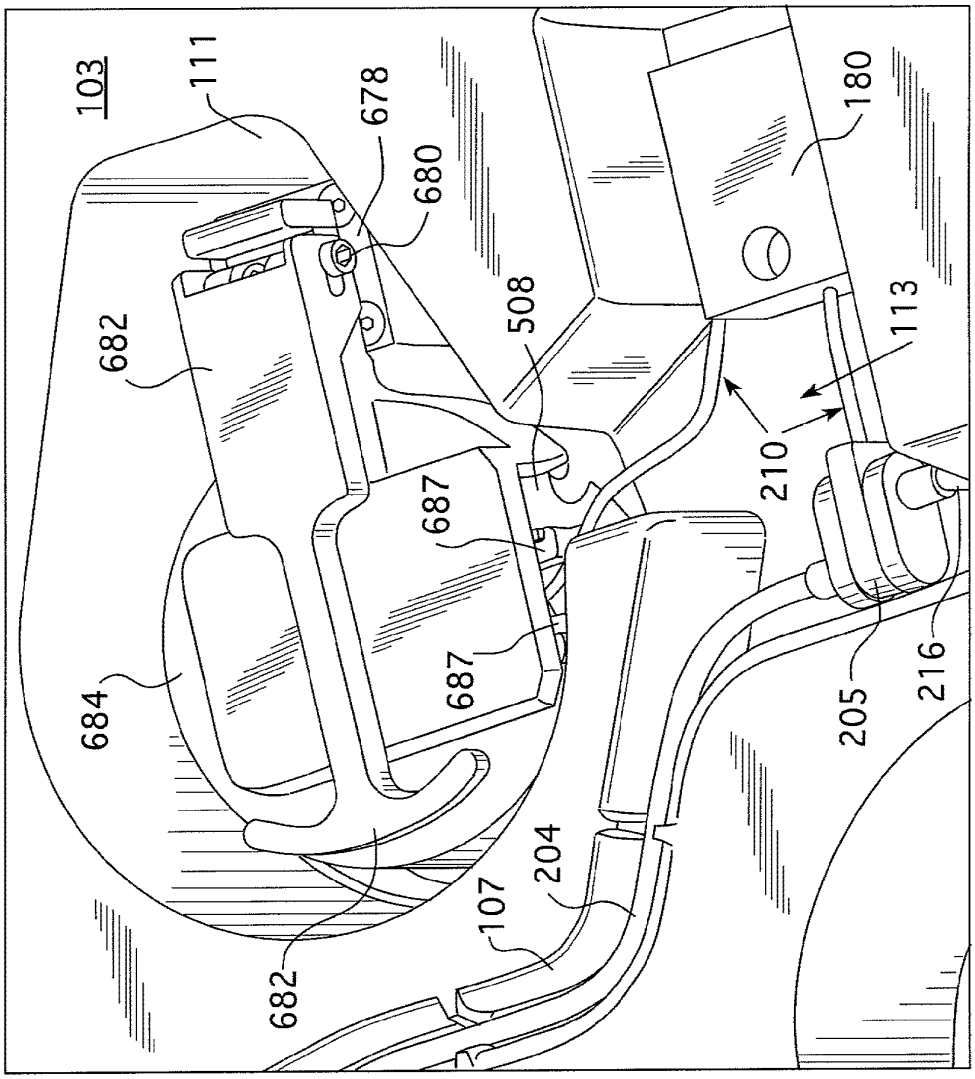
103
111
678
680
180
682
508
113
210
687
687
684
205
216
204
107
682

FIG. 6E

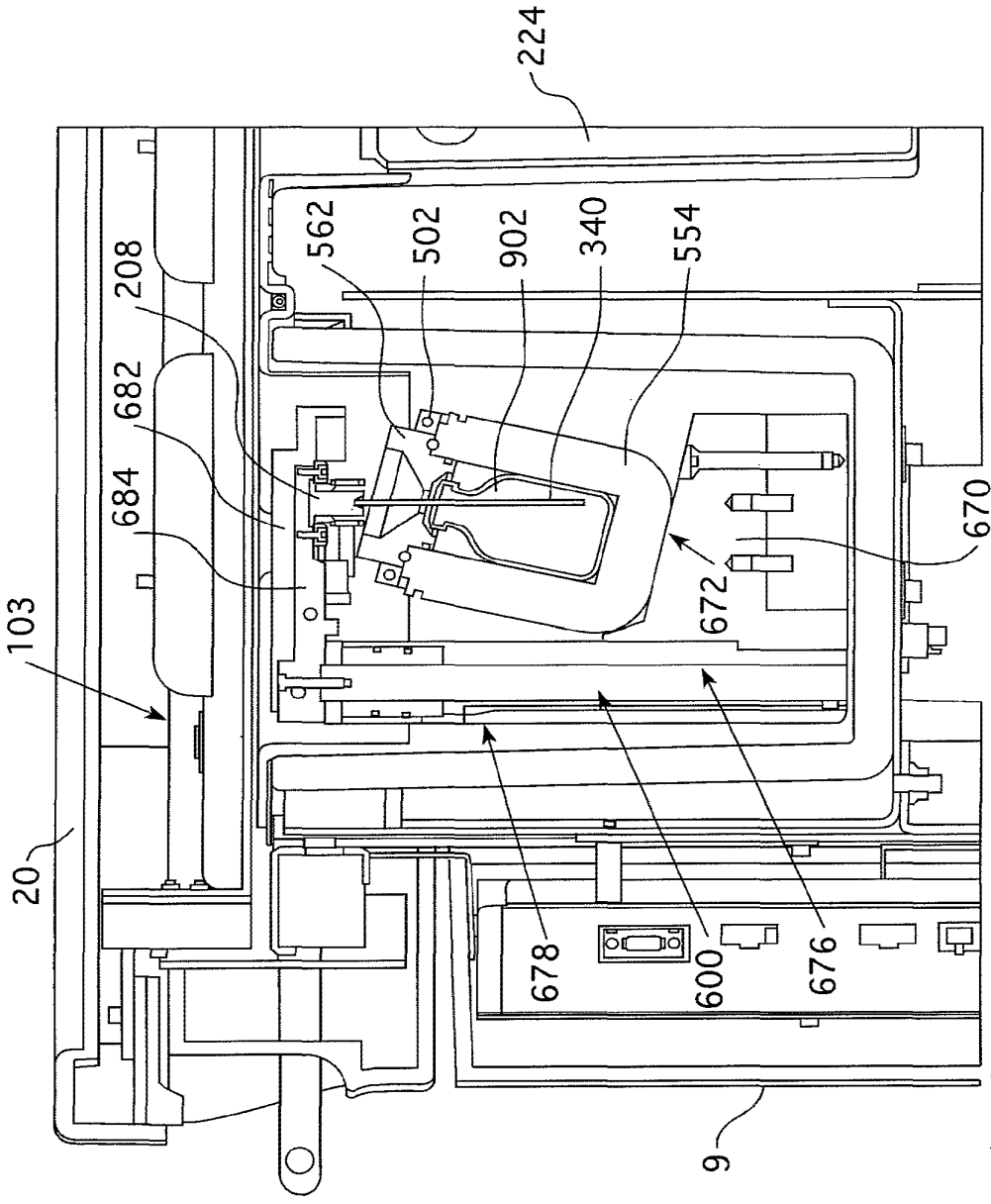

FIG. 6F

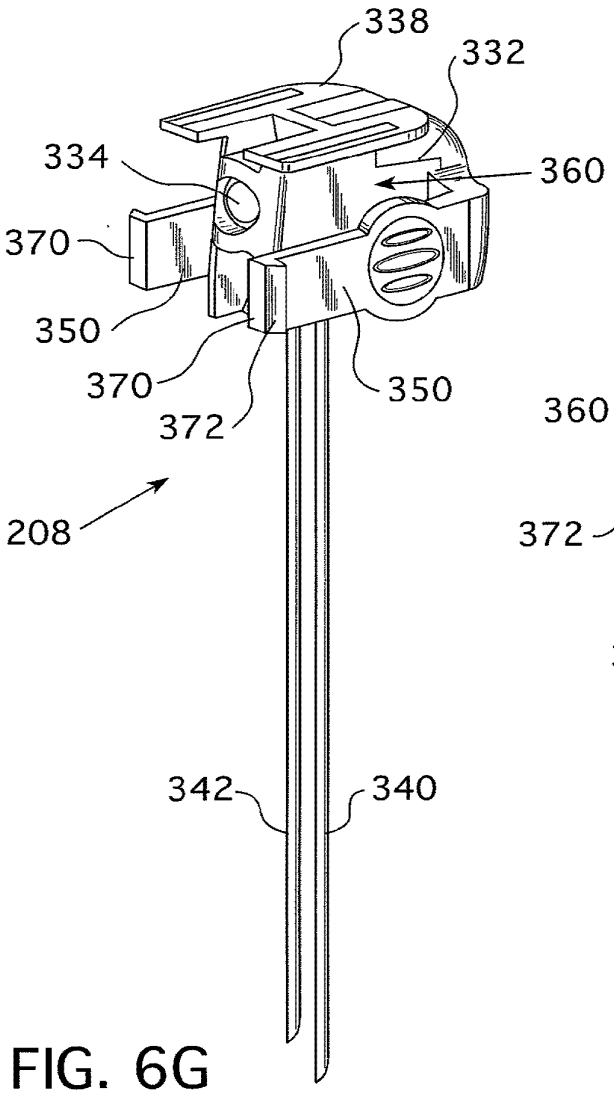
338
332
334
360
370
350
370
372
350
208
342
340

FIG. 6G

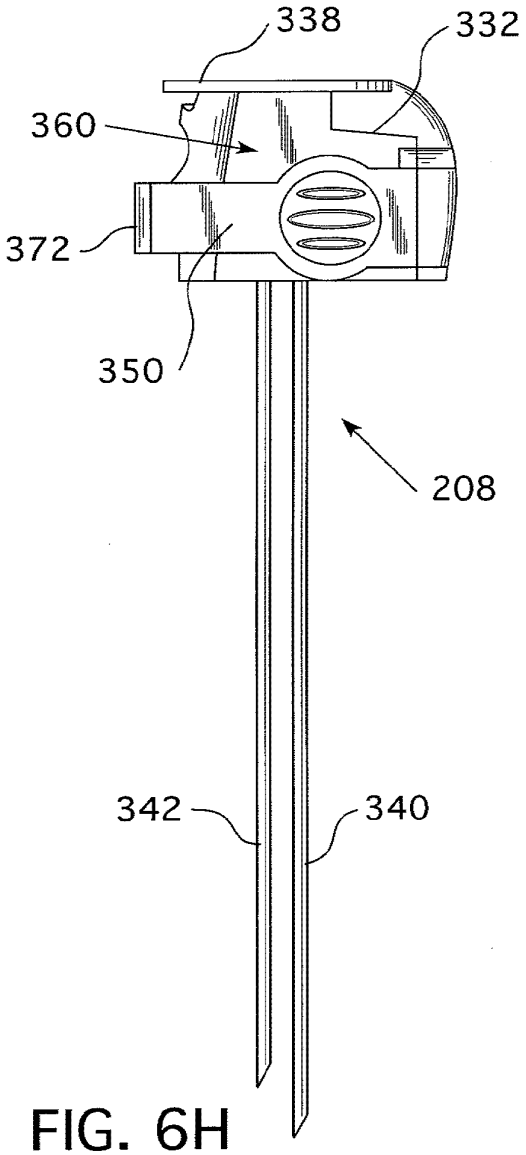
338
332
360
372
350
208
342
340

FIG. 6H

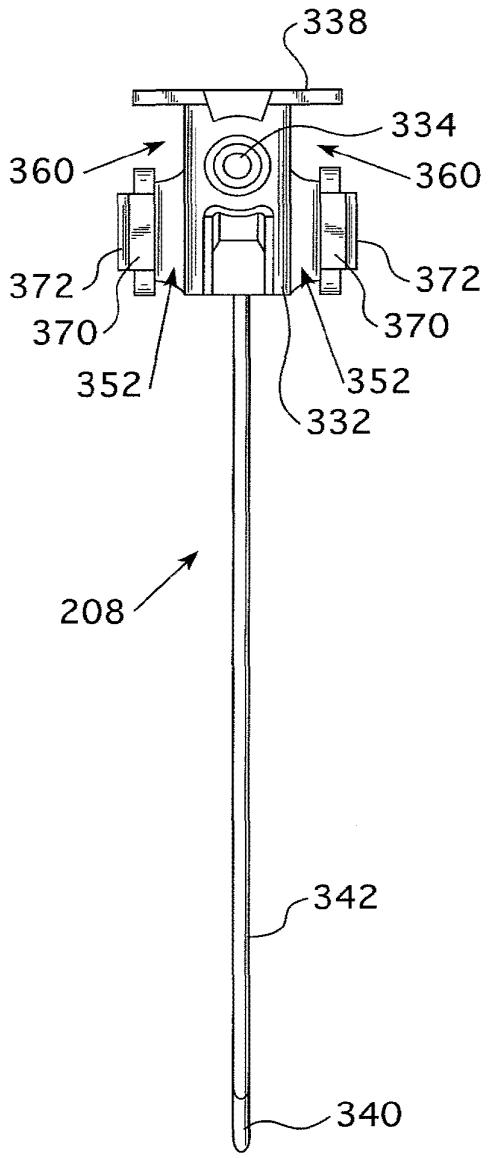
338
334
360
360
372
372
370
370
352
352
332
208
342
340

FIG. 6I

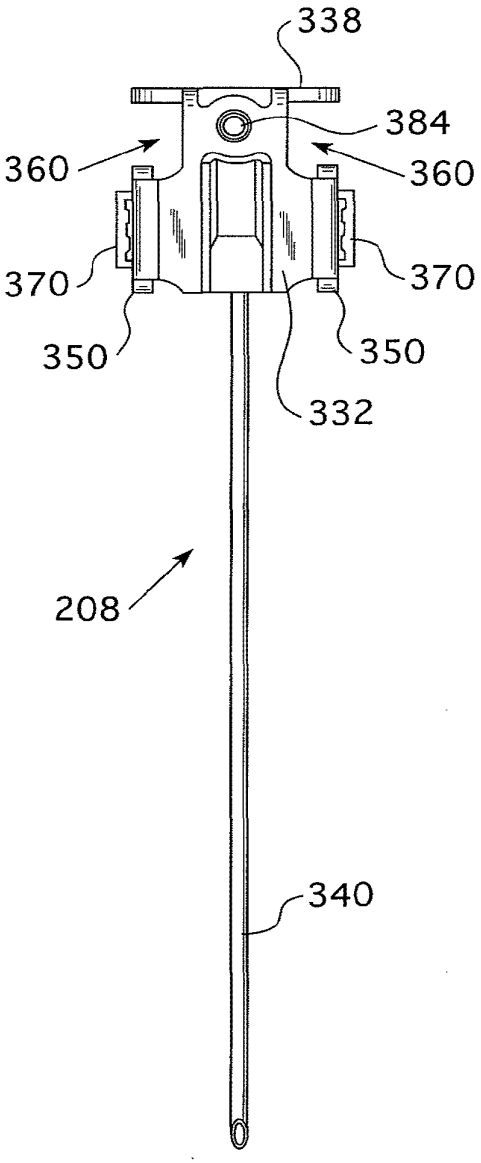
338
384
360
360
370
370
350
350
332
208
340

FIG. 6J

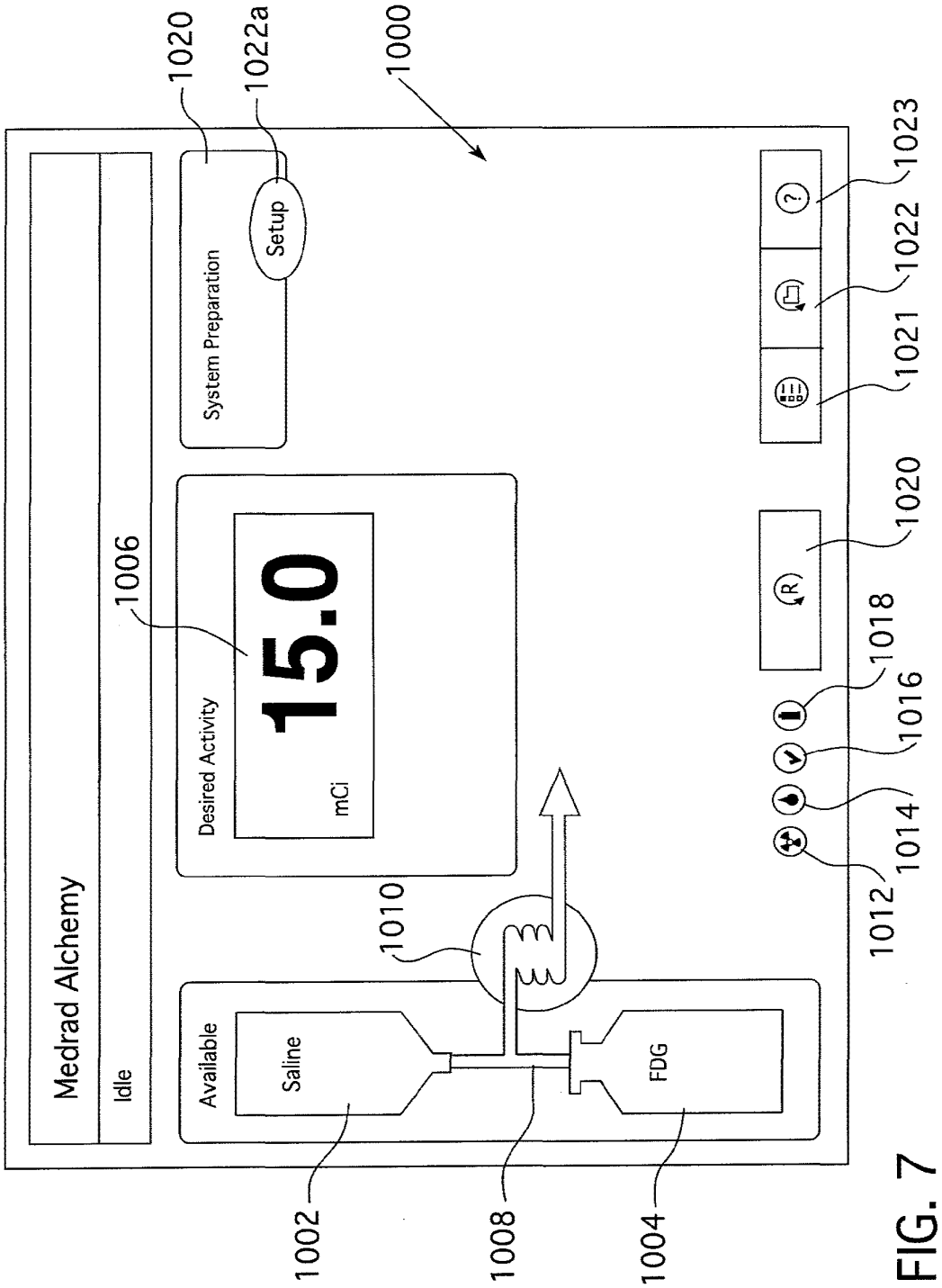
1020
1022a
1000
1023
1022
1021
1006
1020
1018
1016
1014
1012
1010
1002
1008
1004
Medrad Alchemy
Idle
System Preparation
Setup
Desired Activity
15.0
mCi
Available
Saline
FDG
R

FIG. 7

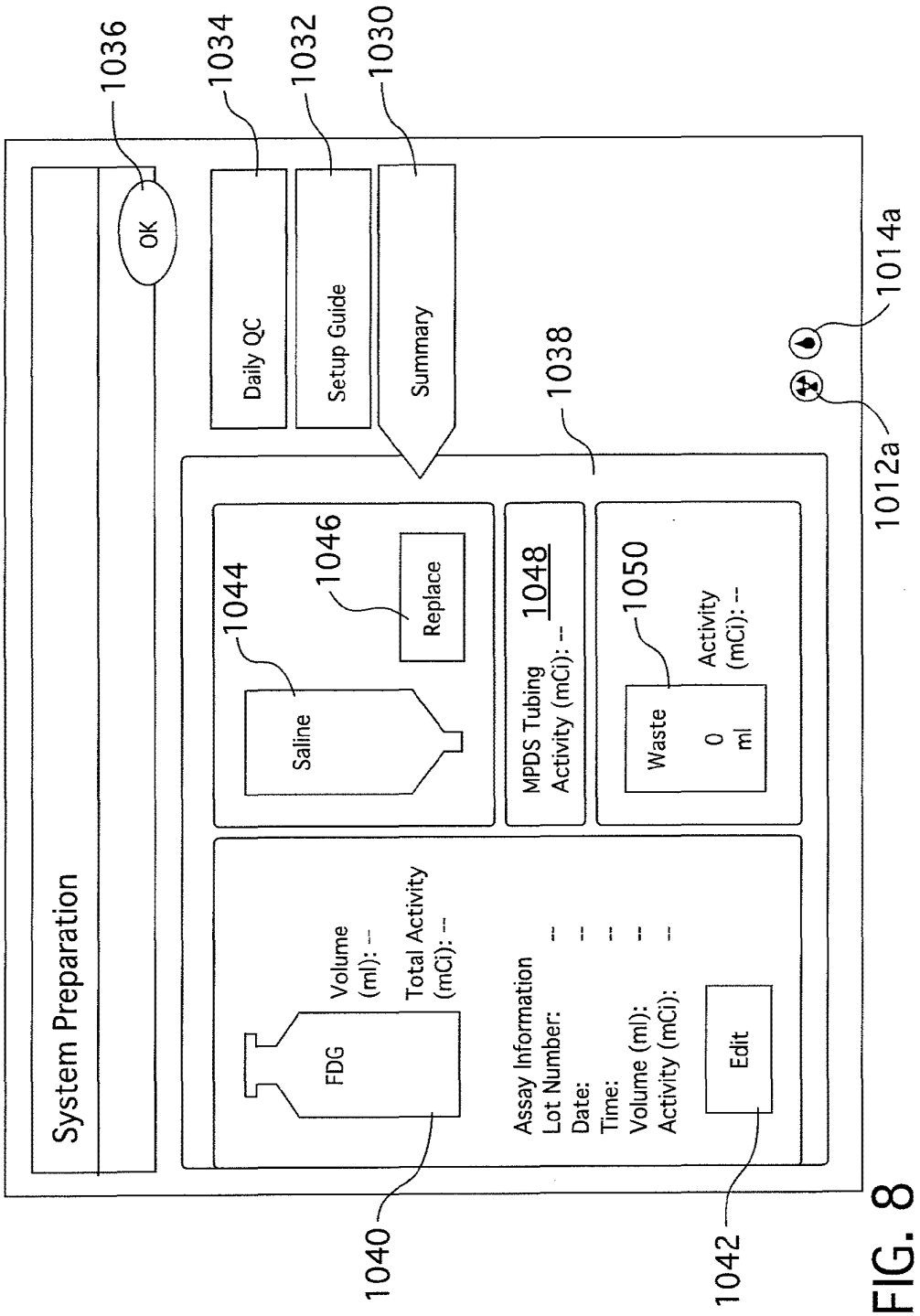
System Preparation
OK
Daily QC
Setup Guide
Summary
1036
1034
1032
1030
1038
1014a
1012a
Saline
Replace
1044
1046
MPDS Tubing
Activity (mCi): --
1048
Waste
0
ml
Activity
(mCi): --
1050
FDG
Volume
(ml): --
Total Activity
(mCi): --
Assay Information
Lot Number: --
Date: --
Time: --
Volume (ml): --
Activity (mCi): --
Edit
1040
1042

FIG. 8

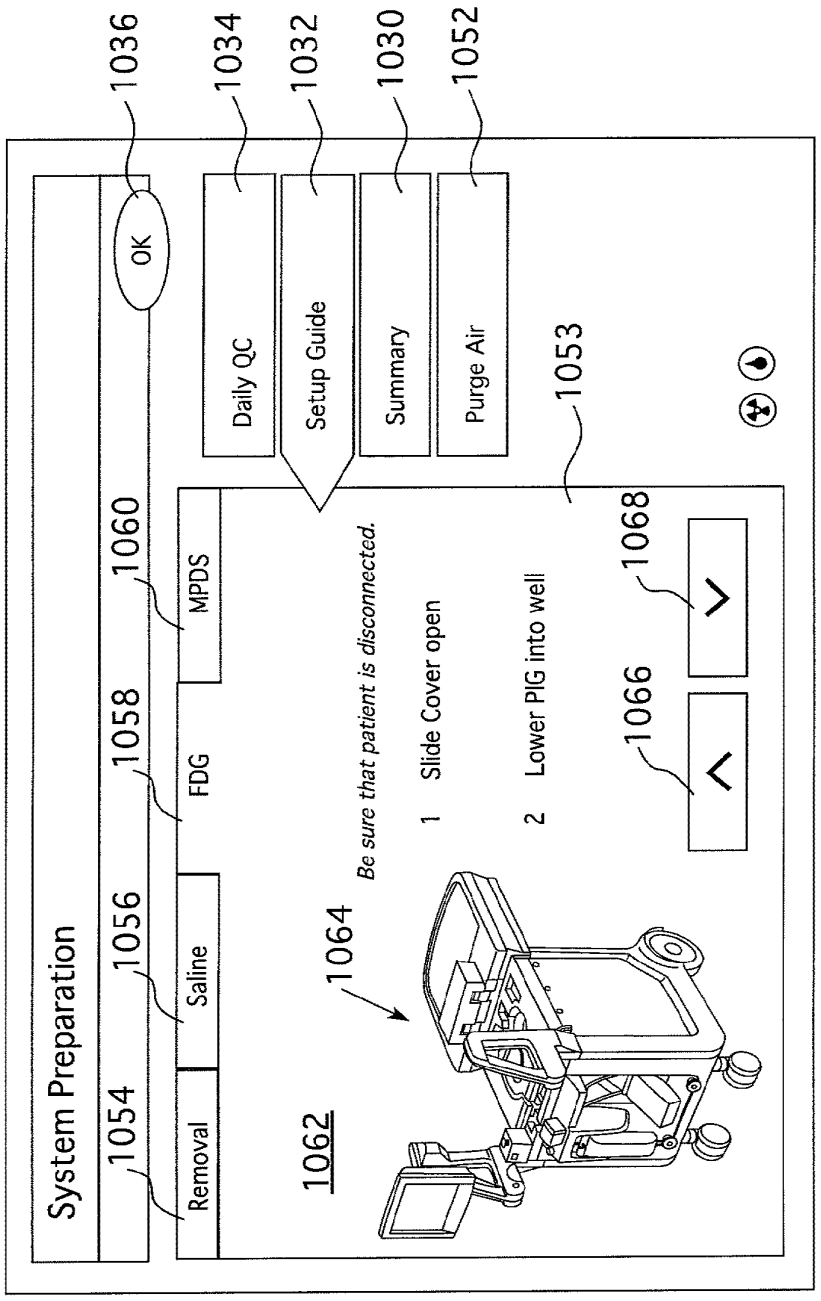
System Preparation
1054
Removal
1056
Saline
1058
FDG
1060
MPDS
OK
1036
Daily QC
1034
Setup Guide
1032
Summary
1030
Purge Air
1052
1053
Be sure that patient is disconnected.
1 Slide Cover open
2 Lower PIG into well
1062
1064
1066
1068

FIG. 9

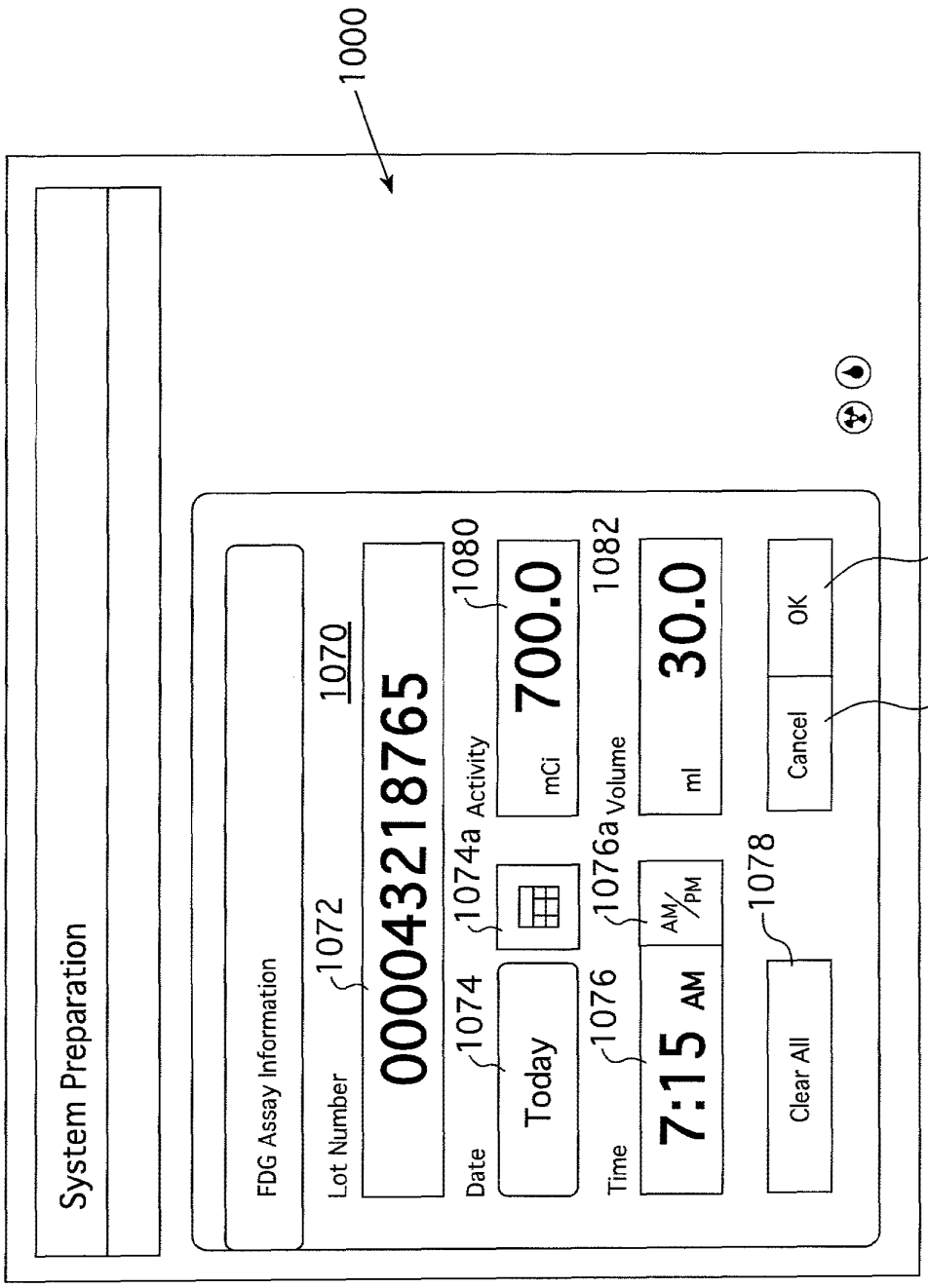
1000
System Preparation
FDG Assay Information
Lot Number
1072
1070
0000432187 65
Date
1074
Today
1074a
Activity
1080
700.0
mCi
Time
1076
7:15 AM
1076a
AM/PM
Volume
1082
30.0
ml
Clear All
1078
Cancel
OK
1084
1086

FIG. 10

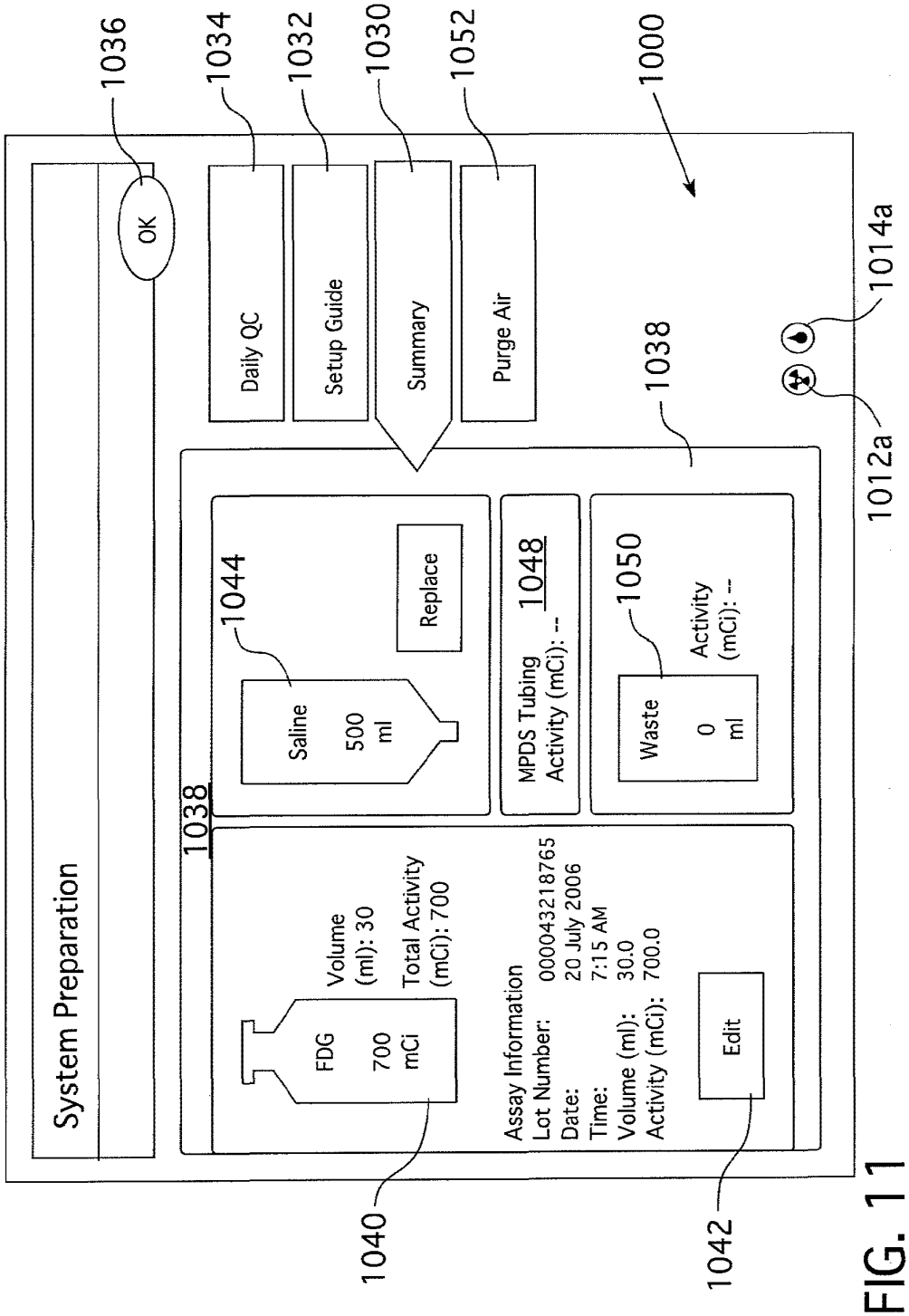
1036
1034
1032
1030
1052
1000
OK
Daily QC
Setup Guide
Summary
Purge Air
1038
1014a
1012a
1038
1044
Saline
500
ml
Replace
MPDS Tubing 1048
Activity (mCi): --
1050
Waste
0
ml
Activity
(mCi): --
System Preparation
FDG
700
mCi
Volume
(ml): 30
Total Activity
(mCi): 700
Assay Information
Lot Number: 000043218765
Date: 20 July 2006
Time: 7:15 AM
Volume (ml): 30.0
Activity (mCi): 700.0
Edit
1040
1042

FIG. 11

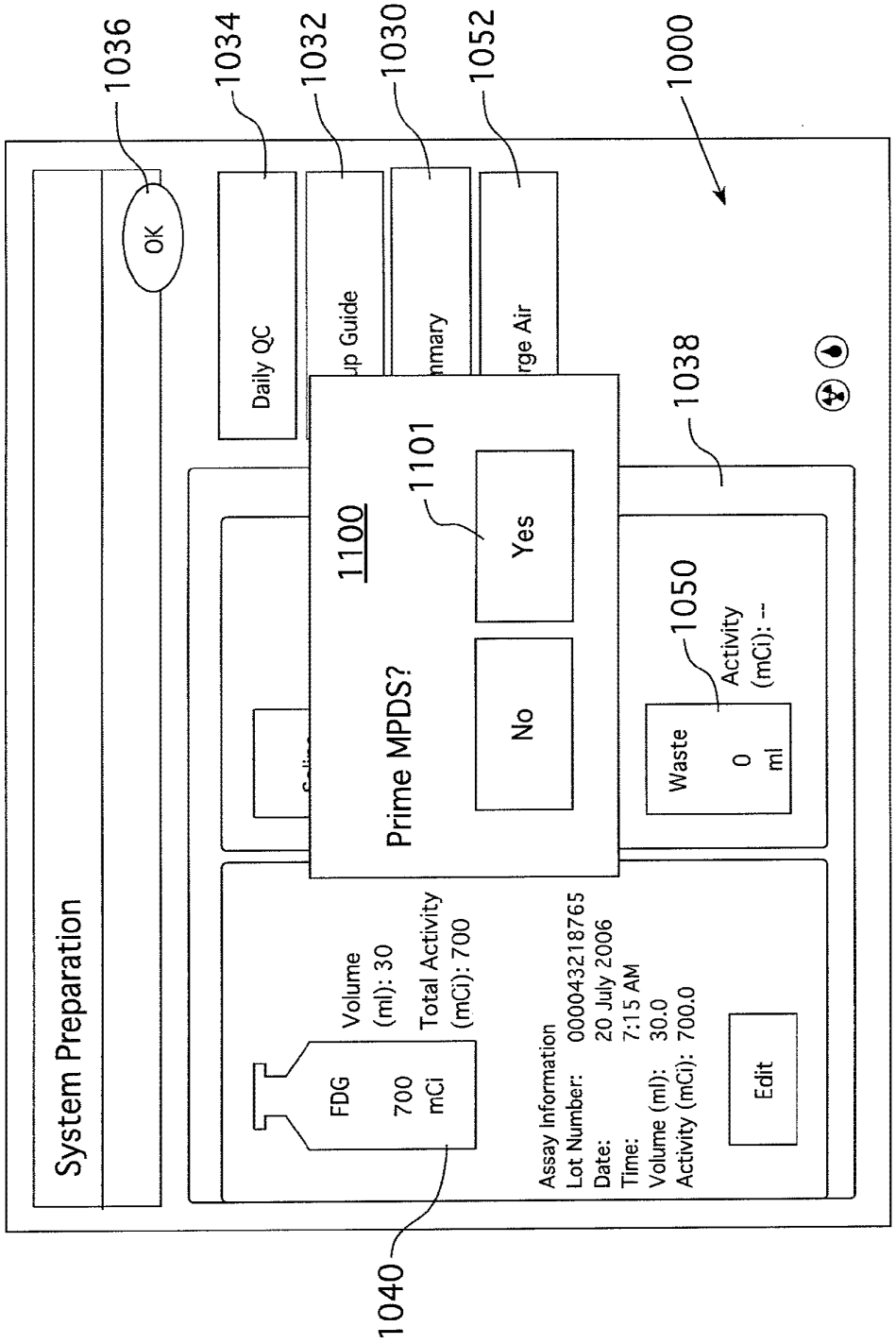
1036
1034
1032
1030
1052
1000
OK
Daily QC
up Guide
nmary
rge Air
1038
1101
1100
Yes
Prime MPDS?
No
1050
Activity
(mCi): --
Waste
0
ml
System Preparation
Volume
(ml): 30
Total Activity
(mCi): 700
FDG
700
mCi
Assay Information
Lot Number: 00004321876S
Date: 20 July 2006
Time: 7:15 AM
Volume (ml): 30.0
Activity (mCi): 700.0
Edit
1040

FIG. 12A

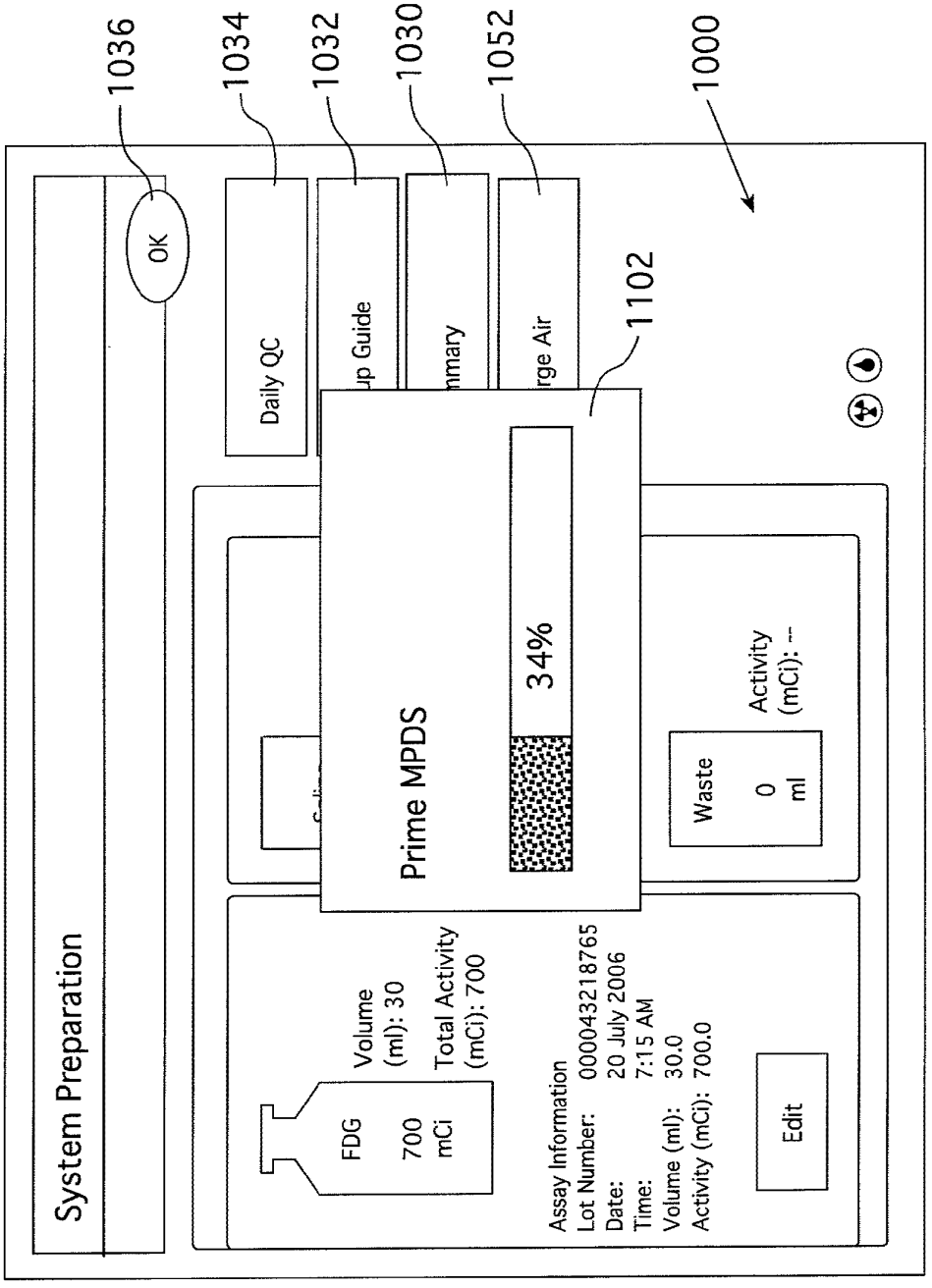
1036
1034
1032
1030
1052
1000
1102
OK
Daily QC
Prime MPDS
34%
System Preparation
FDG
700
mCi
Volume
(ml): 30
Total Activity
(mCi): 700
Waste
0
ml
Activity
(mCi): --
Edit
Assay Information
Lot Number: 000043218765
Date: 20 July 2006
Time: 7:15 AM
Volume (ml): 30.0
Activity (mCi): 700.0

FIG. 12B

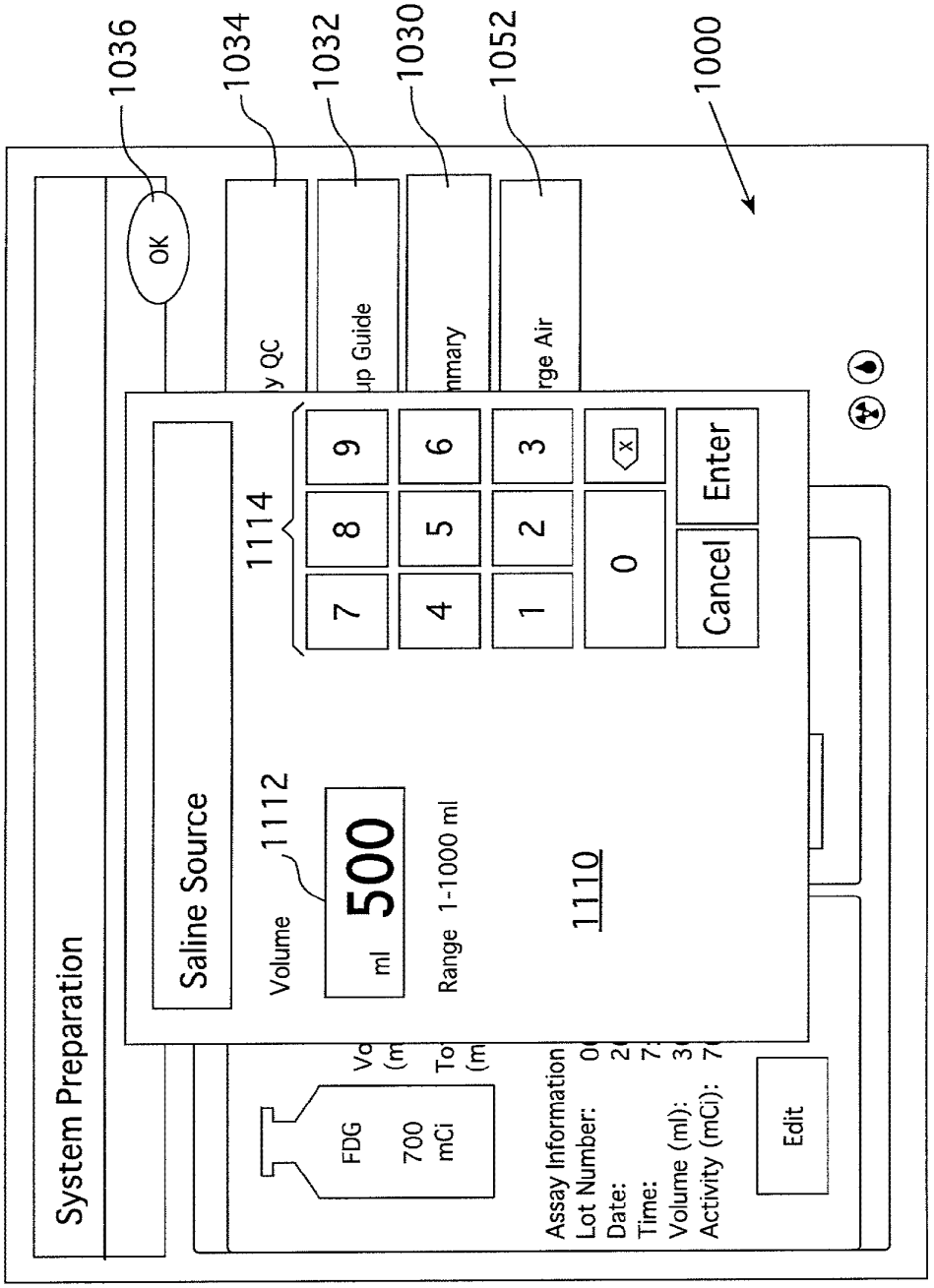
1036
1034
1032
1030
1052
1000
OK
y QC
up Guide
mmary
rge Air
System Preparation
Saline Source
1112
Volume
500
ml
Range 1-1000 ml
1114
7
8
9
4
5
6
1
2
3
0
Cancel
Enter
1110
FDG
700
mCi
Assay Information
Lot Number:
Date:
Time:
Volume (ml):
Activity (mCi):
Edit

FIG. 13

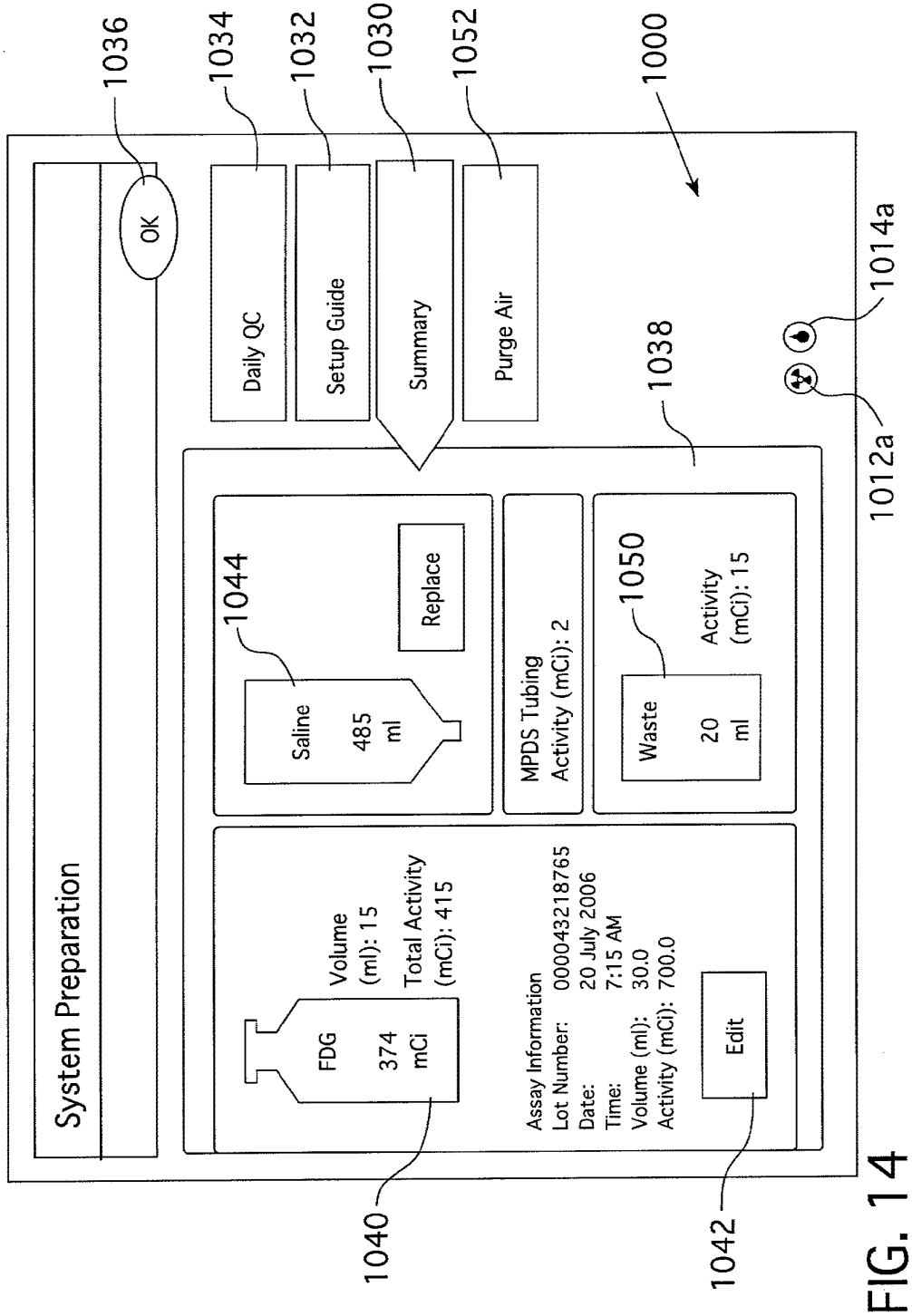
1036
1034
1032
1030
1052
1000
OK
Daily QC
Setup Guide
Summary
Purge Air
1014a
1012a
1038
System Preparation
1044
Saline
485
ml
Replace
MPDS Tubing
Activity (mCi): 2
1050
Waste
20
ml
Activity
(mCi): 15
FDG
374
mCi
Volume
(ml): 15
Total Activity
(mCi): 415
Assay Information
Lot Number: 000043218765
Date: 20 July 2006
Time: 7:15 AM
Volume (ml): 30.0
Activity (mCi): 700.0
Edit
1040
1042

FIG. 14

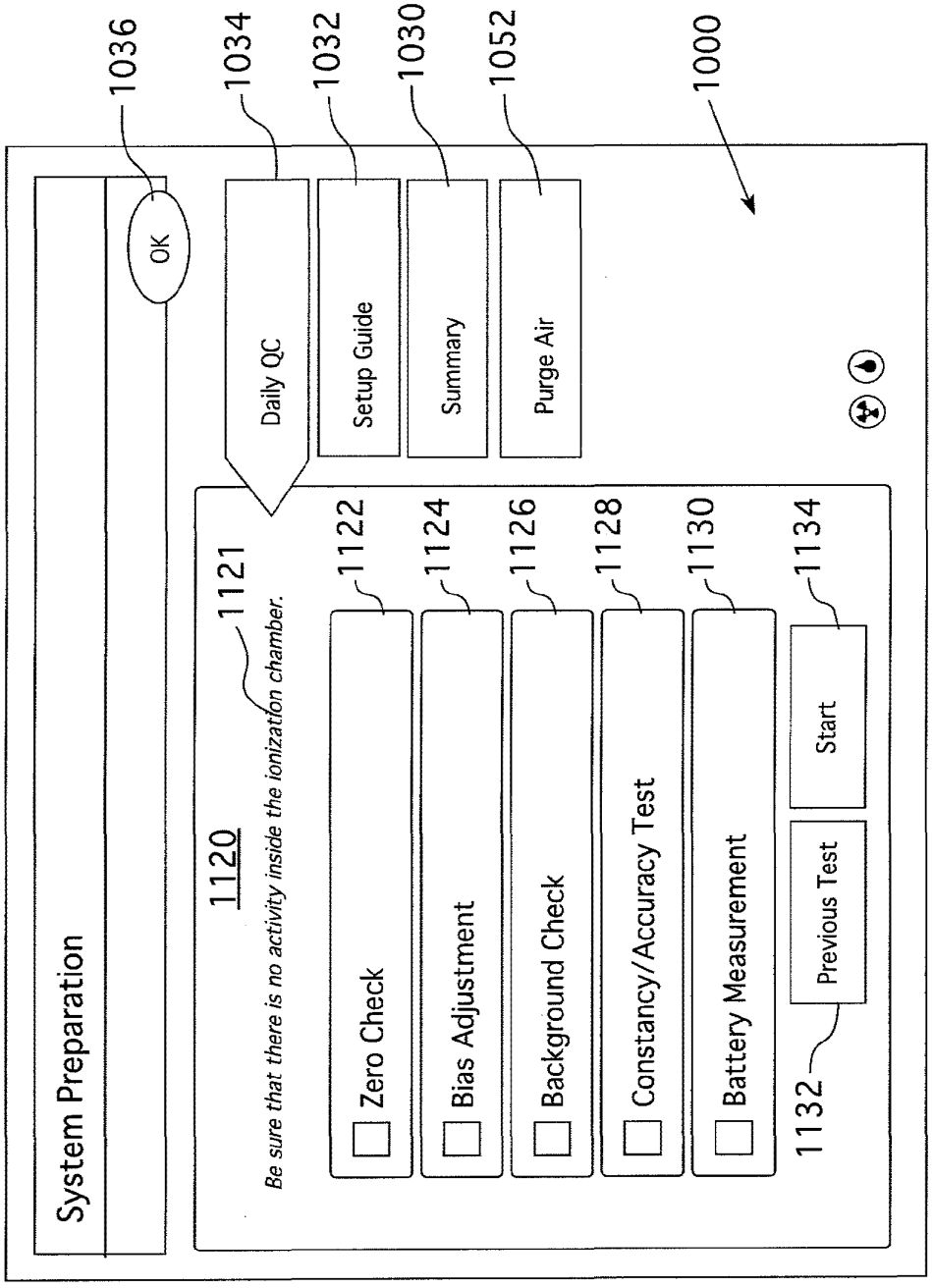
1036
1034
1032
1030
1052
1000
System Preparation
OK
Daily QC
Setup Guide
Summary
Purge Air
1120
1121
Be sure that there is no activity inside the ionization chamber.
1122
1124
1126
1128
1130
1134
Zero Check
Bias Adjustment
Background Check
Constancy/Accuracy Test
Battery Measurement
Start
Previous Test
1132

FIG. 15

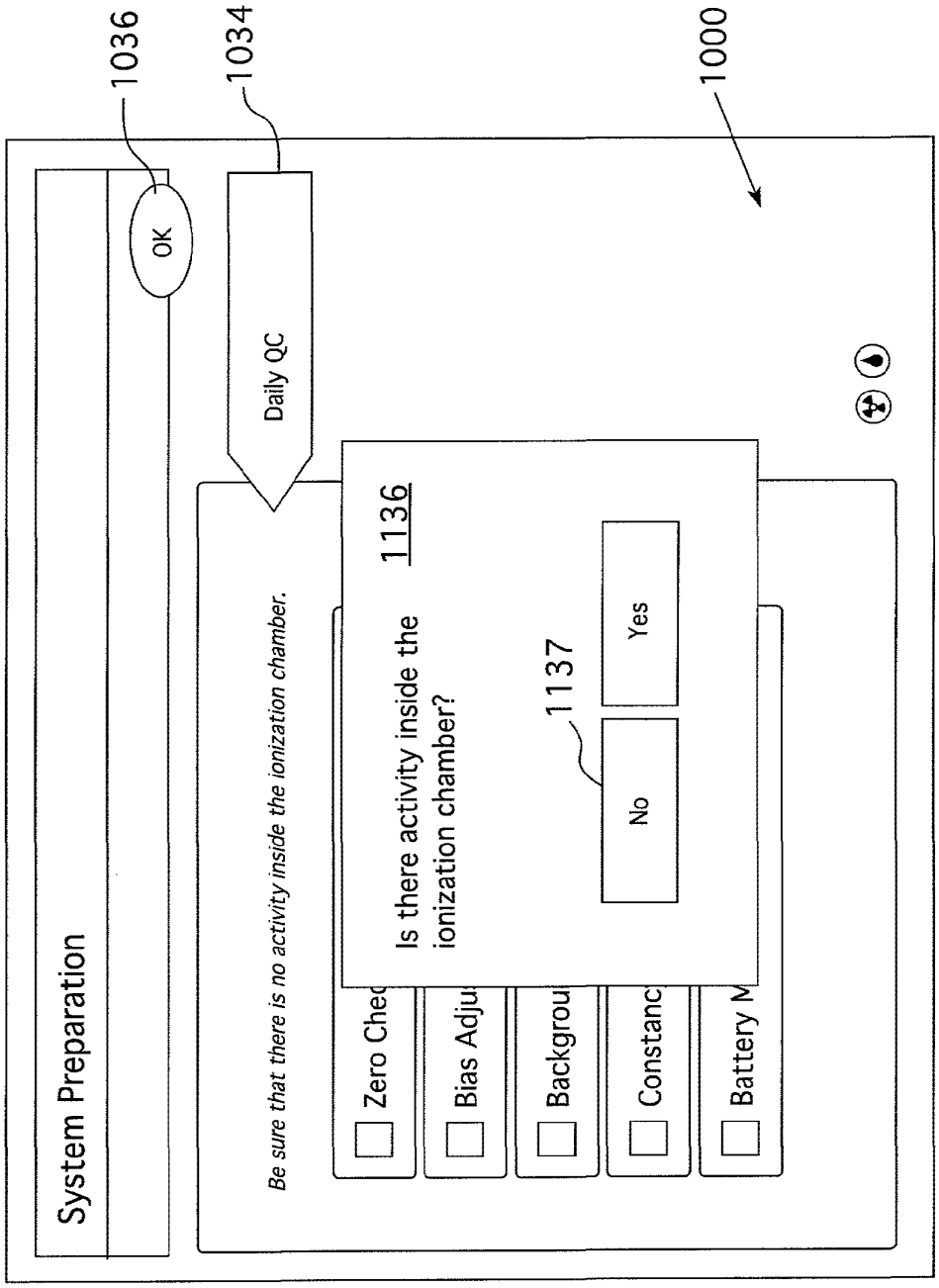
1036
1034
1000
OK
Daily QC
System Preparation
Be sure that there is no activity inside the ionization chamber.
Is there activity inside the ionization chamber?
1136
1137
No
Yes
Zero Chec
Bias Adju
Backgrou
Constanc
Battery M

FIG. 16A

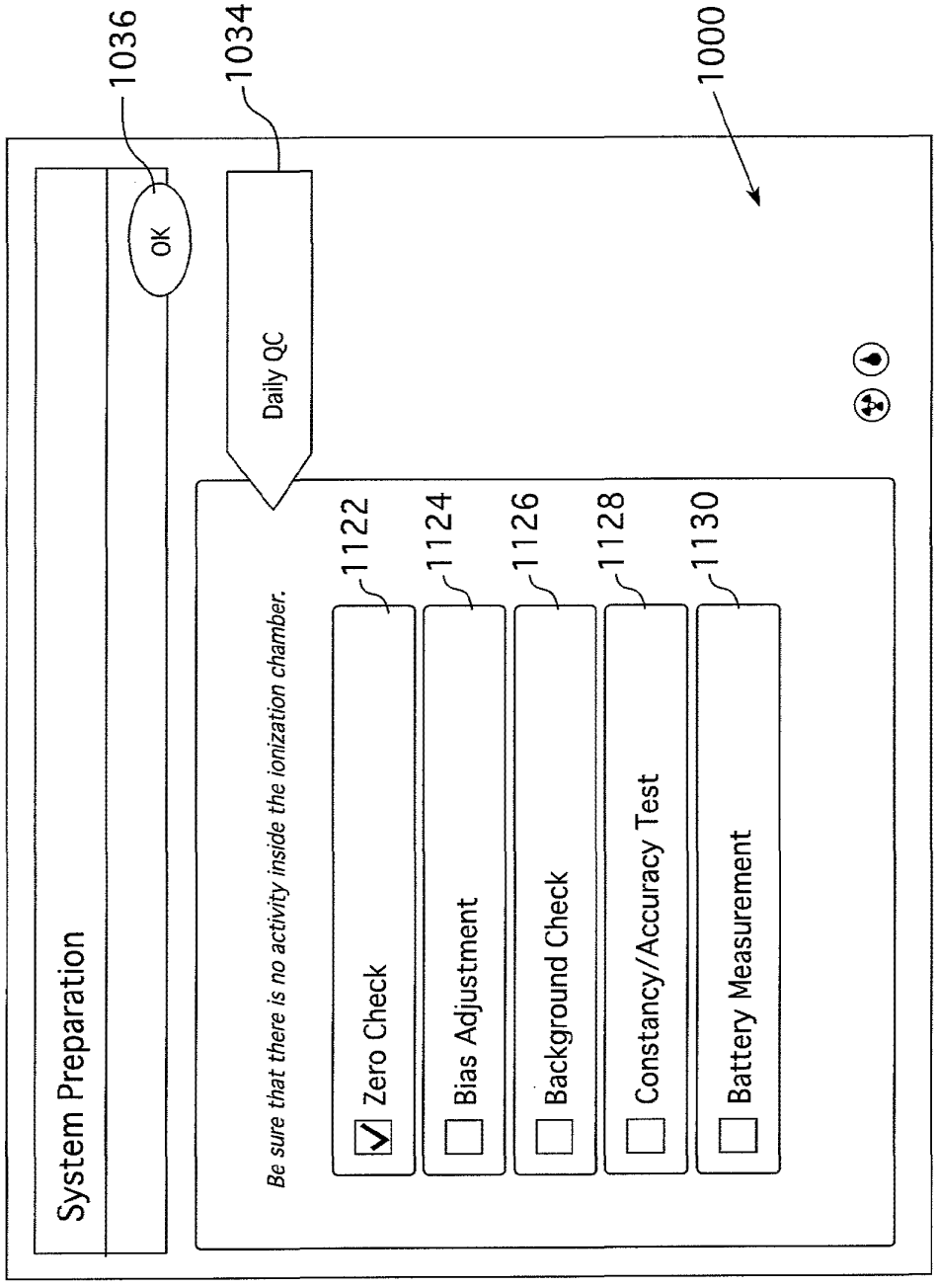
1036
1034
1000
OK
Daily QC
System Preparation
Be sure that there is no activity inside the ionization chamber.
1122
1124
1126
1128
1130
Zero Check
Bias Adjustment
Background Check
Constancy/Accuracy Test
Battery Measurement

FIG. 16B

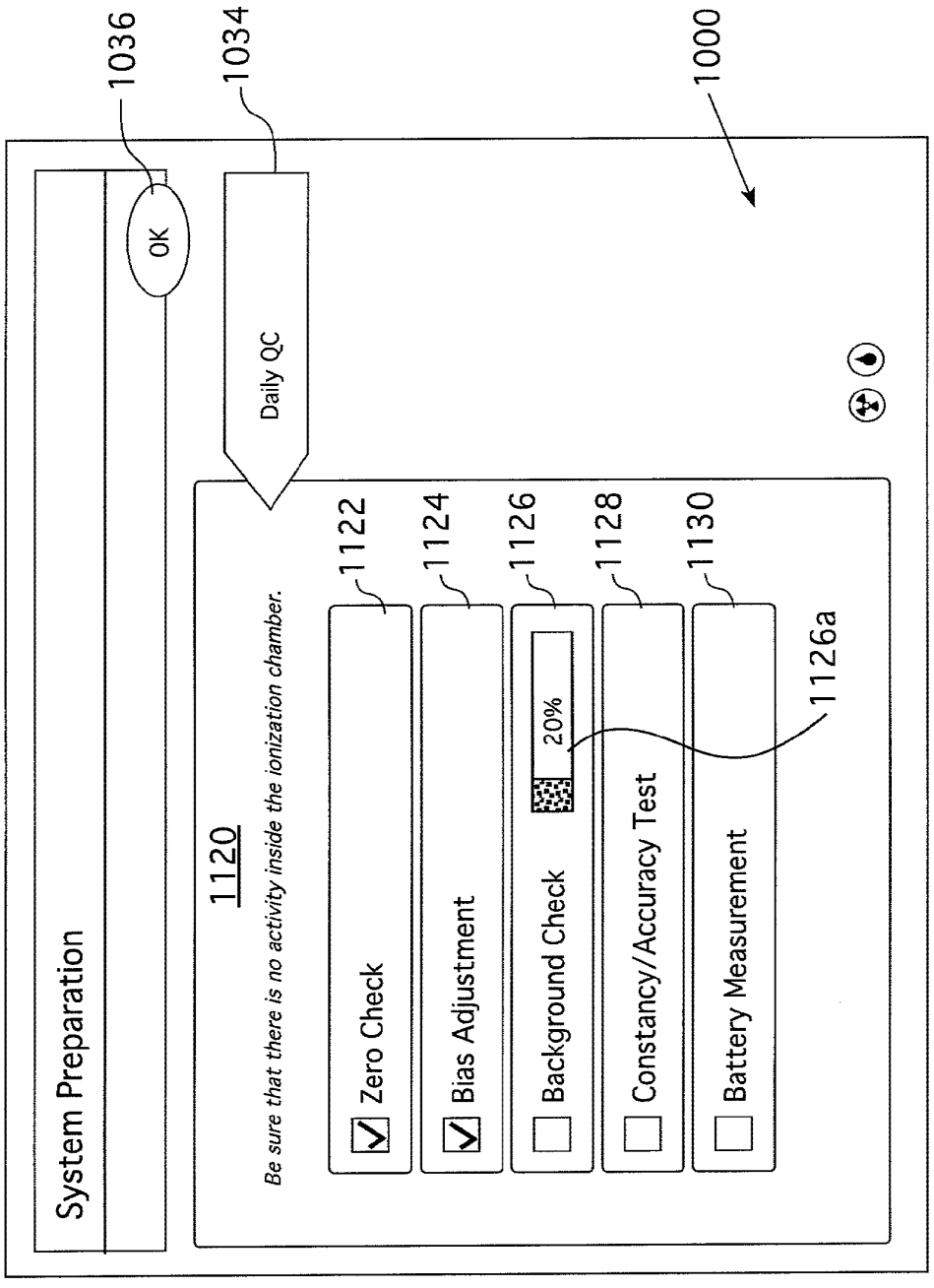
1036
1034
1000
System Preparation
OK
Daily QC
1120
Be sure that there is no activity inside the ionization chamber.
1122
1124
1126
1128
1130
Zero Check
Bias Adjustment
Background Check
20%
Constancy/Accuracy Test
Battery Measurement
1126a

FIG. 17

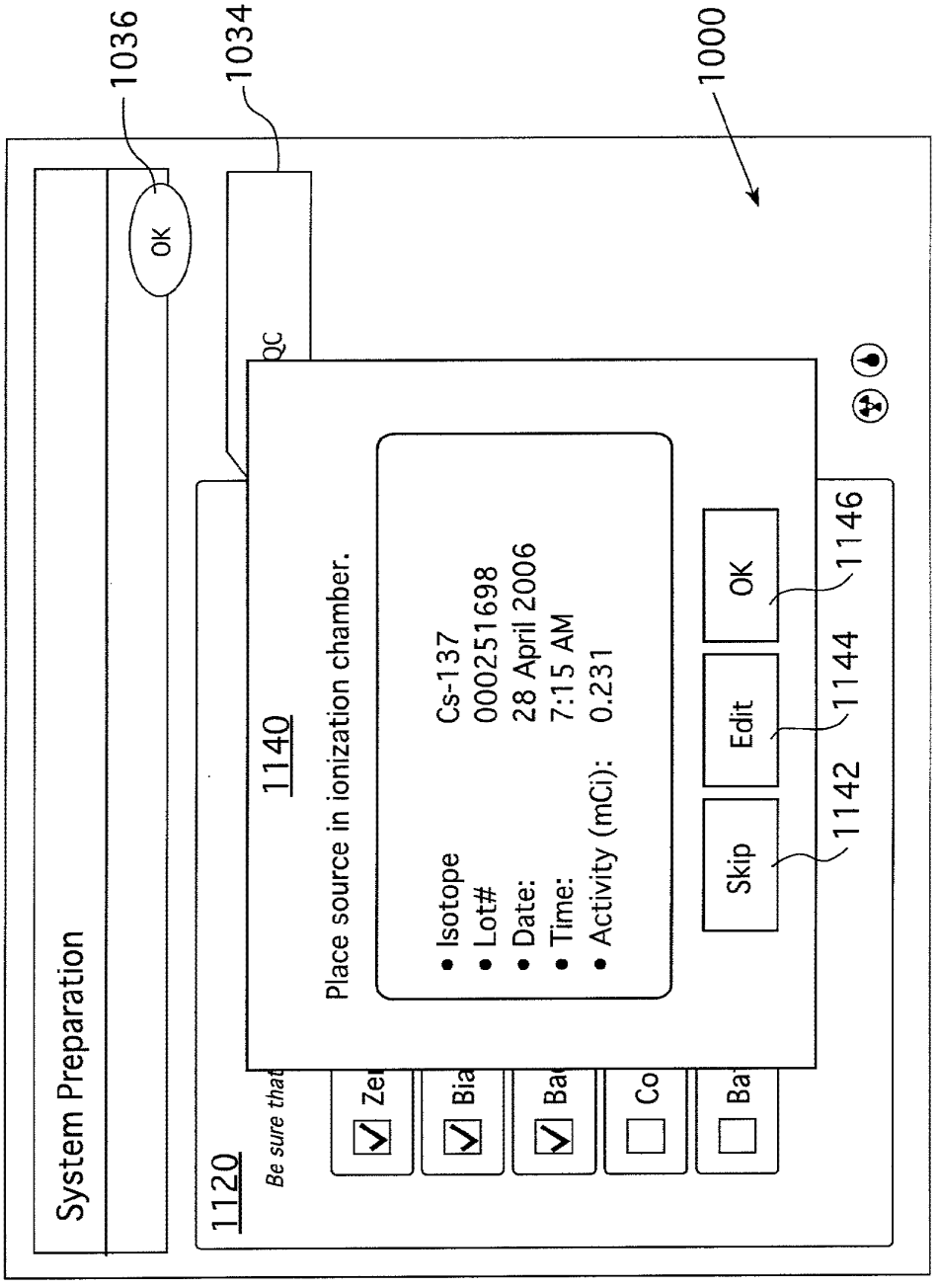
1036
1034
1000
System Preparation
OK
QC
1120
1140
Place source in ionization chamber.
• Isotope Cs-137
• Lot# 000251698
• Date: 28 April 2006
• Time: 7:15 AM
• Activity (mCi): 0.231
Skip
Edit
OK
1142
1144
1146

FIG. 18

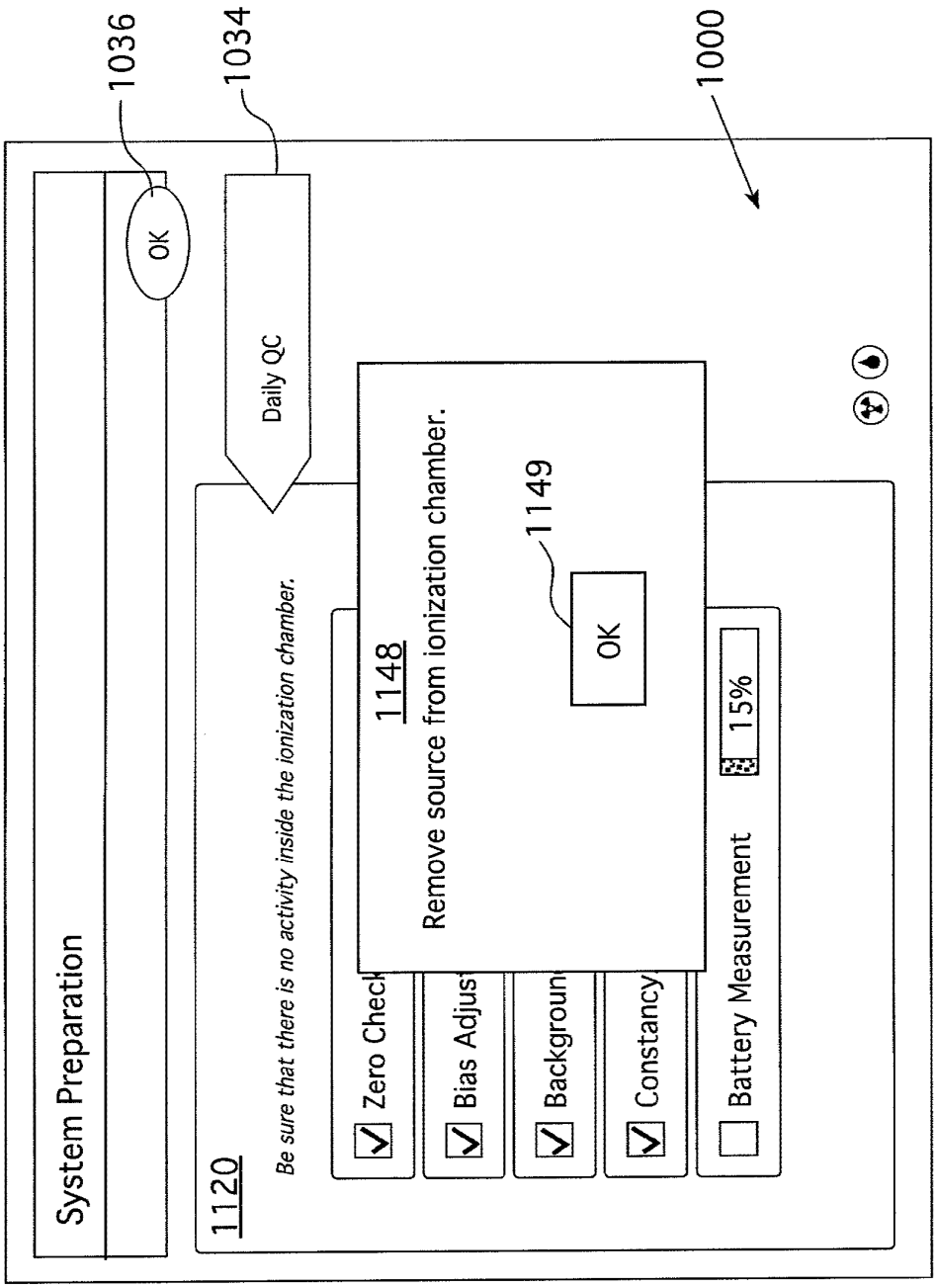
1036
1034
1000
System Preparation
OK
Daily QC
1120
Be sure that there is no activity inside the ionization chamber.
Zero Check
Bias Adjust
Background
Constancy
Battery Measurement
15%
1148
Remove source from ionization chamber.
1149
OK

FIG. 19

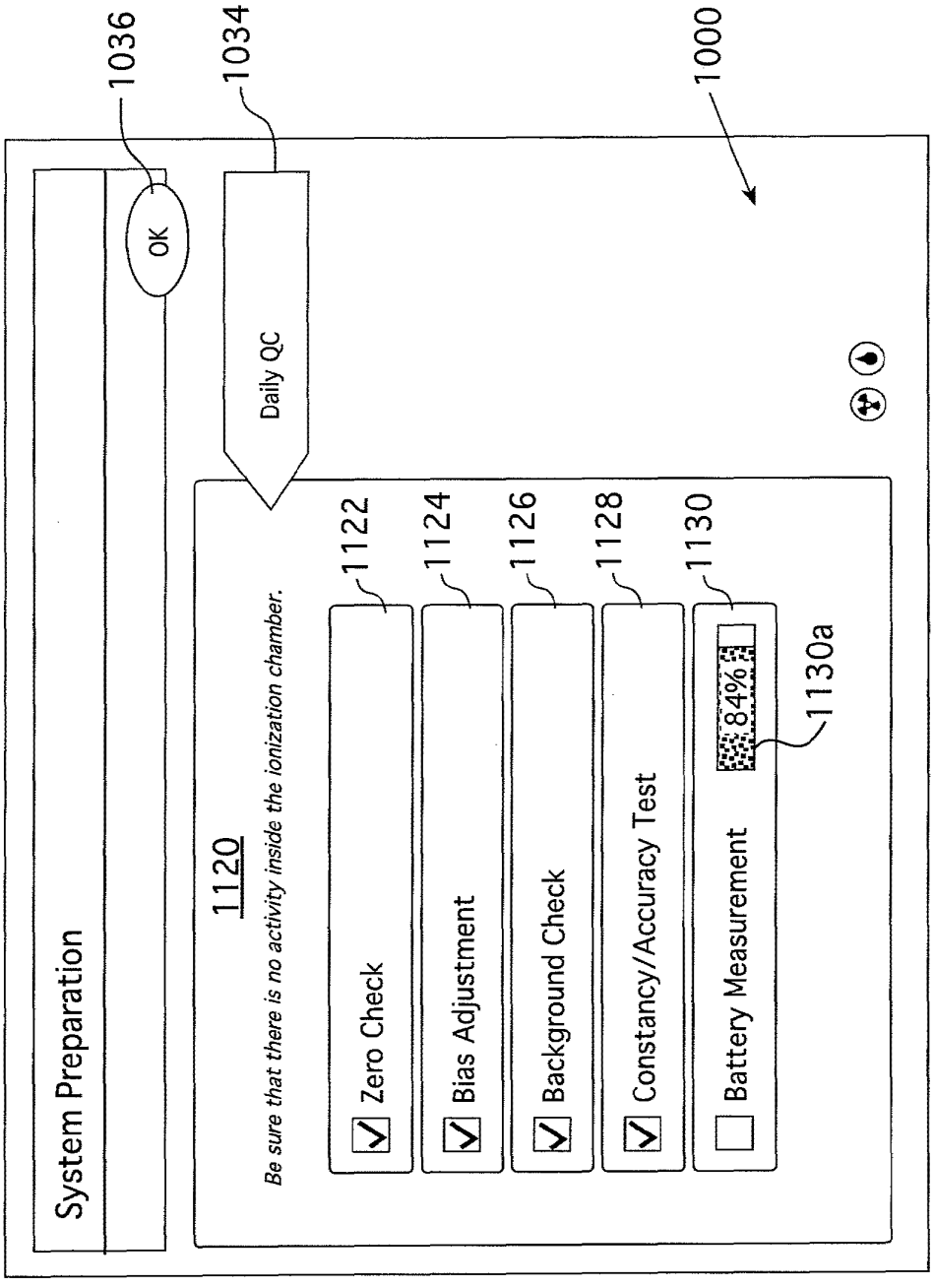
1036
1034
1000
System Preparation
OK
Daily QC
1120
Be sure that there is no activity inside the ionization chamber.
1122
Zero Check
1124
Bias Adjustment
1126
Background Check
1128
Constancy/Accuracy Test
1130
Battery Measurement
84%
1130a

FIG. 20

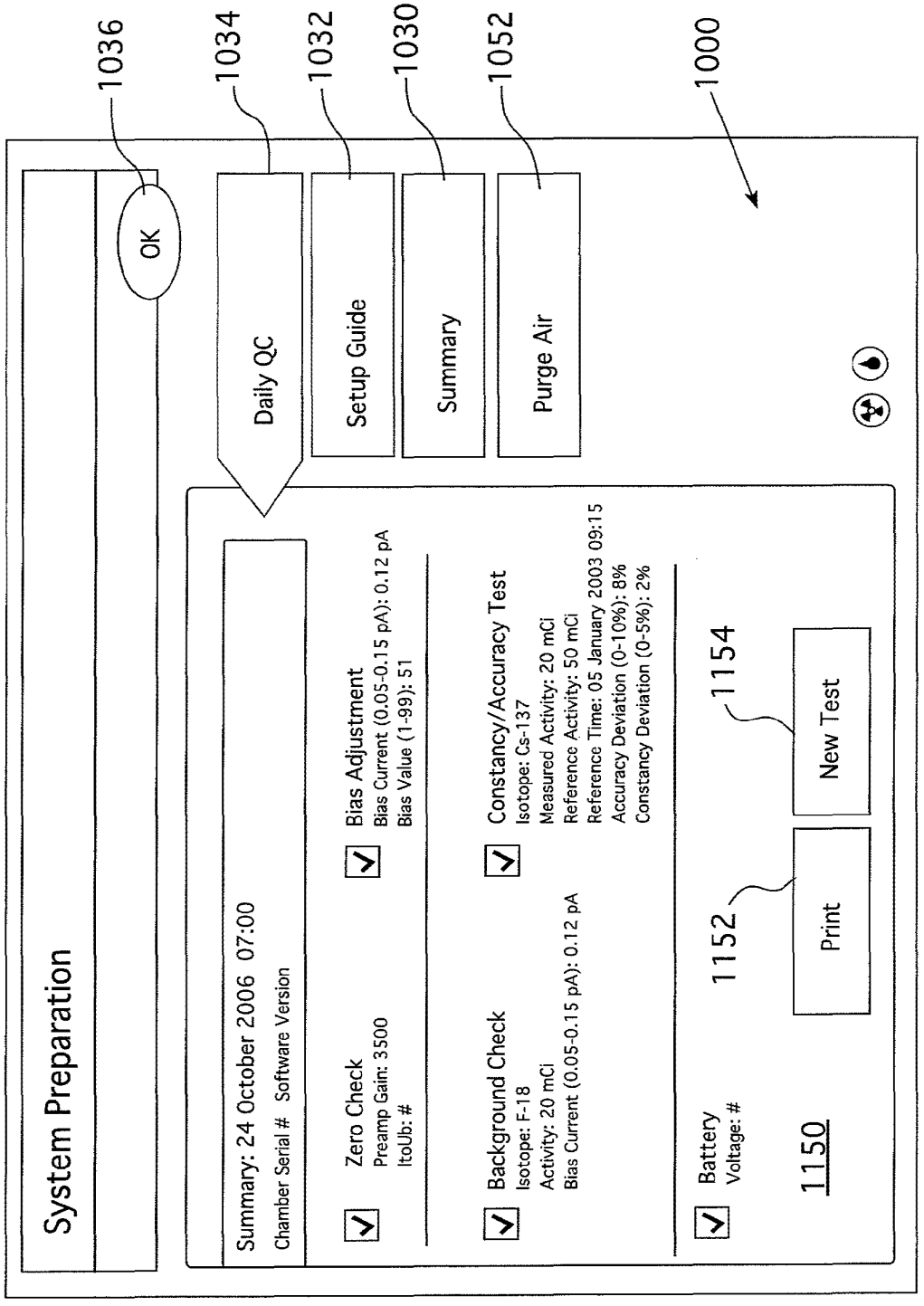
System Preparation
OK
1036
Daily QC
1034
Setup Guide
1032
Summary
1030
Purge Air
1052
1000
Summary: 24 October 2006 07:00
Chamber Serial # Software Version
Zero Check
Preamp Gain: 3500
ItoUb: #
Bias Adjustment
Bias Current (0.05-0.15 pA): 0.12 pA
Bias Value (1-99): 51
Background Check
Isotope: F-18
Activity: 20 mCi
Bias Current (0.05-0.15 pA): 0.12 pA
Constancy/Accuracy Test
Isotope: Cs-137
Measured Activity: 20 mCi
Reference Activity: 50 mCi
Reference Time: 05 January 2003 09:15
Accuracy Deviation (0-10%): 8%
Constancy Deviation (0-5%): 2%
Battery
Voltage: #
1150
1152
Print
1154
New Test

FIG. 21

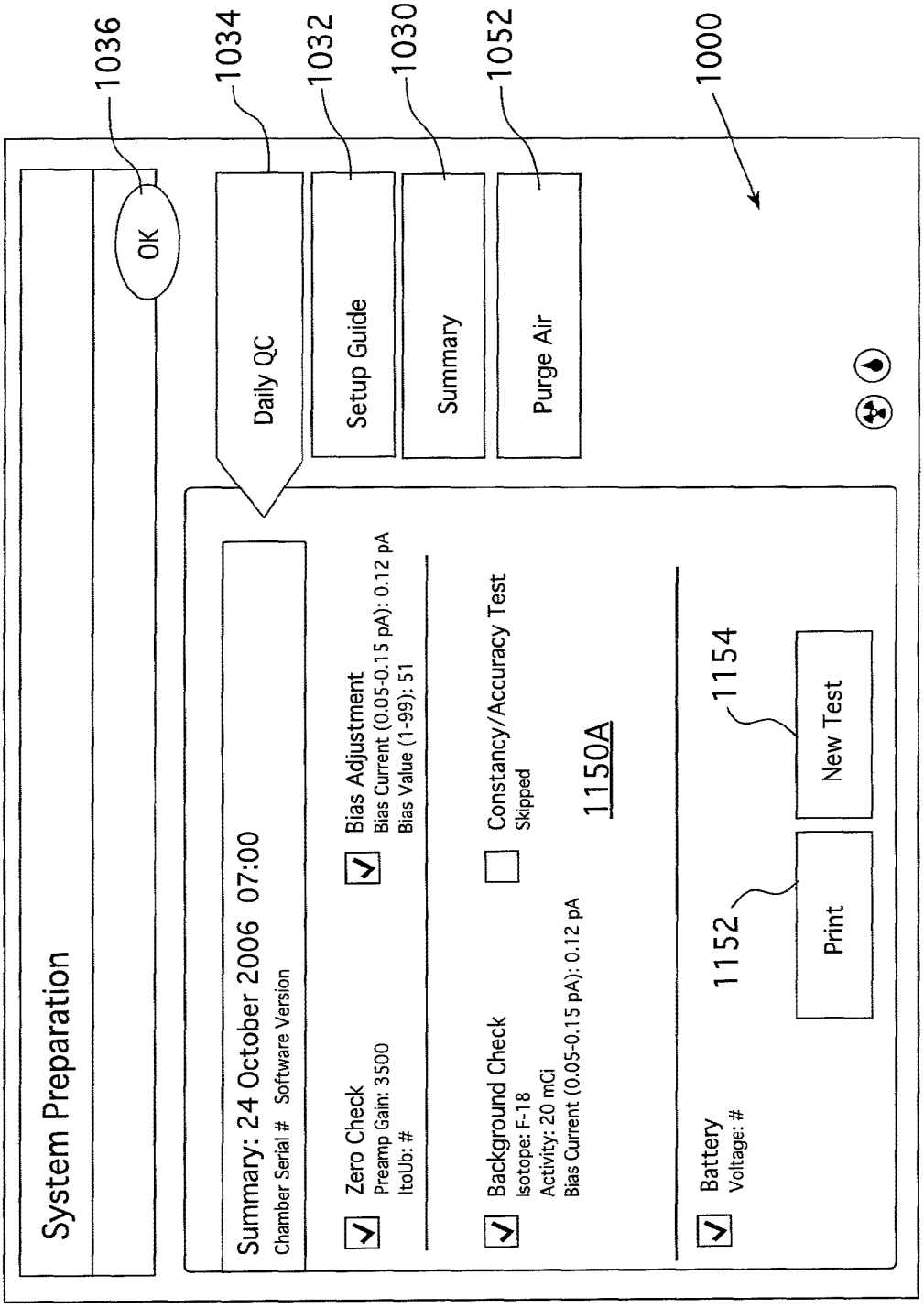
System Preparation
OK
1036
1034
1032
1030
1052
1000
Daily QC
Setup Guide
Summary
Purge Air
Summary: 24 October 2006 07:00
Chamber Serial # Software Version
Zero Check
Preamp Gain: 3500
ItoUb: #
Bias Adjustment
Bias Current (0.05-0.15 pA): 0.12 pA
Bias Value (1-99): 51
Background Check
Isotope: F-18
Activity: 20 mCi
Bias Current (0.05-0.15 pA): 0.12 pA
Constancy/Accuracy Test
Skipped
1150A
Battery
Voltage: #
1152
Print
New Test
1154

FIG. 22

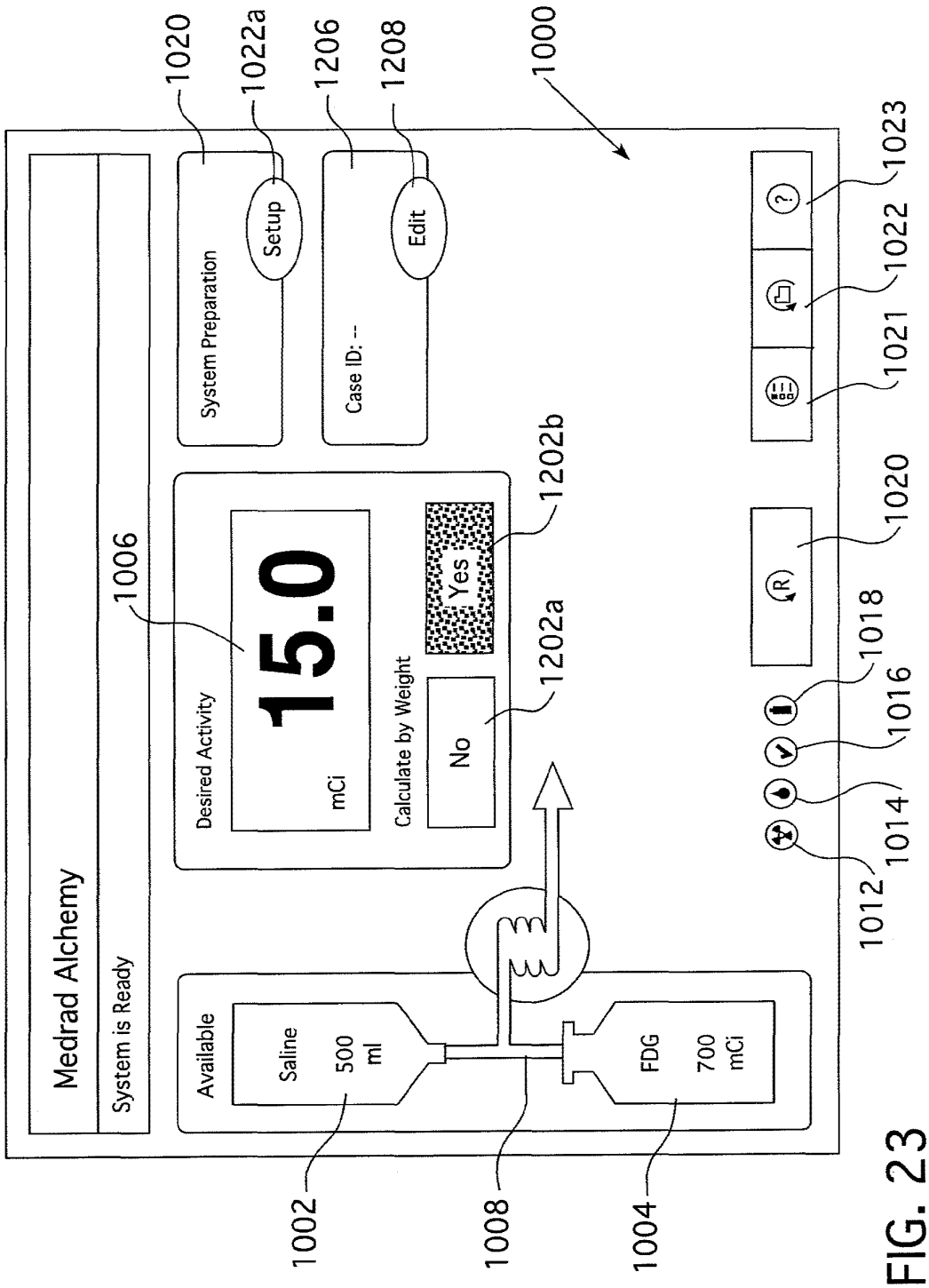
Medrad Alchemy
System is Ready
1006
Available
Saline
500
ml
FDG
700
mCi
1002
1008
1004
Desired Activity
15.0
mCi
Calculate by Weight
No
Yes
1202a
1202b
System Preparation
Setup
1020
1022a
Case ID: --
Edit
1206
1208
1000
1012
1014
1016
1018
1020
1021
1022
1023

FIG. 23

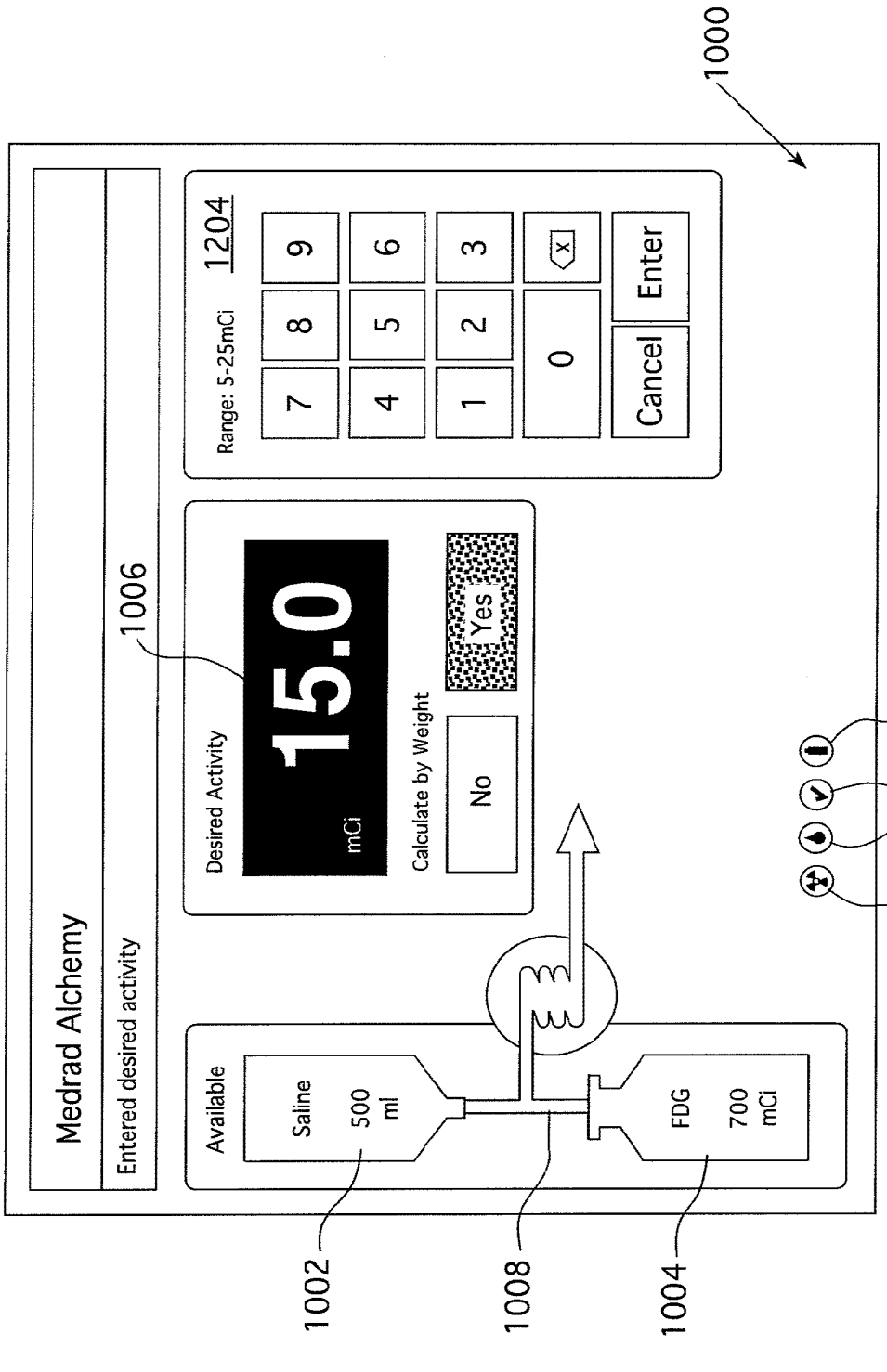
1000
Medrad Alchemy
Entered desired activity
1006
Desired Activity
15.0
mCi
Calculate by Weight
No
Yes
Range: 5-25mCi
1204
7
8
9
4
5
6
1
2
3
0
X
Cancel
Enter
Available
Saline
500
ml
FDG
700
mCi
1002
1008
1004
1012
1014
1016
1018

FIG. 24A

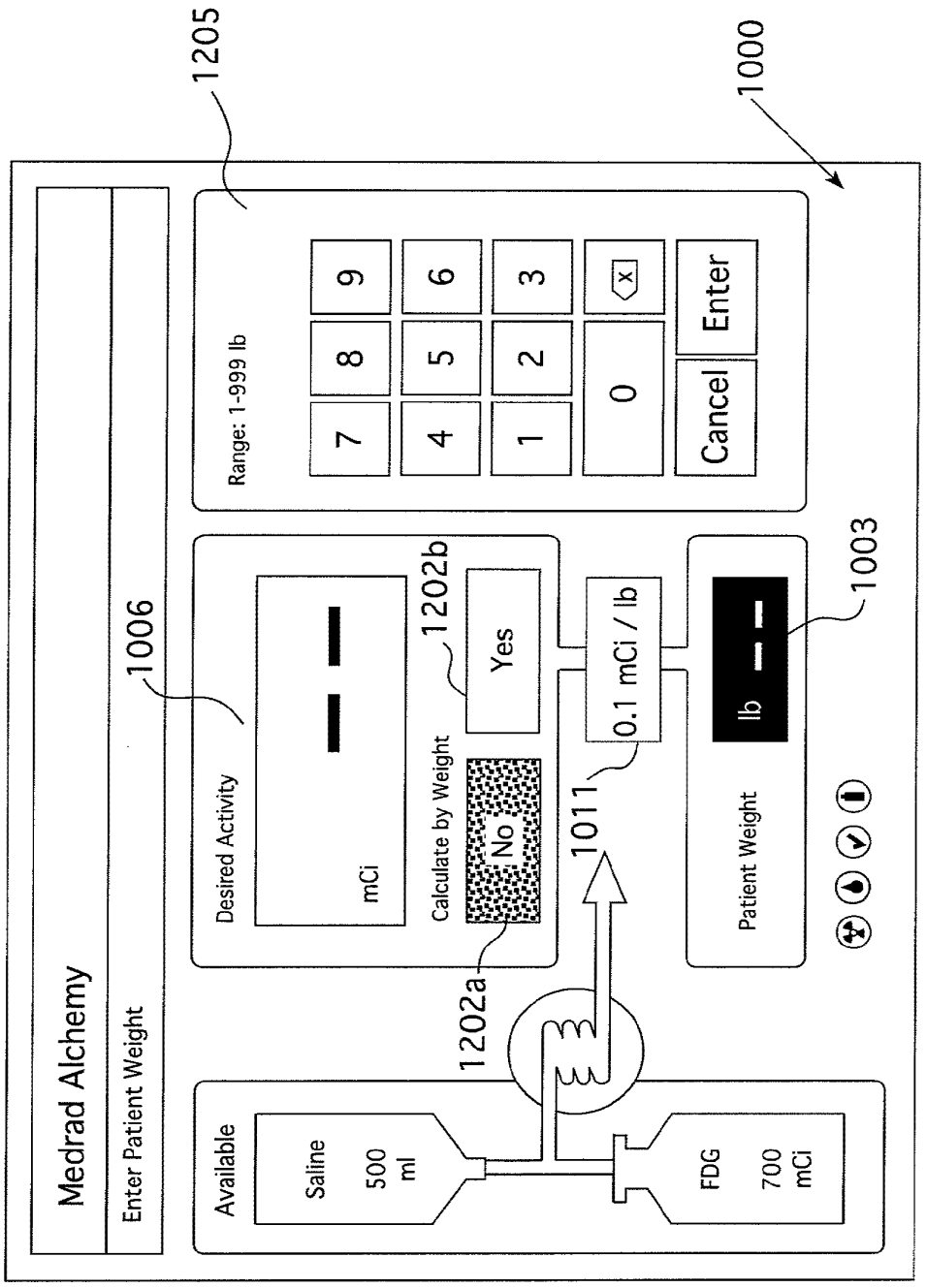
1205
1000
Medrad Alchemy
Enter Patient Weight
1006
Range: 1-999 lb
7
8
9
4
5
6
1
2
3
0
x
Cancel
Enter
Desired Activity
mCi
Calculate by Weight
1202b
Yes
No
1202a
1011
0.1 mCi / lb
Patient Weight
lb
1003
Available
Saline
500
ml
FDG
700
mCi

FIG. 24B

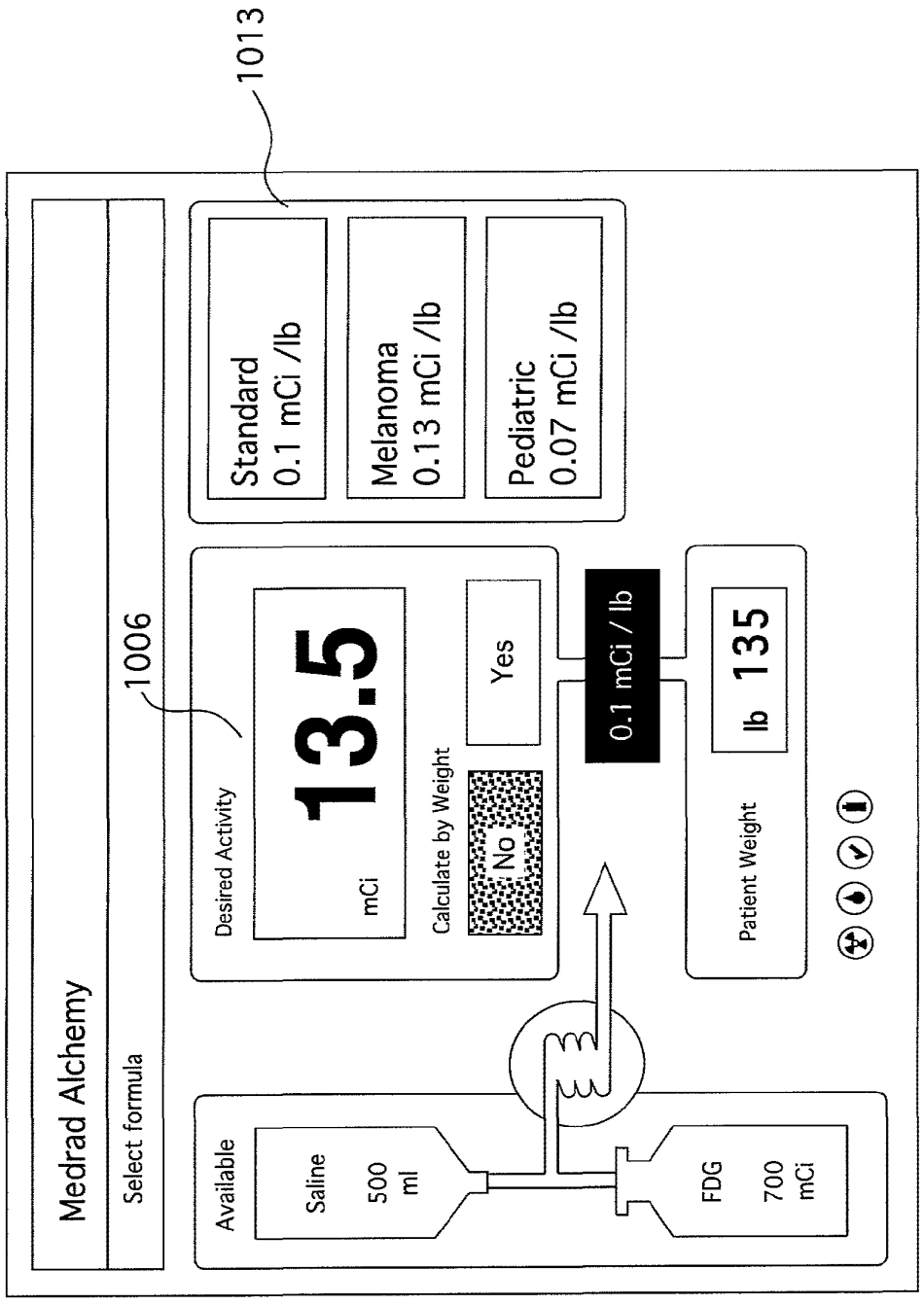
1013
Medrad Alchemy
Select formula
1006
Desired Activity
13.5
mCi
Calculate by Weight
No
Yes
0.1 mCi / lb
Patient Weight
lb 135
Standard
0.1 mCi /lb
Melanoma
0.13 mCi /lb
Pediatric
0.07 mCi /lb
Available
Saline
500
ml
FDG
700
mCi

FIG. 24C

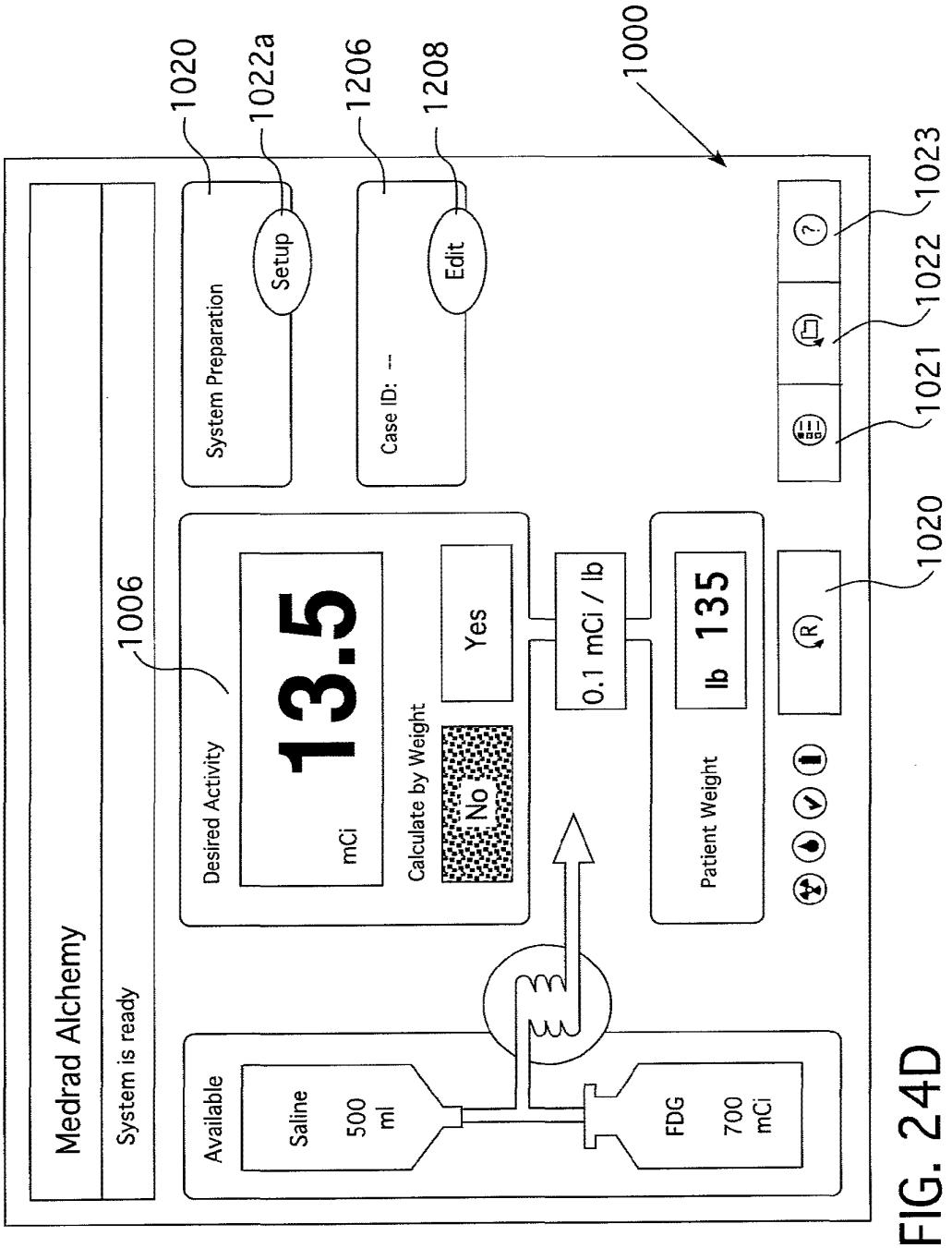
1000
1020
1022a
1206
1208
1023
1022
1021
1020
1006
Medrad Alchemy
System is ready
System Preparation
Setup
Case ID: --
Edit
Desired Activity
13.5
mCi
Calculate by Weight
No
Yes
0.1 mCi / lb
Patient Weight
lb 135
R
Available
Saline
500
ml
FDG
700
mCi

FIG. 24D

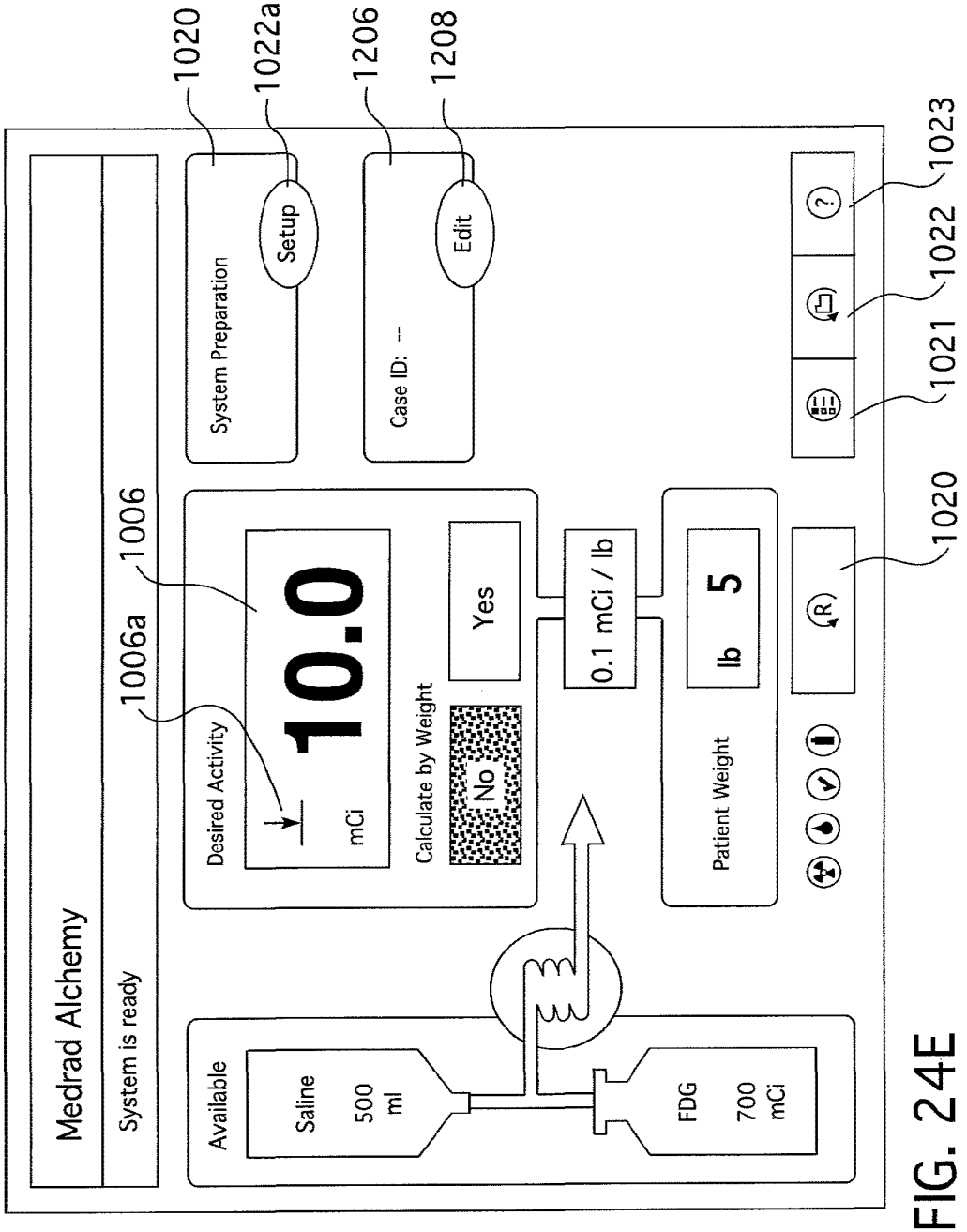
Medrad Alchemy
System is ready
1006
1006a
Desired Activity
10.0
mCi
Calculate by Weight
No
Yes
0.1 mCi / lb
Patient Weight
lb
5
Available
Saline
500
ml
FDG
700
mCi
System Preparation
Setup
Case ID: --
Edit
1020
1022a
1206
1208
1020
1021
1022
1023

FIG. 24E

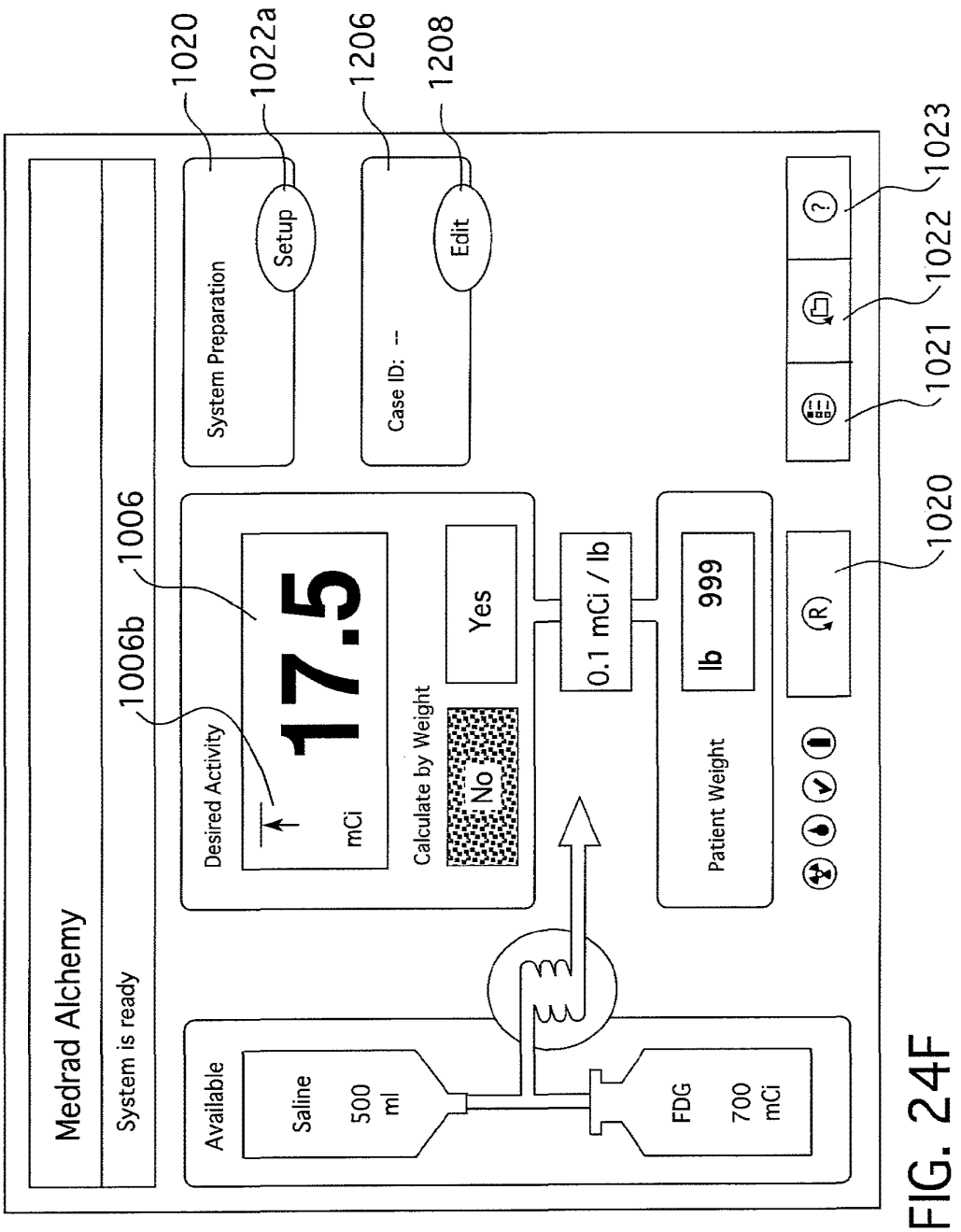
Medrad Alchemy
System is ready
1006
1006b
Desired Activity
17.5
mCi
Calculate by Weight
No
Yes
0.1 mCi / lb
Patient Weight
lb 999
1020
1020
1022a
1206
1208
System Preparation
Setup
Case ID: --
Edit
1023
1022
1021
Available
Saline
500
ml
FDG
700
mCi

FIG. 24F

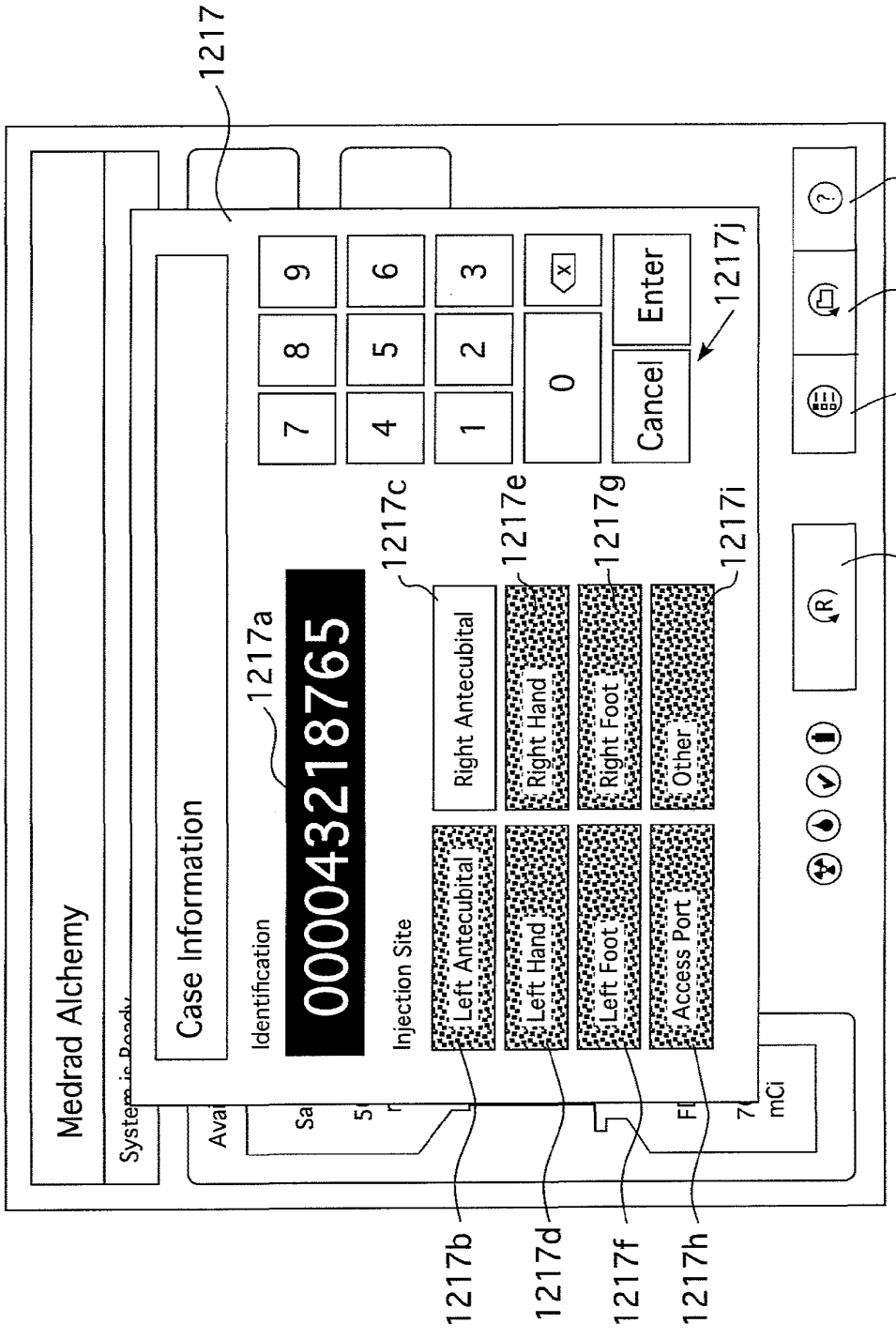
1217
Medrad Alchemy
Case Information
Identification
1217a
00004321876 5
Injection Site
1217c
1217e
1217g
1217i
Right Antecubital
Right Hand
Right Foot
Other
Left Antecubital
Left Hand
Left Foot
Access Port
1217b
1217d
1217f
1217h
7 8 9
4 5 6
1 2 3
0
Cancel
Enter
1217j
1020
1021
1022
1023
mCi

FIG. 25A

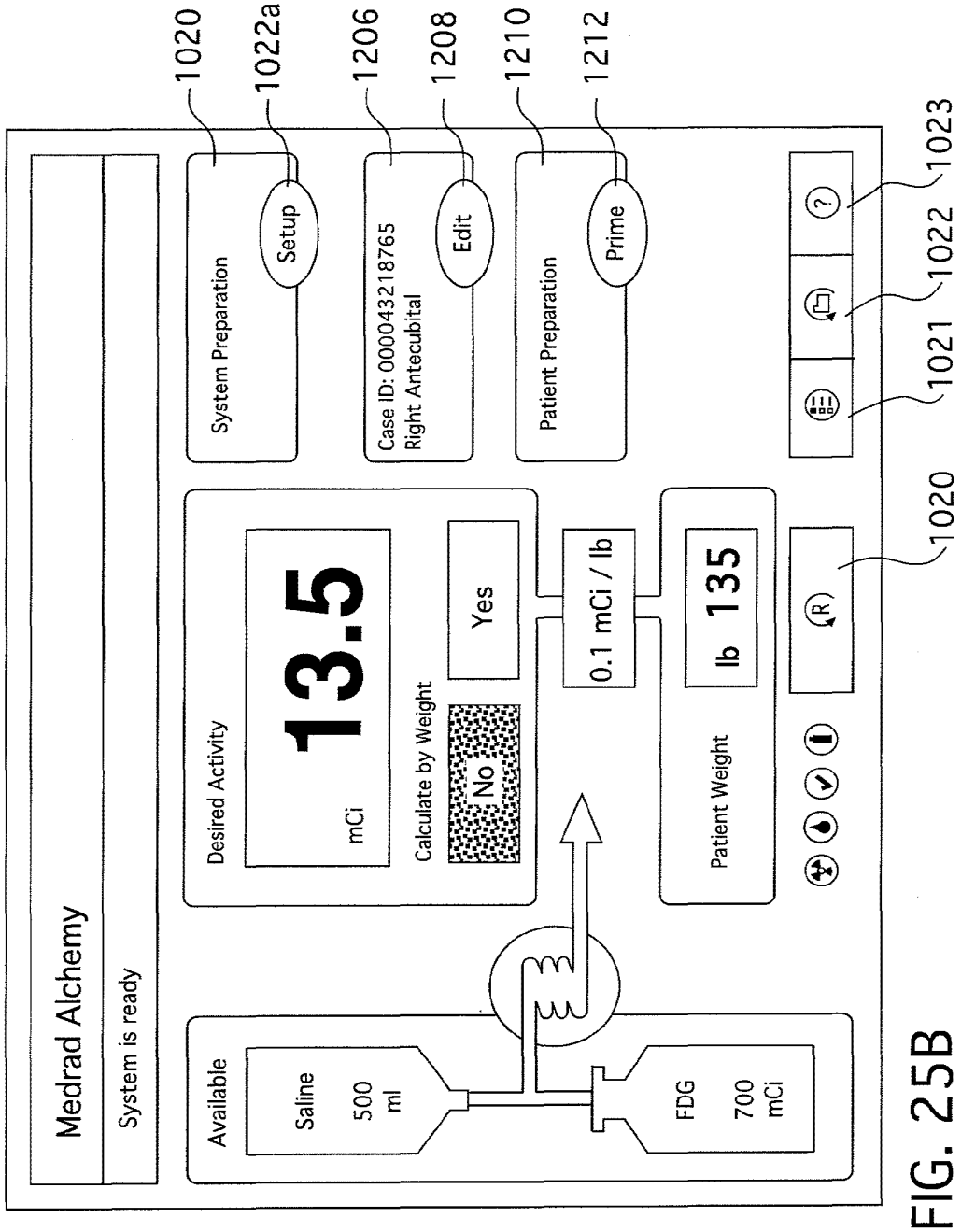
1020
1022a
1206
1208
1210
1212
1023
1022
1021
1020
Medrad Alchemy
System is ready
Available
Saline
500
ml
FDG
700
mCi
System Preparation
Setup
Case ID: 000043218765
Right Antecubital
Edit
Patient Preparation
Prime
Desired Activity
13.5
mCi
Calculate by Weight
No
Yes
0.1 mCi / lb
Patient Weight
lb 135
R
?

FIG. 25B

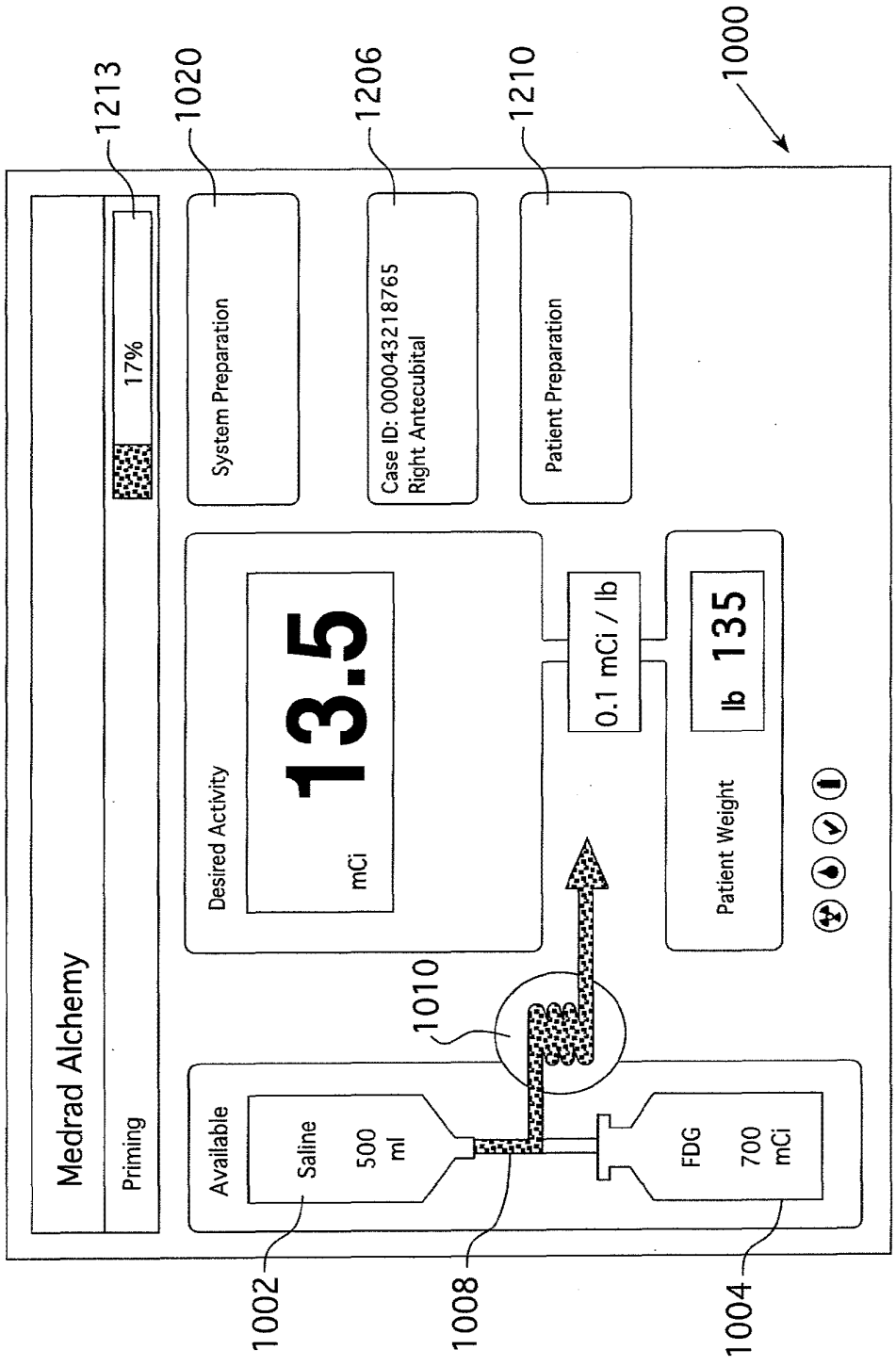
1213
1020
1206
1210
1000
Medrad Alchemy
Priming
17%
System Preparation
Case ID: 000043218765
Right Antecubital
Patient Preparation
Desired Activity
13.5
mCi
0.1 mCi / lb
Patient Weight
lb 135
1010
Available
Saline
500
ml
FDG
700
mCi
1002
1008
1004

FIG. 26A

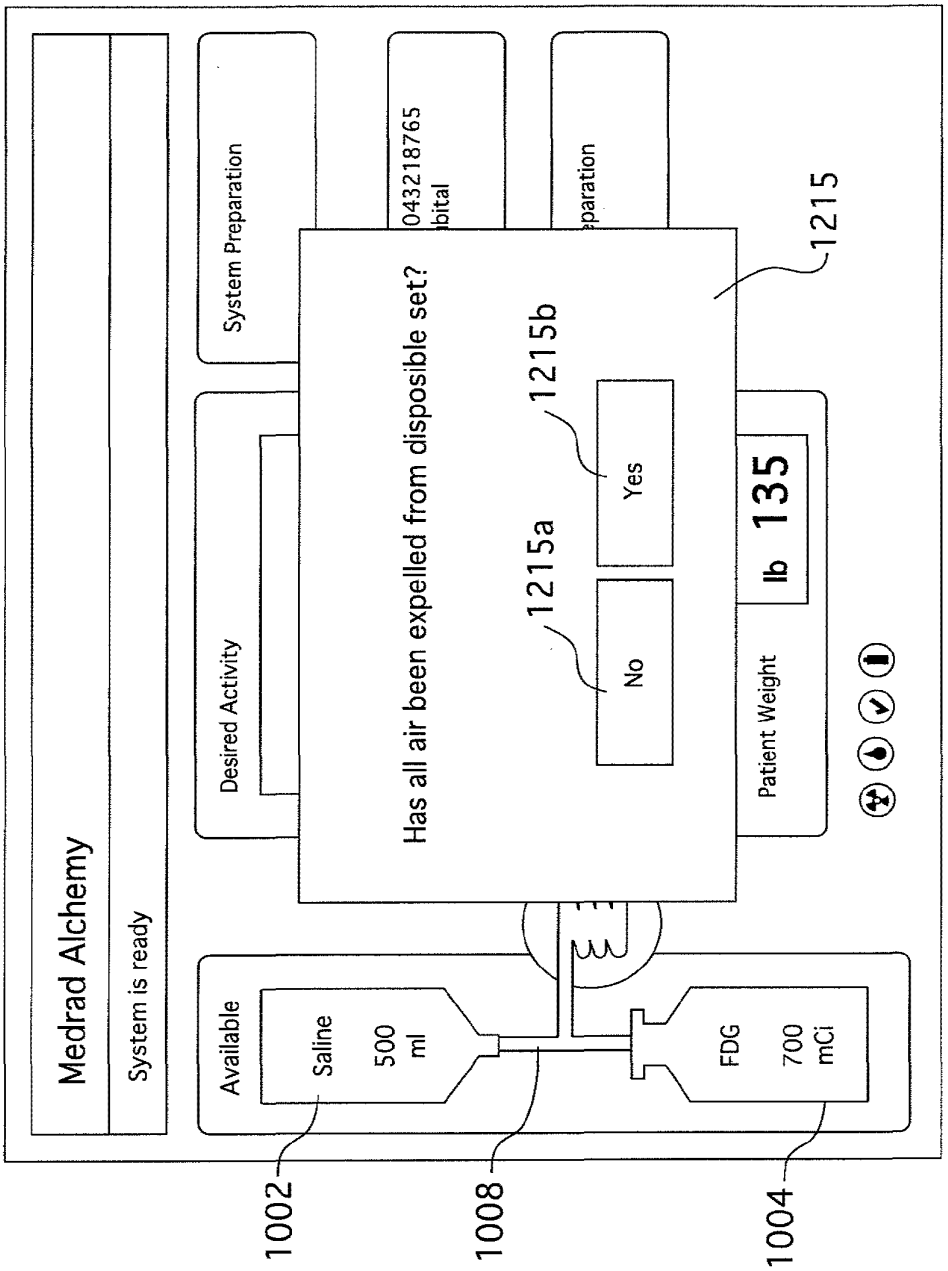
Medrad Alchemy
System is ready
Available
Saline
500
ml
FDG
700
mCi
Desired Activity
System Preparation
Has all air been expelled from disposible set?
No
Yes
1215a
1215b
1215
Patient Weight
lb 135
1002
1008
1004

FIG. 26B

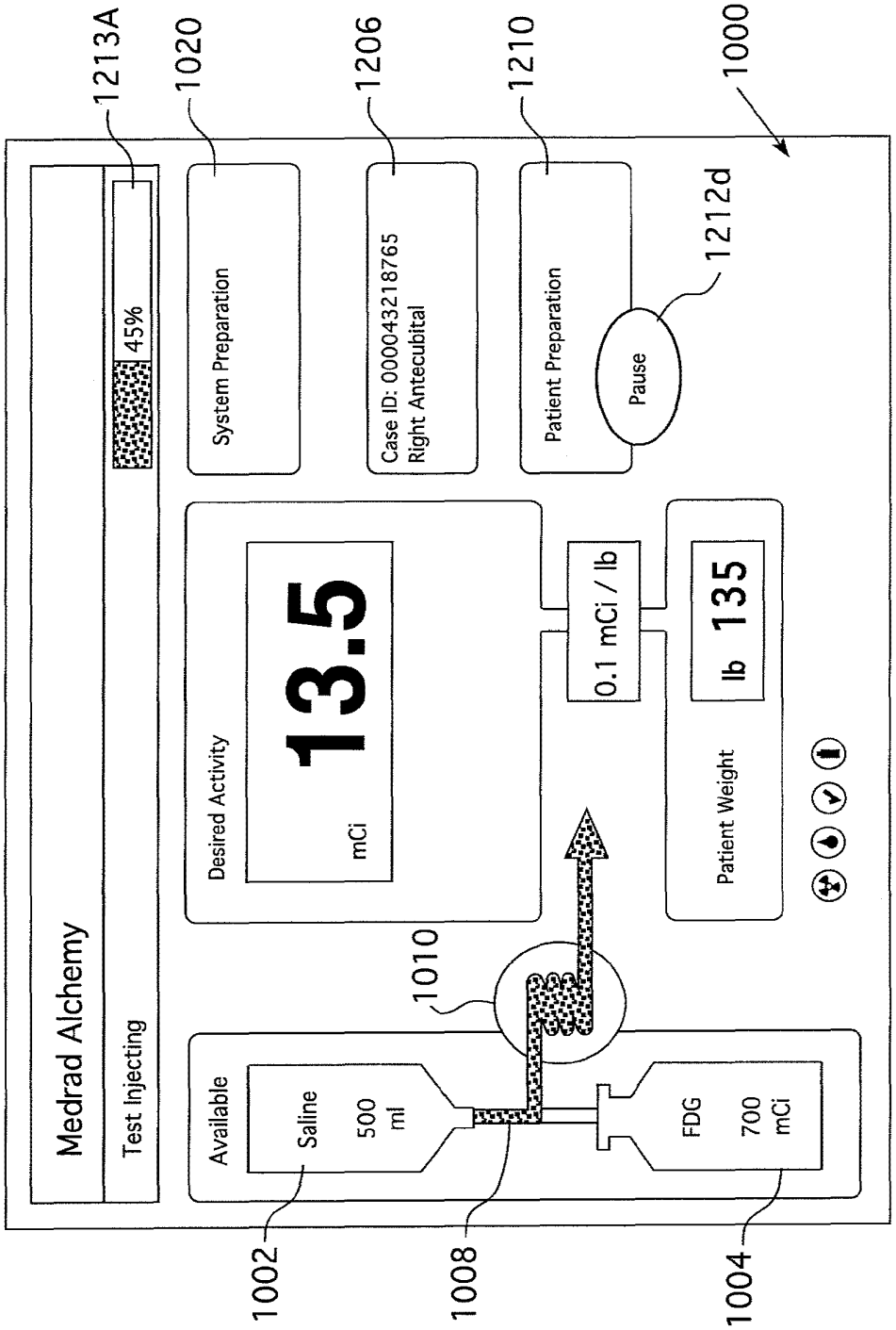
1213A
1020
1206
1210
1000
Medrad Alchemy
Test Injecting
45%
System Preparation
Case ID: 000043218765
Right Antecubital
Patient Preparation
Pause
1212d
Desired Activity
13.5
mCi
0.1 mCi / lb
Patient Weight
lb 135
1010
Available
Saline
500
ml
FDG
700
mCi
1002
1008
1004

FIG. 27A

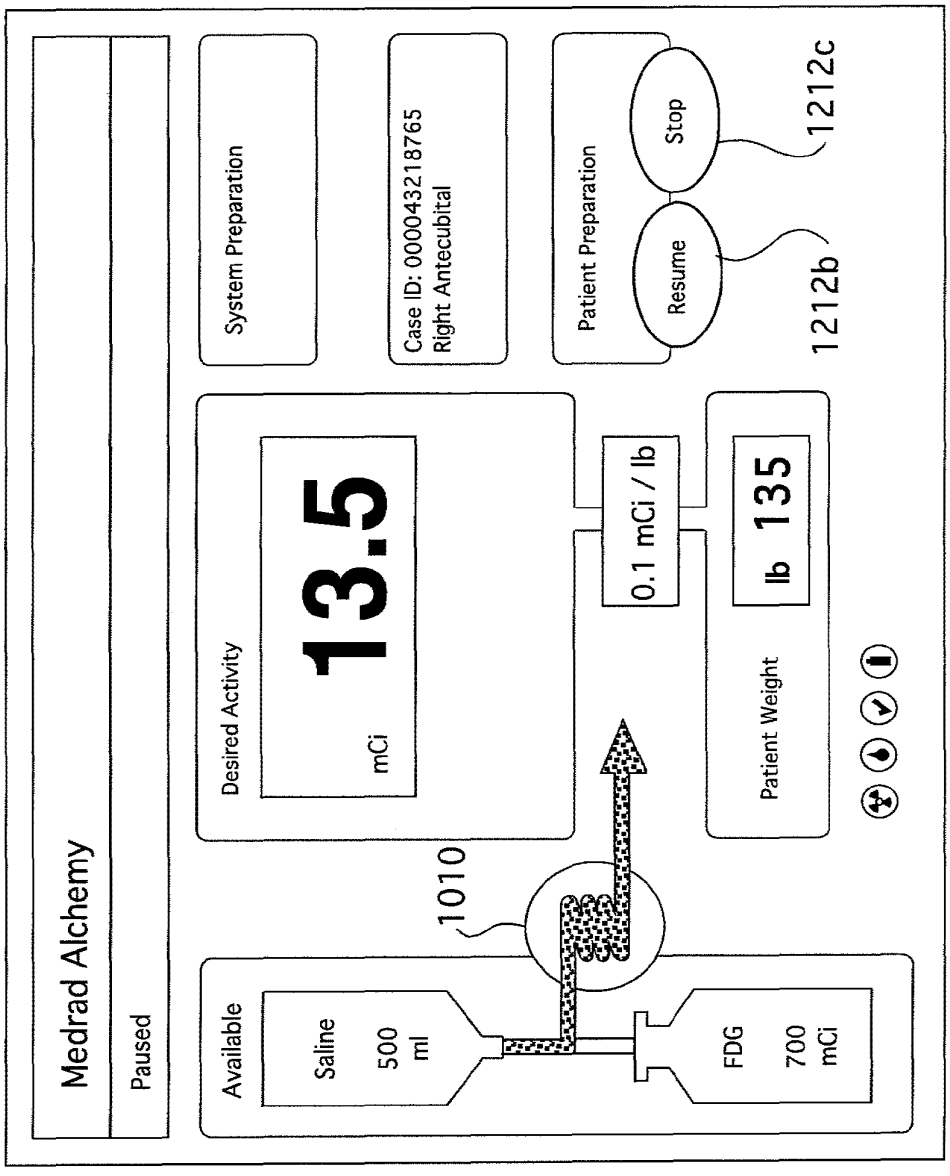
Medrad Alchemy
Paused
System Preparation
Case ID: 000043218765
Right Antecubital
Patient Preparation
Stop
Resume
1212c
1212b
Desired Activity
13.5
mCi
0.1 mCi / lb
Patient Weight
lb 135
1010
Available
Saline
500
ml
FDG
700
mCi

FIG. 27B

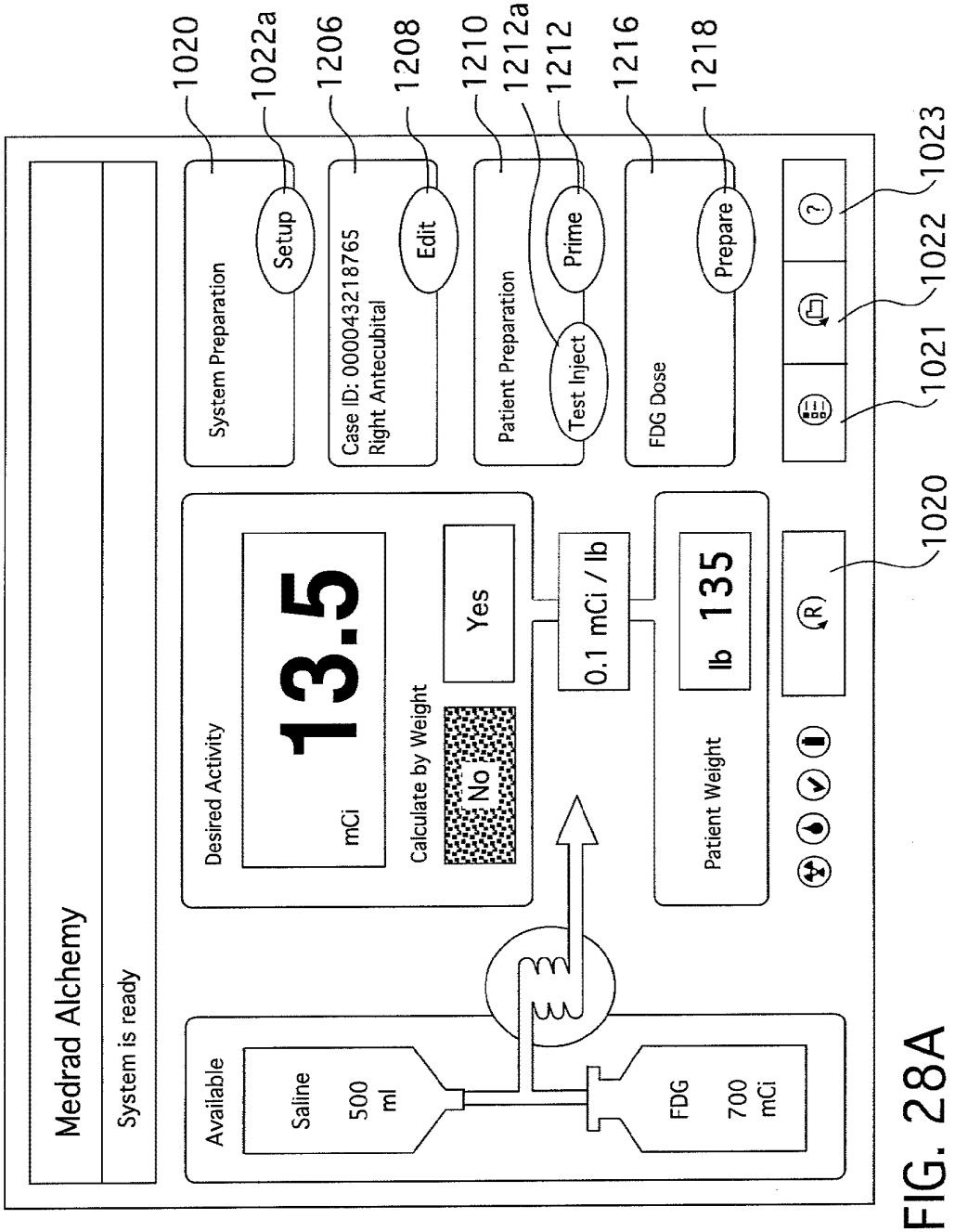
Medrad Alchemy
System is ready
Available
Saline
500
ml
FDG
700
mCi
Desired Activity
13.5
mCi
Calculate by Weight
No
Yes
0.1 mCi / lb
Patient Weight
lb 135
System Preparation
Setup
Case ID: 000043218765
Right Antecubital
Edit
Patient Preparation
Prime
Test Inject
FDG Dose
Prepare
1020
1022a
1206
1208
1210
1212a
1212
1216
1218
1020
1021
1022
1023

FIG. 28A

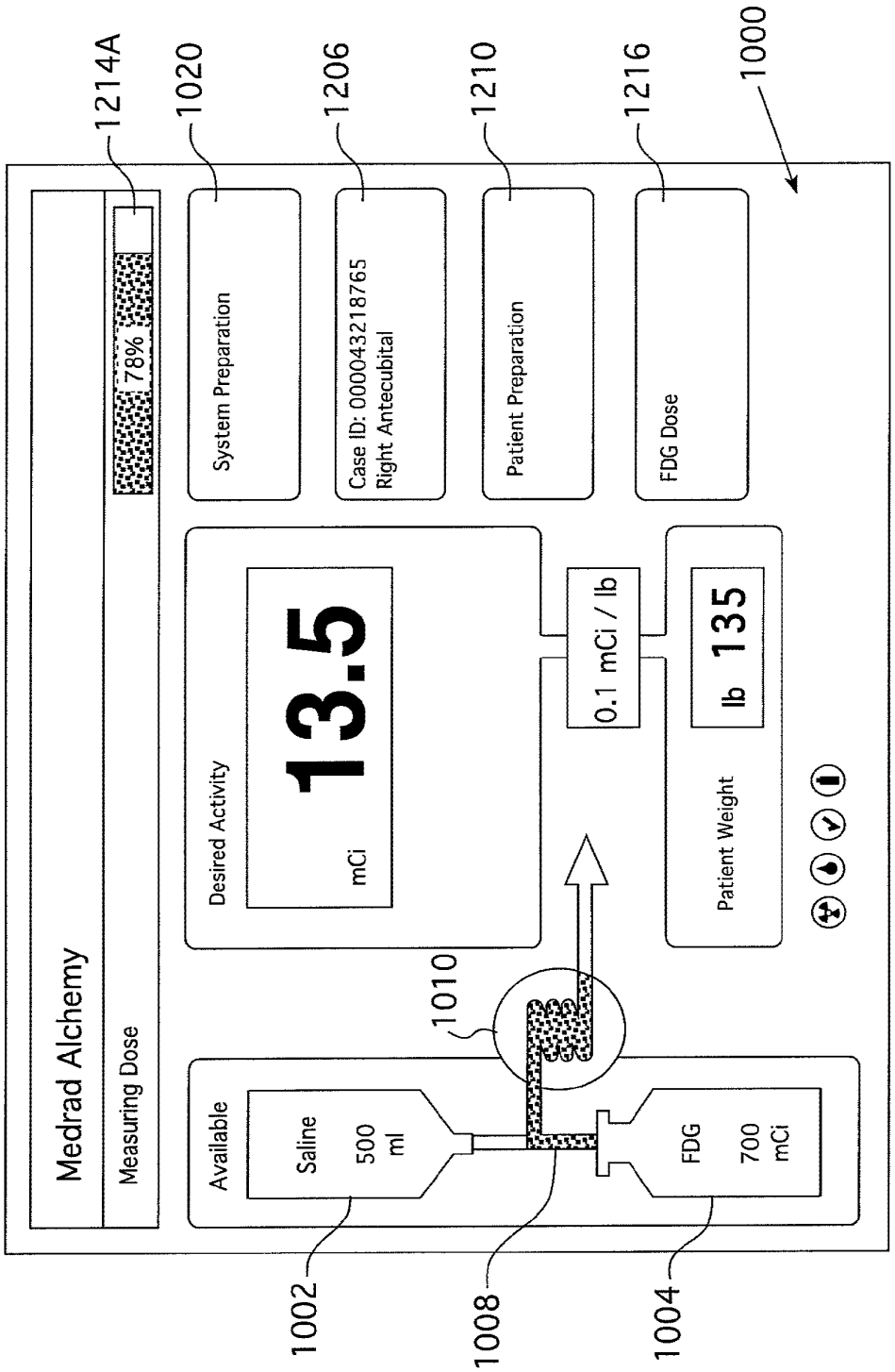
1214A
1020
1206
1210
1216
1000
Medrad Alchemy
Measuring Dose
78%
System Preparation
Case ID: 000043218765
Right Antecubital
Patient Preparation
FDG Dose
Desired Activity
13.5
mCi
0.1 mCi / lb
lb 135
Patient Weight
1010
Available
Saline
500
ml
FDG
700
mCi
1002
1008
1004

FIG. 28B

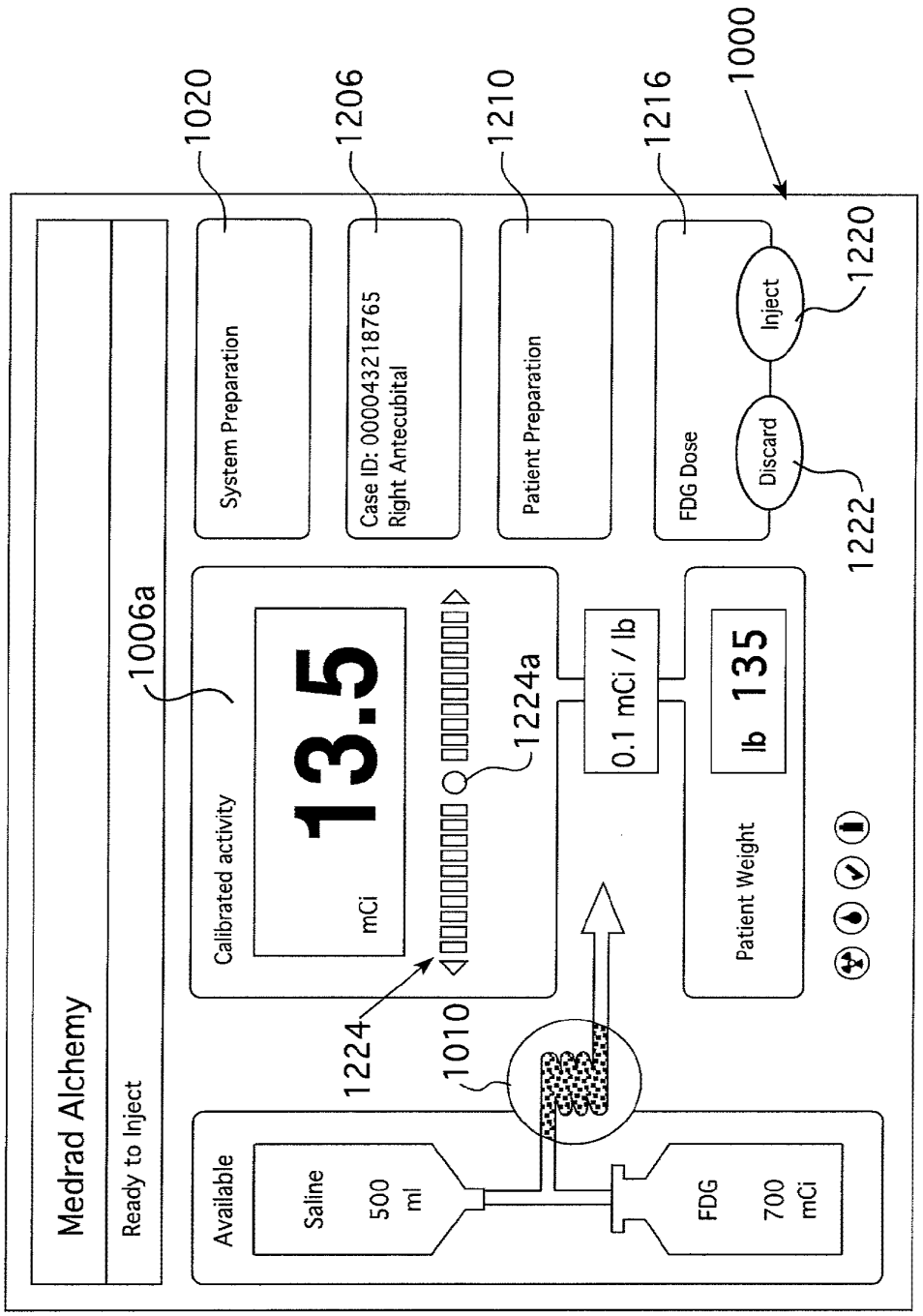
1020
1206
1210
1216
1000
Medrad Alchemy
Ready to Inject
1006a
System Preparation
Case ID: 000043218765
Right Antecubital
Patient Preparation
FDG Dose
Inject
Discard
1220
1222
Calibrated activity
13.5
mCi
1224a
0.1 mCi / lb
Patient Weight
lb 135
1224
1010
Available
Saline
500
ml
FDG
700
mCi

FIG. 29

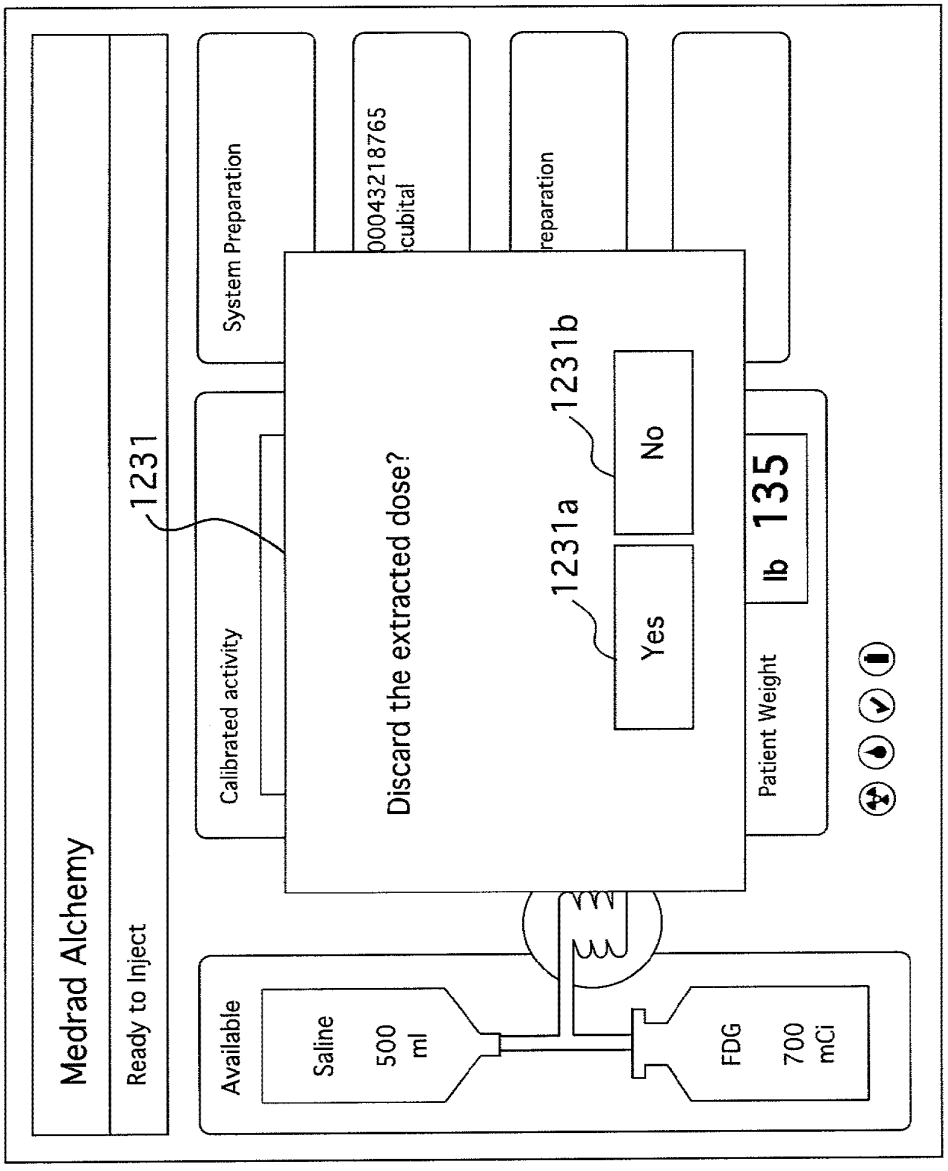
Medrad Alchemy
Ready to Inject
1231
System Preparation
Calibrated activity
Discard the extracted dose?
1231a
Yes
1231b
No
Patient Weight
lb 135
Available
Saline
500
ml
FDG
700
mCi

FIG. 30A

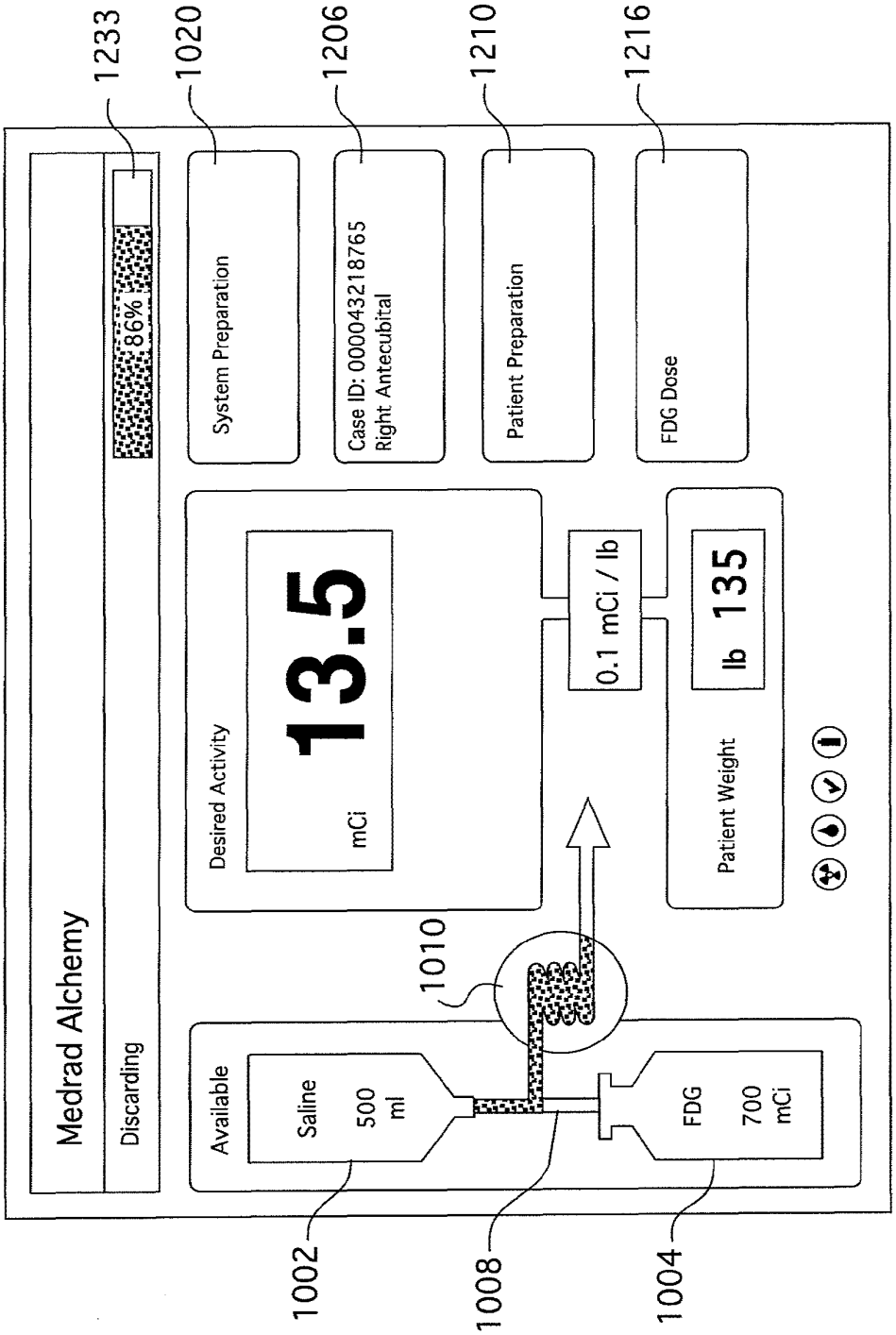
1233
1020
1206
1210
1216
Medrad Alchemy
Discarding
86%
System Preparation
Case ID: 000043218765
Right Antecubital
Patient Preparation
FDG Dose
Desired Activity
13.5
mCi
0.1 mCi / lb
lb 135
Patient Weight
1010
Available
Saline
500
ml
FDG
700
mCi
1002
1008
1004

FIG. 30B

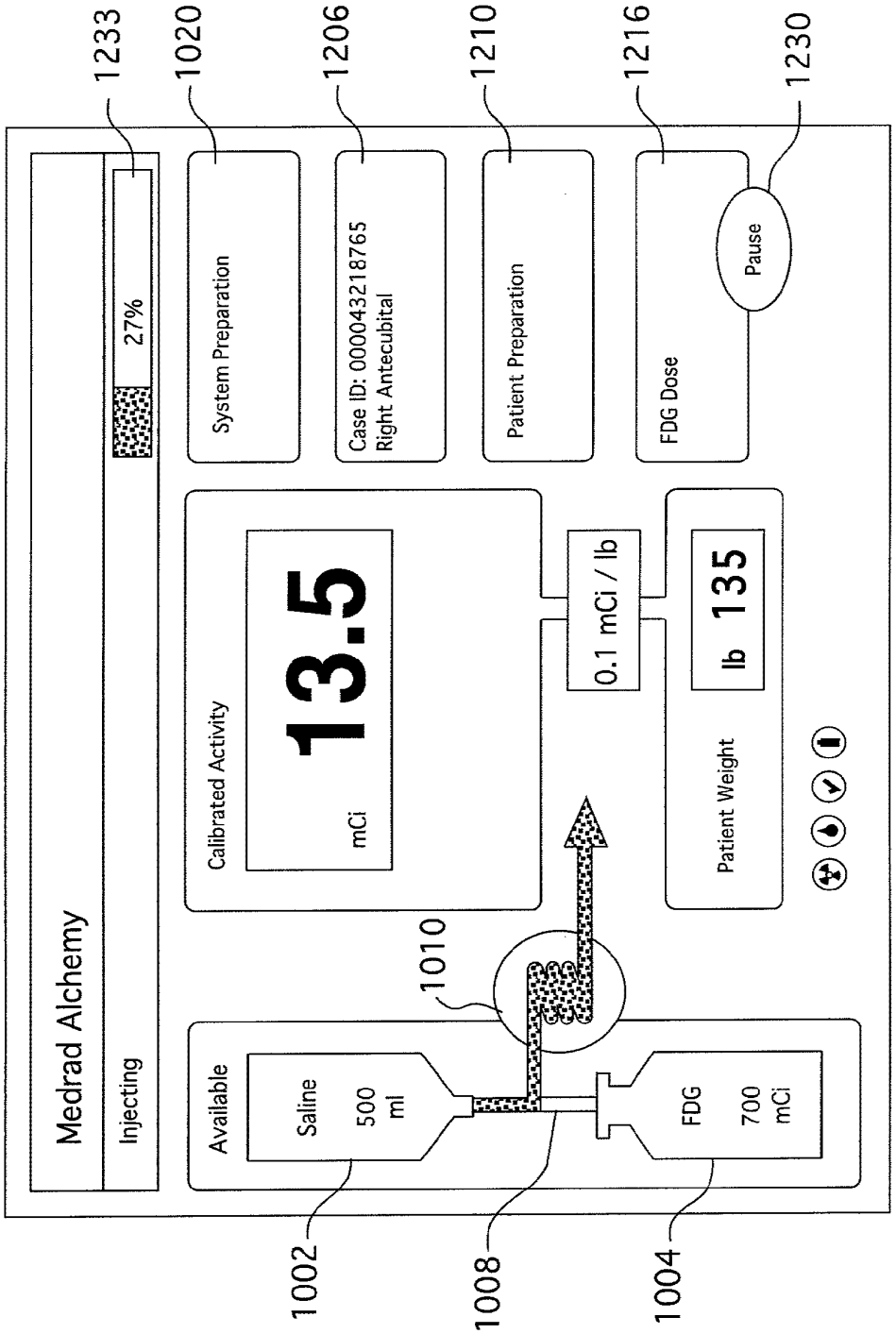
1233
1020
1206
1210
1216
1230
Medrad Alchemy
Injecting
27%
System Preparation
Case ID: 000043218765
Right Antecubital
Patient Preparation
FDG Dose
Pause
Calibrated Activity
13.5
mCi
0.1 mCi / lb
Patient Weight
lb 135
1010
Available
Saline
500
ml
FDG
700
mCi
1002
1008
1004

FIG. 31

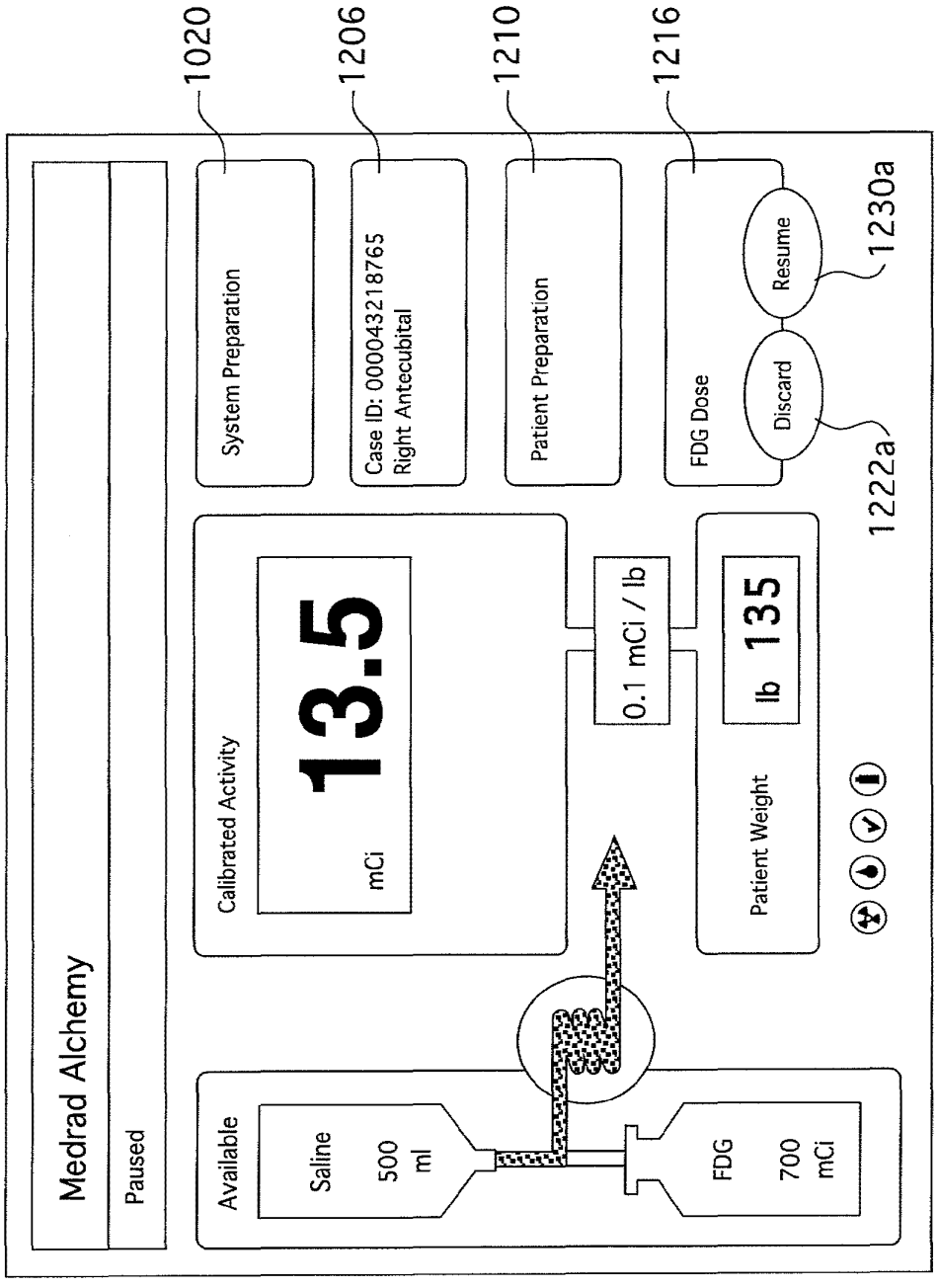
1020
1206
1210
1216
Medrad Alchemy
Paused
System Preparation
Case ID: 000043218765
Right Antecubital
Patient Preparation
FDG Dose
Resume
Discard
1230a
1222a
Calibrated Activity
13.5
mCi
0.1 mCi / lb
Patient Weight
lb 135
Available
Saline
500
ml
FDG
700
mCi

FIG. 32A

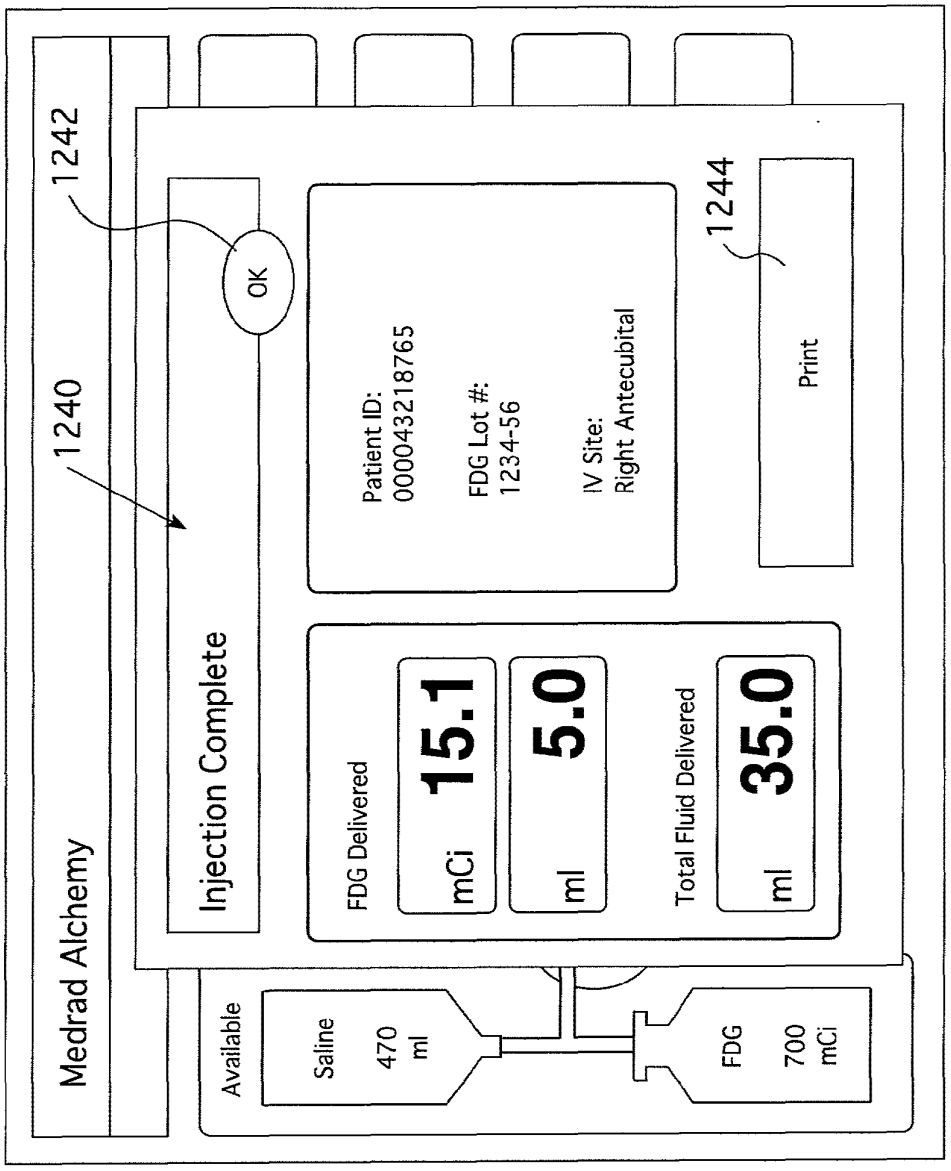
Medrad Alchemy
1240
1242
1244
Injection Complete
OK
Patient ID:
0000043218765
FDG Lot #:
1234-56
IV Site:
Right Antecubital
Print
FDG Delivered
15.1
mCi
5.0
ml
Total Fluid Delivered
35.0
ml
Available
Saline
470
ml
FDG
700
mCi

FIG. 32B

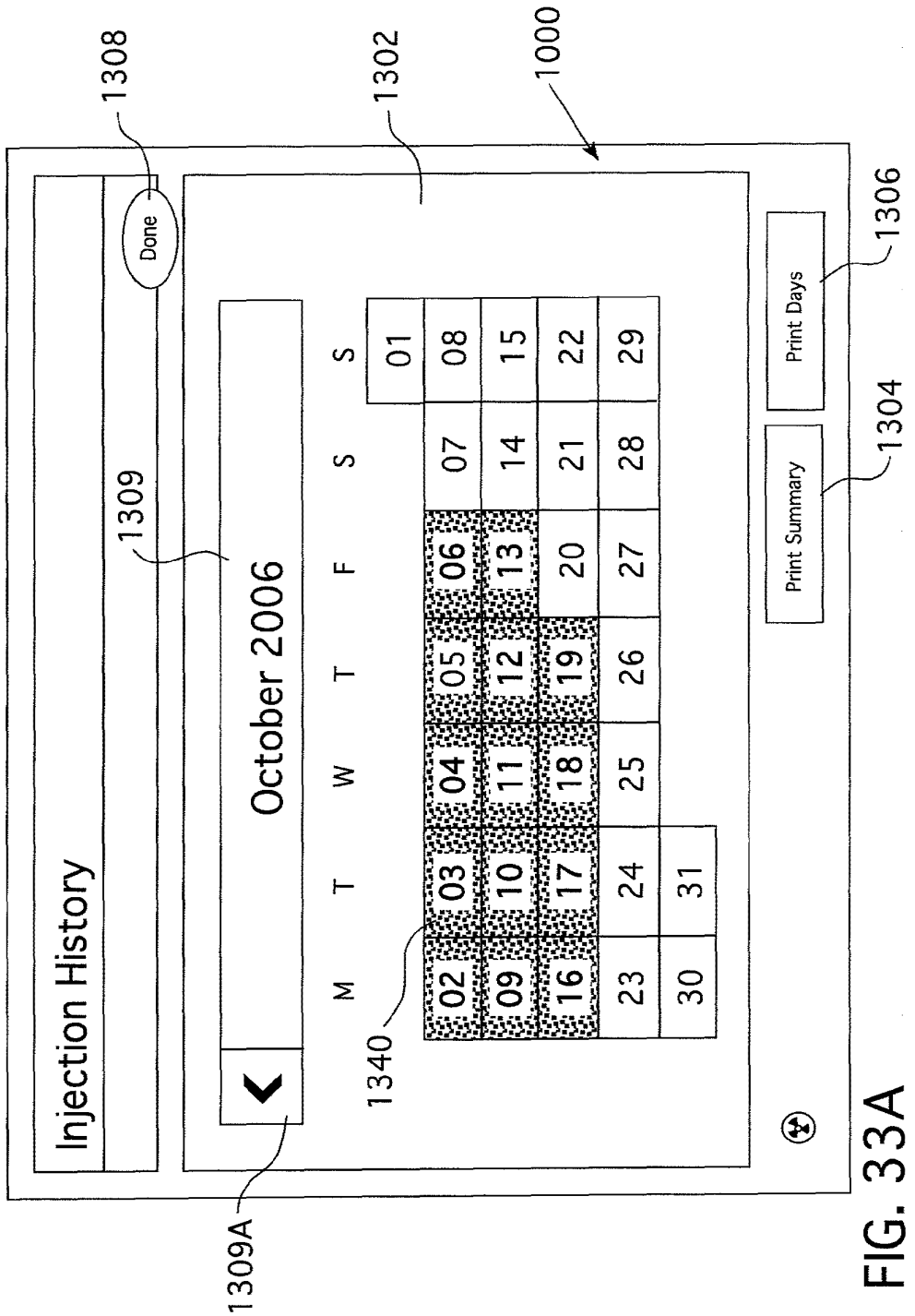
1308
1302
1000
Done
Injection History
1309
October 2006
M T W T F S S
01
02 03 04 05 06 07 08
09 10 11 12 13 14 15
16 17 18 19 20 21 22
23 24 25 26 27 28 29
30 31
1340
Print Days
1306
Print Summary
1304
1309A

FIG. 33A

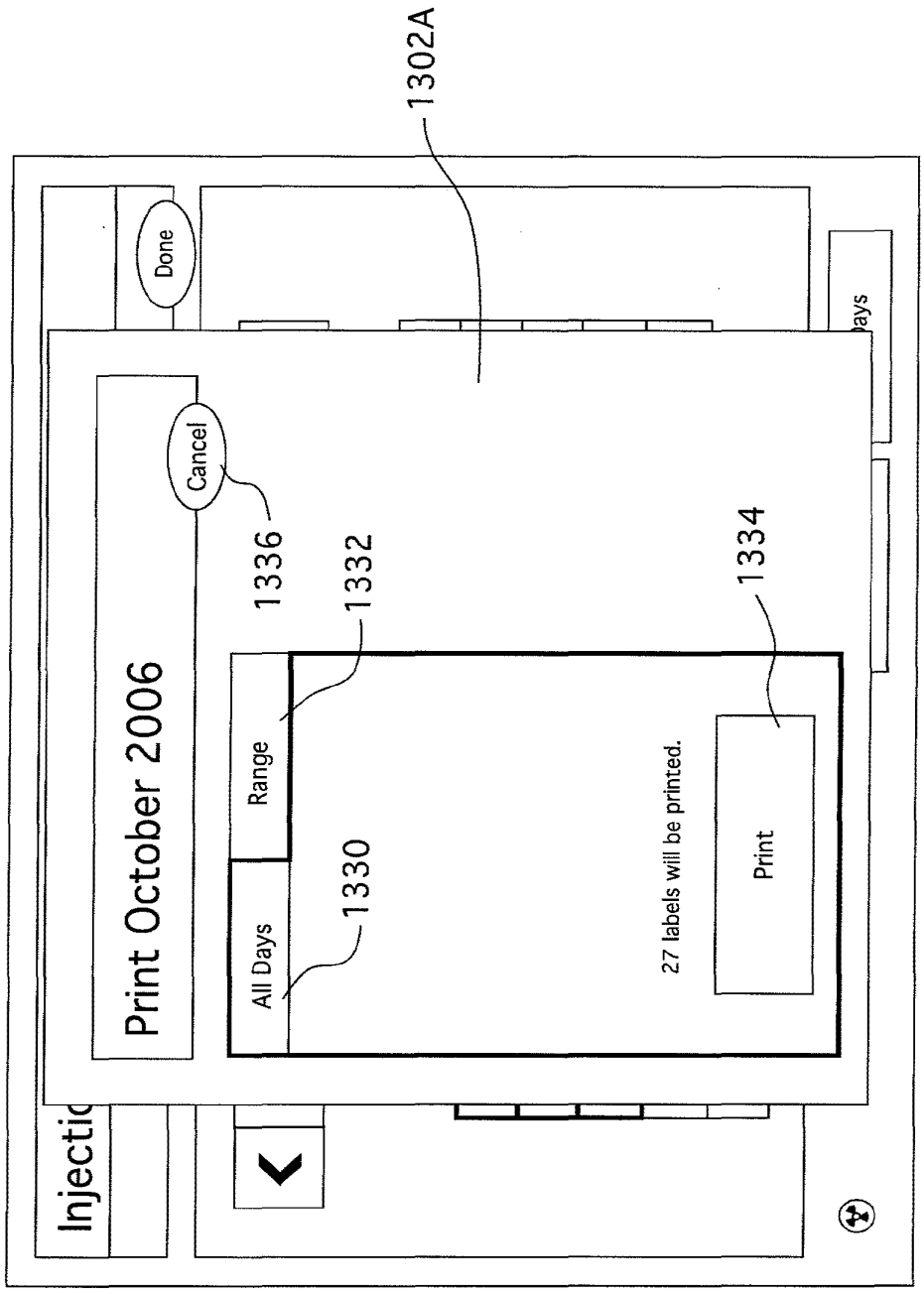
1302A
Done
Cancel
1336
1332
1334
Print October 2006
Range
All Days
1330
27 labels will be printed.
Print

FIG. 33B

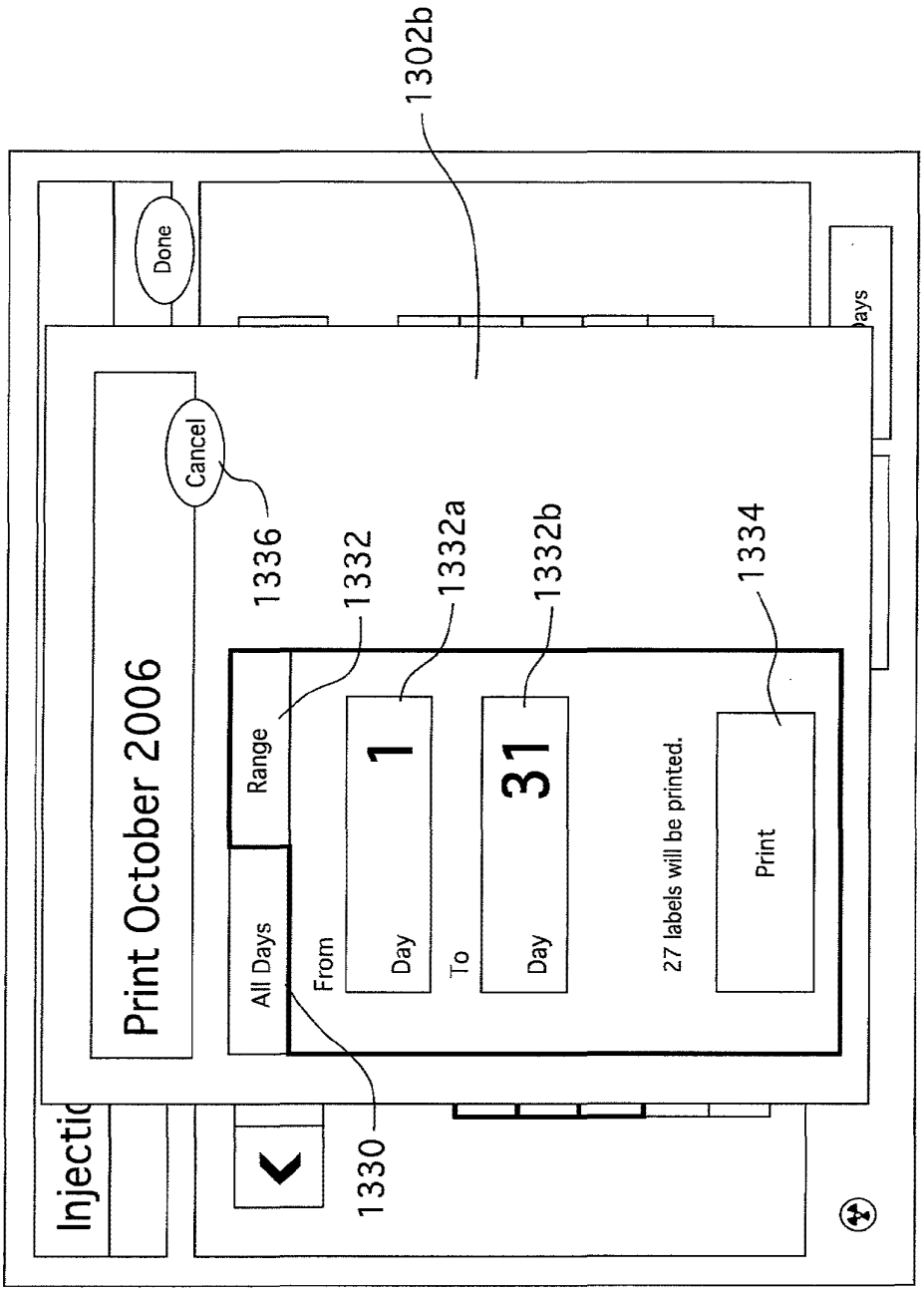
1302b
Done
Cancel
1336
1332
1332a
1332b
1334
Print October 2006
Range
All Days
From
1
Day
To
31
Day
27 labels will be printed.
Print
1330
Injecti

FIG. 33C

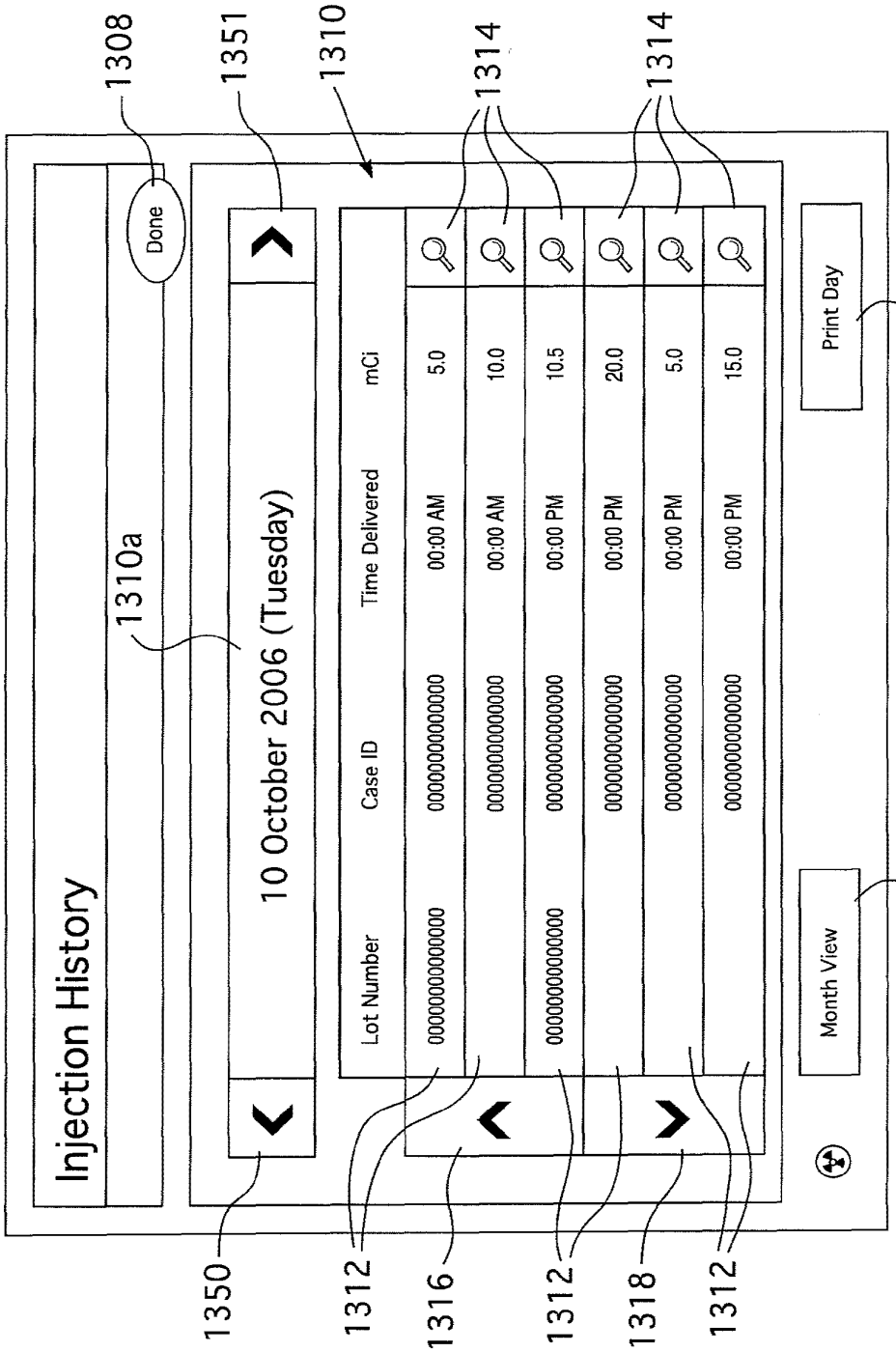
Injection History
Done
1308
1310a
1351
1310
10 October 2006 (Tuesday)
1314
1314
Lot Number
Case ID
Time Delivered
mCi
0000000000000
0000000000000
00:00 AM
5.0
0000000000000
0000000000000
00:00 AM
10.0
0000000000000
0000000000000
00:00 PM
10.5
0000000000000
0000000000000
00:00 PM
20.0
0000000000000
0000000000000
00:00 PM
5.0
0000000000000
0000000000000
00:00 PM
15.0
Print Day
1306a
Month View
1320
1350
1312
1316
1312
1318
1312

FIG. 34A

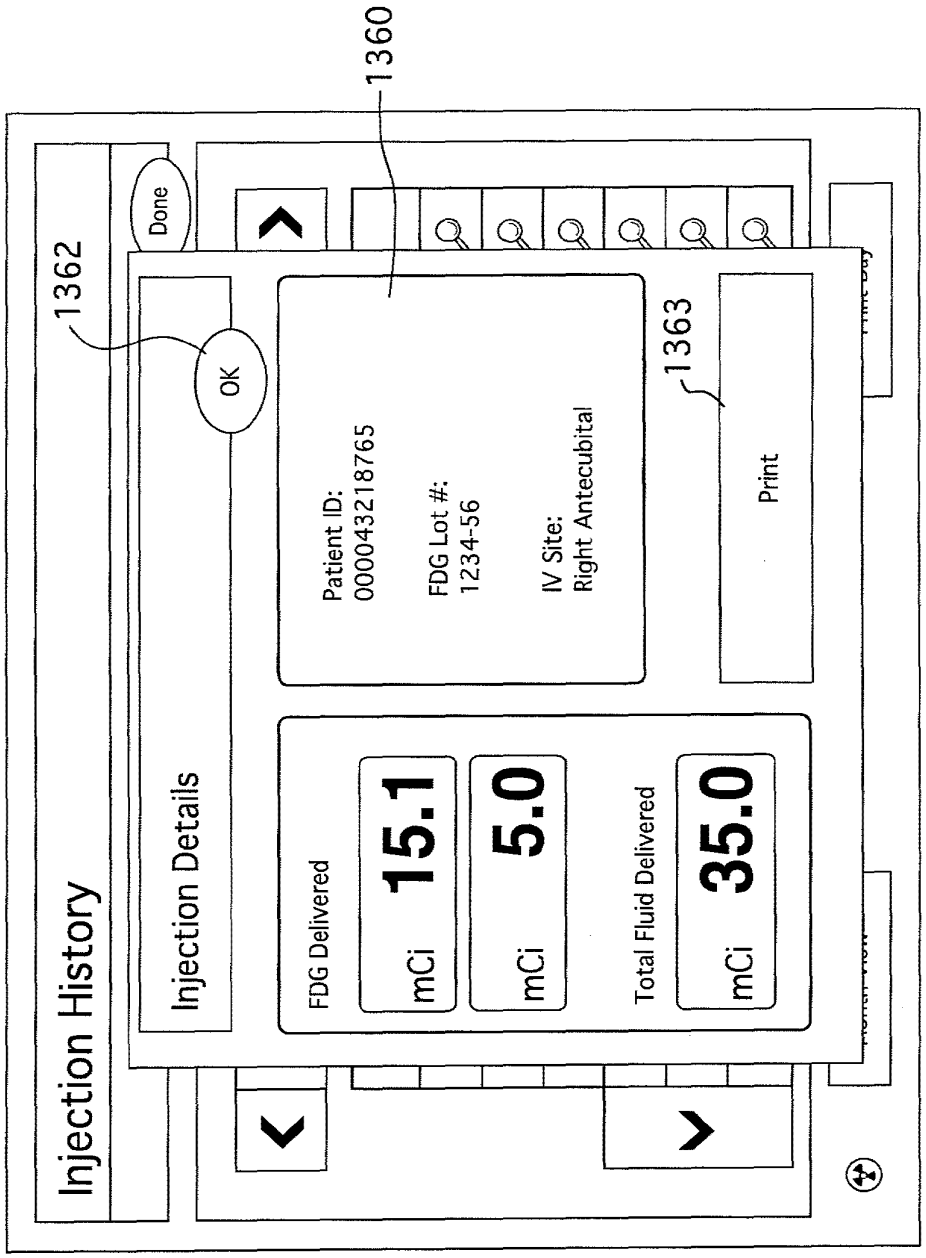
1360
1362
1363
Injection History
Done
OK
Injection Details
Patient ID:
000043218765
FDG Lot #:
1234-56
IV Site:
Right Antecubital
Print
FDG Delivered
15.1
mCi
5.0
mCi
Total Fluid Delivered
35.0
mCi

FIG. 34B

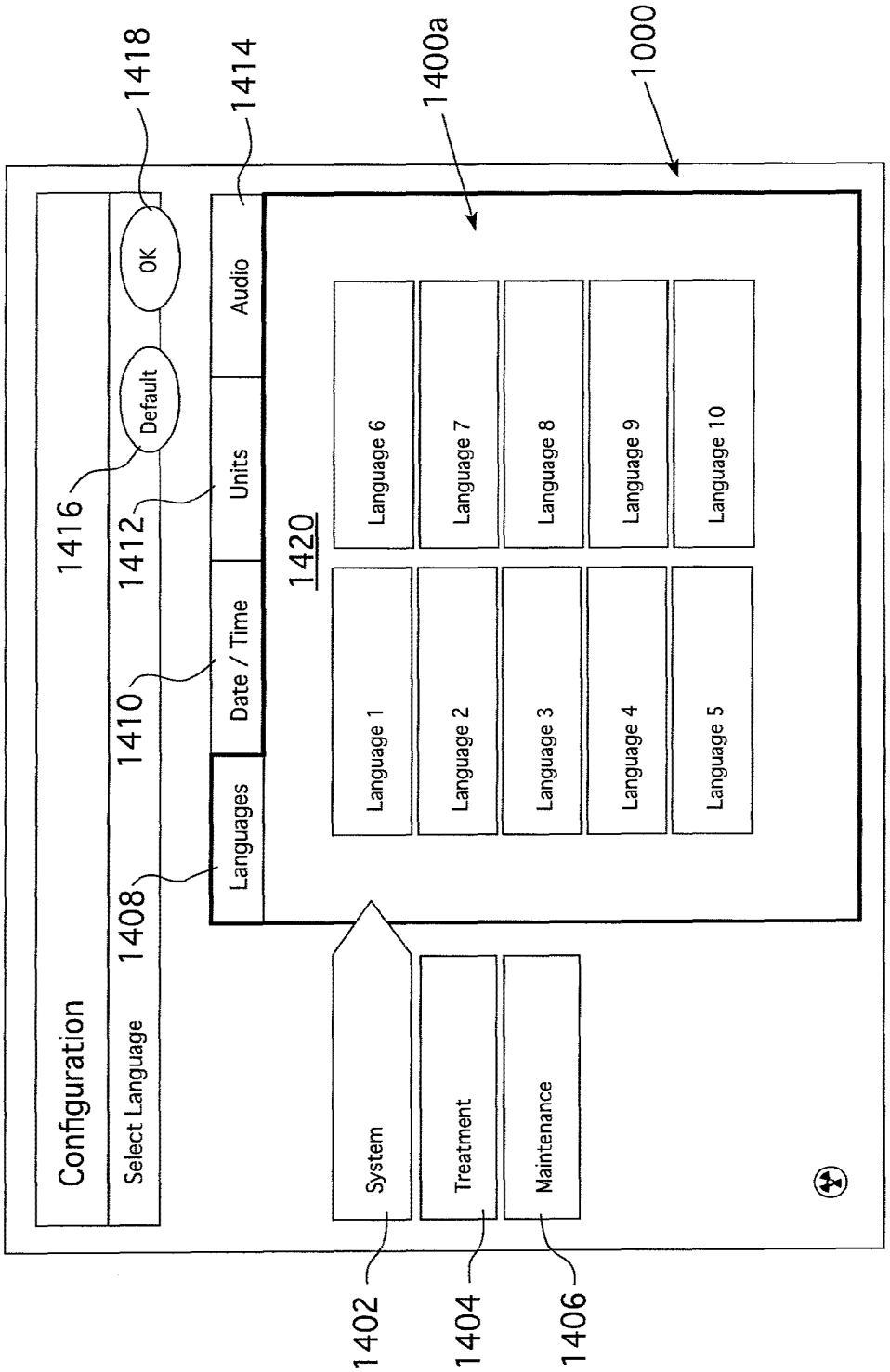
1000
1400a
1418
1414
1416
1412
1410
1408
1420
Configuration
Select Language
Languages
Date / Time
Units
Audio
OK
Default
Language 1
Language 2
Language 3
Language 4
Language 5
Language 6
Language 7
Language 8
Language 9
Language 10
System
Treatment
Maintenance
1402
1404
1406

FIG. 35

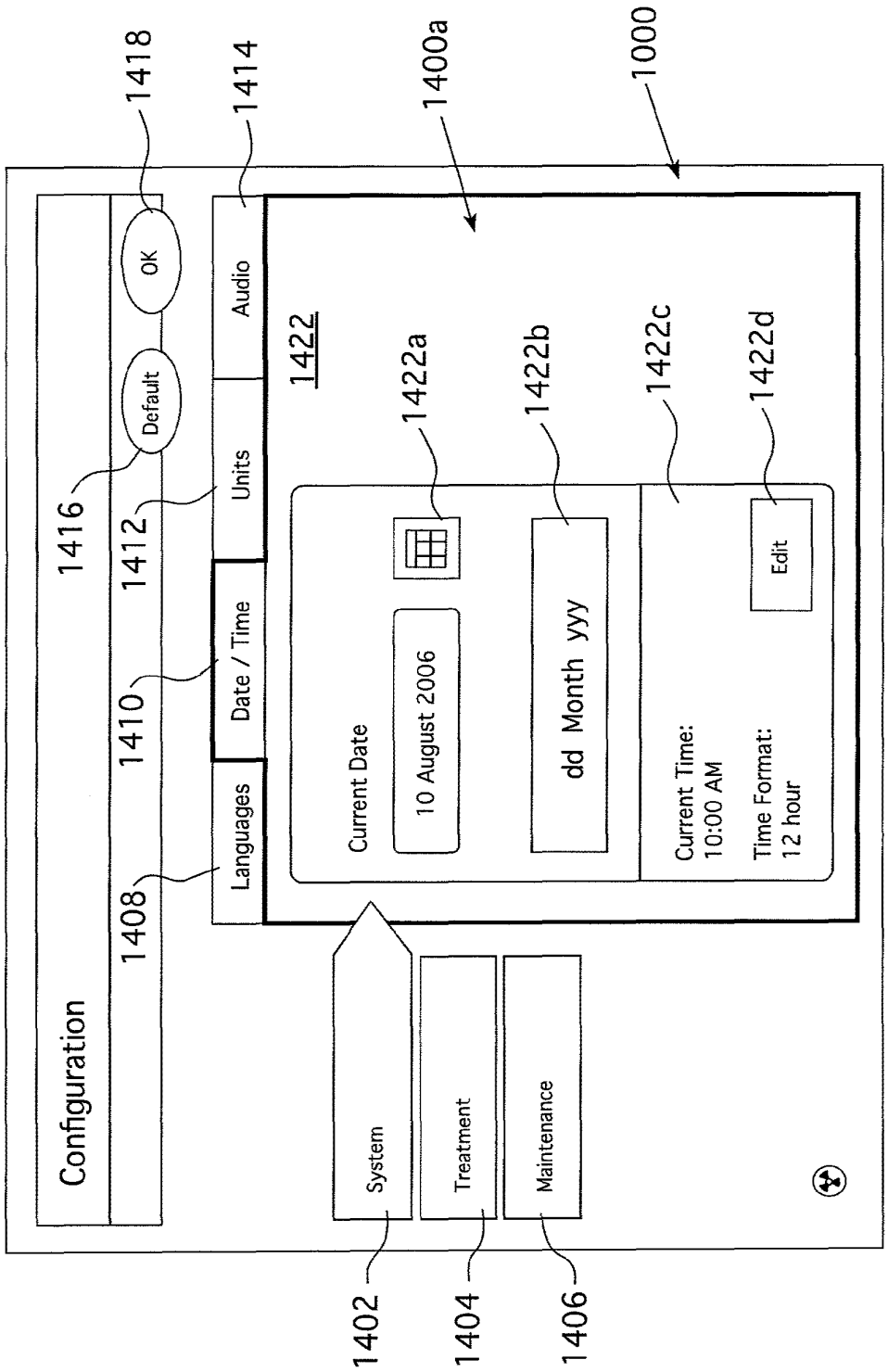
1000
1400a
1414
1418
Configuration
1408
1410
1412
1416
Languages
Date / Time
Units
Default
OK
Audio
1422
1422a
1422b
1422c
1422d
Current Date
10 August 2006
dd Month yyy
Current Time:
10:00 AM
Time Format:
12 hour
Edit
System
Treatment
Maintenance
1402
1404
1406

FIG. 36

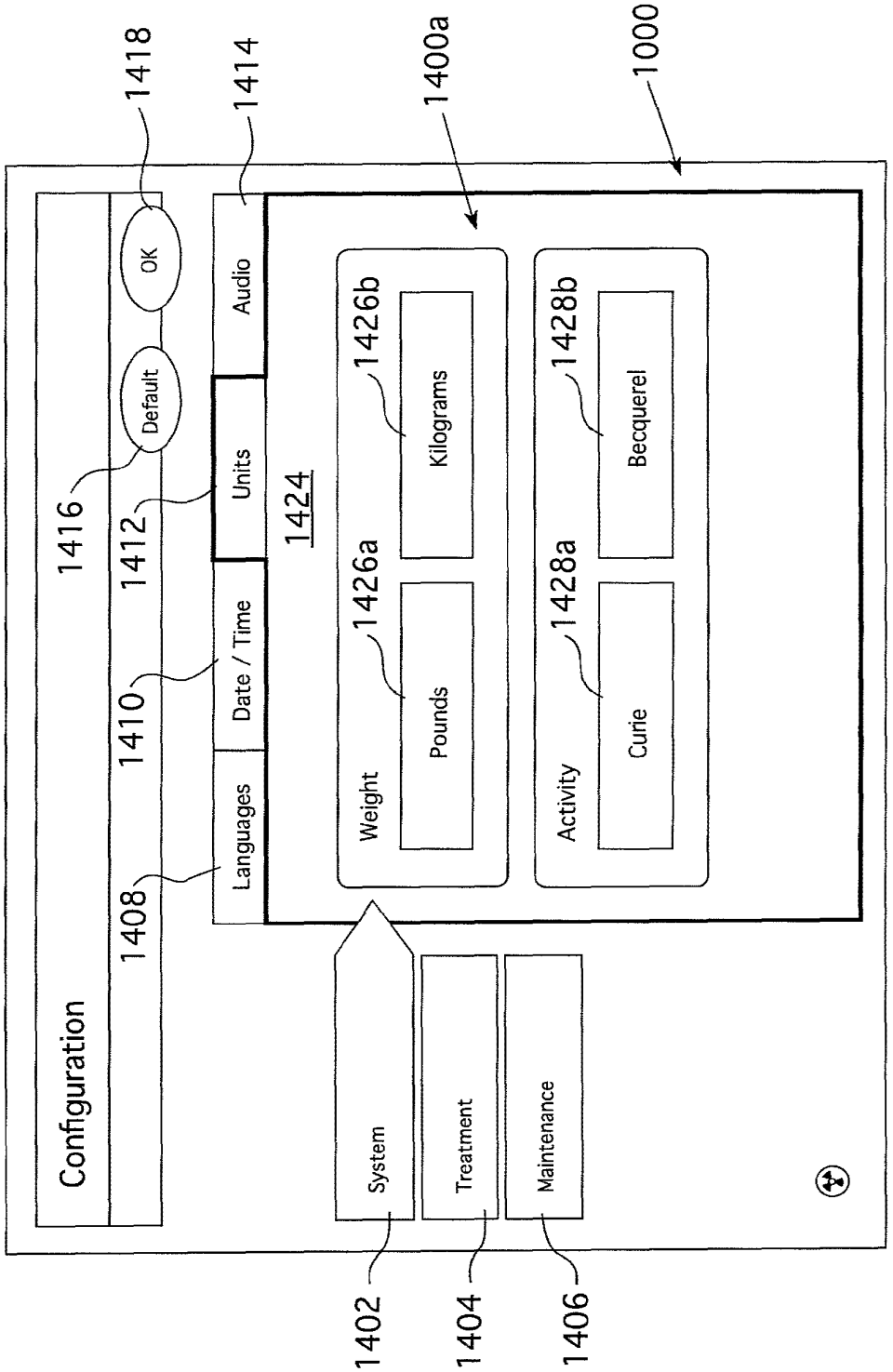
1000
1400a
1414
1418
Configuration
OK
Default
Audio
Units
Date / Time
Languages
1424
1426b
Kilograms
1426a
Pounds
Weight
1428b
Becquerel
1428a
Curie
Activity
System
Treatment
Maintenance
1402
1404
1406
1408
1410
1412
1416

FIG. 37

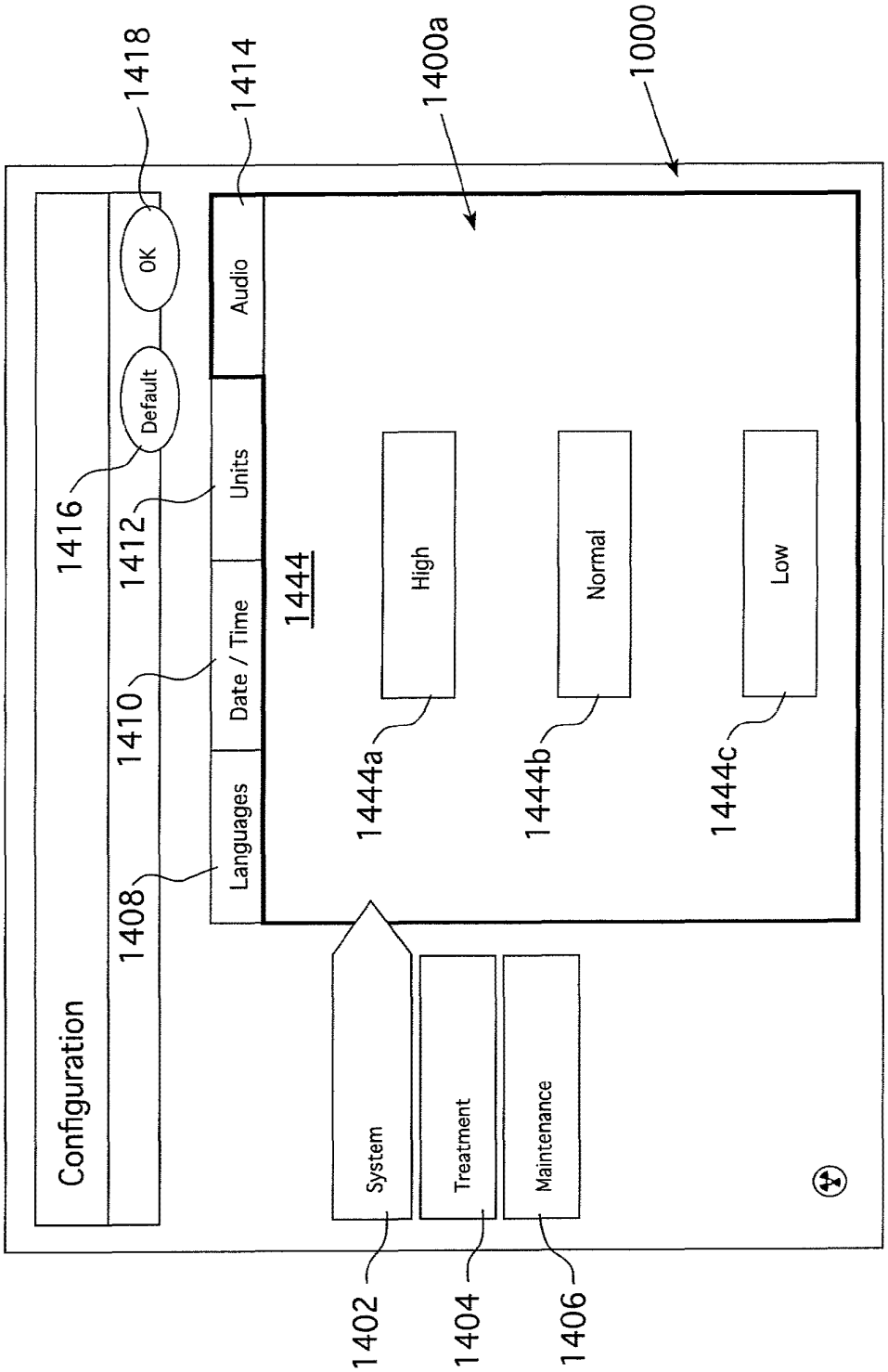
1418
1414
1400a
1000
OK
Audio
Default
Units
1416
1412
1444
High
Normal
Low
Date / Time
1410
1444a
1444b
1444c
Languages
1408
Configuration
System
Treatment
Maintenance
1402
1404
1406

FIG. 38

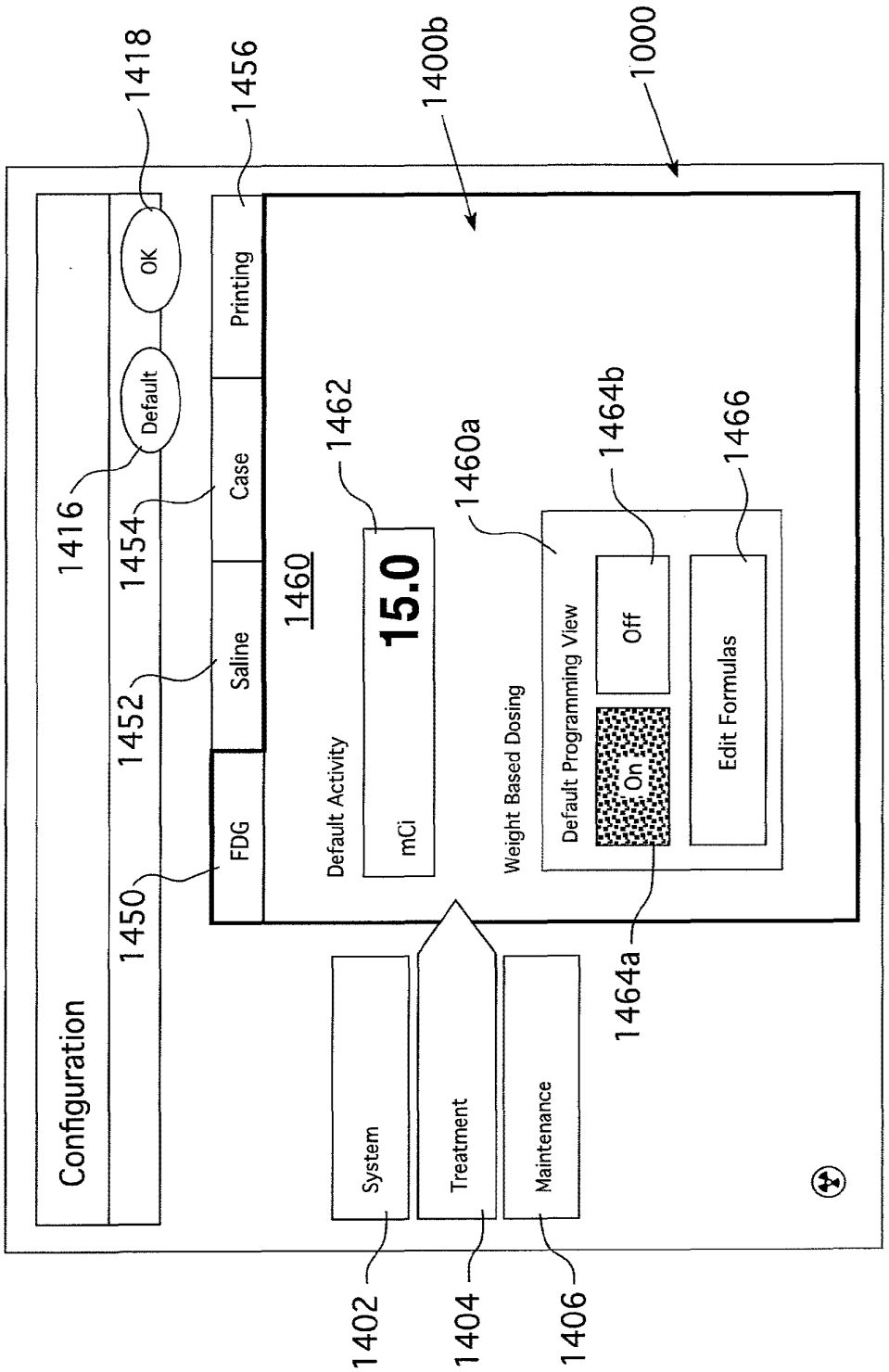
1000
1400b
1418
1456
OK
Default
Printing
Case
Saline
FDG
1416
1454
1452
1450
1460
1462
1460a
1464b
1466
Default Activity
15.0
mCi
Weight Based Dosing
Default Programming View
Off
On
Edit Formulas
1464a
Configuration
System
Treatment
Maintenance
1402
1404
1406

FIG. 39A

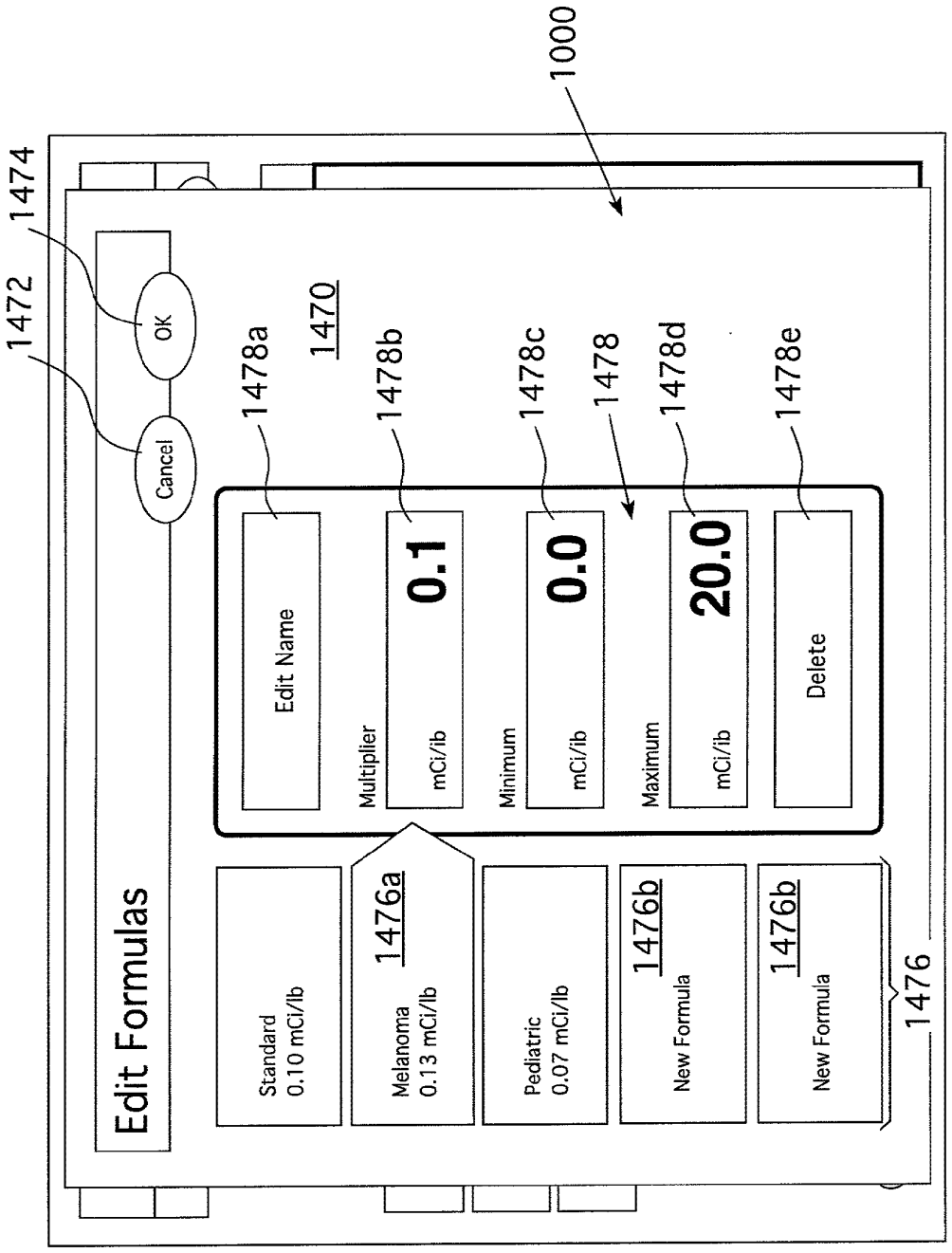
1000
1474
1472
OK
Cancel
Edit Formulas
1470
1478a
1478b
1478c
1478
1478d
1478e
Edit Name
Multiplier
0.1
mCi/lb
Minimum
0.0
mCi/lb
Maximum
20.0
mCi/lb
Delete
Standard
0.10 mCi/lb
1476a
Melanoma
0.13 mCi/lb
Pediatric
0.07 mCi/lb
1476b
New Formula
1476b
New Formula
1476

FIG. 39B

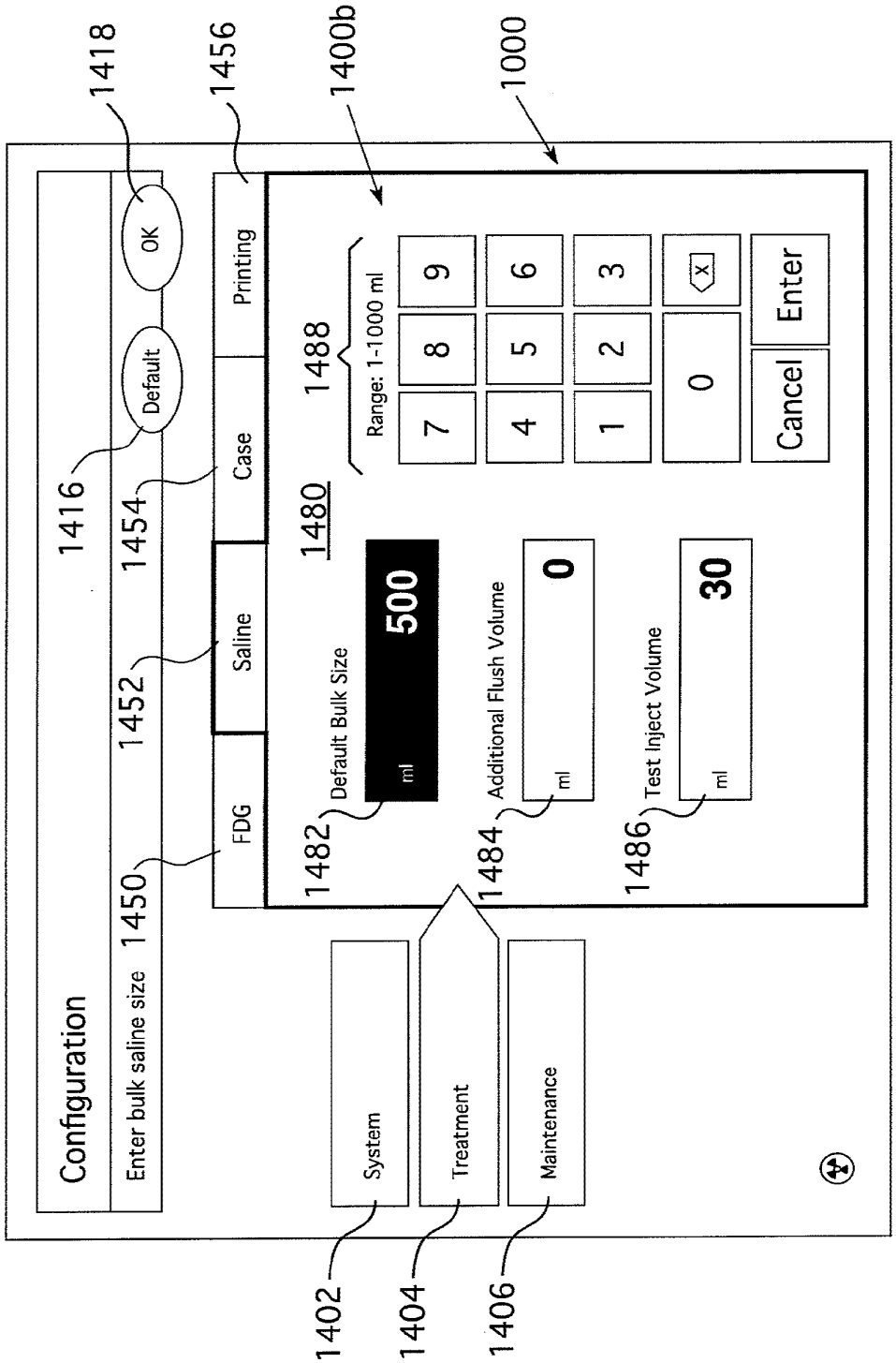
1418
1456
1400b
1000
1416
1454
1452
1450
1480
1488
1482
1484
1486
1402
1404
1406
Configuration
Enter bulk saline size
OK
Default
FDG
Saline
Case
Printing
Range: 1-1000 ml
7
8
9
4
5
6
1
2
3
0
X
Cancel
Enter
Default Bulk Size
500
ml
Additional Flush Volume
0
ml
Test Inject Volume
30
ml
System
Treatment
Maintenance

FIG. 40

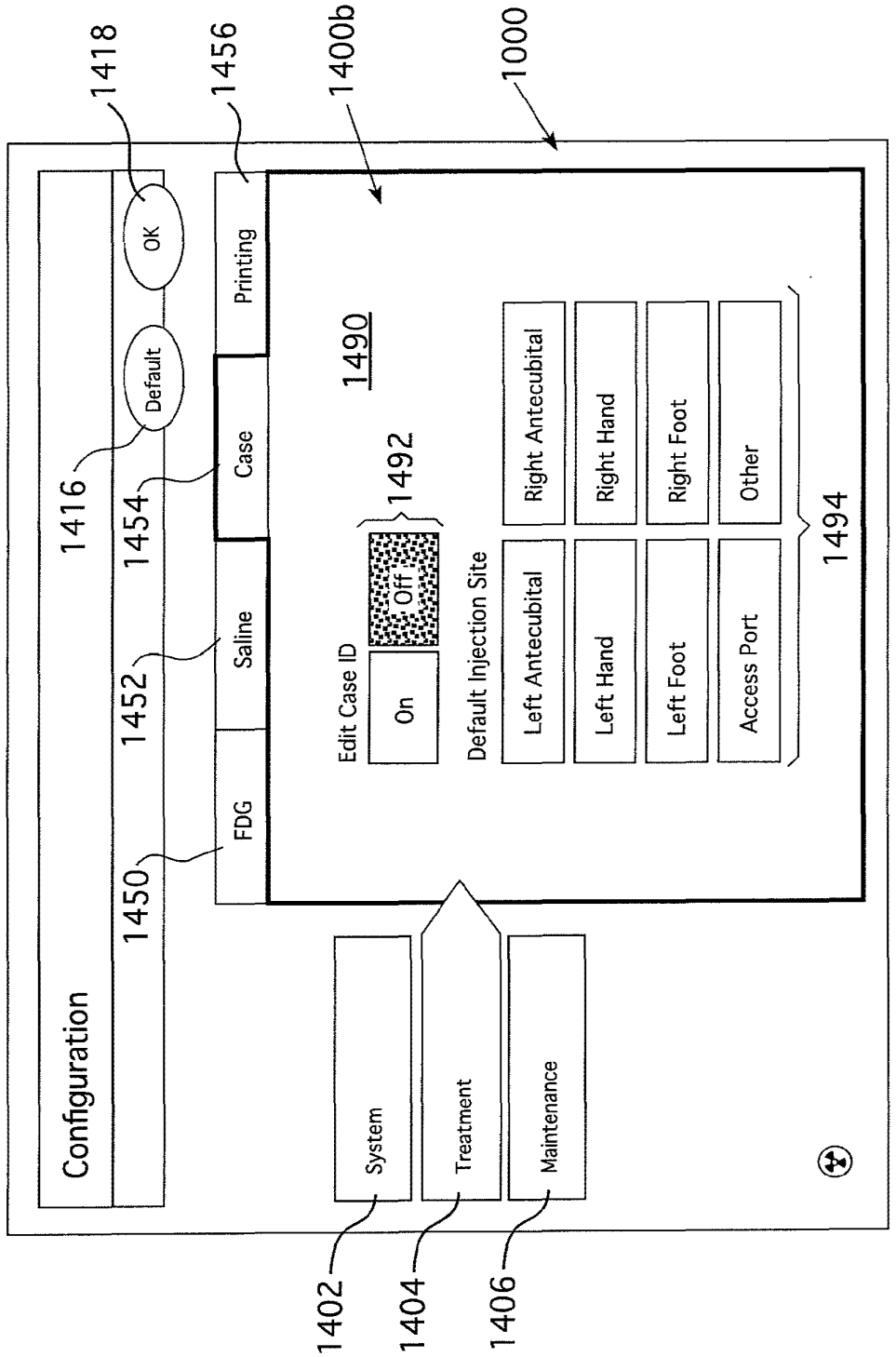
1418
1456
1400b
1000
OK
Default
Printing
Case
Saline
FDG
1416
1454
1452
1450
Configuration
1490
1492
Edit Case ID
On
Off
Default Injection Site
Left Antecubital
Left Hand
Left Foot
Access Port
Right Antecubital
Right Hand
Right Foot
Other
1494
System
Treatment
Maintenance
1402
1404
1406

FIG. 41

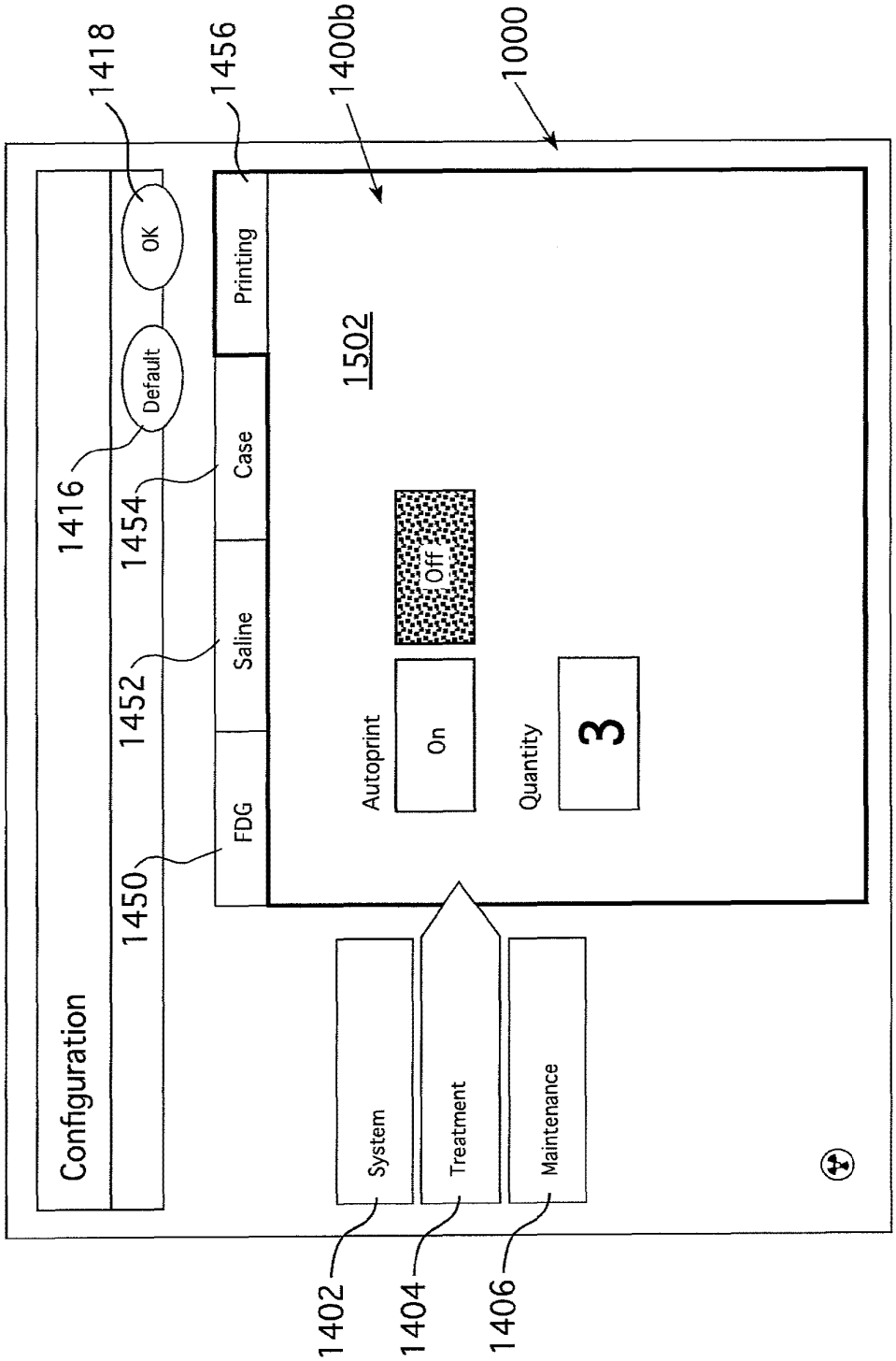
1418
1456
1400b
1000
OK
Default
Printing
1502
1416
1454
Case
Saline
1452
Off
On
Autoprint
Quantity
3
FDG
1450
Configuration
System
Treatment
Maintenance
1402
1404
1406

FIG. 42

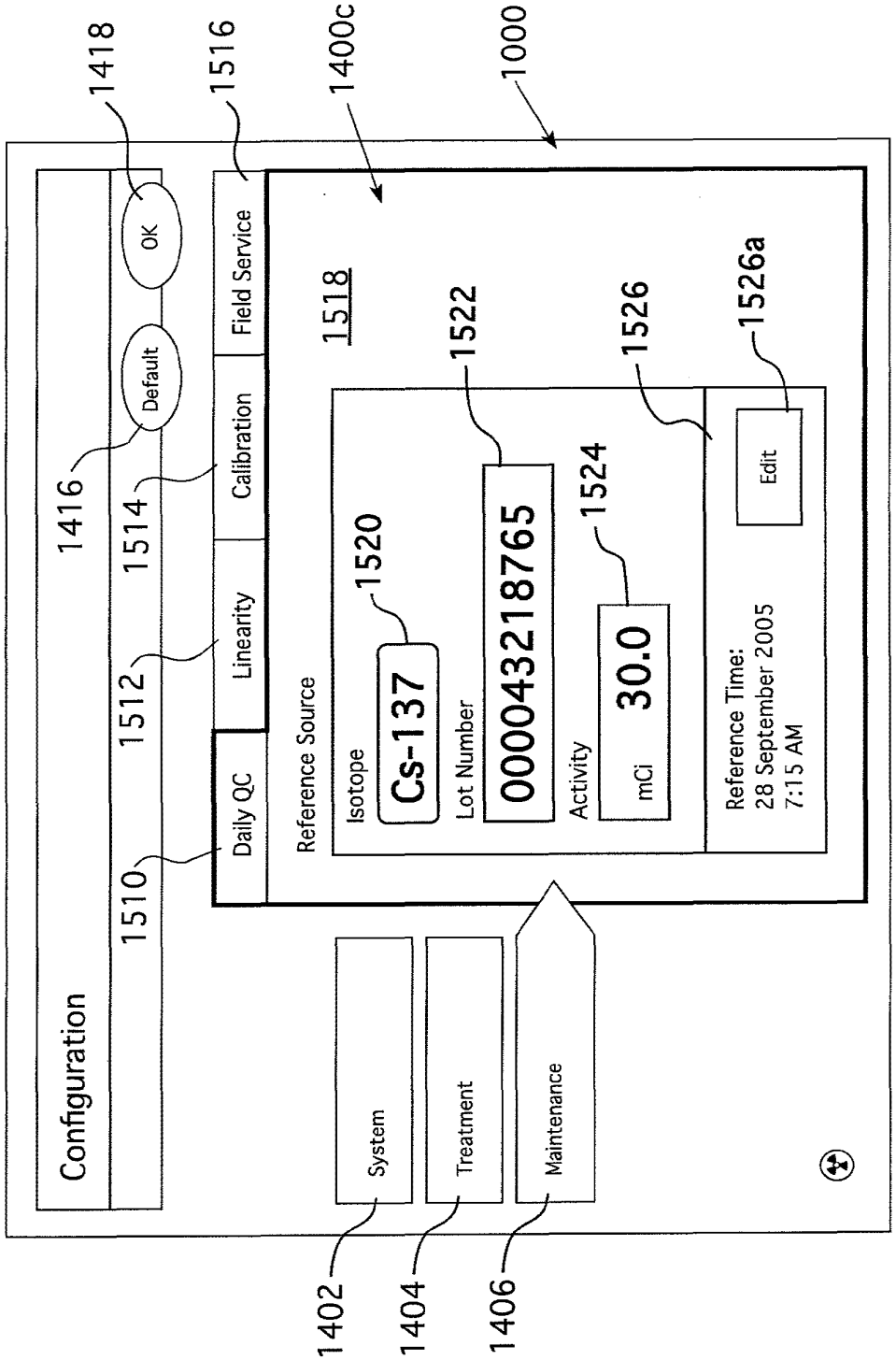
1418
1516
1400c
1000
OK
Default
Field Service
Calibration
Linearity
Daily QC
1416
1514
1512
1510
Configuration
1518
1522
1526
1526a
Reference Source
Isotope
Cs-137
1520
Lot Number
0000432218765
Activity
30.0
mCi
1524
Edit
Reference Time:
28 September 2005
7:15 AM
System
Treatment
Maintenance
1402
1404
1406

FIG. 43

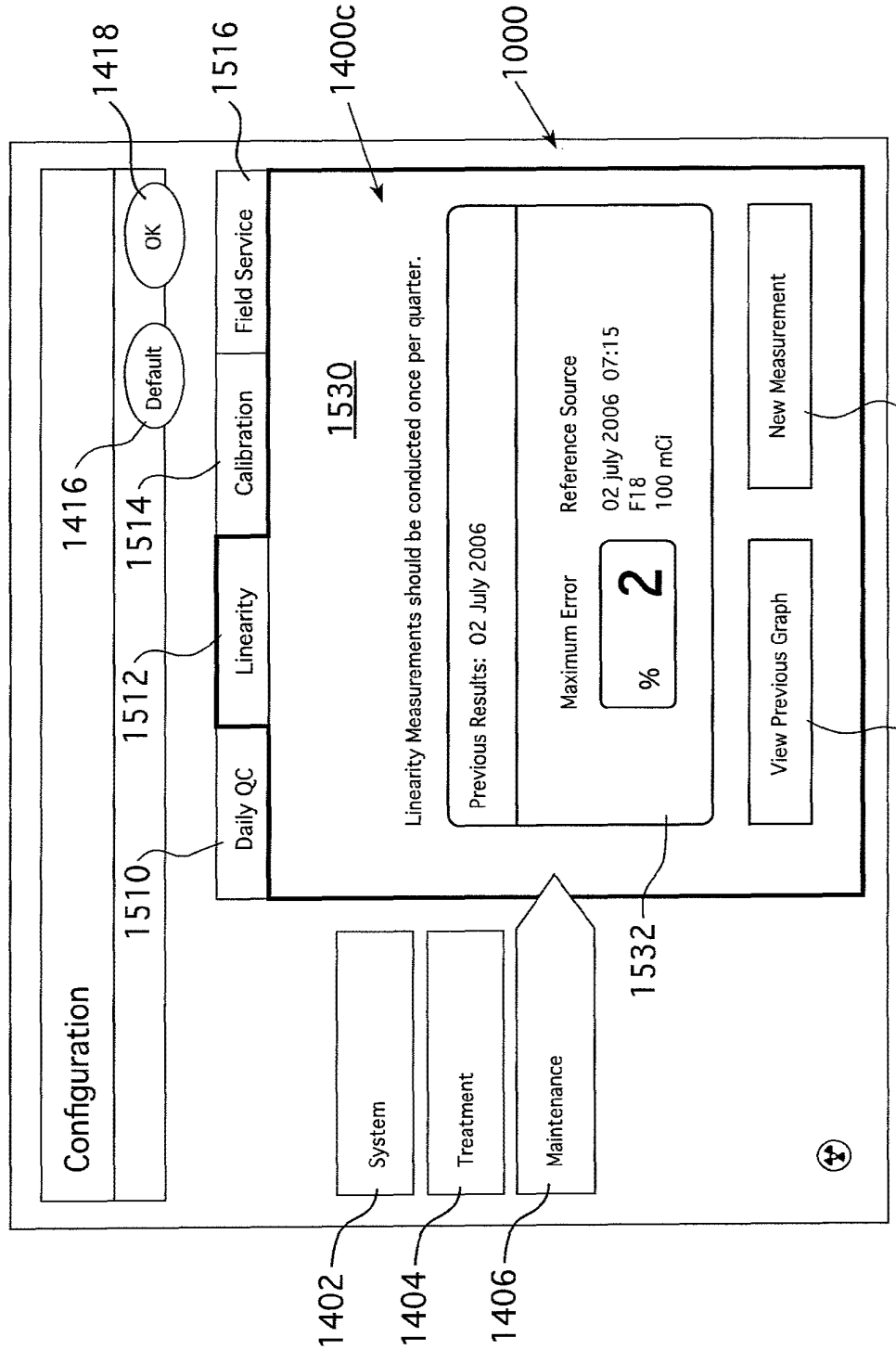
1418
1516
1400c
1000
OK
Default
Field Service
Calibration
Linearity
Daily QC
Configuration
1416
1514
1512
1510
1530
Linearity Measurements should be conducted once per quarter.
Previous Results: 02 July 2006
Maximum Error
2
%
Reference Source
02 july 2006 07:15
F18
100 mCi
New Measurement
View Previous Graph
1536
1534
1532
System
Treatment
Maintenance
1402
1404
1406

FIG. 44A

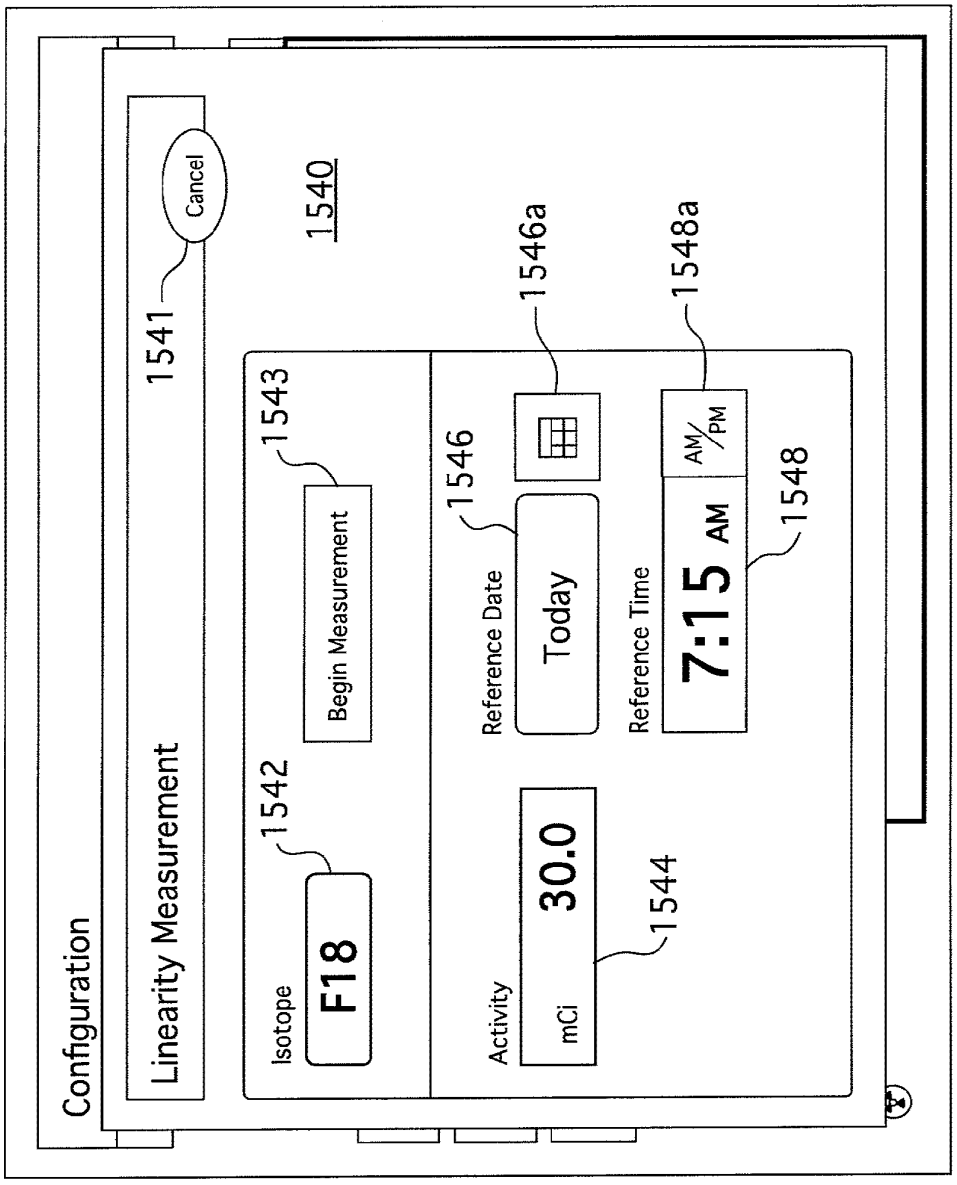
Configuration
Linearity Measurement
Cancel
1541
1540
1542
Isotope
F18
1543
Begin Measurement
1546
Reference Date
Today
1546a
1548
Reference Time
7:15 AM
AM/PM
1548a
Activity
30.0
mCi
1544

FIG. 44B

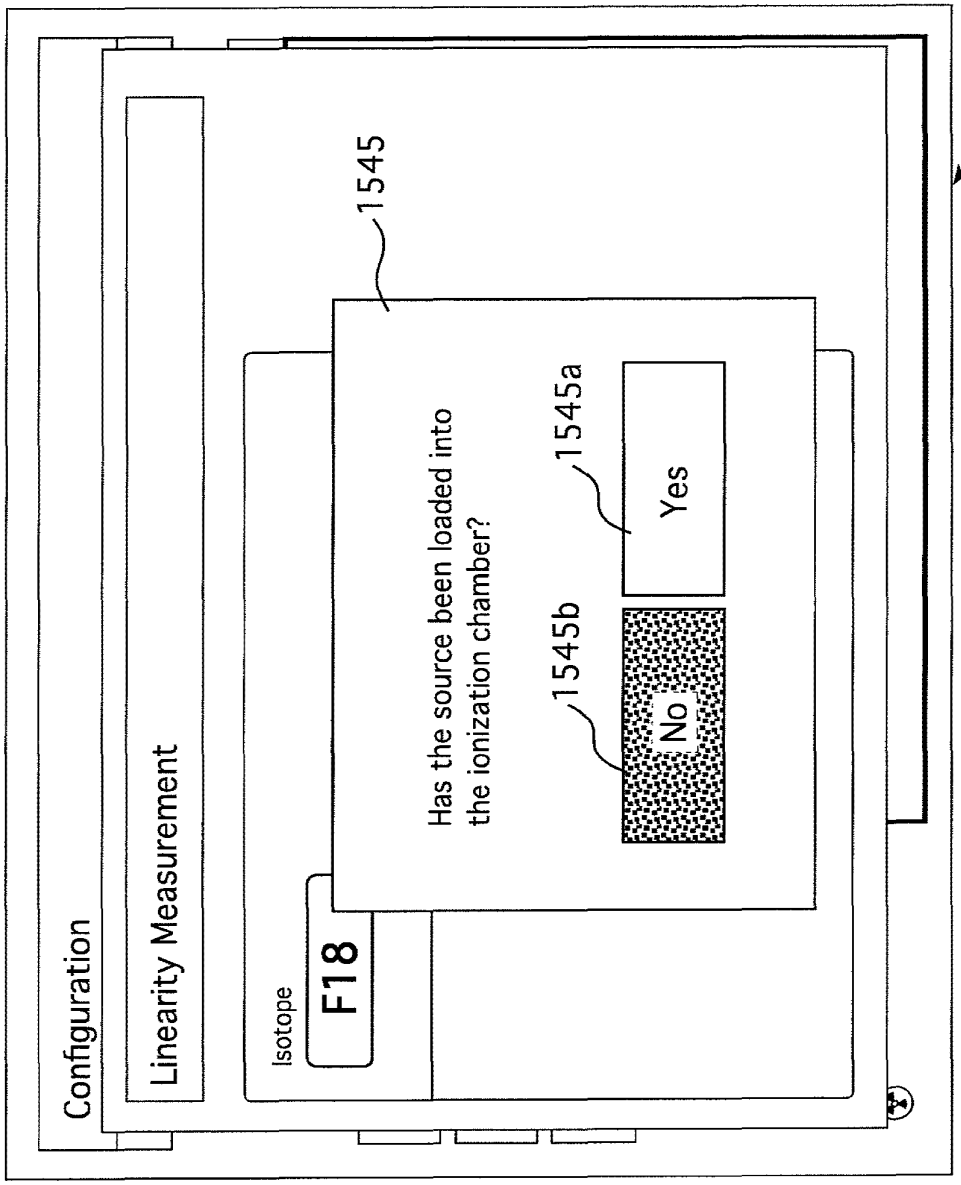
Configuration
Linearity Measurement
Isotope
F18
1545
Has the source been loaded into the ionization chamber?
1545a
Yes
1545b
No
1000

FIG. 44C

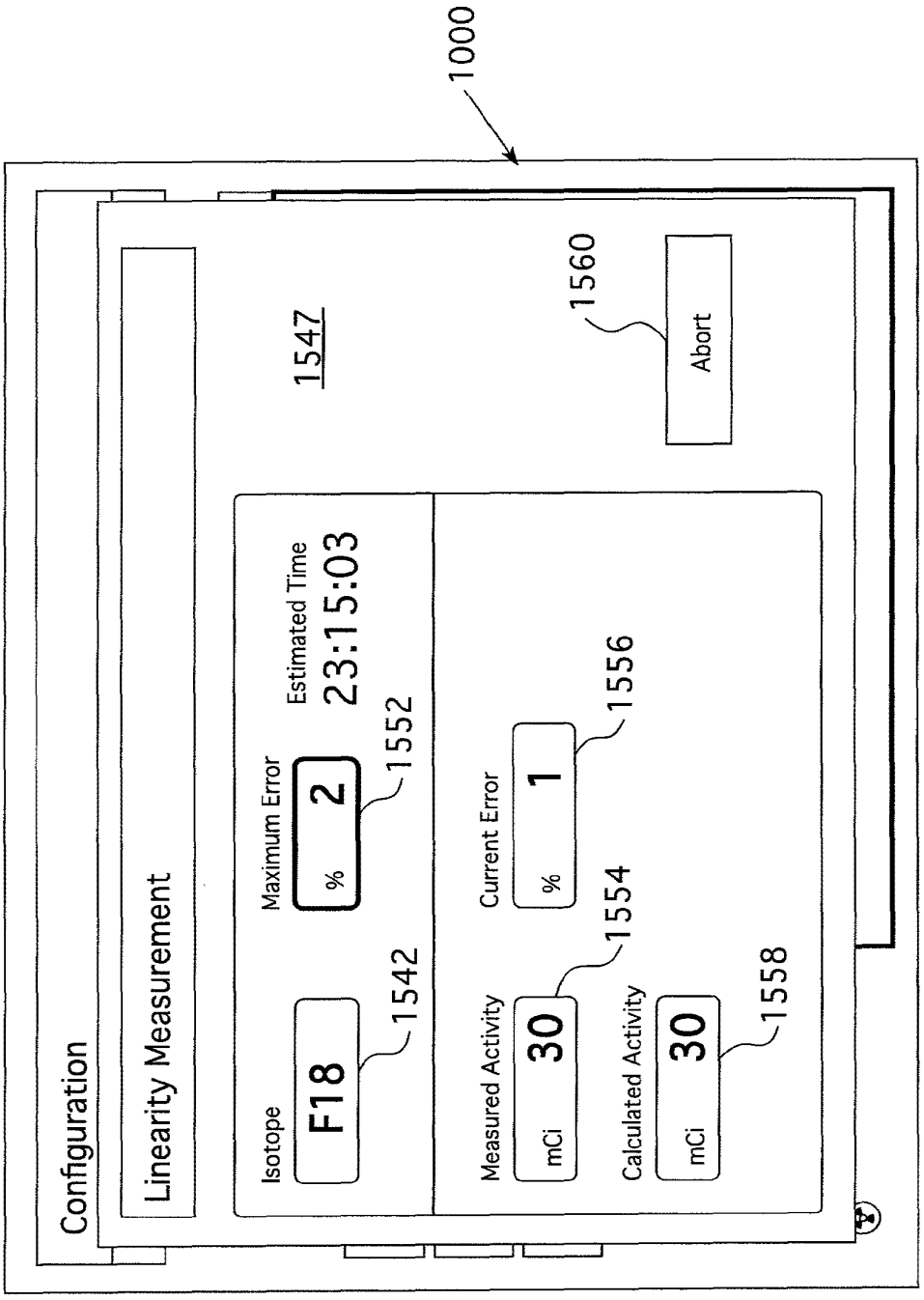
1000
Configuration
Linearity Measurement
1547
1560
Abort
Isotope
F18
1542
Maximum Error
%
2
1552
Estimated Time
23:15:03
Current Error
%
1
1556
Measured Activity
mCi
30
1554
Calculated Activity
mCi
30
1558

FIG. 44D

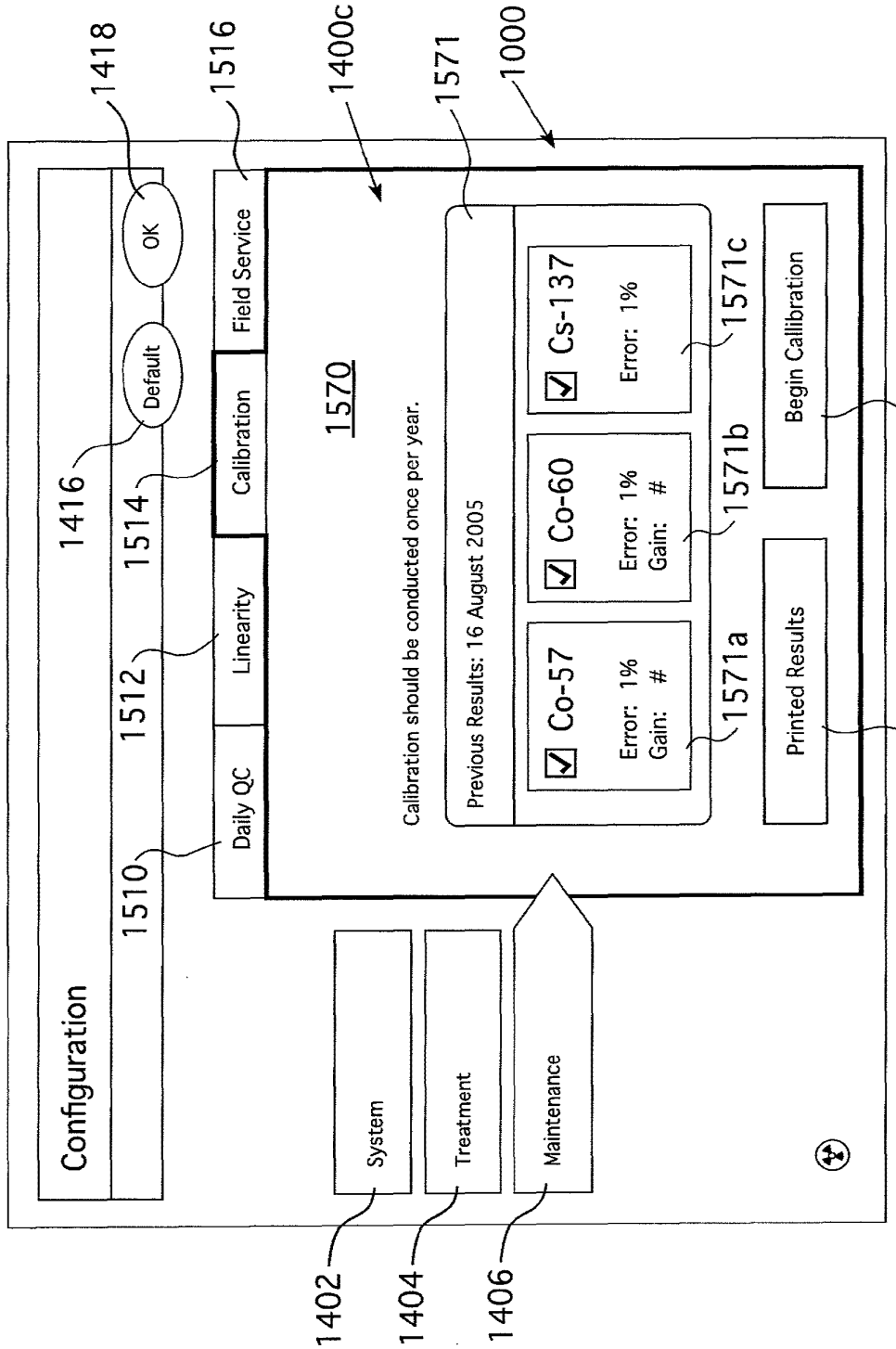
1000
1400c
1571
1516
1418
1570
Configuration
1510
1512
1514
1416
Daily QC
Linearity
Calibration
Field Service
OK
Default
Calibration should be conducted once per year.
Previous Results: 16 August 2005
Co-57
Error: 1%
Gain: #
Co-60
Error: 1%
Gain: #
Cs-137
Error: 1%
1571a
1571b
1571c
Printed Results
Begin Calibration
1572
1574
System
Treatment
Maintenance
1402
1404
1406

FIG. 45A

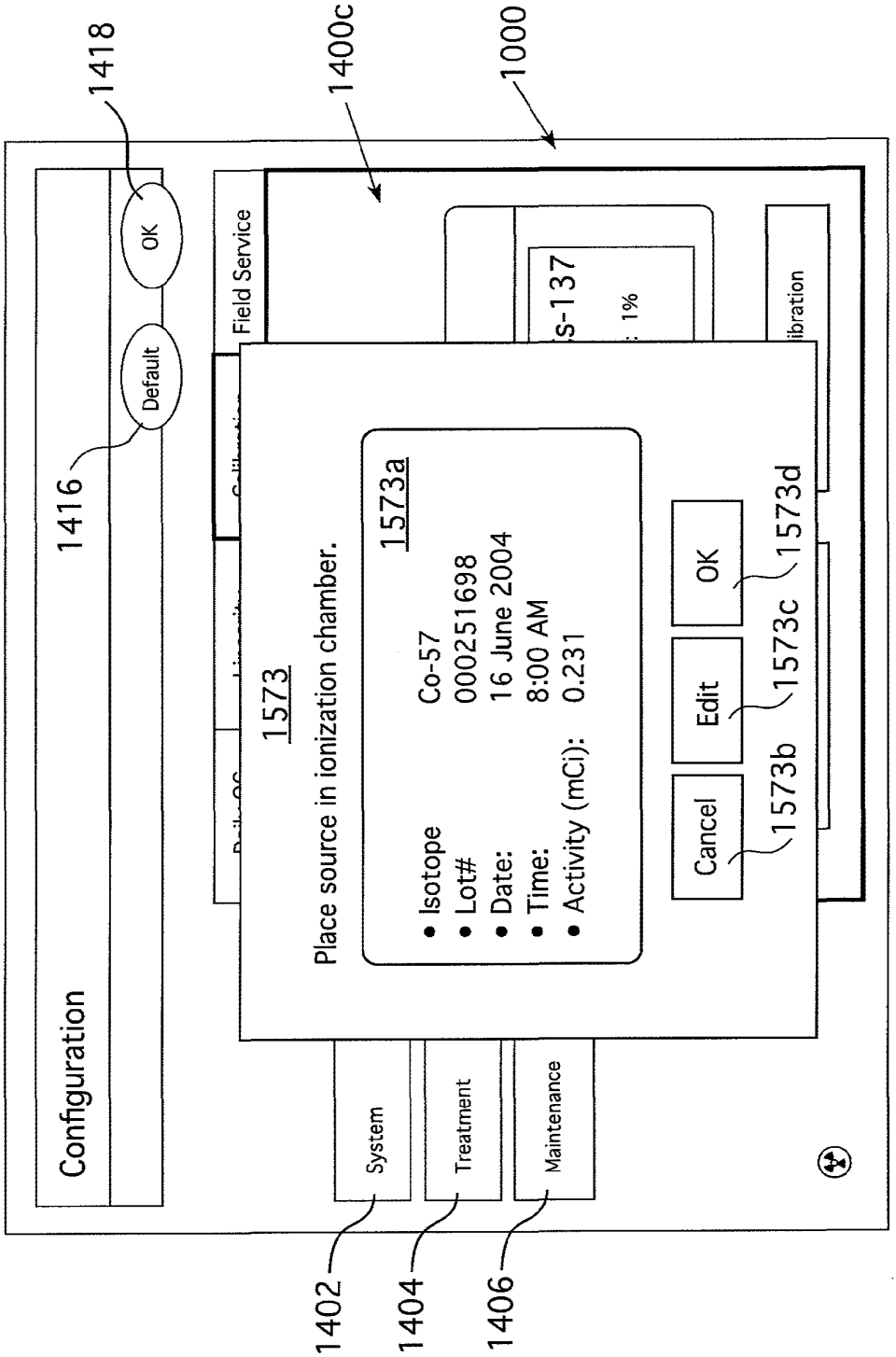
1418
1400c
1000
1416
OK
Default
Configuration
Field Service
1573
Place source in ionization chamber.
1573a
• Isotope Co-57
• Lot# 00251698
• Date: 16 June 2004
• Time: 8:00 AM
• Activity (mCi): 0.231
Cancel
Edit
OK
1573b
1573c
1573d
System
Treatment
Maintenance
1402
1404
1406

FIG. 45B

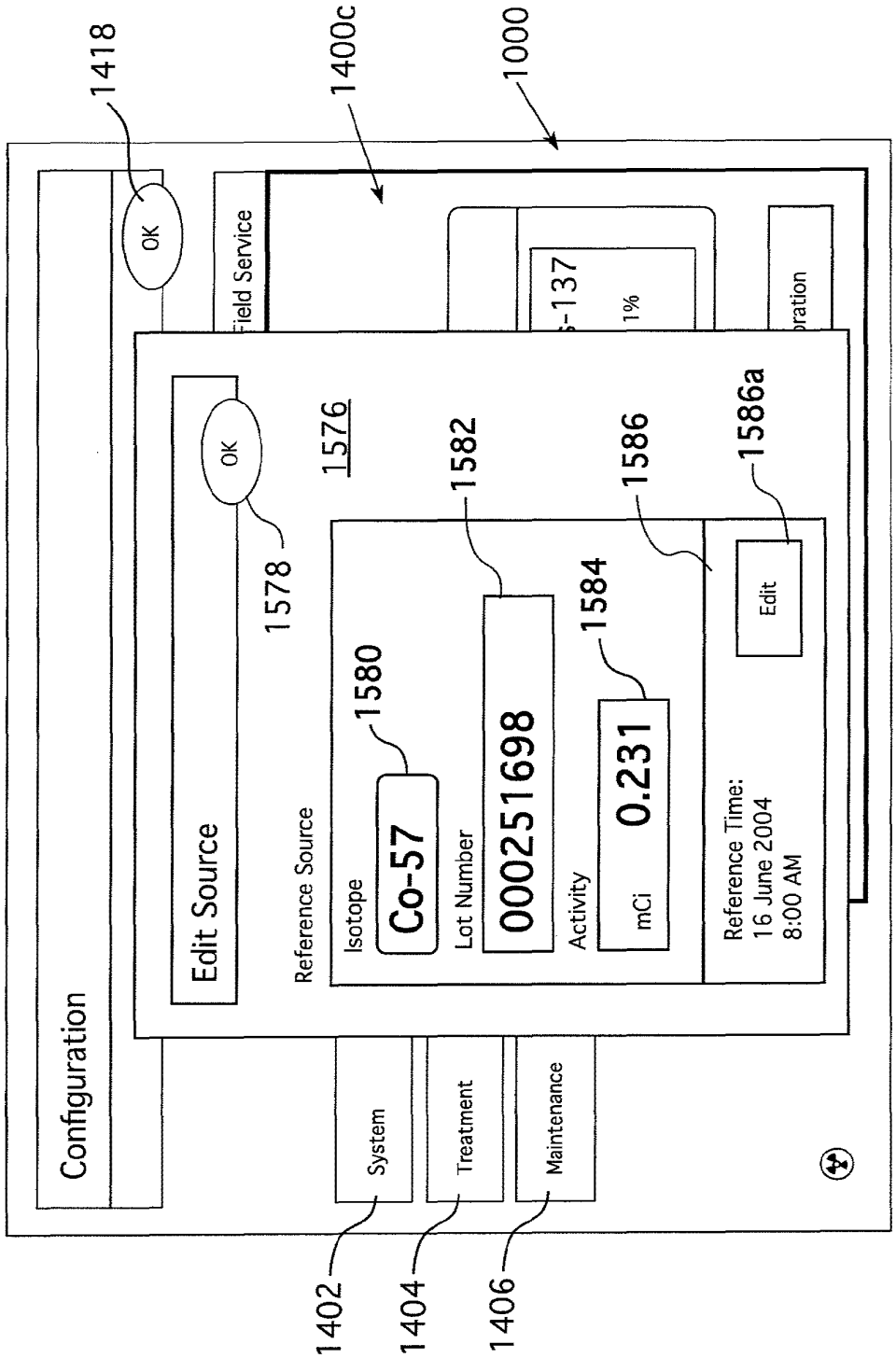
1418
1400c
1000
OK
Field Service
Configuration
Edit Source
OK
1578
1576
1582
1586
1586a
Reference Source
Isotope
Co-57
1580
Lot Number
000251698
Activity
mCi
0.231
1584
Edit
Reference Time:
16 June 2004
8:00 AM
System
Treatment
Maintenance
1402
1404
1406

FIG. 45C

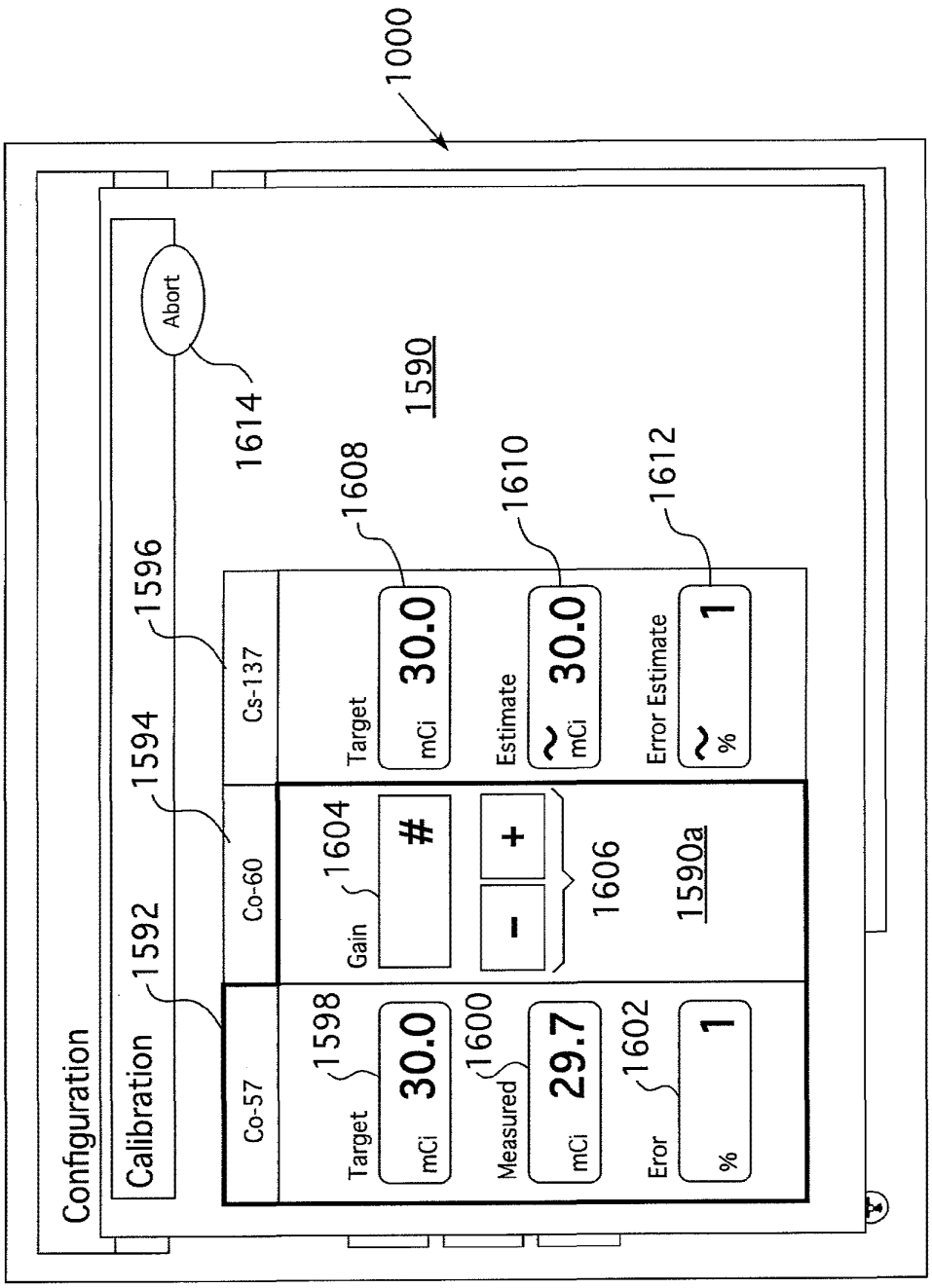
1000
Configuration
Calibration
1592
1594
1596
Co-57
Co-60
Cs-137
Abort
1614
1590
1608
1610
1612
Target
30.0
mCi
Estimate
~ 30.0
mCi
Error Estimate
~ 1
%
Gain
1604
#
+
-
1606
1590a
1598
Target
30.0
mCi
1600
Measured
29.7
mCi
1602
Eror
1
%

FIG. 45D

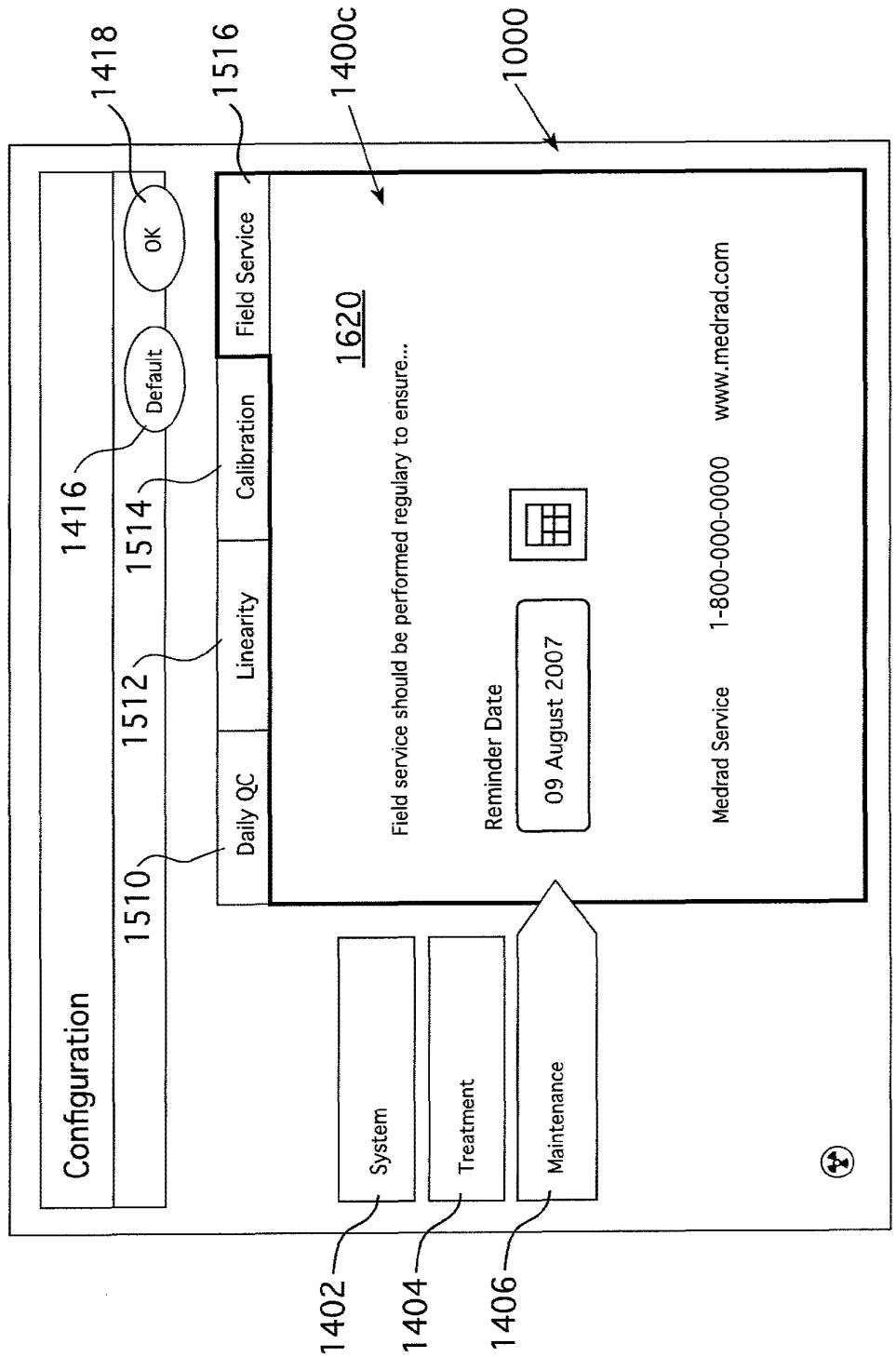
1418
1516
1400c
1000
OK
Default
Field Service
Calibration
Linearity
Daily QC
1416
1514
1512
1510
Configuration
1620
Field service should be performed regulary to ensure...
Reminder Date
09 August 2007
Medrad Service
1-800-000-0000
www.medrad.com
System
Treatment
Maintenance
1402
1404
1406

FIG. 46

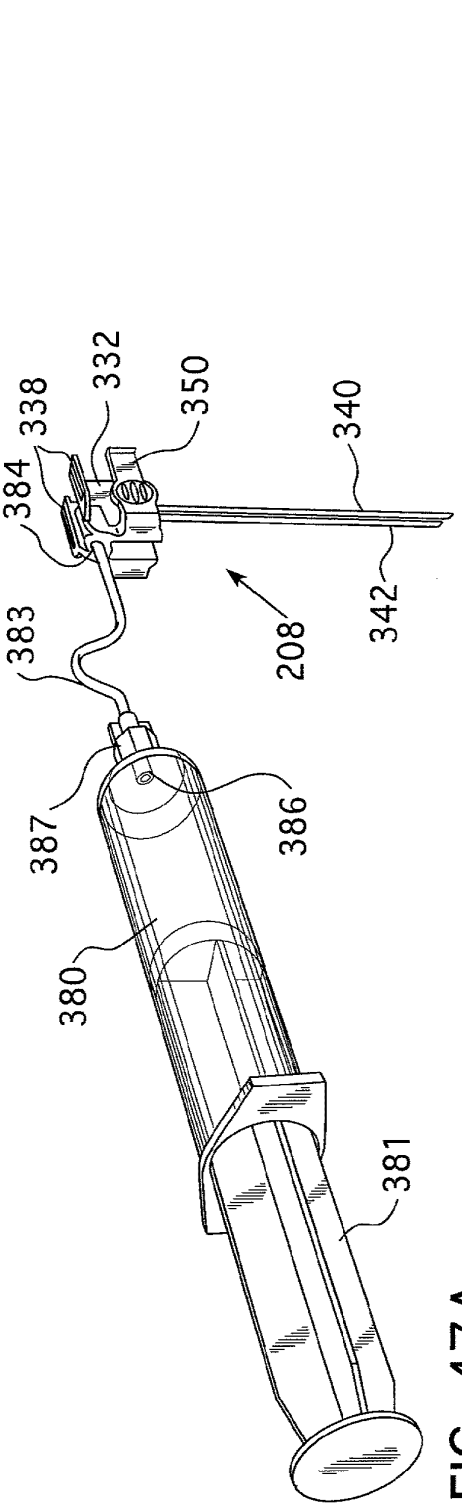

FIG. 47A

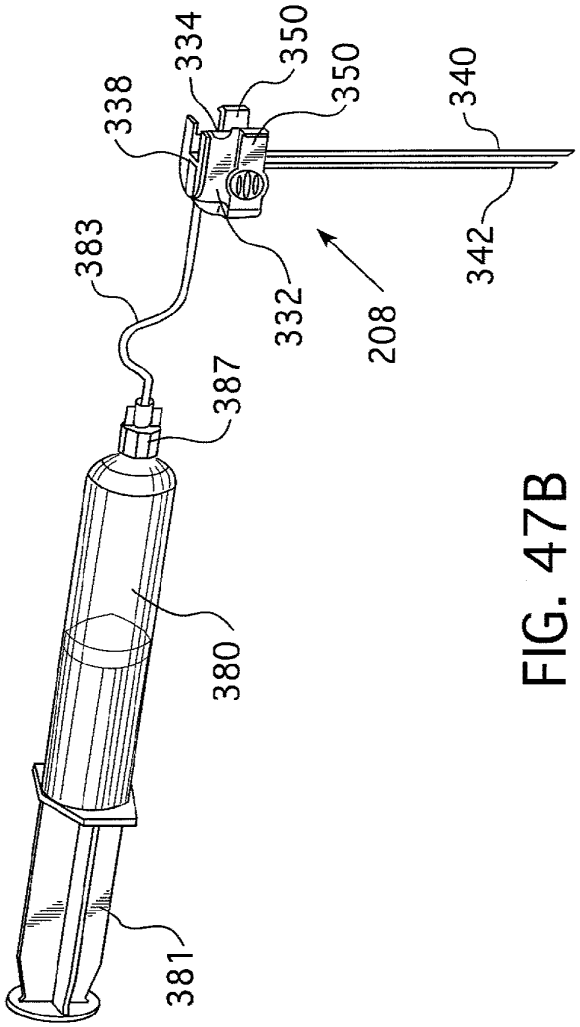

FIG. 47B

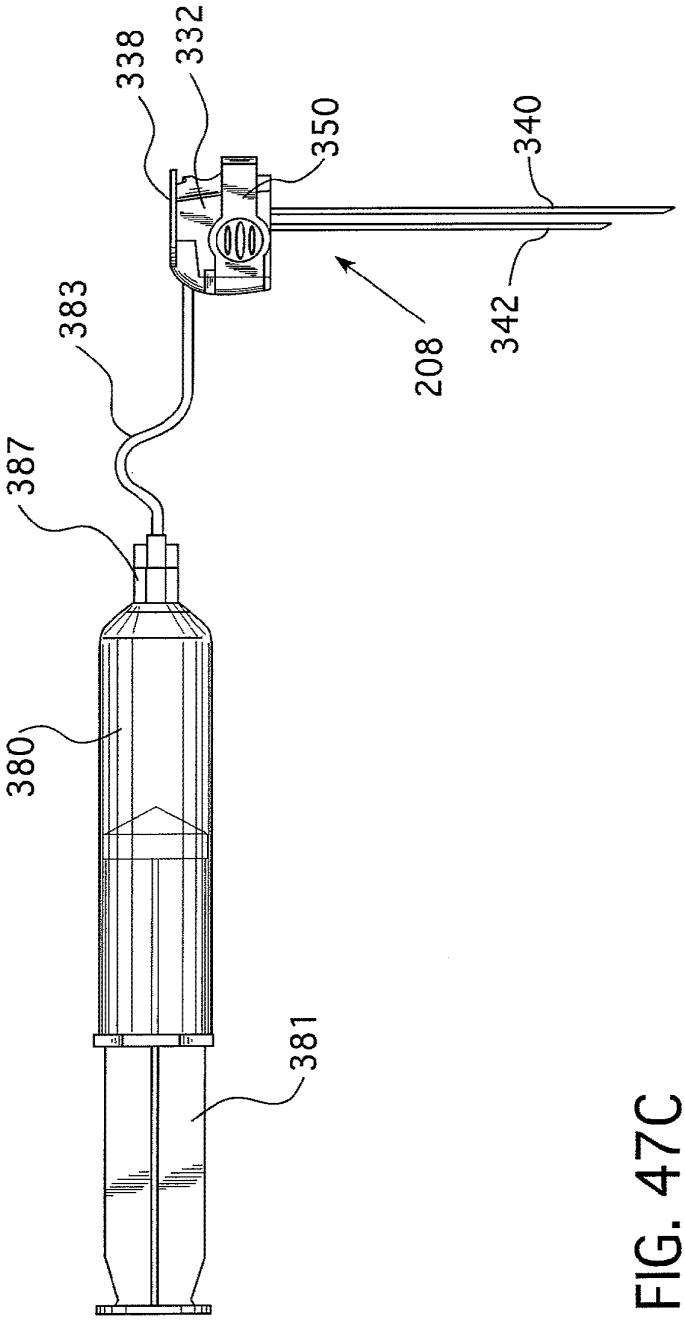

FIG. 47C

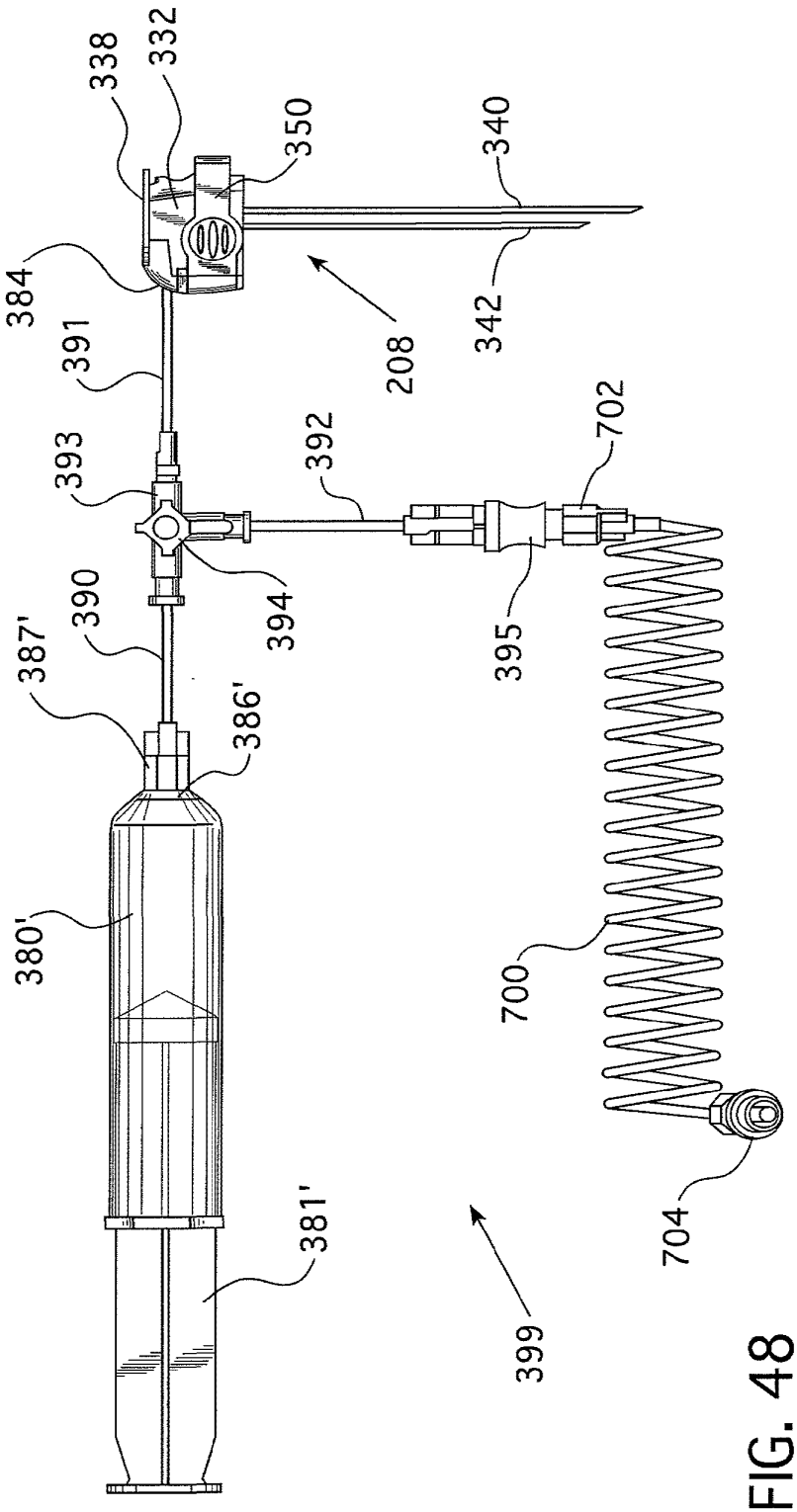
338
332
350
340
384
342
391
208
393
392
702
390
394
395
387'
386'
380'
700
381'
704
399

FIG. 48

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European Patent Office
Office européen des brevets

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A2

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(54) Strontium-rubidium infusion system.

(57) This novel strontium-rubidium infusion system includes means for generating a solution containing Rubidium-82, measuring the radioactivity in the solution, and infusing it into a patient in order to perform various studies on the patient's heart. The new system includes a wash syringe which can be used by a physician to manually inject a bolus containing a large amount of radioactivity directly into a patient in order to perform first pass ventriculography studies.

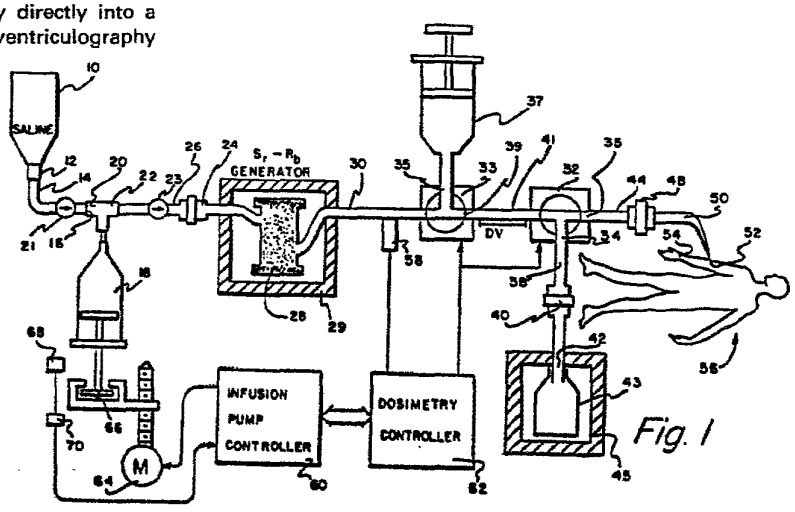

Fig. 1

EP 0 160 303 A2

Croydon Printing Company Ltd.

STRONTIUM-RUBIDIUM INFUSION SYSTEM

The present invention relates to a strontium-rubidium infusion system. More specifically, it relates to a strontium-rubidium infusion system which has an in-line, real time dosimetry system which can be used to infuse patients with Rubidium-82, particularly for first pass ventriculography studies. More precisely, the present invention provides a strontium-rubidium infusion system comprising:

(a) means for generating rubidium-82 in a solution which can be infused into a patient;

(b) means for collecting a predefined volume of solution containing rubidium-82;

(c) means for measuring the radioactivity present in said predefined volume before it is infused into said patient; and

(d) means for quickly infusing said predefined volume of rubidium-82 into said patient as a single bolus.

The present application is related to European Patent Application 84301269.1, entitled DOSIMETRY SYSTEM FOR STRONTIUM-RUBIDIUM INFUSION PUMP, filed February 27, 1984 and published September 5, 1984 under No. EP 0117752 A2.

Current statistics show that approximately one-third of all deaths in the United States are related to coronary artery disease. See, for example, Pohost, G., McKusick, K., and Strauss, W., "Physiologic Basis and Utility of Myocardial Perfusion Imaging", Proceedings of the Second International Symposium on Radiopharmaceuticals, Society of Nuclear Medicine, New York 1979, pp. 465-473. This fact has prompted extensive research to more efficiently diagnose and manage this disease. Recent advances in radiopharmaceutical development and instrument design have established myocardial scintigraphy as an important new approach for evaluating coronary artery disease and myocardial perfusion. See, for example, Pierson, R., Friedman, M., Tansley, W., Castellana, F., Enlander, D., and Huang, P., "Cardiovascular Nuclear Medicine: An Overview", Sem. Nucl. Med.,

9, 224-240 (1979); Leppo, J., Scheuer, J., Pohost, G., Freeman, L., and Strauss, H., "The Evaluation of Ischemic Heart Disease Thallium-201 with Comments on Radionuclide Angiography"; Sem. Nucl. Med., 10, 115-126 (1980); Vogel, R., "Quantitative Aspects of Myocardial Perfusion Imaging", Sem. Nucl. Med., 10, 146-156 (1980); Chervu, R., "Radiopharmaceuticals in Cardiovascular Nuclear Medicine", Sem. Nucl. Med., 9, 241-256 (1979); and Pitt, B., and Strauss, H., "Cardiovascular Nuclear Medicine", Sem. Nucl. Med., 7, 3-6 (1977).

Myocardial scintigraphy studies have been performed with several isotopes of potassium, rubidium, cesium, and thallium (Tl-201), although the usefulness of all of these nuclides is limited by their non-optimal physical properties. In spite of its long half-life and low-gamma energy, Tl-201 is currently the most widely used agent for myocardial imaging. See, for example, Poe, N., "Rationale and Radiopharmaceuticals for Myocardial Imaging", Sem. Nucl. Med., 7, 7-14 (1977); Strauss, H. and Pitt, B., "Thallium-201 as a Myocardial Imaging Agent", Sem. Nucl. Med., 7, 49-58 (1977); Botvinick, E., Dunn, R., Hattner, R., and Massie, B., "A Consideration of Factors Affecting the Diagnostic Accuracy of Tl-201 Myocardial Perfusion Scintigraphy in Detecting Coronary Artery Disease", Sem. Nucl. Med., 10, 157-167 (1980); and Wackers, F., "Thallium-201 Myocardial Scintigraphy in Acute Myocardial Infarction and Ischemia", Sem. Nucl. Med., 10, 127-145 (1980).

In diagnostic procedures in which the heart is involved, it is desirable for a diagnostician to be able to view a patient's heart. Heretofore, various radioactive materials have been used

together with radiological procedures for viewing internal organs of patients. It has been difficult, however, to view a heart, because the radioactive substances which could be used for viewing the heart have had a very long half-life. Thus, using them with patients has involved an element of danger and each use reduces the number of times that a patient could be infused within any given time period. It would, therefore, be desirable to have a diagnostic apparatus and procedure which could be used with relative safety for viewing the heart.

Rubidium-82 is a potassium analog. That means it acts in a manner similar to potassium when it is infused into a patient. Thus it builds up at a very rapid rate, i.e., within seconds, in the patient's heart. Rubidium-82 also has the advantage of having a very short half-life, approximately 76 seconds. Therefore, it decays after a very short period of time following entry into the body, thereby allowing numerous procedures to be performed within a relatively short time period in a given patient. Rubidium-82 also has the advantage of being observable using a modified gamma camera, such as a gamma camera of the type manufactured by Searle Radiographics, Inc., called the PHO Gamma IV. A problem with using Rubidium-82 in a patient involves measuring the amount of radiation infused into the patient. In view of the very short half-life of Rubidium-82, it has heretofore been impractical to measure the radioactivity of a particular dose and to then infuse it into the patient using conventional means. An accurate method for measuring the amount of radiation being infused into the patient would

be highly desirable for this particular application.

The availability of improved instrumentation has stimulated interest in the use of the positron emitter, Rubidium-82, for myocardial imaging. See, for example, Beller G., and Smith, T., "Radionuclide Techniques in the Assessment of Myocardial Ischemia and Infarction", Circulation, 53 (3, Supp. 1) 123-125 (1976); Budinger, T., Yano, Y., Derenzo, S., et al., "Myocardial Uptake of Rubidium-82 Using Positron Emission Tomography", J., Nucl. Med. 20, 603 (1979); Budinger, T., Yano, Y., Derenzo, S., et al., "Infarction Sizing and Myocardial Perfusion Measurements Using Rb-82 and Positron Emission Tomography", Amer. J. Cardiol., 45, 399 (1980). Rubidium-82, an analog of the alkali metal potassium, is rapidly cleared from the blood and concentrated by the myocardium. The short half-life of the Rubidium-82 (76 sec) offers the unique advantage of permitting repeat perfusion and blood flow studies in patients whose clinical status is rapidly changing.

Rubidium-82 is produced by the decay of its parent, strontium-82. E. R. Squibb and Sons, Inc. has developed a Rubidium-82 generator and infusion system which yields an isotonic saline solution of Rubidium-82 at physiological pH for rapid administration. In animal experiments, the safety and myocardial uptake of Rubidium-82 has been demonstrated. Therefore, this agent has been selected as a candidate for clinical trials.

In the European patent application identified above, a system for infusing Rubidium-82 into a patient while measuring the dose going into the patient

was described. That system is useful in myocardial scintigraphy studies. In a modification to that system, described herein, a system which permits both myocardial scintigraphy studies, as well as first pass ventriculography studies, is described.

In accordance with the present invention, a strontium-rubidium infusion system is described. The system includes means for generating rubidium-82 in a solution which can be infused into a patient. In particular, the strontium-rubidium generator, described above, is typically used. Generated rubidium-82 is then collected in a piece of tubing having a predefined volume. This tubing is called the "dose volume" tubing, and it contains the dose volume of rubidium-82 solution which is to be infused.

The system also includes means for measuring the radioactivity present in the dose volume before the dose volume is infused into the patient and a wash syringe for quickly infusing the dose volume into the patient as a single bolus.

In the Drawings:-

FIG. 1 is an overall schematic diagram of the strontium-rubidium infusion system of the present invention;

FIG. 2 is a front view of the infusion pump control used with the strontium-rubidium infusion system;

FIG. 3 is a front view of the dosimetry control used with the strontium-rubidium infusion system;

FIG. 4 is a graph of radioactivity measured (on the y-axis) by the dosimeter probe versus time

(on the x-axis);

FIG. 5 is a perspective view of the dosimetry probe;

FIG. 6 is a schematic diagram of the interface between the dosimetry probe of FIG. 4 and the dosimetry control circuitry;

FIG. 7 is a schematic diagram of the circuit for the Single Channel Analyzer used to convert and shape the raw pulses from the dosimetry probe of FIG. 4;

FIG. 8 is a schematic diagram of the circuit for the Multiply-Divide circuit used to carry out the formula which converts pulses from the Single Channel Analyzer into radioactivity present in front of the dosimetry probe;

FIG. 9 is a schematic diagram of one of the Display Controller circuits used to interface the switches and the displays to the other circuitry;

FIG. 10 is a schematic diagram of the Dose Rate circuit used to provide a display of the amount of radiation present in the eluate;

FIG. 11 is a schematic diagram of the Control Circuit which oversees the operation of the remainder of the circuitry; and

FIG. 12 is a schematic diagram of a valve driver circuit.

Referring now to FIG. 1, a saline bag 10 is connected, through a bullet nose fitting 12 and a piece of tubing 14, to a T-shaped two-way check valve 16 having three arms. A first arm 20 is attached to a one-way valve 21 which permits saline to enter the check valve 16, but does not allow it to exit back into the tubing 14. A second arm 22 includes a check valve 23 which permits saline to

exit from the check valve 16 into a filter 24 through a tube 26, but does not allow it to re-enter the check valve 16 from the tube 26. An automatic syringe 18, connected to the check valve 16 fills from the saline bag 10 and pumps out through the tubing 26 into the filter 24. Saline pumped through the filter 24 enters a strontium-rubidium generator 28 which is of the type described more fully in U. S. Patent 4,405,716, issued September 27, 1983, entitled ^{82}RB GENERATING METHOD AND ELUENT. The generator 28 is preferably enclosed in a lead shield 29.

Saline pumped through the strontium-rubidium generator 28 exits the generator 28 through tubing 30 containing Rubidium-82. The tubing 30 is connected to a diverter valve 33 having a first arm 35 which connects to a manually operated wash syringe 37. The remaining arm 39 is connected to a diverter valve 32 through a length of tubing 41 which is called the "dose volume" tubing 41, which has a length, DV. The length, DV, of the dose volume tubing, times its cross-sectional area, gives its volume, hereinafter referred to as the "dose volume".

Diverter valve 32 has a first arm 34 which leads through tubing 38, an antibacterial filter 40, through a tube 42, and ultimately to a waste collection container 43. The waste collection container 43 is preferably enclosed in a lead shield 45. A second arm 35 of the diverter valve 32 is connected through tubing 44, an antibacterial filter 48, additional tubing 50, and into an infusion needle 52. The infusion needle 52 is typically inserted into the arm 54 of a patient 56.

In the preferred embodiment of the invention, the check valve 16 is a dual back check valve of the type made by Beckton Dickenson Inc., and the antibacterial filters 24, 40, 48 are of the type made by Schleicher & Schull as their type FP030/3.

In the operation of the device to perform first pass ventriculography studies, the amount of radioactivity in the saline eluted from the strontium-rubidium generator 28 must be measured. Accordingly, a dosimetry probe 58 is placed adjacent to the tubing 30 where it measures the radioactivity of the rubidium-containing saline as it enters the the diverter valve 33. The diverter valve 33 is a three-part valve which permits flow from either the generator to the diverter valve 32 or from the wash syringe 37 to the diverter valve 32.

The diverter valves 32, 33 are connected to a dosimetry controller 62 for automatic operation. The operation of the dosimetry controller 62 will be further explained hereinafter. Based upon the signal sent by the dosimetry controller 62 to the valves 32, 33, the elution from the generator 28 is directed through the valves 32, 33 and the dose volume tubing 41 into the waste container 43 until such time as the minimum dose rate is met. Once the minimum dose rate for a first pass study has been reached, the dosimetry controller 62 starts integrating patient volume and dose to fill the dose volume tubing 41 with highly radioactive eluate. At that point, the valve 33 is switched to open the valve between the dose volume tubing 41 and the wash syringe 37 and close the valve leading through tubing 30 to the generator 28. Similarly,

the diverter valve 32 is switched from the waste position to the patient position, and the physician performing the study quickly injects saline from the wash syringe 37 directly into the patient 56. That operation performs a number of different functions. In particular, it pushes the dose volume of radioactive eluate from the dose volume tubing 41 into the patient as a single highly radioactive bolus. Thereafter, the remaining saline in the wash syringe 37 clears the lines 41, 44, 50, purging them of radioactivity.

An advantage of the wash solution clearing the patient line of radioactivity is that the line does not "glow" in photos taken of the patient. Such a glowing interferes with data from the patient. An advantage of using the manually operated wash syringe 37 is that it allows a high infusion rate, on the order of 300 milliliters per minute, rather than about 50 milliliters per minute which can be obtained through automatic operation. The dose volume line 41 is typically of a length such that, together with its diameter, it holds between 3 and 10 ccs of fluid. Accordingly, it could be 3 to 4 feet long. Because of the length of the dose volume line 41, the dose volume line 41 can be placed within a standard dose calibrator of the type normally used in such studies. Accordingly, while the probe 58 and associated electronics are used to determine when to switch the divertor valves 32, 33 and while the electronics of the present device can also be used to measure the dose which is to be infused into the patient 56, a standard dose calibrator can also be used in first pass ventriculargraphy applications.

As will be explained hereinafter, the

present device can also be used in performing myocardial perfusion studies of the type described in the patent applications referred to earlier.

In order to use the infusion system, various procedures must be performed and controlled. In particular, the syringe 18 must be purged of air, and filled with saline, and the diverter valves 32, 33 must be positioned. These operations are contingent upon a number of factors including the total volume to be infused into the patient 56, the total dosage to be infused into the patient 56, the minimum radioactivity which must be present in the tubing 30 before any eluate is infused into the patient 56, the total volume to be infused (Note: The total volume eluted may differ from the total volume infused into the patient 56 as some volume is likely to be diverted to waste.).

The foregoing parameters may be altered from the front panel of two different controllers shown in FIGS. 2 and 3. These are the infusion pump controller 60 and the dosimetry controller 62, repectively. The infusion pump controller 60 controls the mechanical movement of the syringe's plunger 66 via a stepping motor 64 which is connected to the plunger 66.

In the preferred embodiment of the invention, the syringe 18 is a sterile, disposable plastic syringe of the type made by Sherwood Medical and designated as Part. No. 881-514031. The infusion pump controller 60 limits the movement of the syringe plunger 66 based upon optical limit detectors 68, 70 which limit the fully displaced and fully extended positions of the plunger 66, respectively. The volume control function performed by the infusion pump controller 60 is

accomplished by counting the number of pulses sent to the stepping motor 64.

With reference to FIG. 2, the front panel of the infusion pump controller 60 is shown. The infusion pump controller 60 includes an on/off power switch 72 which is used to turn on the power to the unit.

A set of thumbwheel switches 74 is used to select the total volume (ml) to be eluted. An LED display 76 shows the total volume (ml) which has been eluted. A momentary contact push-button switch 78 is used to start and to stop the movement of the plunger 66 in the forward (inject) direction.

A set of push-button potentiometers comprise the Flow Rate Control 80 which is used to determine the volume per unit time which is infused. The Flow Rate Control 80 sets the pulse rate into the stepping motor 64. An LED 82 lights when the end of travel of the plunger 66, as indicated by the optical limit detectors 68, 70 is reached. A pair of momentary contact push-button switches 84, 86 are used to control the purge and refill functions, respectively, of the syringe 18. Thus, if the purge control switch 84 is pushed, and held, the plunger 66 continues to move in the forward direction until it reaches the forward limit detector 68. Similarly, while the refill control switch 84 is pressed and held, the plunger 66 continues to move toward the rear limit detector 70. The speed of movement of the plunger 66 during purge and refill operations are controlled by adjustable screw-type potentiometers 88, 90, respectively.

The infusion pump controller 60 is comprised

of a Superior Electric Company STM103 Translator Module which is interfaced to provide signals representative of flow rate, volume eluted, and injection. It is also interfaced to be remotely controlled. A pulse called "INIT" indicates that the Translator Module has been powered. The "INIT" pulse is used to reset the displays on the dosimetry module. An "INJECT" signal indicates that the pump is injecting. Output pulses, corresponding to .1 ml steps of the syringe 18, are provided. An "End of Elution" signal is used to remotely disable the infusion pump controller 60.

With reference now to FIG. 3, the dosimetry controller 62, is comprised of a number of LED displays and thumbwheel switch sets. In addition, the dosimetry controller 62 includes an on/off switch 92 for providing power to the unit.

The first set of thumbwheel switches 94 is used to set the volume (ml) to be infused into the patient 56. The LED display 96, immediately above the thumbwheel switches 94, displays the volume of eluate which has been infused into the patient 56.

The thumbwheel switches 98 are used to set the total dose (mCi) which is to be infused into the patent 56 and the LED display 100 immediately above the total dose thumbwheel switches 98 displays the total dose which has been infused into the patient 56. Similarly, the thumbwheel switches 102 are used to set the dose rate (mCi/sec.) which is to be used to determine when to switch the diverter valve 32 from the waste position to the patient 56 position. The actual dose rate which is present in the eluate within the tube 30 in front of the dosimetry probe 58 is displayed on the LED display 104. The description of the dose present

in the eluate at any given time from the start of infusion will be provided hereafter. The dosimetry controller 62 further comprises a pair of LED's 106, 108 which indicate the position of the diverter valves 32, 33. Only one of these two LED's 106, 108, should be on at any given time.

While the normal position of the diverter valves 32, 33 is toward waste from the generator 28, except when eluate is being manually infused into a patient 56, provision must be made to clear the tubing 44, 50 of any air prior to infusing a patient 56. Accordingly, the dosimetry controller 62 includes a toggle switch 110 which is used to hard wire the diverter valve 32 in the patient 56 position.

The present preferred embodiment of the invention also includes a set of thumbwheel switches 112 which are used to set the flow rate which will be used in internal calculations of dosimetry controller 62. It is presently anticipated by the inventor that a future version of the present invention will include automatic means for determining the flow rate based upon the settings used in the infusion pump controller 60.

Referring now to FIG. 4, a graph of the radioactive dosage present in the tubing 30 in front of the dosimetry probe 58, is shown. In the graph, the dosage is measured on the y-axis and time is measured on the x-axis. The time is referenced with zero being the time that the start/stop inject button 78 on the infusion controller 60 is pushed to commence infusion.

For approximately 10 seconds there will be no radioactivity present in the eluate from the strontium-rubidium generator 28. Thereafter, the

dose rate rises at a rapid rate up to a maximum, after which the dose rate falls to a level value indicative of the steady state regeneration rate of the Sr-Rb generator 28. Thus, when the infusion starts, there is a delay initially as the dose rate builds up, a reduction in dosage after the generator 28 is partially eluted, and then there is a dosage representative of the steady state regeneration rate of the generator 28.

The setting of the dose rate thumbwheel switches 102 tells the dosimetry controller 62 at what point along the upward slope of the dosage curve to start integrating the patient volume (i.e., the volume in dose volume line 41 which will be infused into the patient 56) and the patient dose. At that point the dose indicated by the LED's 100 will start accumulating from zero, where it had been until that point. Similarly, the patient 56 volume indicated by the LED's 96 will start to accumulate as of that time.

Once highly radioactive eluate is infused into the dose volume line 41 it continues to be infused until one of various stop indications occurs. In particular, when the total patient 56 dose, set by the thumbwheel switches 98, is reached, the diverter valve 32 is opened to the patient position, diverter valve 33 is closed from the generator 28 and opened to the wash syringe 37, and the stepping motor 64 stops, thereby preventing further infusion. Similarly, the diverter valves 32, 33 are switched, and the stepping motor 64 is stopped when the patient volume 96, preset by the thumbwheel switches 94 reaches its preset value or after the total volume to be eluted, set by the volume thumbwheel switches 74 reaches its preset

value; or when the purge limit optical stop 68 of the syringe 18 is reached; or if the start/stop inject button 78 is pushed. Any of the foregoing events causes the diverter valves 32, 33 to switch, and causes the stepping motor 64 to stop. Note, however, that the purge and refill switches 84, 86 are disabled as of the time that the start/stop inject button 78 is pushed to commence the infusion.

Quantizing Radioactivity in a Liquid Stream

In order to measure the radioactivity in the saline solution which passes through the line 30 in front of the dosimetry probe 58, it is necessary to count the number of disintigrations which occur in front of the probe 58, while at the same time keeping track of the flow rate of the saline through the tube 30. Given that these quantities are known, it is possible to measure the total activity in milliCuries (mCi) in accordance with the following formula:

$$A = \frac{(C)(F)}{(V)(E)(CM)(Y)}$$

Where, A = total activity (mCi);
C = net counts;
F = flow rate (ml/min);
V = volume in detector view (ml);
E = net efficiency (counts per minute/disintegration per minute);
CM = disintegrations/minute to milliCurie conversion factor; and
Y = net yield of photon.

In the case of the present invention, the above formula can be simplified to:

$$A = \frac{(C)(F)}{K}$$

Where, A = total activity (in milliCuries);
C = net counts (from probe);
F = the flow rate; and
K = the calibration factor.

As noted, the calibration factor, K, takes into account the volume in the detector's view, the net efficiency of the probe, the conversion factor in terms of disintigrations per minute to milliCuries, and the net yield of photons. These factors are substantially constant for any given probe and tubing combination for a reasonable amount of time. Accordingly, provision is made on the circuit board to adjust the calibration factor, K, when the instrument is serviced. However, the calibration factor, K, is not user adjustable in the normal course of operation.

Dosimetry Probe

Referring now to FIG. 5, the dosimetry probe 58 is comprised of a photomultiplier tube 120, such as the RCA C83009E 14 mm diameter 10-stage photomultiplier tube manufactured by the Electro Optics Division of RCA Corporation in Lancaster, Pennsylvania. The photomultiplier tube 120 has a face 122 through which input signals in the form of light are received. On the face 122, a plastic scintillator 124, such as a Nuclear Enterprises Type 102A manufactured in Edinburgh, Scotland, is mounted. In the preferred embodiment of the invention, the plastic scintillator 124 is glued or bonded to the face 122 of the photomultiplier tube 120. After the plastic scintillator 124 has been bonded to the face 122 of the photomultiplier tube 120, an aluminum foil covering (not shown) is placed over the face end of the photomultiplier tube 120, including the plastic

scintillator 124. The purpose of the aluminum foil covering is to reflect back into the tube 120 any light which scintillates from the plastic scintillator 124 away from the tube 120. In addition, the aluminum foil covering prevents any stray light which might come into the area of the face 122 from getting into the tube 120. Following the application of the aluminum foil, a light tight material, such as black electrical tape is wrapped over the aluminum foil covered tube 120 in order to further prevent any light from entering into the tube 120. The tape-wrapped tube 120 is then inserted into a mu metal shield 126 which is intended to prevent any electromagnetic radiation effects from affecting the output of the dosimetry probe 58. In the preferred embodiment of the invention, the dosimetry probe 58 is plugged into a standard photomultiplier tube socket base 128 containing a standard resistive biasing network.

Dosimetry Circuitry

Referring now to FIG. 6, the photomultiplier tube socket base 128 includes a resistive network containing biasing resistors for placing appropriate bias voltages on the ten dynodes in the photomultiplier tube 120. Accordingly, the high voltage connection to the photomultiplier tube base 128 is automatically biased to provide appropriate operating voltages to the photomultiplier tube 120. The high voltage supply 130 used in the preferred embodiment of the invention is a 0-1000 volt, adjustable Bertan PMT-10A-P power supply manufactured by Bertan Associates, Inc., Three Aerial Way, Syosset, New York. In the present application, the high voltage supply 130 is adjusted to provide an output voltage

of 950 volts. The photomultipler tube socket base 128 is an RCA photomultipler tube socket base, Part No. AJ2273.

An output signal goes from the dosimetry probe 58 on a line 132 to a coupling network comprising a pull up resistor 134, a coupling capacitor 136, and a output resistor 138. Accordingly, an AC signal having a peak to peak maximum of approximately 250 millivolts with negative going pulses, is provided on output line 140.

Single Channel Analyzer

Referring now to FIG. 7, the schematic diagram for a Single Channel Analyzer circuit is shown. The Single Channel Analyzer is used, because the pulses on output line 140 from the Dosimetry circuitry are very sharply defined pulses which may occur at very high frequencies. In view of the fact that it is important to count all the pulses, a very high speed comparator, such as an AM685 voltage comparator 142, manufactured by Advanced Micro Devices, 901 Thompson Place, Sunnyvale, California, with emitter-coupled logic (ECL) output, or other suitable very high speed comparator, must be used.

A biasing network 141 consisting of a series of resistors and capacitors is used as one input to the comparator 142. In view of the fact that the pulses which are handled by the comparator 142 are of very short duration, a one-shot circuit 144, comprised in the preferred embodiment of the invention, of a Motorola Type 1670 master-slave flip-flop integrated circuit, is used to stretch the pulse width up to a uniform pulse width of approximately 50 nanoseconds. The output signal

from the one-shot 144 is fed into a programmable divide-by-N circuit 146, which in the preferred embodiment of the invention is comprised of a Motorola Type 10136 universal hexadecimal counter integrated circuit. The divide-by-N circuit 146 is programmable. Accordingly, a very high pulse repetition rate coming into the comparator with very short pulse widths is reformed by the one-shot to have wider, uniform pulses, and the input signal is further reformed by the divide-by-N circuit to bring the pulse repetition rate down into any desirable range. In particular, outputs of the divide-by-N circuit 146 are provided for N equal to 2, 4, 8, and 16.

Up through this point in the circuit, the devices have all been of ECL type in order to be able to handle the very high speed pulses which are detected by the dosimetry probe 58. In view of the fact that it is conventional to use transistor-transistor-logic (TTL) integrated circuits, a type 10125 ECL-to-TTL level converter circuit 150 is hooked to the output of the divide-by-N circuit 146. Thus, the ECL-to-TTL level converter circuit 150 transforms the ECL signal levels into TTL signal levels for further processing. The TTL outputs leave the ECL-to-TTL level converter circuit 150 on four lines 152, 154, 156, 158, which correspond to the TTL level of the counts into the Single Channel Analyzer divided by 2, 4, 8, and 16, respectively. The counts out on the lines 152-158 will be referred to hereafter as the "net counts".

Multiplier-Divider Circuit

Referring now to FIG. 8, there is a Multiplier-Divider circuit 160 which converts the

net counts from the Single Channel Analyzer circuit, described above, into a meaningful quantity (milliCuries). The Multiplier-Divider circuit 160 accepts the "net counts" on an input line 162 which is connected to one of the lines 152-158 from the Single Channel Analyzer (i.e., the raw counts converted into TTL levels and then divided by 2, 4, 8, or 16) and multiplies them by the eluate Flow Rate divided by 100. The result is then divided by a constant, K, in order to carry out the formula:

$$A = \frac{(N)(F)}{K}$$

Where, A = total activity (in milliCuries);
N = net counts (from Single Channel Analyzer);
F = Flow Rate; and
K = the calibration factor.

The net counts, N, are first multiplied by a two digit number corresponding to the eluate Flow Rate (entered on the Flow Rate thumbwheel switches 112A, 112B, corresponding to the most significant digit (MSD) and the least significant digit (LSD), respectively, the thumbwheel switches 112A, 112B are on the front panel of the dosimetry controller 62, shown in FIG. 3. The multiplication is accomplished by cascading two TTL Synchronous Decade Rate Multiplier circuits (F74167), and sending their outputs through a NAND gate 168. The resulting output corresponds to F_{out}, where:

$$F_{out} = \frac{(N)(F)}{100}$$

The output pulses are of varying duration, so they are next fed through a pair of one-shots

which process them to have a fixed duration. In the preferred embodiment of the invention, the first one-shot is comprised of one-half of an SN74123 integrated circuit 170. The first one-shot is negative edge triggered, and it provides a pulse output of approximately 200 nanoseconds. Its output is double buffered through buffers 172, 174 into a second one-shot which is comprised of one-half of a CD4098BE integrated circuit 176 in order to increase the width of the output pulses, so they will be acceptable to a CMOS divider integrated circuit 178. The second one-shot is configured to be leading edge triggered.

The output of the second one-shot is then divided by the calibration factor, K, which may have a range of between 3 and 9,999. A CD4059A integrated circuit 178 is used as a programmable divide-by-N counter. Programming is accomplished via a series of 16 DIP switches 180 mounted on the printed circuit card. Each set of four switches corresponds to the BCD settings for 1's, 10's, 100's and 1000's. Pull up resistors (not shown) are employed in the standard manner so that when the DIP switches are open the inputs to the divide-by-N circuit 178 are pulled high.

The output of the divider 178 has pulses of random widths, so another one-shot, made up of the second half of the CD4098BE 176 configured for leading edge triggering, is used. This one-shot provides an output pulse duration of approximately 20 microseconds. Before leaving the Multiplier-Divider circuit 160, the output is double buffered through buffers 182, 184 and the output signal on line 186 is sent to the Dose Rate circuit. There will be one dose corrected output

pulse on line 186 for each 0.01 milliCurie of activity which passes by the dosimetry probe 58.

Display Controller Circuit

Referring now to FIG. 9, the schematic diagram for a Display Controller Circuit 190 is shown. There are three Display Controller Circuits within the dosimetry controller 62. Each Display Controller 190 is used both to interface a set of thumbwheel switches 192 and to display the quantity associated with the particular set of thumbwheel switches 192. Thus, there is one Display Controller of 190 for Dose Rate (which works with thumbwheel switches 102 and LEDs 104), one for Patient Volume (which works with thumbwheel switches 94 and LEDs 96), and one for Dose (which works with thumbwheel switches 98 and LEDs 100). Each Display Controller Circuit 190 drives four seven-segment displays 194, such as MAN71 displays.

The major component of the Display Controller Circuit 190 of the preferred embodiment of the invention is an Intersil ICM7217IJI integrated circuit 196, which is a device which provides a direct interface to the seven-segment displays 194. Each Display Controller Circuit 190 allows the user to set a level, by programming binary coded decimal (BCD) thumbwheel switches 192. The levels can then be detected. In this way, a preset limit for Dose, for example, will be detected and will be used to shut down the infusion pump. For Dose Rate, the preset level is used to switch the position of the diverter valve 32, through the valve driver circuit which will be explained hereinafter. The Patient Volume can also be preset, and the infusion pump can be stopped at the preset limit.

Dose Rate Circuit

The Dose Rate circuit 200, shown in FIG. 10, provides a visual display of the amount of radiation present in the eluate. The Dose Rate circuit 200 employs a Display Controller Circuit, of the type described above. The Dose Rate display is constantly updated to provide the user with Dose Rate information. The Dose Rate circuit 200, with the Display Controller, is programmed to set a trigger level for switching the eluate from waste to the patient 56.

The Dose Rate circuit 200 uses signals from the Multiplier-Divider circuit 160, described above, and from the Control Board which will be described hereinafter. The dose corrected output pulses on line 186 from the Multiplier-Divider circuit 160 described above (i.e., 1 pulse/.01/mCi) enter the Dose Rate circuit 200, and are double buffered by buffers 202, 204. The buffered pulses are then fed through one-half of a one-shot 206, comprised of a CD4098BE integrated circuit in the preferred embodiment of the invention. The output from the one-shot 206 is gated through NAND gate 207 to the Dose Rate Display 104 since there are three Display Controller Circuits 190, which are used for Dose (circuit "A"), Dose Rate (circuit "B"), and Patient Volume (circuit "C"), the designation "B10" at the output of NAND gate 207 means pin 10 on input connector 197 (see FIG. 9).

The heart of the Dose Rate circuit 200 is an Intersil ICM7207A Oscillator Controller integrated circuit 208. This unit, along with a dual one-shot comprised of a CD4098BE integrated circuit 210, in the preferred embodiment of the invention, provides all of the control necessary for gating, storing,

and resetting the display.

The outputs of the Dose Rate Display Controller Circuit provide an easy interface to determine when a predetermined count (corresponding to the dose rate which was set on thumbwheel switches 102) has been reached, and to generate a signal which is used to enable the Dose and Patient Volume Displays, 100, 96, respectively.

In the preferred embodiment of the invention, the signal utilized to enable the Dose and Patient Volume Displays 100, 96, respectively, is derived from one half of a dual D-type flip-flop, such as a CD4013BE integrated circuit 212. The flip-flop 212 is only enabled during an injection. The enabling "INJECT" signal is generated when the pump is injecting. Once an injection is started and a user pre-set Dose Rate limit set on thumbwheel switches 102 is met, the flip-flop 212 latches a positive Q output to enable the Dose Display and the Patient Volume Display.

Control Circuit

Referring now to FIG. 11, the schematic diagram of the Control circuit 220 is shown. The purpose of the Control circuit 220 is to "oversee" all other operations. Specifically, the Control circuit 220 controls the Dose Display and Patient Volume Display. The Control circuit 220 also provides timing for resetting the Multiplier-Divider circuit 160, and it buffers various inputs and outputs to and from the infusion pump control module 60.

The basic function for turning the infusion pump off is the End of Elution signal. The End of Elution signal is derived from either the Dose Display 100 or the Patient Volume Display 96.

These displays 100, 96 are gated to begin counting once the Dose Rate trigger level, the Q output from flip-flop 212, reaches its preset limit, as defined by the Dose Rate thumbwheel switches 102. Then, once the Dose or Patient Volume is met, as defined by the Dose thumbwheel switches 98 and by the Patient Volume thumbwheel switches 94, respectively, the Control circuit 220 signals the pump to stop.

Valve Driver Circuit

The Valve Driver circuit 230, shown schematically in FIG. 12, is used to control the switching of the diverter valves 32, 33 which direct the eluate either to the patient 56 or to waste. The Valve Driver circuit 230 accepts its input from the infusion pump controller or from the Patient Line Purge Switch 110. The Patient Line Purge Switch 110 directly controls the valves 32, 33.

The diverter valves 32, 33 are two position valves which include electrical switches which close individually when the valves 32, 33 are fully in one of their two positions, i.e., either the patient or waste position for valve 32. Movement of the valves 32, 33 from one position to the other is controlled by an AC motor which includes two windings. When the first winding is energized, the motor moves in a clockwise direction. When the second winding is energized, the motor moves in a counterclockwise direction. In the preferred embodiment, one motor controls both diverter valves 32, 33. At each limit of the valves' movement, there is a microswitch 232, 234 which senses when the valve limit has been reached.

When one of the microswitches 232, 234 is

open, i.e. switch 232, the input to an associated inverter 236 is essentially at ground. When the switch 232 closes, the input to the inverter 236 increases to approximately five volts. After the switch 232 again opens, it takes some time, due to the RC time constant of the associated resistors and capacitor, before the voltage at the input of the first inverter 236 returns to approximately zero. Accordingly, the combination of inverters and the RC network to which each of the switches 232, 234 are connected acts as a switch debouncer. Thus, the output of inverter 238 will be low when switch 232 is closed and high when switch 232 is opened. Similarly, the output of inverter 240 will be low when switch 234 is closed and high when switch 234 is opened.

NAND gate 242 normally has a high output voltage. Accordingly, as will be obvious to those of ordinary skill in the digital circuitry art, LED 106 will be on when switch 232 is closed. Otherwise, LED 106 will be off. Similarly, LED 108 will be on when switch 234 is closed. Note that these LEDs 106, 108 were previously described with reference to the dosimetry controller 62 (See FIG. 3).

When both switches 232, 234 are opened at the same time, there will be two high signals at the input of NAND gate 254. That will cause NAND gate 256 to trigger a monostable multivibrator comprised of one half of a CD4098BE integrated circuit 258 which provides a low going output pulse having a duration of approximately 700 milliseconds in the preferred embodiment of the invention. The particular time period during which this pulse is low must exceed the time period which it would take

for the diverter valves 32, 33 to be moved from one position to the other position. In the preferred embodiment of the invention the movement of the diverter valves 32, 33 takes approximately 600 milliseconds. The outputs from the monostable multivibrator are fed via EXCLUSIVE OR gate 260 into a D-type flip-flop 262 comprised of a CD4013BE integrated circuit. In the event that the diverter valves 32, 33 did not move from one position to the other within the prescribed time period, it is presumed that a fault condition occurred, e.g. one of the diverter valves 32, 33 jammed. Accordingly, the operator is advised of the fault condition by both LEDs 106, 108 flashing simultaneously. The flashing occurs as a result of the output of the flip-flop 262 which is connected on line 264 to NAND gate 242 being kept high, thereby causing NAND gate 242 to act as an astable multivibrator which oscillates between high and low outputs thereby causing the EXCLUSIVE OR gates 248, 250 to change states and to flash the LEDs 106, 108.

At the same time that one output of the flip-flop 262 goes high, the other output, on line 266 goes low. The signal on line 266 is normally high, as it is one input to NAND gate 268. The other input to NAND gate 268 is the "End of Elution" signal previously discussed. When both inputs to NAND gate 268 are high the output on line 270 is high. The output signal on line 270 turns off the infusion pump when it is low. This is the signal which remotely controls the infusion pump, as heretofore described. Thus, in the fault condition, when the signal on line 266 goes low the infusion pump is turned off. When there is no fault condition, the infusion pump will be enabled

when the End of Elution signal is high.

The "INJECT" line which indicates when the pump is injecting enters the Valve Controller Circuit 230 on line 252. A series of inverters are used to buffer the INJECT signal in order to obtain an output on line 253. The output on line 253 is used as the input to a pair of solid state relays (not shown) which select between the two windings of the motor which drives the diverter valves 32, 33. Thus, when the INJECT line is low the motor drives the diverter valves 32, 33 into the Patient position, and when the INJECT line is high, the motor drives the diverter valves 32, 33 into the Waste position.

What we claim is:

1. A strontium-rubidium infusion system comprising:

(a) means for generating rubidium-82 in a solution which can be infused into a patient;

(b) means for collecting a predefined volume of solution containing rubidium-82;

(c) means for measuring the radioactivity present in said predefined volume before it is infused into said patient; and

(d) means for quickly infusing said predefined volume of rubidium-82 into said patient as a single bolus.

2. The strontium-rubidium infusion system of Claim 1 wherein said means for generating rubidium-82 in a solution which can be infused into a patient comprises a strontium-rubidium generator.

3. The strontium-rubidium infusion system of Claim 1 or 2 wherein said means for infusing said solution into a patient comprises a syringe.

4. The strontium-rubidium infusion system of Claim 3 wherein said means for infusing said solution into a patient further comprises means for electromechanically operating said syringe.

5. The strontium-rubidium infusion system of Claim 4 wherein said means for electromechanically operating said syringe comprises a stepper motor which drives means for moving the plunger of said syringe.

6. The strontium-rubidium infusion system of Claim 5 further comprising electronic means for controlling said stepper motor.

7. The strontium-rubidium infusion system of any one of Claims 1 to 6 wherein said means for measuring the radioactivity present in said solution as it is infused into said patient comprises a dosimetry system.

8. The strontium-rubidium infusion system of Claim 7 wherein said dosimetry system is connected to means for controlling said means for infusing.

9. The strontium-rubidium infusion system of any one of Claims 1 to 8 wherein said means for quickly infusing said predefined volume of rubidium-82 into said patient as a single bolus comprises a manually operated wash syringe.

10. The strontium-rubidium infusion system of Claim 9 wherein said manually operated wash syringe is initially filled with saline solution.

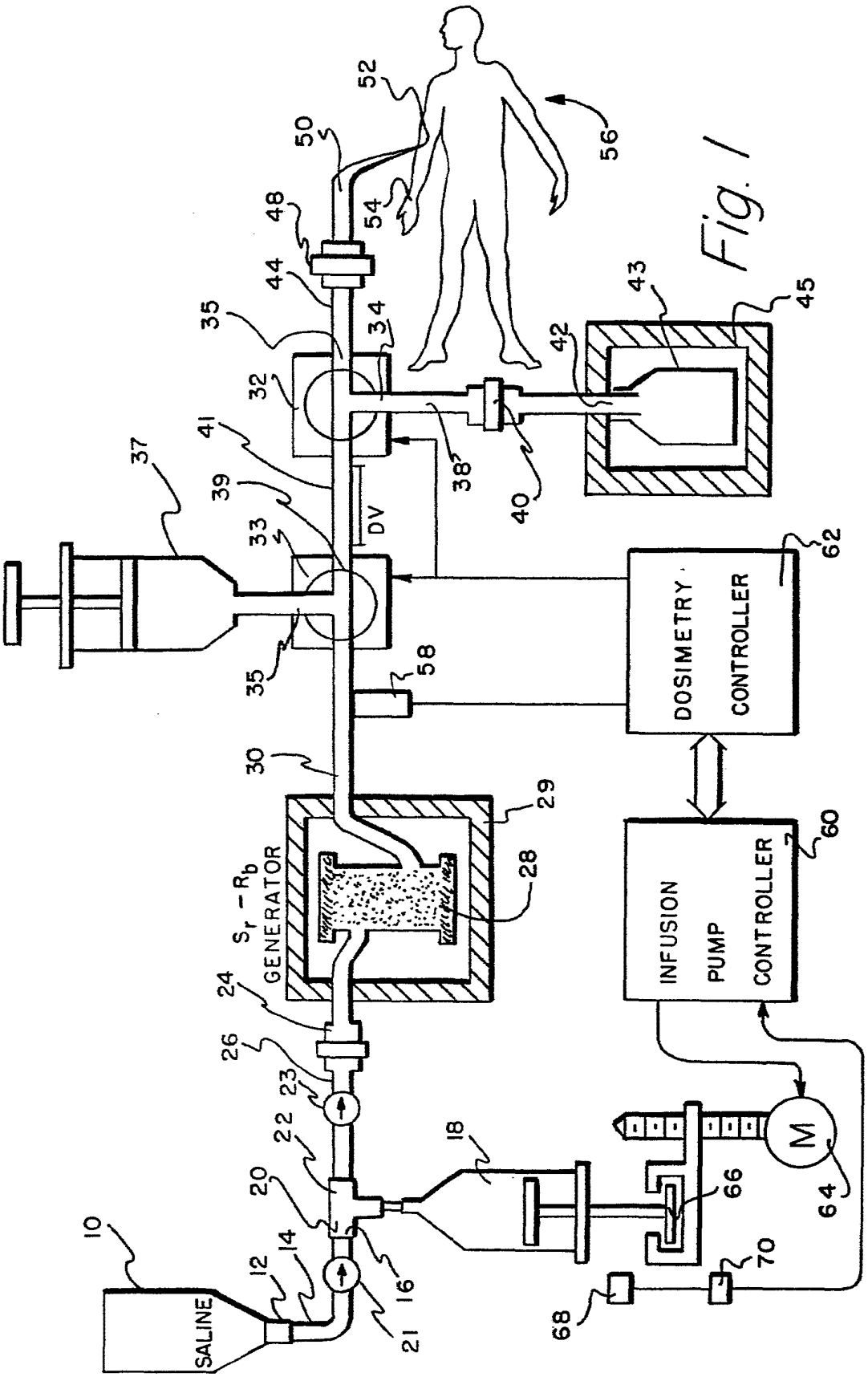
SALINE
10
12
14
16
18
20
21
22
23
24
26
28
29
30
32
33
34
35
37
38
39
40
41
42
43
44
45
48
50
52
54
56
58
60
62
64
66
68
70
DV
$S_r - R_b$ GENERATOR
DOSIMETRY CONTROLLER
INFUSION PUMP CONTROLLER
M

Fig. 1

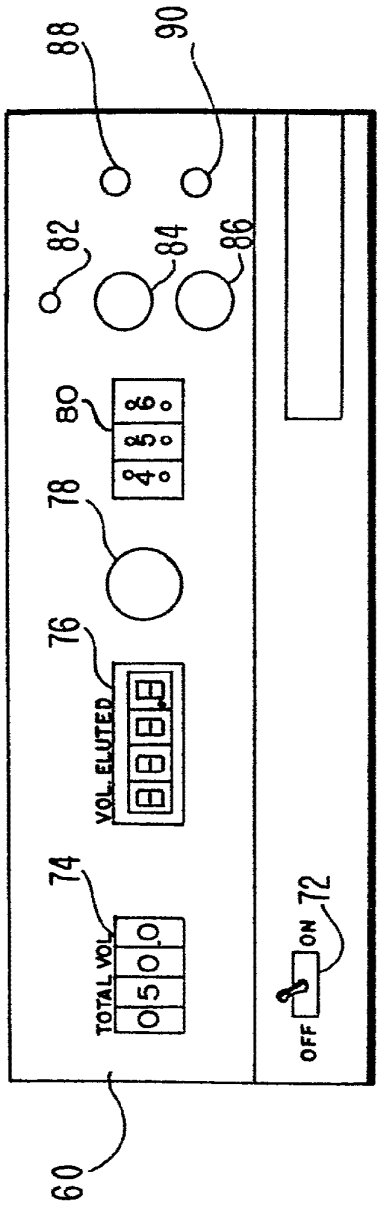
88
90
82
84
86
80
78
76
VOL. ELUTED
74
TOTAL VOL
0500
OFF
ON
72
60

Fig. 2

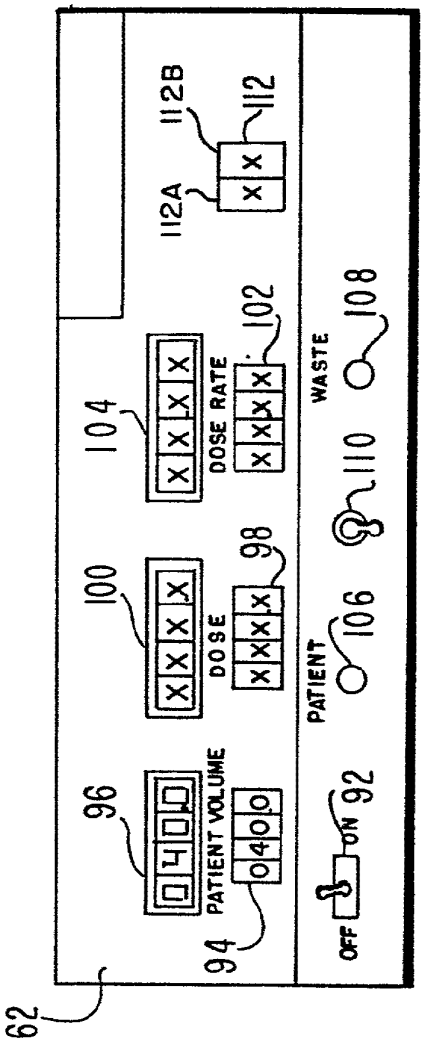
112B
112A
112
104
DOSE RATE
102
108
WASTE
110
100
DOSE
98
PATIENT
106
96
PATIENT VOLUME
0400
94
OFF
ON
92
62

Fig. 3

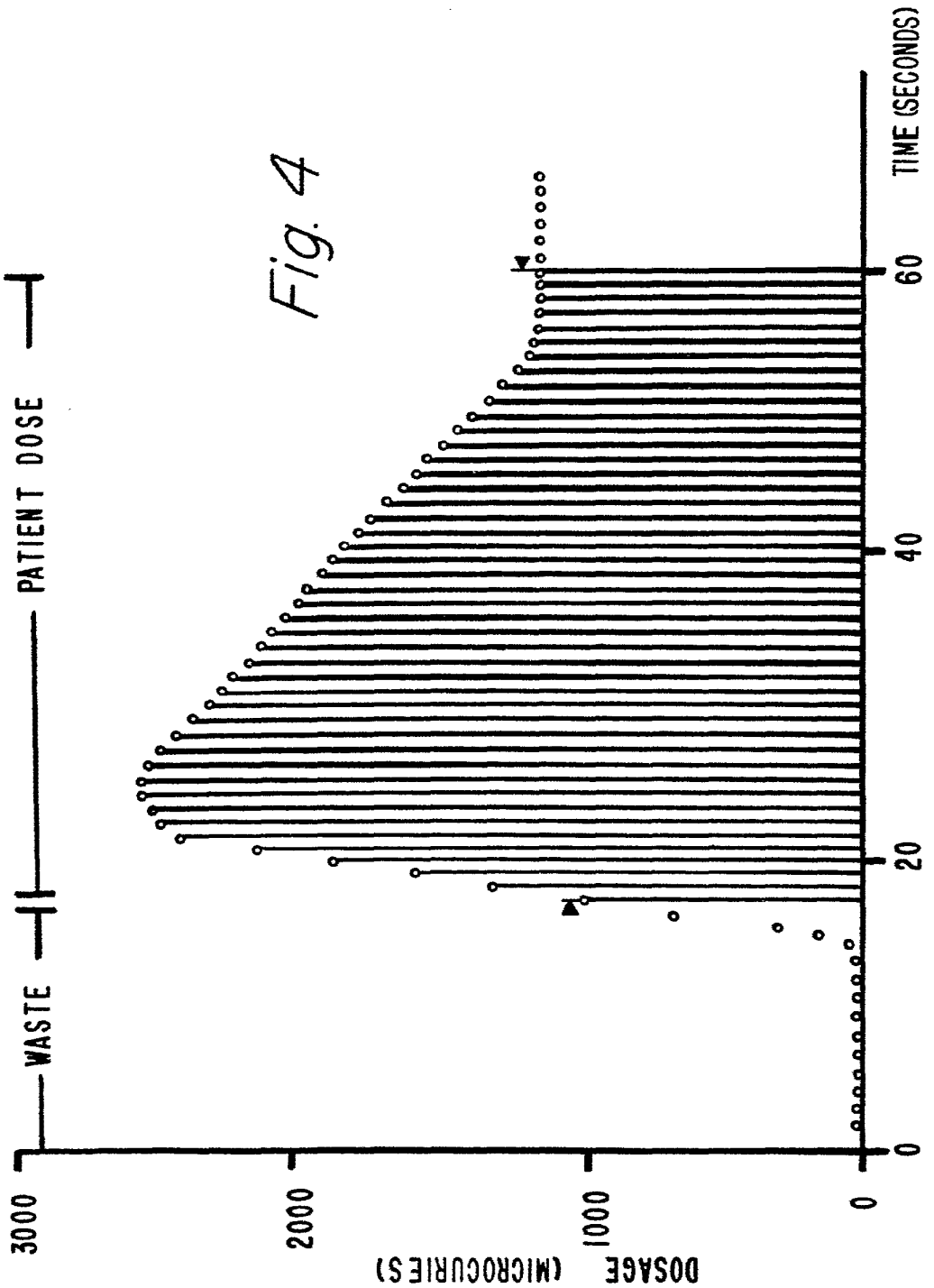
WASTE
PATIENT DOSE
3000
2000
1000
0
DOSAGE (MICROCURIES)
0
20
40
60
TIME (SECONDS)

Fig. 4

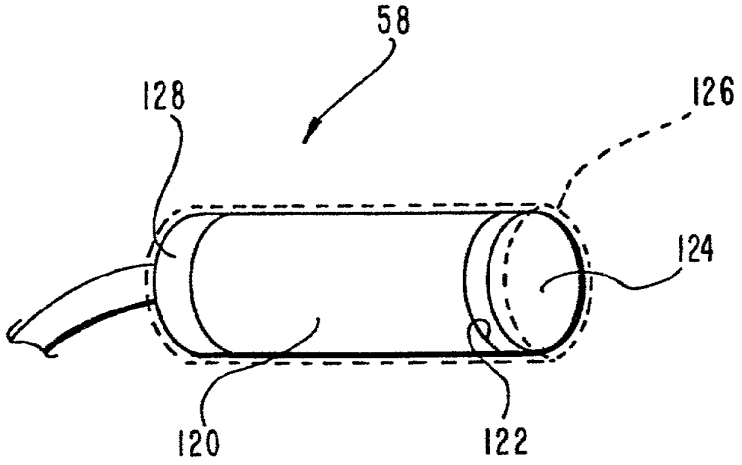
58
128
126
124
120
122

Fig. 5

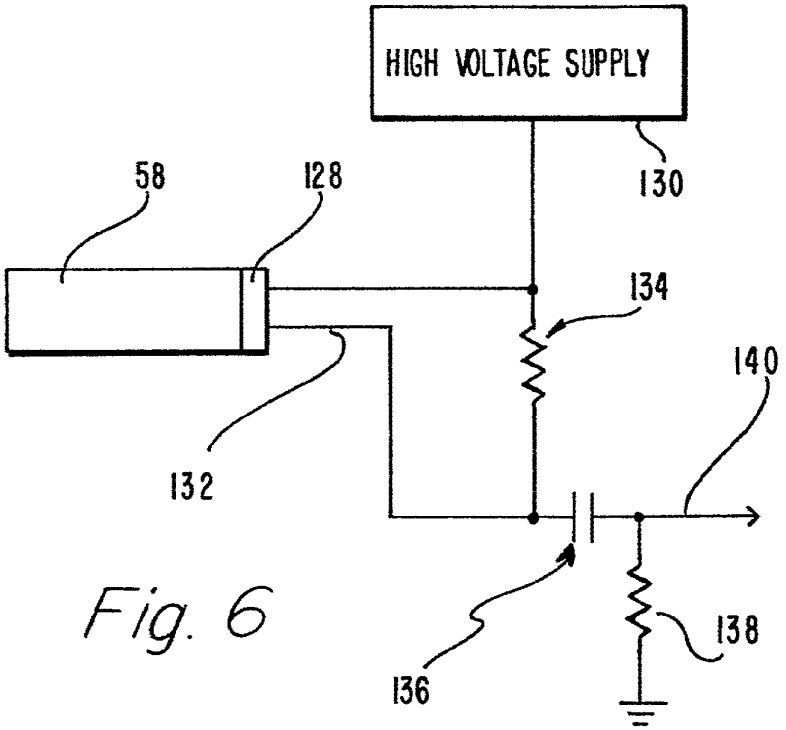
HIGH VOLTAGE SUPPLY
130
58
128
134
140
132
136
138

Fig. 6

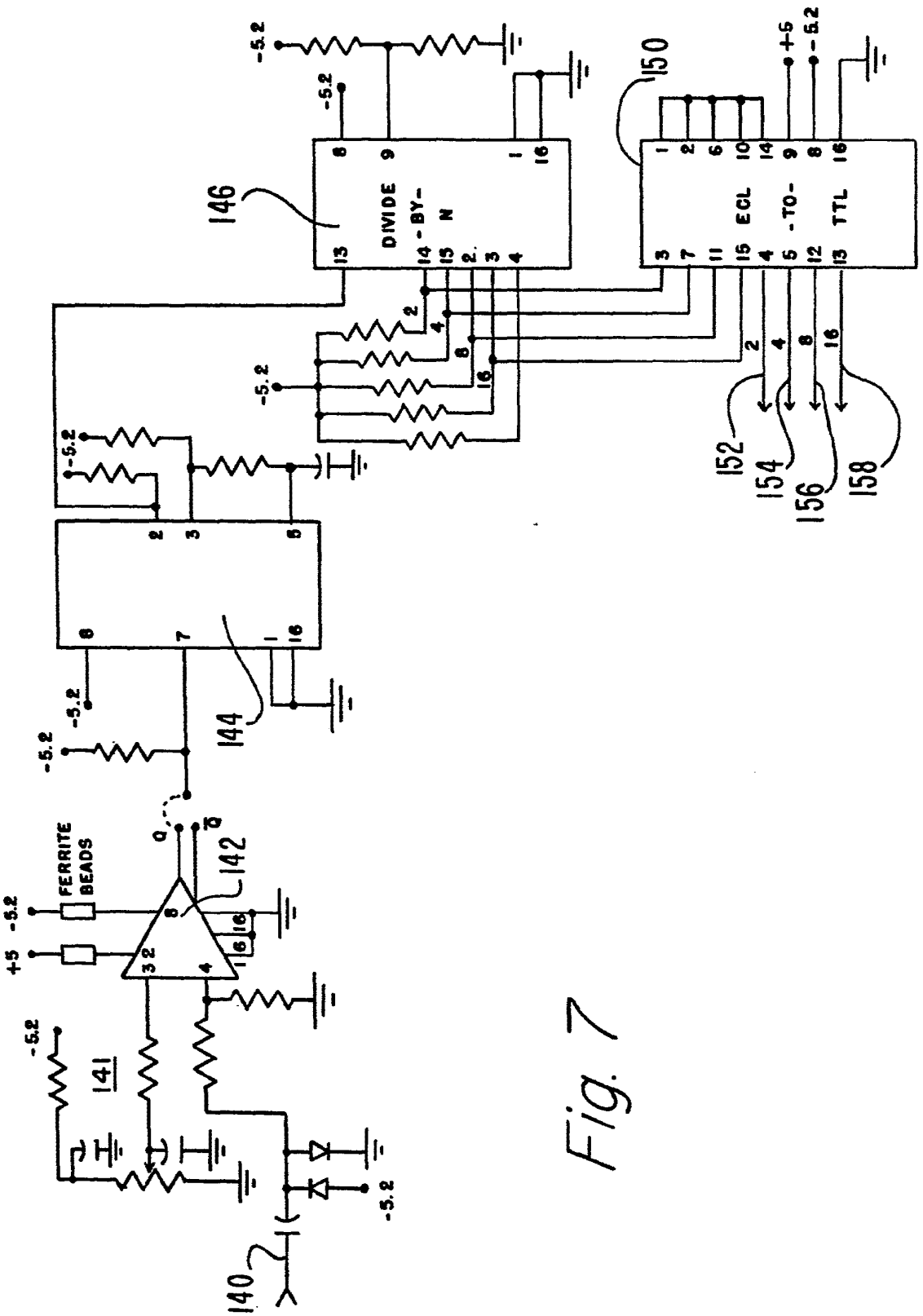
-5.2
146
DIVIDE -BY- N
150
ECL -TO- TTL
+5
152
154
156
158
144
142
FERRITE BEADS
141
140

Fig. 7

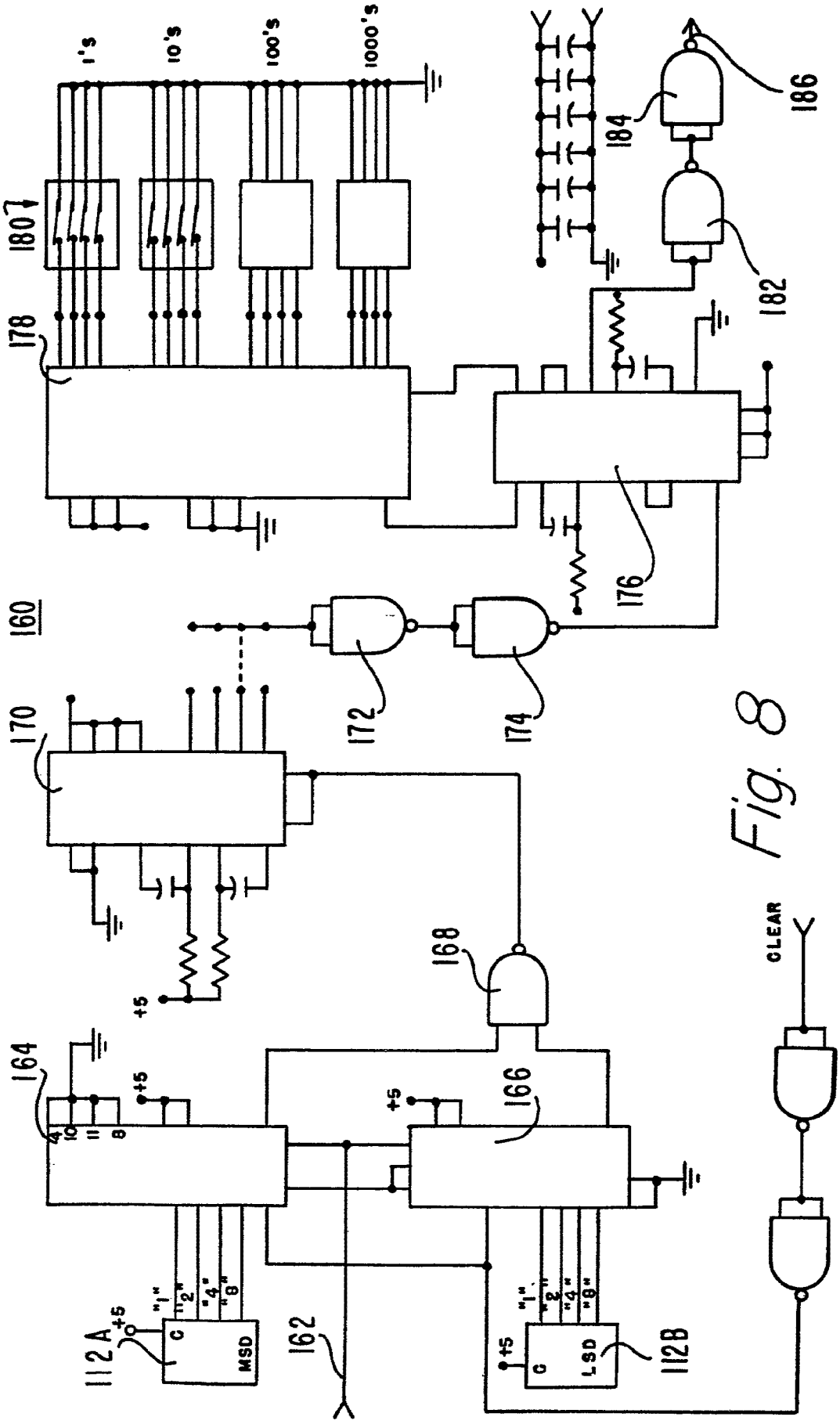
1's
10's
100's
1000's
180
178
184
186
182
176
160
172
174
170
168
164
166
162
112A
112B
MSD
LSD
CLEAR
+5
"1"
"2"
"4"
"8"

Fig. 8

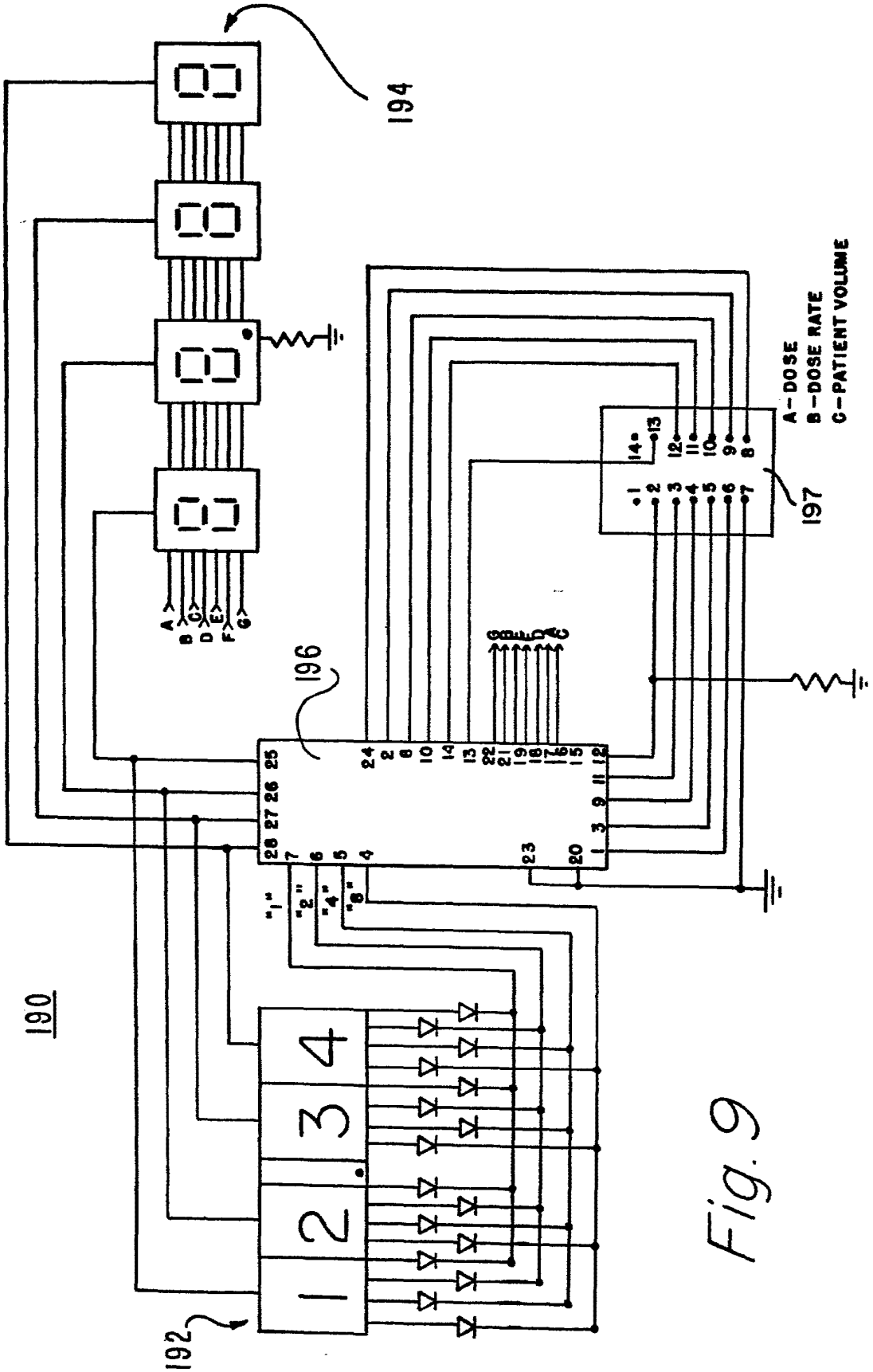
194
A
B
C
D
E
F
G
196
24 2 6 10 14 13 22 21 19 18 17 15
25 26 27 28
12 11 9 3 1
7 6 5 4
23 20
"1"
"2"
"4"
"8"
190
192
1
2
3
4
197
A-DOSE
B-DOSE RATE
C-PATIENT VOLUME

Fig. 9

0160303

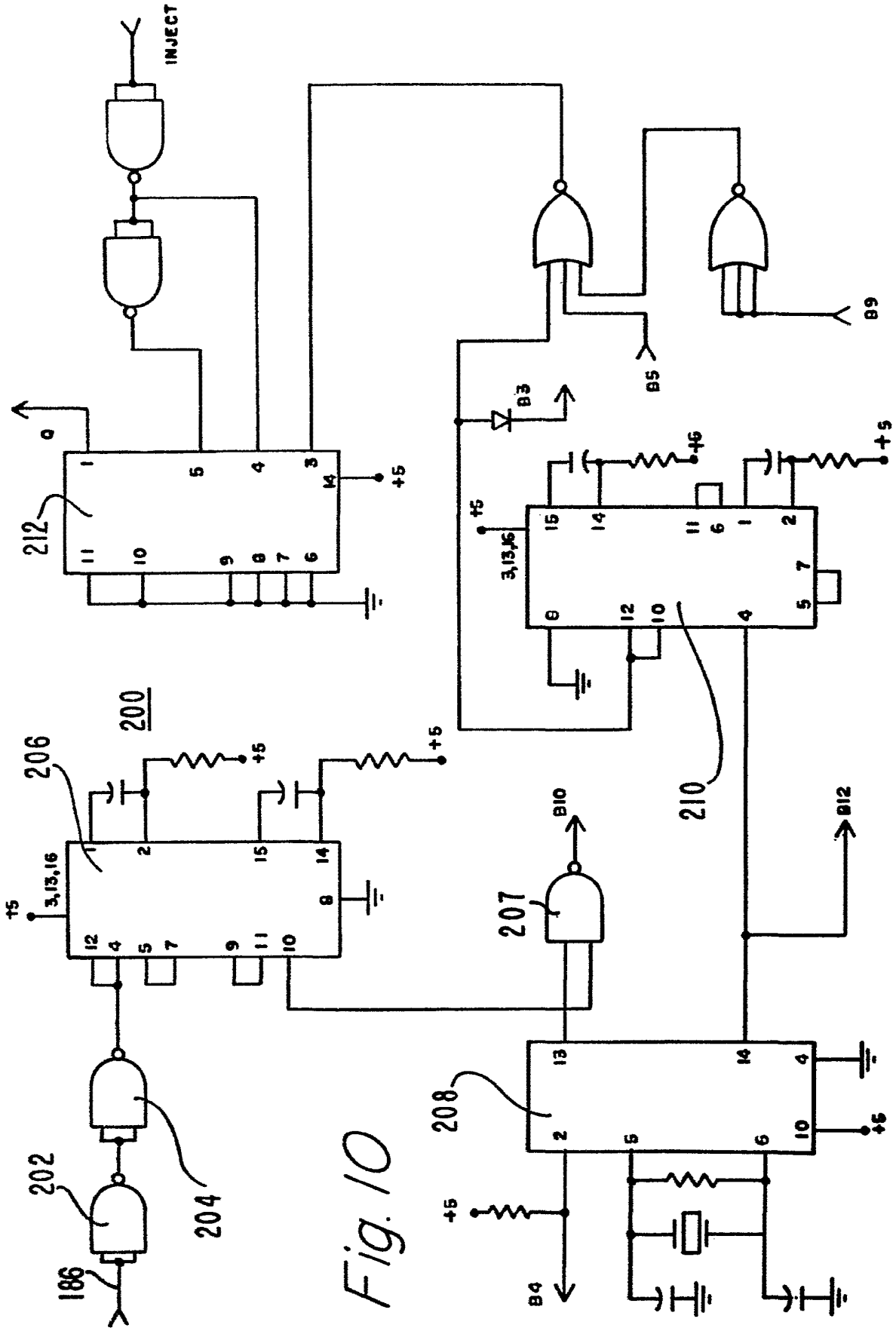

Fig. 10

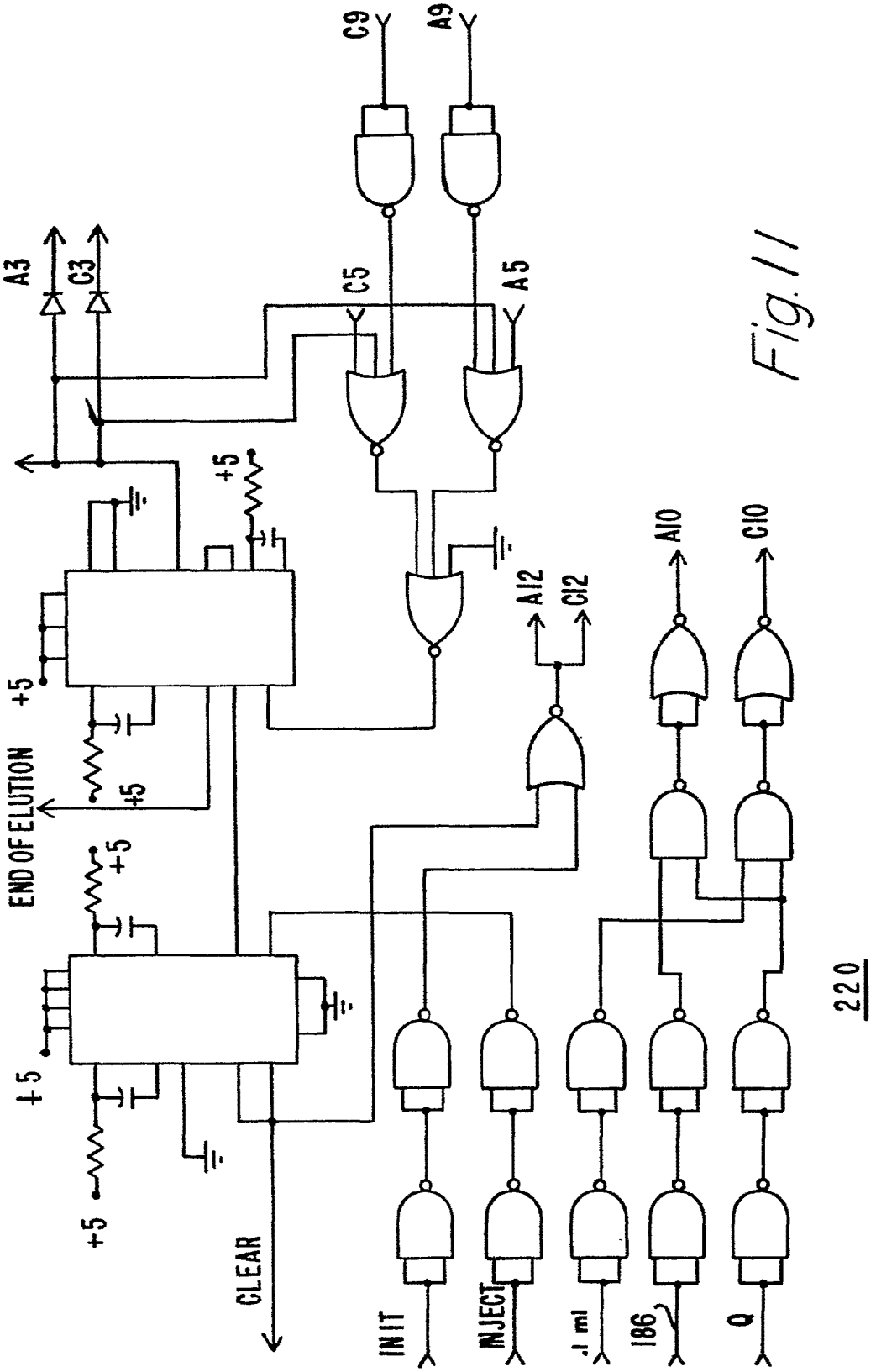
C9
A9
A3
C3
C5
A5
+5
A12
C12
A10
C10
END OF ELUTION
+5
+5
+5
+5
CLEAR
INIT
INJECT
.1 ml
186
Q
220

Fig. 11

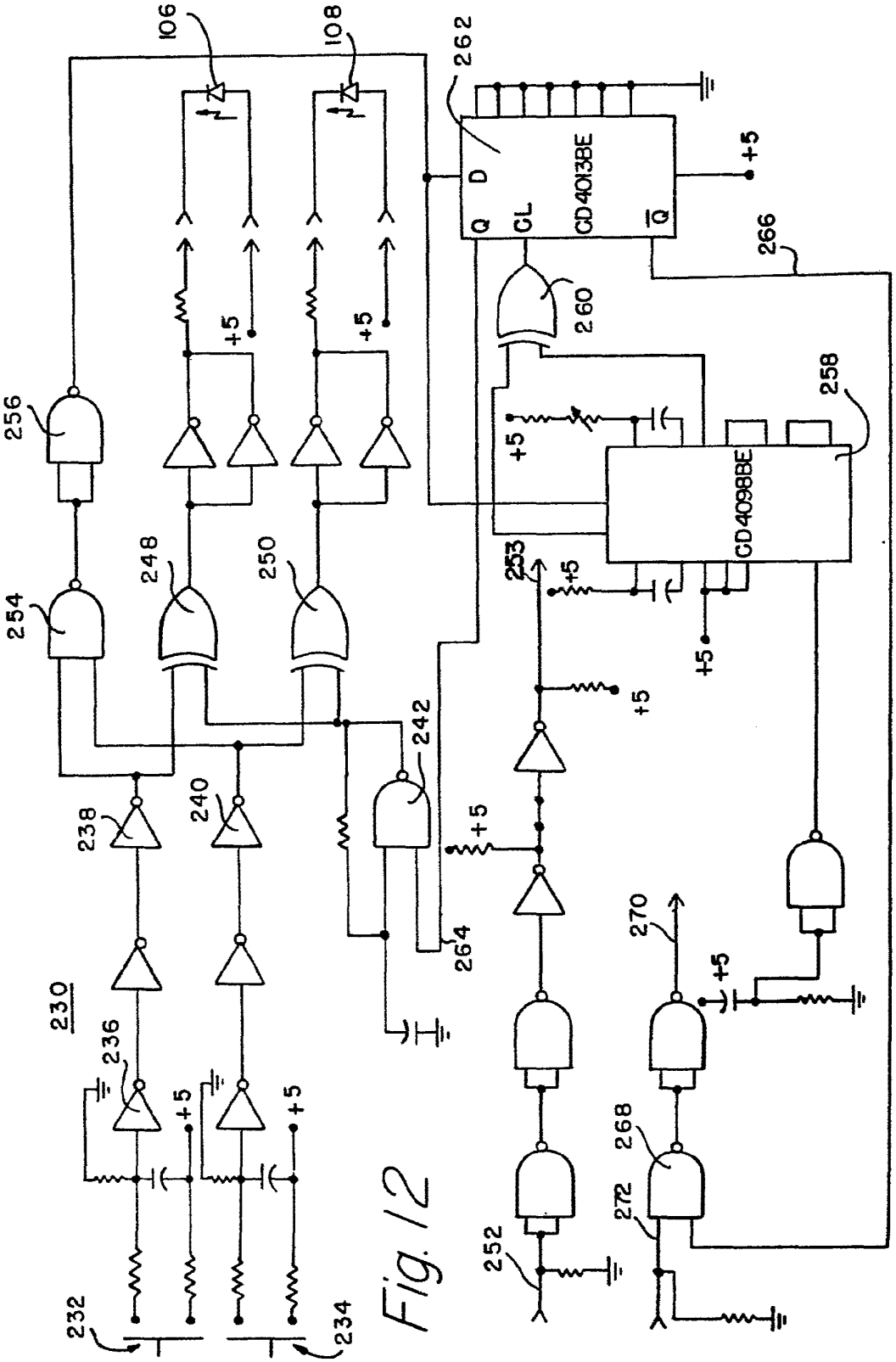
106
108
262
CD4013BE
D
Q
CL
Q̄
+5
266
260
256
258
CD4098BE
248
250
254
253
242
238
240
264
230
236
232
234
270
268
272
252

Fig. 12

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(54) Dosimetry system for strontium-rubidium infusion pump.

(57) The dosimetry system used with a strontium-rubidium infusion system is a very high speed circuit capable of measuring the radioactive dosage infused into a patient in real time. The dosimetry system is capable of receiving very short duration input pulses generated by a photomultiplier tube in response to the presence of radioactivity.

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DOSIMETRY SYSTEM FOR STRONTIUM-RUBIDIUM INFUSION PUMP

The present invention relates to a strontium-rubidium infusion system. In particular, it relates to a strontium-rubidium infusion system which has an in-line, real time dosimetry system which can be used to infuse patients with Rubidium-82.

Current statistics show that approximately one-third of all deaths in the United States are related to coronary artery disease. See, for example, Pohost, G., McKusick, K., and Strauss, W., "Physiologic Basis and Utility of Myocardial Perfusion Imaging" Proceedings of the Second International Symposium on Radiopharmaceuticals, Society of Nuclear Medicine, New York 1979, pp. 465-473, and this fact has prompted extensive research to more efficiently diagnose and manage this disease. Recent advances in radiopharmaceutical development and instrument design have established myocardial scintigraphy as an important new approach for evaluating coronary artery disease and myocardial perfusion. See, for example, Pierson, R., Friedman, M., Tansley, W., Castellana, F., Enlander, D., and Huang, P., "Cardiovascular Nuclear Medicine: An Overview", Sem. Nucl. Med., 9, 224-240 (1979); Leppo, J., Scheuer, J., Pohost, G., Freeman, L., and Strauss, H., "The Evaluation of Ischemic Heart Disease Thallium-201 with Comments on Radionuclide Angiography": Sem. Nucl. Med., 10, 115-126 (1980); Vogel, R., "Quantitative Aspects of Myocardial Perfusion Imaging", Sem. Nucl. Med., 10, 146-156 (1980); Chervu, R., "Radiopharmaceuticals in Cardiovascular Nuclear Medicine", Sem. Nucl. Med., 9, 241-256 (1979); and Pitt, B., and Strauss, H., "Cardiovascular Nuclear Medicine", Sem. Nucl. Med., 7, 3-6 (1977).

Myocardial scintigraphy studies have been performed with several isotopes of potassium, rubidium, cesium, and thallium (T1-201), although the usefulness of all of these nuclides is limited by their non-optimal physical properties. In spite of its long half-life and low-gamma energy, T1-201 is currently the most widely used agent for myocardial imaging. See, for example, Poe, N., "Rationale and Radiopharmaceuticals for Myocardial Imaging", Sem. Nucl. Med., 7, 7-14 (1977); Strauss, H. and Pitt, B., "Thallium-201 as a Myocardial Imaging Agent", Sem. Nucl. Med., 7, 49-58 (1977); Botvinick, E., Dunn, R., Hattner, R., and Massie, B., "A Consideration of Factors Affecting the Diagnostic Accuracy of T1-201 Myocardial Perfusion Scintigraphy in Detecting Coronary Artery Disease", Sem. Nucl. Med., 10, 157-167 (1980); and Wackers, F., "Thallium-201 Myocardial Scintigraphy in Acute Myocardial Infarction and Ischemia", Sem. Nucl. Med., 10, 127-145 (1980).

In diagnostic procedures in which the heart is involved, it is desirable for a diagnostician to be able to view a patient's heart. Heretofore, various radioactive materials have been used together with radiological procedures for viewing internal organs of patients. It has been difficult, however, to view a heart because the radioactive substances which could be used for viewing the heart have had a very long half-life. Thus, using them with patients involves an element of danger and also reduces the number of times that a patient could be infused within any given time period. It would therefore be desirable to have a diagnostic apparatus and procedure which could be used with relative safety for viewing the heart.

Rubidium-82 is a potassium analog. That means it acts similar to potassium when it is infused into a patient. Thus it builds up at a very rapid rate, i.e., within seconds, in the patient's heart. Rubidium-82 also has the advantage of having a very short half-life, approximately 76 seconds. Therefore, it decays after a very short period of time following entry into the body, thereby allowing numerous procedures to be performed within a relatively short time period in a given patient. Rubidium-82 also has the advantage of being observable using a modified gamma camera such as a gamma camera of the type manufactured by Searle Radiographics, Inc., called the PHO Gamma IV. A problem with using Rubidium-82 in a patient involves keeping track of the amount of radiation infused into the patient. In view of the very short half-life of Rubidium-82, it is impractical to measure the radioactivity of a particular dose and to then infuse it into the patient using conventional means. An accurate method for measuring the amount of radiation being infused into the patient would be highly desirable for this particular application.

The availability of improved instrumentation has stimulated interest in the use of the positron emitter, Rubidium-82, for myocardial imaging. See for example, Beller G., and Smith, T., "Radionuclide Techniques in the Assessment of Myocardial Ischemia and Infarction," Circulation, 53 (3, Supp. 1) 123-125 (1976); Budinger, T., Yano, Y., Derenzo, S., et al., "Myocardial Uptake of Rubidium-82 Using Positron Emission Tomography," J., Nucl. Med. 20, 603 (1979); Budinger, T., Yano, Y., Derenzo, S., et al., "Infarction Sizing and Myocardial Perfusion Measurements Using Rb-82 and Positron Emission Tomography," Amer. J. Cardiol., 45, 399 (1980). Rubidium-82, an analog of the alkali metal potassium, is rapidly cleared from the blood and concentrated by the myocardium. The short half-life of the Rubidium-82 (76 sec) offers

the unique advantage of permitting repeat perfusion and blood flow studies in patients whose clinical status is rapidly changing.

Rubidium-82 is produced by the decay of its parent, strontium-82. E. R. Squibb and Sons, Inc. has developed a Rubidium-82 generator and infusion system which yields an isotonic saline solution of Rubidium-82 at physiological pH for rapid administration. In animal experiments, the safety and myocardial uptake of Rubidium-82 has been demonstrated. Therefore this agent has been selected as a candidate for clinical trials.

In the Drawing:

FIG. 1 is an overall schematic diagram of the strontium-rubidium infusion system used in conjunction with the present invention;

FIG. 2 is a front view of the infusion pump control used with the strontium-rubidium infusion system;

FIG. 3 is a front view of the dosimetry control used with the strontium-rubidium infusion system;

FIG. 4 is a graph of radioactivity measured (on the y-axis) by the dosimeter probe versus time (on the x-axis);

FIG. 5 is a perspective view of the dosimetry probe;

FIG. 6 is a schematic diagram of the interface between the dosimetry probe of FIG. 4 and the dosimetry control circuitry;

FIG. 7 is a schematic diagram of the circuit for the Single Channel Analyzer used to convert and

No. 156,285, entitled ^{82}RB GENERATING METHOD AND ELUENT, filed on June 4, 1980 by Rudi D. Neirinckx, et al.

Saline pumped through the strontium-rubidium generator 28 exits the generator 28 through tubing 30 containing Rubidium-82. The tubing 30 is connected to a diverter valve 32 having a first arm 34 which leads through tubing 38, an antibacterial filter 40, and ultimately to waste 42. A second arm 35 of the diverter valve 32 is connected through tubing 44, an antibacterial filter 48, additional tubing 50, and into an infusion needle 52. The infusion needle 52 is typically inserted into the arm 54 of a patient 56.

In the preferred embodiment of the invention, the check valve 16 is a dual back check valve of the type made by Beckton Dickenson Inc., and the antibacterial filters are of the type made by Schleicher & Schull as their type FP030/3.

In the operation of the device, the amount of radioactivity in the saline eluted from the strontium-rubidium generator 28 must be measured as it is introduced into the patient 56. Accordingly, a dosimetry probe 58 is placed adjacent to the tubing 30 where it measures the radioactivity of the rubidium-containing saline as it leaves the generator 28 and enters the diverter valve 32.

In order to use the infusion system, various procedures must be performed and controlled. In particular, the syringe 18 must be purged of air, and filled with saline, and the diverter valve 32 must be positioned. These operations are contingent upon a number of factors including the total volume to be infused into the patient 56, the total dosage to be infused into the patient 56, the minimum radioactivity which must be present in the tubing 30 before any eluate is infused into the patient 56, the total volume to be infused (Note: The total volume eluted may differ from the total volume infused into the patient 56 as some volume is likely to be diverted to waste.)

The foregoing parameters may be altered from the front panel of two different controllers shown in FIGS. 2 and 3. These are the infusion pump controller 60 and the dosimetry controller 62, repectively. The infusion pump controller 60 controls the mechanical movement of the syringe's plunger 66 via a stepping motor 64 which is connected to the plunger 66.

In the preferred embodiment of the invention, the syringe 18 is a sterile, disposable plastic syringe of the type made by Sherwood Medical and designated as Part. No. 881-514031. The infusion pump controller 60 limits the movement of the syringe plunger 66 based upon optical limit detectors 68, 70 which limit the fully displaced and fully extended positions of the plunger 66, respectively. The volume control function performed by the infusion pump controller 60 is accomplished by counting the number of pulses sent to the stepping motor 64.

With reference to FIG. 2, the front panel of the infusion pump controller 60 is shown. The infusion pump controller 60 includes an on/off power switch 72 which is used to turn on the power to the unit.

A set of thumbwheel switches 74 is used to select the total volume (ml) to be eluted. An LED display 76 shows the total volume (ml) which has been eluted. A momentary contact push-button switch 78 is used to start and to stop the movement of the plunger 66 in the forward (inject) direction.

A set of push-button potentiometers comprise the Flow Rate Control 80 which is used to determine the volume per unit time which is infused. The Flow Rate Control 80 sets the pulse rate into the stepping motor 64. An LED 82 lights when the end of travel of the plunger 66, as indicated by the optical limit detectors 68, 70 is reached. A pair of momentary contact push-button switches 84, 86 are used to control the purge and refill functions, respectively, of the syringe 18. Thus, if the purge

control switch 84 is pushed, and held, the plunger 66 continues to move in the forward direction until it reaches the forward limit detector 68. Similarly, while the refill control switch 84 is pressed and held, the plunger 66 continues to move toward the rear limit detector 70. The speed of movement of the plunger 66 during purge and refill operations are controlled by adjustable screw-type potentiometers 88, 90, respectively.

The infusion pump controller 60 is comprised of a Superior Electric Company STM103 Translator Module which is interfaced to provide signals representative of flow rate, volume eluted, and injection. It is also interfaced to be remotely controlled. A pulse called "INIT" indicates that the Translator Module has been powered. The "INIT" pulse is used to reset the displays on the dosimetry module. An "INJECT" signal indicates that the pump is injecting. Output pulses, corresponding to .1 ml steps of the syringe 18, are provided. An "End of Elution" signal is used to remotely disable the infusion pump controller 60.

With reference now to FIG. 3, the dosimetry controller 62, is comprised of a number of LED displays and thumbwheel switch sets. In addition, the dosimetry controller 62 includes an on/off switch 92 for providing power to the unit.

The first set of thumbwheel switches 94 is used to set the volume (ml) to be infused into the patient 56. The LED display 96, immediately above the thumbwheel switches 94, displays the volume of eluate which has been infused into the patient 56.

The thumbwheel switches 98 are used to set the total dose (mCi) which is to be infused into the patent 56 and the LED display 100 immediately above the total dose thumbwheel switches 98 displays the total dose which has been infused into the patient 56. Similarly, the thumbwheel switches 102 are used to set the dose rate (mCi sec.) which is to be used to determine when to switch the diverter valve 32 from the waste position to the patient 56 position. The actual dose rate which is present in the eluate within the tube 30 in front of the dosimetry probe 58 is displayed on the LED display 104. The description of the dose present in the eluate at any given time from the start of infusion will be provided hereafter. The dosimetry controller 62 further comprises a pair of LED's 106, 108 which indicate the position of the diverter valve 32. Only one of these two LED'S 106, 108, should be on at any given time.

While the normal position of the diverter valve 32 is toward waste, except when eluate is being infused into a patient 56, provision must be made to clear the tubing 44, 50 of any air prior to infusing a patient 56. Accordingly, the dosimetry controller 62 includes a toggle switch 110 which is used to hard wire the diverter valve 32 in the patient 56 position.

The present preferred embodiment of the invention also includes a set of thumbwheel switches 112 which are used to set the flow rate which will be used in internal calculations of dosimetry controller 62. It is presently anticipated by the inventor that a future version of the present invention will include automatic means for determining the flow rate based upon the settings used in the infusion pump controller 60.

Referring now to FIG. 4, a graph of the radioactive dosage present in the tubing 30 in front of the dosimetry probe 58, is shown. In the graph, the dosage is measured on the y-axis and time is measured on the x-axis. The time is referenced with zero being the time that the start/stop inject button 78 on the infusion controller 60 is pushed to commence infusion.

For approximately 10 seconds there will be no radioactivity present in the eluate from the strontium-rubidium generator 28. Thereafter, the dose rate rises at a rapid rate up to a maximum, after which the dose rate falls to a level value indicative of the steady state regeneration rate of the Sr-Rb generator 28. Thus, when the infusion starts, there is a delay initially as the dose rate builds up, a reduction in dosage after the generator 28 is partially eluted, and then there is a dosage representative of the steady state regeneration rate of the generator 28.

The setting of the dose rate thumbwheel switches 102 tells the dosimetry controller 62 at what point along the upward slope of the dosage curve to switch the diverter valve 32 from the waste position to the patient 56 position whereby the eluate will be infused into the patient 56. At that point the dose indicated by the LED's 100 will start accumulating from zero, where it had been until that point. Similarly, the patient 56 volume indicated by the LED's 96 will start to accumulate as of that time.

Once eluate is infused into the patient 56, it continues to be infused until one of various stop indications occurs. In particular, when the total patient 56 dose, set by the thumbwheel switches 98, is reached, the diverter valve 32 is returned to the waste position, and the stepping motor 64 stops, thereby preventing further infusion. Similarly, the diverter valve 32 is switched, and the stepping motor 64 is stopped when the patient 56 volume, preset by the thumbwheel switches 94 reaches its preset value or after the total volume to be eluted, set by the volume thumbwheel switches 74 reaches its preset value; or when the purge limit optical stop 68 of the syringe 18 is reached; or if the start stop inject button 78 is pushed. Any of the foregoing events causes the diverter valve 32 to

switch to the waste position, and causes the stepping motor 64 to stop. Note, however, that the purge and refill switches 84, 86 are disabled as of the time that the start/stop inject button 78 is pushed to commence the infusion.

Quantizing Radioactivity in a Liquid Stream

In order to measure the radioactivity in the saline solution which passes through the line 30 in front of the dosimetry probe 58, it is necessary to count the number of disintigrations which occur in front of the probe 58, while at the same time keeping track of the flow rate of the saline through the tube 30. Given that these quantities are known, it is possible to measure the total activity in milliCuries (mCi) in accordance with the following formula:

$$A = \frac{(C)(F)}{(V)(E)(CM)(Y)}$$

Where, A = total activity (mCi);
C = net counts;
F = flow rate (ml/min);
V = volume in detector view (ml);
E = net efficiency (counts per minute/disintegration per minute);
CM = disintegrations/minute to milliCurie conversion factor; and
Y = net yield of photon.

In the case of the present invention, the above formula can be simplified to:

$$A = \frac{(C)(F)}{K}$$

Where, A = total activity (in milliCuries);
C = net counts (from probe);
F = the flow rate; and
K = the calibration factor.

As noted, the calibration factor, K, takes into account the volume in the detector's view, the net efficiency of the probe, the conversion factor in terms of disintigrations pet minute to milliCuries, and the net yield of photons. These factors are substantially constant for any given probe and tubing combination for a reasonable amount of time. Accordingly, provision is made on the circuit board to adjust the calibration factor, K, when the instrument is serviced. However, the calibration factor, K, is not user adjustable in the normal course of operation.

Dosimetry Probe

Referring now to FIG. 5, the dosimetry probe 58 is comprised of a photomultiplier tube 120, such as the RCA C83009E 14 mm diameter 10-stage photomultiplier tube manufactured by the Electro Optics Division of RCA Corporation in Lancaster, Pennsylvania. The photomultiplier tube 120 has a face 122 through which input signals in the form of light are received. On the face 122, a plastic scintillator 124, such as a Nuclear Enterprises Type 102A manufactured in Edinburgh, Scotland, is mounted. In the preferred embodiment of the invention, the plastic scintillator 124 is glued or bonded to the face 122 of the photomultiplier tube 120. After the plastic scintillator 124 has been bonded to the face 122 of the photomultiplier tube 120, an aluminum foil covering (not shown) is placed over the face end of the photomultiplier tube 120, including the plastic scintillator 124. The purpose of the aluminum foil covering is to reflect back into the tube 120 any light which scintillates from the plastic scintillator 124 away from the tube 120. In addition, the aluminum foil covering prevents any stray light which might come into the area of the face 122 from getting into the tube 120. Following the application of the aluminum foil, a light tight material, such as black electrical tape is wrapped over the aluminum foil covered tube 120 in order to further prevent any light from entering into the tube 120. The tape-wrapped tube 120 is then inserted into a mu metal shield 126 which is intended to prevent any electromagnetic radiation effects from affecting the output of the dosimetry probe 58. In the preferred embodiment of the invention, the dosimetry probe 58 is plugged into a standard photomultiplier tube socket base 128 containing a standard resistive biasing network.

Dosimetry Circuitry

Referring now to FIG. 6, the photomultiplier tube socket base 128 includes a resistive network containing biasing resistors for placing appropriate bias voltages on the ten dynodes in the photomultiplier tube 120. Accordingly, the high voltage connection to the photomultiplier tube base 128 is automatically biased to provide appropriate operating voltages to the photomultiplier tube 120. The high voltage supply 130 used in the preferred embodiment of the invention is a 0-1000 volt, adjustable Bertan PMT-10A-P power supply manufac-

tured by Bertan Associates, Inc., Three Aerial Way, Syosset, New York. In the present application, the high voltage supply 130 is adjusted to provide an output voltage of 950 volts. The photomultipler tube socket base 128 is an RCA photomultipler tube socket base, part No. AJ2273.

An output signal goes from the dosimetry probe 58 on a line 132 to a coupling network comprising a pull up resistor 134, a coupling capacitor 136, and a output resistor 138. Accordingly, an AC signal having a peak to peak maximum of approximately 250 millivolts with negative going pulses, is provided on output line 140.

Single Channel Analyzer

Referring now to FIG. 7, the schematic diagram for a Single Channel Analyzer circuit is shown. The Single Channel Analyzer is used, because the pulses on output line 140 from the Dosimetry circuitry are very sharply defined pulses which may occur at very high frequencies. In view of the fact that it is important to count all the pulses, a very high speed comparator, such as an AM685 voltage comparator 142, manufactured by Advanced Micro Devices, 901 Thompson Place, Sunnyvale, California, with emitter-coupled logic (ECL) output, or other suitable very high speed comparator, must be used.

A biasing network 141 consisting of a series of resistors and capacitors is used as one input to the comparator 142. In view of the fact that the pulses which are handled by the comparator 142 are of very short duration, a one-shot circuit 144, comprised in the preferred embodiment of the invention, of a Motorola Type 1670 master-slave flip-flop integrated circuit, is used to stretch the pulse width up to a uniform pulse width of approximately 50 nanoseconds. The output signal from the one-shot 144 is fed into a programmable divide-by-N circuit 146, which in the preferred embodiment of the invention is comprised of a Motorola Type 10136 universal hexadecimal counter integrated circuit. The divide-by-N circuit 146 is programmable. Accordingly, a very high pulse repetition rate coming into the comparator with very short pulse widths is reformed by the one-shot to have wider, uniform pulses, and the input signal is further reformed by the divide-by-N circuit to bring the pulse repetition rate down into any desirable range. In particular, outputs of the divide-by-N circuit 146 are provided for N equal to 2, 4, 8, and 16.

Up through this point in the circuit, the devices have all been of ECL type in order to be able to handle the very high speed pulses which are detected by the dosimetry probe 58. In view of the fact that it is conventional to use transistor-transistor-logic (TTL) integrated circuits, a type 10125 ECL-to-TTL level converter circuit 150 is hooked to the output of the divide-by-N circuit 146. Thus, the ECL-to-TTL level converter circuit 150 transforms the ECL signal levels into TTL signal levels for further processing. The TTL outputs leave the ECL-to-TTL level converter circuit 150 on four lines 152, 154, 156, 158, which correspond to the TTL level of the counts into the Single Channel Analyzer divided by 2, 4, 8, and 16, respectively. The counts out on the lines 152-158 will be referred to hereafter as the "net counts".

Multiplier-Divider Circuit

Referring now to FIG. 8, there is a Multiplier-Divider circuit 160 which converts the net counts from the Single Channel Analyzer circuit, described above, into a meaningful quantity (milliCuries). The Multiplier-Divider circuit 160 accepts the "net counts" on an input line 162 which is connected to one of the lines 152-158 from the Single Channel Analyzer (i.e., the raw counts converted into TTL levels and then divided by 2, 4, 8, or 16) and multiplies them by the eluate Flow Rate divided by 100. The result is then divided by a constant, K, in order to carry out the formula:

$$A = \frac{(N)(F)}{K}$$

Where, A = total activity (in milliCuries);
N = net counts (from Single Channel Analyzer);
F = Flow Rate; and
K = the calibration factor.

The net counts, N, are first multiplied by a two digit number corresponding to the eluate Flow Rate (entered on the Flow Rate thumbwheel switches 112A, 112B, corresponding to the most significant digit (MSD) and the least significant digit (LSD), respectively, the thumbwheel switches 112A, 112B are on the front panel of the dosimetry controller 62, shown in FIG. 3. The multiplication is accomplished by cascading two TTL Synchronous Decade Rate Multiplier circuits (F74167), and sending their outputs through a NAND gate 168. The resulting output corresponds to F_{out}, where:

$$F_{out} = \frac{(N)(F)}{100}$$

The output pulses are of varying duration, so they are next fed through a pair of one-shots which process them to have a fixed duration. In the preferred embodiment of the invention, the first one-shot is comprised of one-half of an SN74123 integrated circuit 170. The first one-shot is negative edge triggered, and it provides a pulse output of approximately 200 nanoseconds. Its output is double buffered through buffers 172, 174 into a second one-shot which is comprised of one-half of a CD4098BE integrated circuit 176 in order to increase the width of the output pulses, so they will be acceptable to a CMOS divider integrated circuit 178. The second one-shot is configured to be leading edge triggered.

The output of the second one-shot is then divided by the calibration factor, K, which may have a range of between 3 and 9,999. A CD4059A integrated circuit 178 is used as a programmable divide-by-N counter. Programming is accomplished via a series of 16 DIP switches 180 mounted on the printed circuit card. Each set of four switches corresponds to the BCD settings for 1's, 10's, 100's and 1000's. Pull up resistors (not shown) are employed in the standard manner so that when the DIP switches are open the inputs to the divide-by-N circuit 178 are pulled high.

The output of the divider 178 has pulses of random widths, so another one-shot, made up of the second half of the CD4098BE 176 configured for leading edge triggering, is used. This one-shot provides an output pulse duration of approximately 20 microseconds. Before leaving the Multiplier-Divider circuit 160, the output is double buffered through buffers 182, 184 and the output signal on line 186 is sent to the Dose Rate circuit. There will be one dose corrected output pulse on line 186 for each 0.01 milliCurie of activity which passes by the dosimetry probe 58.

Display Controller Circuit

Referring now to FIG. 9, the schematic diagram for a Display Controller Circuit 190 is shown. There are three Display Controller Circuits within the dosimetry controller 62. Each Display Controller 190 is used both to interface a set of thumbwheel switches 192 and to display the quantity associated with the particular set of thumbwheel switches 192. Thus, there is one Display Controller of 190 for Dose Rate (which works with thumbwheel switches 102 and LEDs 104), one for Patient Volume (which works with thumbwheel switches 94 and LEDs 96), and one for Dose (which works with thumbwheel switches 98 and LEDs 100). Each Display Controller Circuit 190 drives four seven-segment displays 194, such as MAN71 displays.

The major component of the Display Controller Circuit 190 of the preferred embodiment of the invention is an Intersil ICM7217IJI integrated circuit 196, which is a device which provides a direct interface to the seven-segment displays 194. Each Display Controller Circuit 190 allows the user to set a level, by programming binary coded decimal (BCD) thumbwheel switches 192. The levels can then be detected. In this way, a preset limit for Dose, for example, will be detected and will be used to shut down the infusion pump. For Dose Rate, the preset level is used to switch the position of the diverter valve 32, through the valve driver circuit which will be explained hereinafter. The Patient Volume can also be preset, and the infusion pump can be stopped at the preset limit.

Dose Rate Circuit

The Dose Rate circuit 200, shown in FIG. 10, provides a visual display of the amount of radiation present in the eluate. The Dose Rate circuit 200 employs a Display Controller Circuit, of the type described above. The Dose Rate display is constantly updated to provide the user with Dose Rate information. The Dose Rate circuit 200, with the Display Controller, is programmed to set a trigger level for switching the eluate from waste to the patient 56.

The Dose Rate circuit 200 uses signals from the Multiplier-Divider circuit 160, described above, and from the Control Board which will be described hereinafter. The dose corrected output pulses on line 186 from the Multiplier-Divider circuit 160 described above (i.e., 1 pulse/.01 mCi) enter the Dose Rate circuit 200, and are double buffered by buffers 202, 204. The buffered pulses are then fed through one-half of a one-shot 206, comprised of a CD4098BE integrated circuit in the preferred embodiment of the invention. The output from the one-shot 206 is gated through NAND gate 207 to the Dose Rate Display 104 since there are three Display Controller Circuits 190, which are used for Dose (circuit "A"), Dose Rate (circuit "B"), and Patient Volume (circuit "C"), the designation "B10" at the output of NAND gate 207 means pin 10 on input connector 197 (see FIG. 9).

The heart of the Dose Rate circuit 200 is an Intersil ICM7207A Oscillator Controller integrated circuit 208. This unit, along with a dual one-shot comprised of a CD4098BE integrated circuit 210, in the preferred embodiment of the invention, provides all of the control necessary for gating, storing, and resetting the display.

The outputs of the Dose Rate Display Control-

ler Circuit provide an easy interface to determine when a predetermined count (corresponding to the dose rate which was set on thumbwheel switches 102) has been reached, and to generate a signal which is used for switching the diverter valve 32. The valve switching signal is also used to enable the Dose and Patient Volume Displays, 100, 96, respectively.

In the preferred embodiment of the invention, the valve switching signal is derived from one half of a dual D-type flip-flop, such as a CD4013BE integrated circuit 212. The flip-flop 212 is only enabled during an injection, i.e., when the infusion pump is being used to either infuse eluate into a patient 56 or to divert it to waste. The enabling "INJECT" signal is generated when the pump is injecting. Once an injection is started and a user pre-set Dose Rate limit set on thumbwheel switches 102 is met, the flip-flop 212 latches a positive Q output to switch the diverter valve 32 from the waste position to the patient position and to enable the Dose Display and the Patient Volume Display.

Control Circuit

Referring now to FIG. 11, the schematic diagram of the Control circuit 220 is shown. The purpose of the Control circuit 220 is to "oversee" all other operations. Specifically, the Control circuit 220 controls the Dose Display and Patient Volume Display. The Control circuit 220 also provides timing for resetting the Multiplier-Divider circuit 160, and it buffers various inputs and outputs to and from the infusion pump control module 60.

The basic function for turning the infusion pump off is the End of Elution signal. The End of Elution signal is derived from either the Dose Display 100 or the Patient Volume Display 96. These displays 100, 96 are gated to begin counting once the Dose Rate trigger level, the Q output from flip-flop 212, reaches its preset limit, as defined by the Dose Rate thumbwheel switches 102. Then, once the Dose or Patient Volume is met, as defined by the Dose thumbwheel switches 98 and by the Patient Volume thumbwheel switches 94, respectively, the Control circuit 220 signals the pump to stop.

Valve Driver Circuit

The Valve Driver circuit 230, shown schematically in FIG. 12, is used to control the switching of the diverter valve 32 which directs the eluate either to the patient 56 or to waste. The Valve Driver circuit 230 accepts its input from the Dose Rate circuit or from the Patient Line Purge Switch 110. The Patient Line Purge Switch 110 directly controls the valve 32.

The diverter valve 32 is a two position valve which includes electrical switches which close individually when the valve 32 is fully in either the patient or waste position. Movement of the valve 32 from one position to the other is controlled by an AC motor which includes two windings allowing it to be moved in either direction via an AC motor having two windings. When the first winding is energized, the motor moves in a clockwise direction. When the second winding is energized, the motor moves in a counterclockwise direction. At each limit of the valve movement, there is a microswitch 232, 234 which senses when the valve limit has been reached.

When one of the microswitches 232, 234 is open, i.e. switch 232, the input to an associated inverter 236 is essentially at ground. When the switch 232 closes, the input to the inverter 236 increases to approximately five volts. After the switch 232 again opens, it takes some time, due to the RC time constant of the associated resistors and capacitor, before the voltage at the input of the first inverter 236 returns to approximately zero. Accordingly, the combination of inverters and the RC network to which each of the switches 232, 234 are connected acts as a switch debouncer. Thus, the output of inverter 238 will be low when switch 232 is closed and high when switch 232 is opened. Similarly, the output of inverter 240 will be low when switch 234 is closed and high when switch 234 is opened.

NAND gate 242 normally has a high output voltage. Accordingly, as will be obvious to those of ordinary skill in the digital circuitry art, LED 106 will be on when switch 232 is closed. Otherwise, LED 106 will be off. Similarly, LED 108 will be on when switch 234 is closed. Note that these LEDs 106, 108 were previously described with reference to the dosimetry controller 62 (See FIG. 3).

When both switches 232, 234 are opened at the same time, there will be two high signals at the input of NAND gate 254. That will cause NAND gate 256 to trigger a monostable multivibrator comprised of one half of a CD4098BE integrated circuit 258 which provides a low going output pulse having a duration of approximately 700 milliseconds in the preferred embodiment of the invention. The particular time period during which this pulse is low must exceed the time period which it would take for the diverter valve 32 to be moved from one position to the other position. In the preferred embodiment of the invention the movement of the diverter valve 32 takes approximately 600 milliseconds. The outputs from the monostable multivibra-

tor are fed via EXCLUSIVE OR gate 260 into a D-type flip-flop 262 comprised of a CD4013BE integrated circuit. In the event that the diverter valve 32 did not move from one position to the other within the prescribed time period, it is presumed that a fault condition occurred, e.g. the diverter valve 32 jammed. Accordingly, the operator is advised of the fault condition by both LEDs 106, 108 flashing simultaneously. The flashing occurs as a result of the output of the flip-flop 262 which is connected on line 264 to NAND gate 242 being kept high, thereby causing NAND gate 242 to act as an astable multivibrator which oscillates between high and low outputs thereby causing the EXCLUSIVE OR gates 248, 250 to change states and to flash the LEDs 106, 108.

At the same time that one output of the flip-flop 262 goes high, the other output, on line 266 goes low. The signal on line 266 is normally high, as it is one input to NAND gate 268. The other input to NAND gate 268 is the "End of Elution" signal previously discussed. When both inputs to NAND gate 268 are high the output on line 270 is high. The output signal on line 270 turns off the infusion pump when it is low. This is the signal which remotely controls the infusion pump, as heretofore described. Thus, in the fault condition, when the signal on line 266 goes low the infusion pump is turned off. When there is no fault condition, the infusion pump will be enabled when the End of Elution signal is high.

The Q output from the dose rate circuit 200 enters the Valve Controller Circuit 230 on line 252. A series of inverters are used to buffer the Q output in order to obtain an output on line 254. The output on line 254 is used as the input to a pair of solid state relays (not shown) which selects between the two windings of the motor which drives the diverter valve 32. Thus, when the Q output is high the motor drives the diverter valve 32 into the Patient position, and when the Q output is low, the motor drives the diverter valve 32 into the Waste position.

Claims

1. A dosimetry system suitable for use in a strontium-rubidium infusion system comprising means for generating rubidium 82 in a solution which can be infused into a patient; means for infusing said solution into a patient; means for measuring the radioactivity present in said solution as it is infused into said patient; and means for controlling said means for infusing in response to the amount of radioactivity which has been infused into said patient; said dosimetry system comprising:

(a) a photomultiplier tube, having a face through which input signals in the form of light are received;

(b) a plastic scintillator mounted on said face;

(c) means for reflecting back into said tube any light which scintillates from the plastic scintillator;

(d) means for preventing stray light from striking said plastic scintillator; and

(e) a single channel analyzer electrically connected to said photomultiplier tube for receiveing pulses from said photomultiplier tube, said single channel analyzer comprising:

(i) a very high speed comparator which receives input pulses from said photomultiplier tube; and

(ii) means for accepting input pulses having pulse widths of significantly less than 50 microseconds.

2. The dosimetry system of Claim 1 further comprising means for reducing the pulse reptition rate of said input pulses.

3. The dosimetry system of Claim 2 wherein said means for reducing the pulse reptition rate of said input pulses comprises a programmable divide-by-N circuit capable of receiving a very high pulse repetition rate and bringing the pulse repetition rate down into any desirable range.

4. The dosimetry system of Claim 1, 2 or 3 wherein said means for accepting input pulses having pulse widths of significantly less than 50 microseconds is comprised of a one-shot circuit .

5. The dosimetry system of Claim 4 wherein said one-shot circuit is comprised of an emitter coupled logic flip-flop which can accept input pulses having pulse widths of significantly less than 50 microseconds.

8. The dosimetry system of any one of Claims 1 to 5 further comprising means for converting the output pulses into a measure of radioactivity.

7. The dosimetry system of Claim 6 wherein said means for converting the output pulses into a measure of radioactivity comprises a Multiplier-Divider circuit which accepts said output pulses and multiplies them by a number corresponding to the eluate Flow Rate divided by a constant, K, in order to carry out the formula:

$$A = \frac{(N)(F)}{K}$$

Where, A = total activity (in milliCuries);
N = net counts (from Single Channel Analyzer);

F = Flow Rate; and
K = the calibration factor.

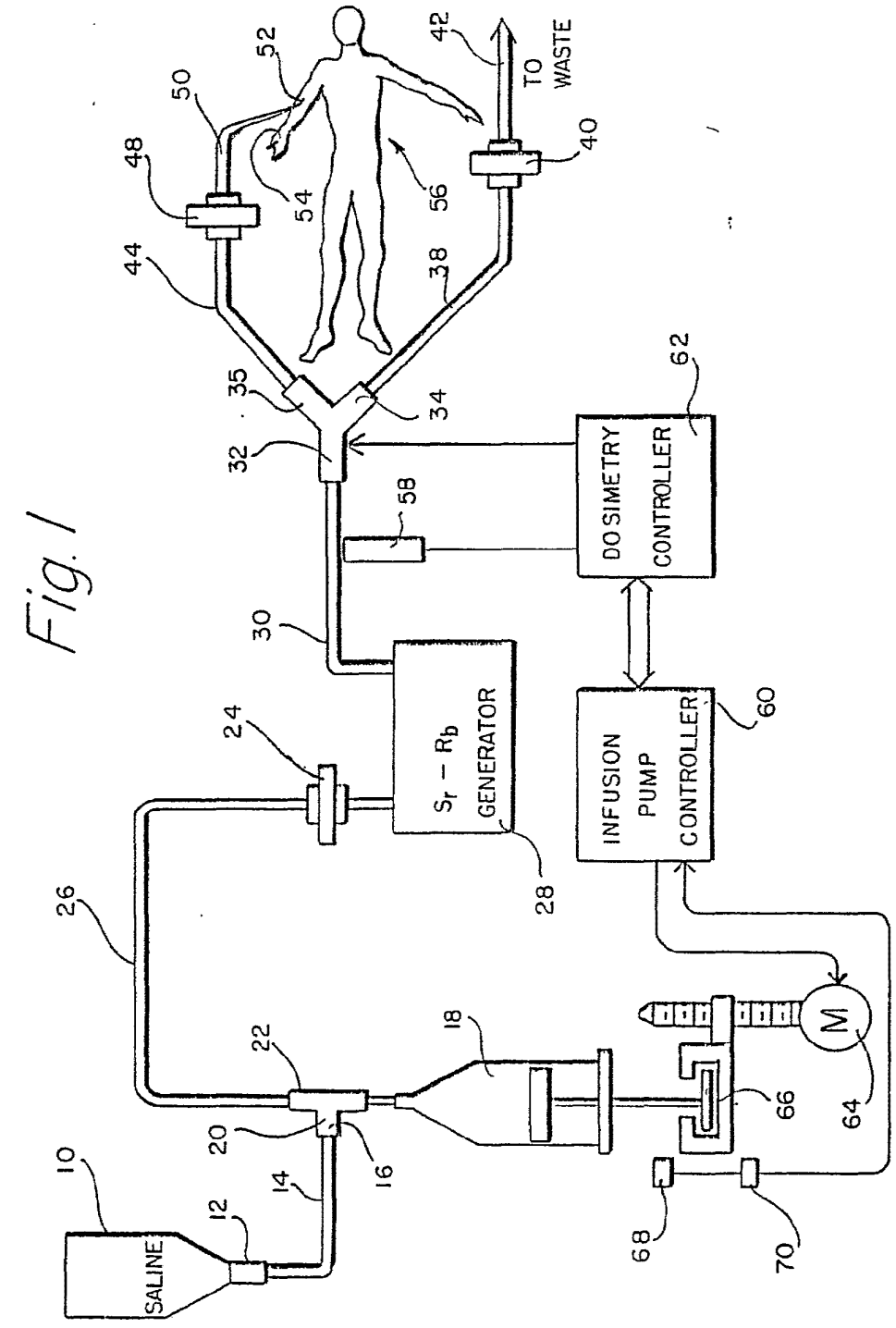
42
TO WASTE
52
50
48
40
54
56
44
38
35
34
32
62
DOSIMETRY CONTROLLER
58
30
24
$S_r - R_b$ GENERATOR
28
INFUSION PUMP CONTROLLER
60
26
M
22
18
66
64
20
16
14
10
12
SALINE
68
70

Fig. 1

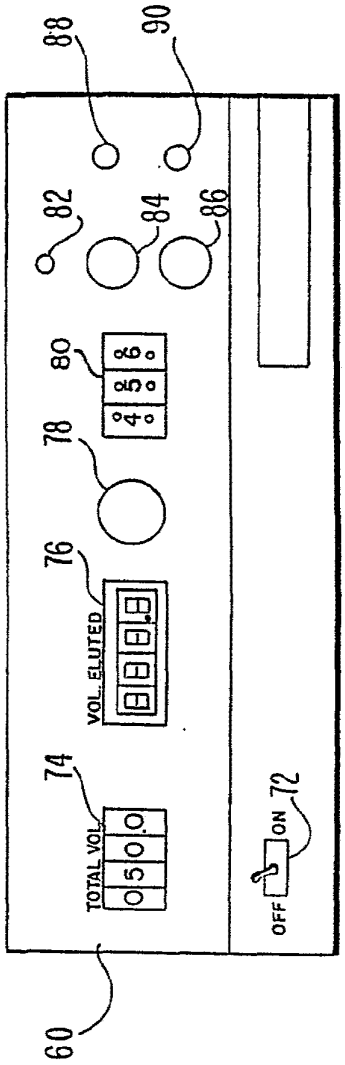
88
90
82
84
86
80
78
76
74
TOTAL VOL
VOL. ELUTED
ON
OFF
72
60

Fig. 2

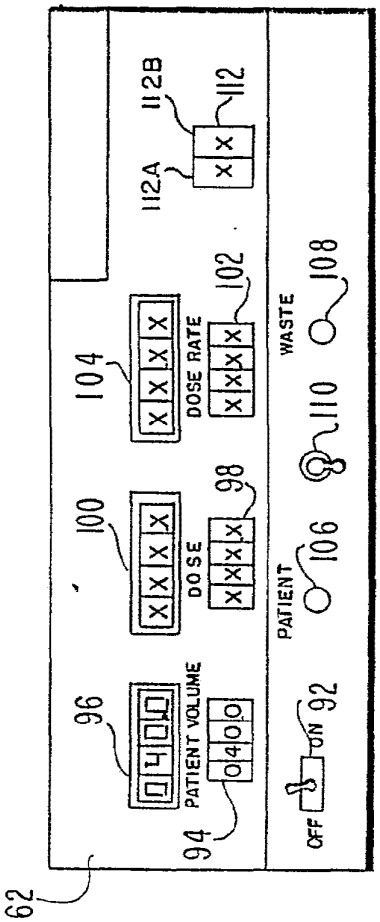
112B
112A
112
104
DOSE RATE
102
108
WASTE
110
100
DOSE
98
PATIENT
106
96
PATIENT VOLUME
94
ON
92
OFF
62

Fig. 3

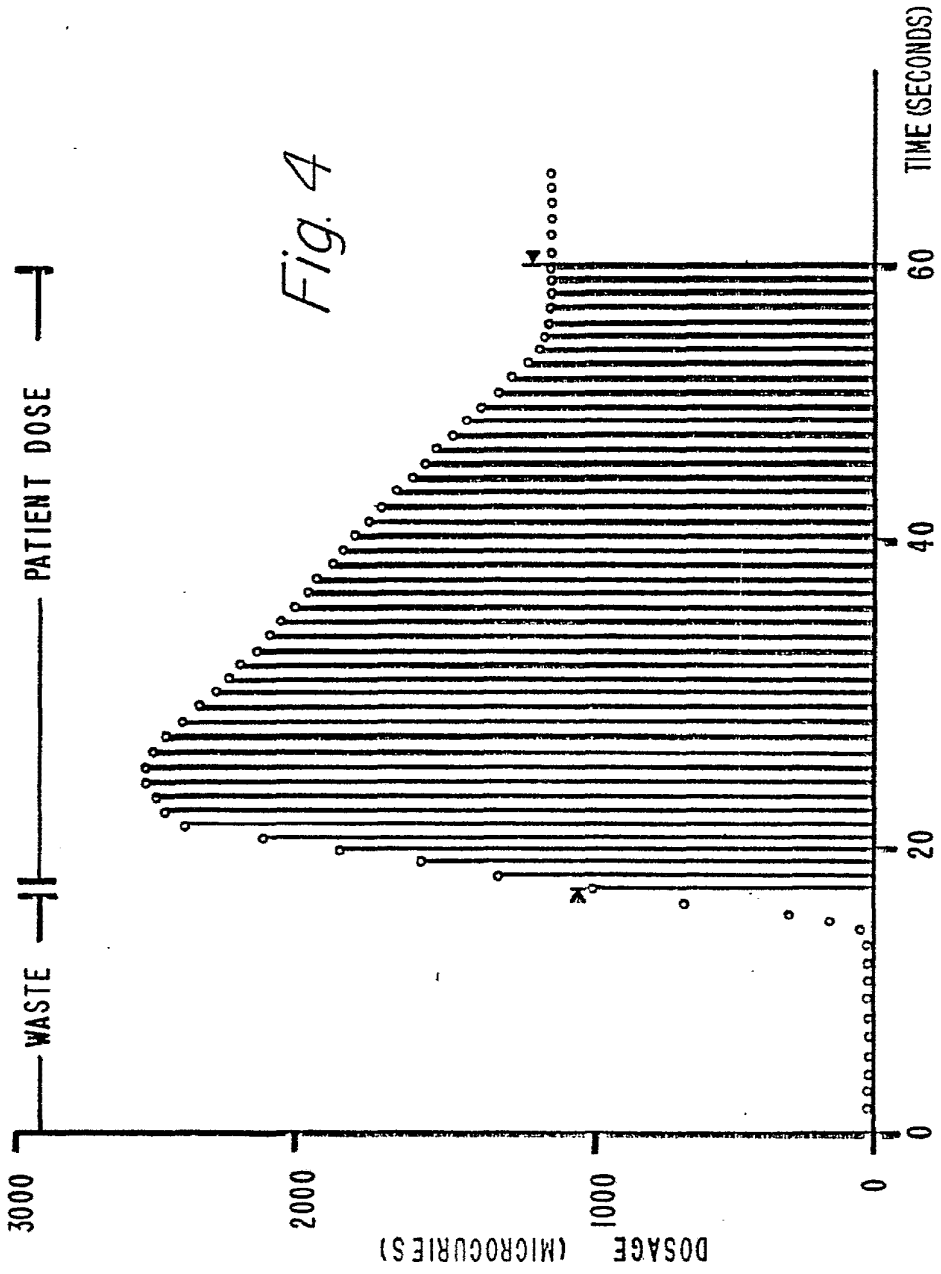
WASTE
PATIENT DOSE
3000
2000
1000
0
DOSAGE (MICROCURIES)
0
20
40
60
TIME (SECONDS)

Fig. 4

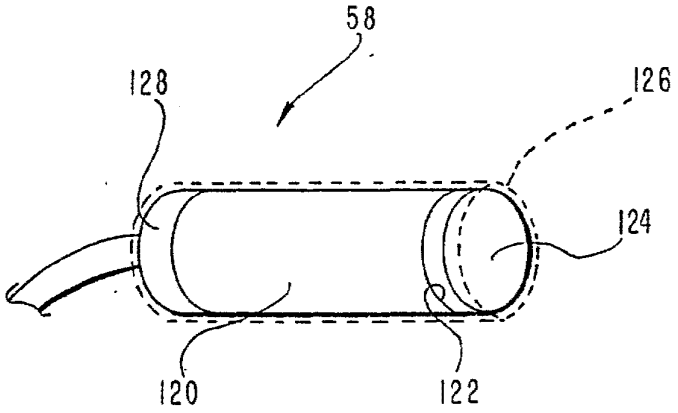
58
128
126
124
120
122

Fig. 5

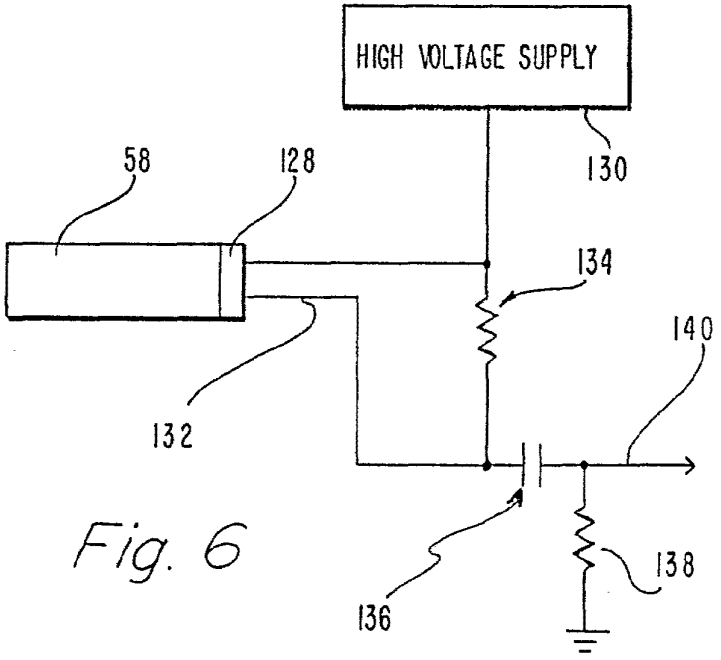
HIGH VOLTAGE SUPPLY
130
58
128
134
140
132
136
138

Fig. 6

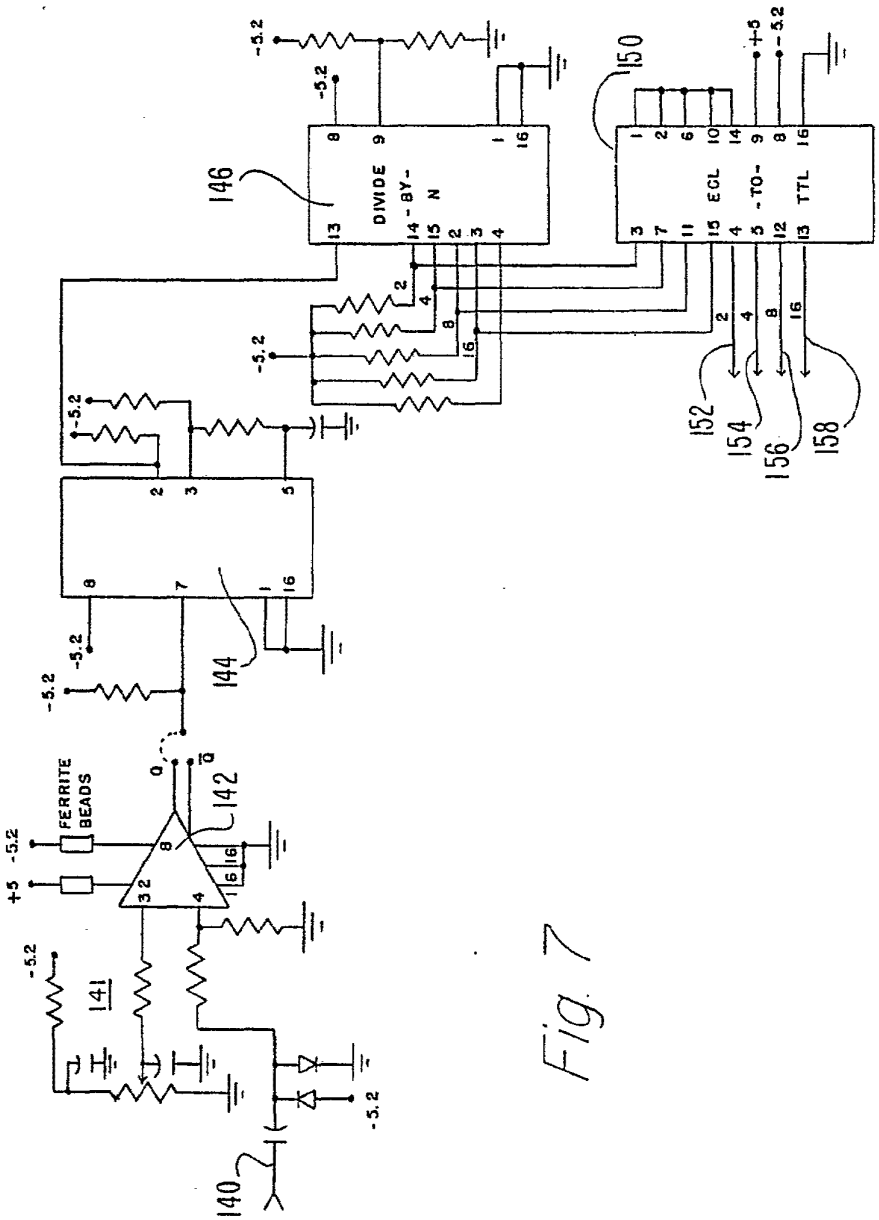
-5.2
146
DIVIDE
-BY-
N
150
ECL
-TO-
TTL
+5
152
154
156
158
144
142
FERRITE
BEADS
141
140

Fig. 7

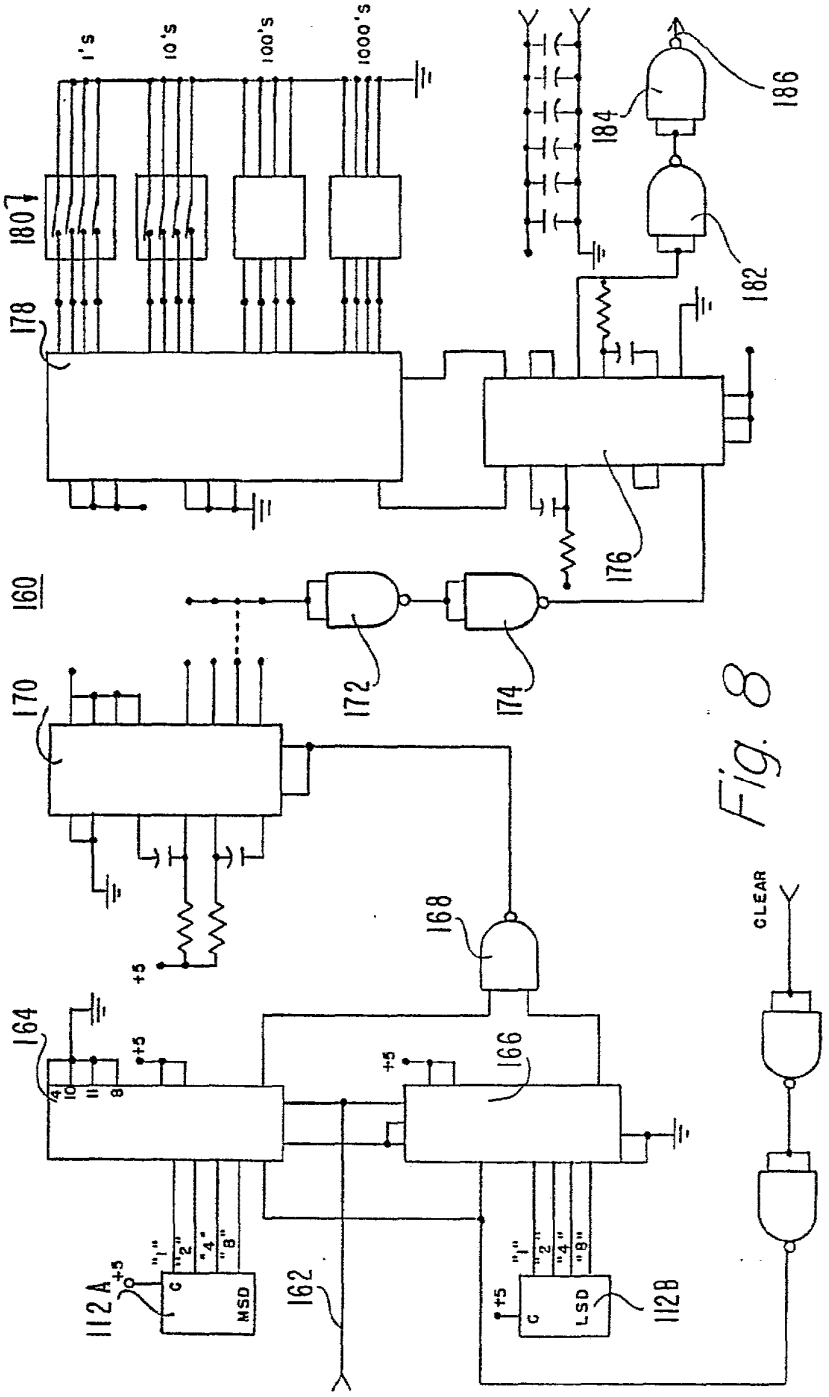
1's
10's
100's
1000's
180
178
184
186
182
176
160
172
174
170
168
164
166
+5
CLEAR
"1"
"2"
"4"
"8"
MSD
LSD
112A
112B
162

Fig. 8

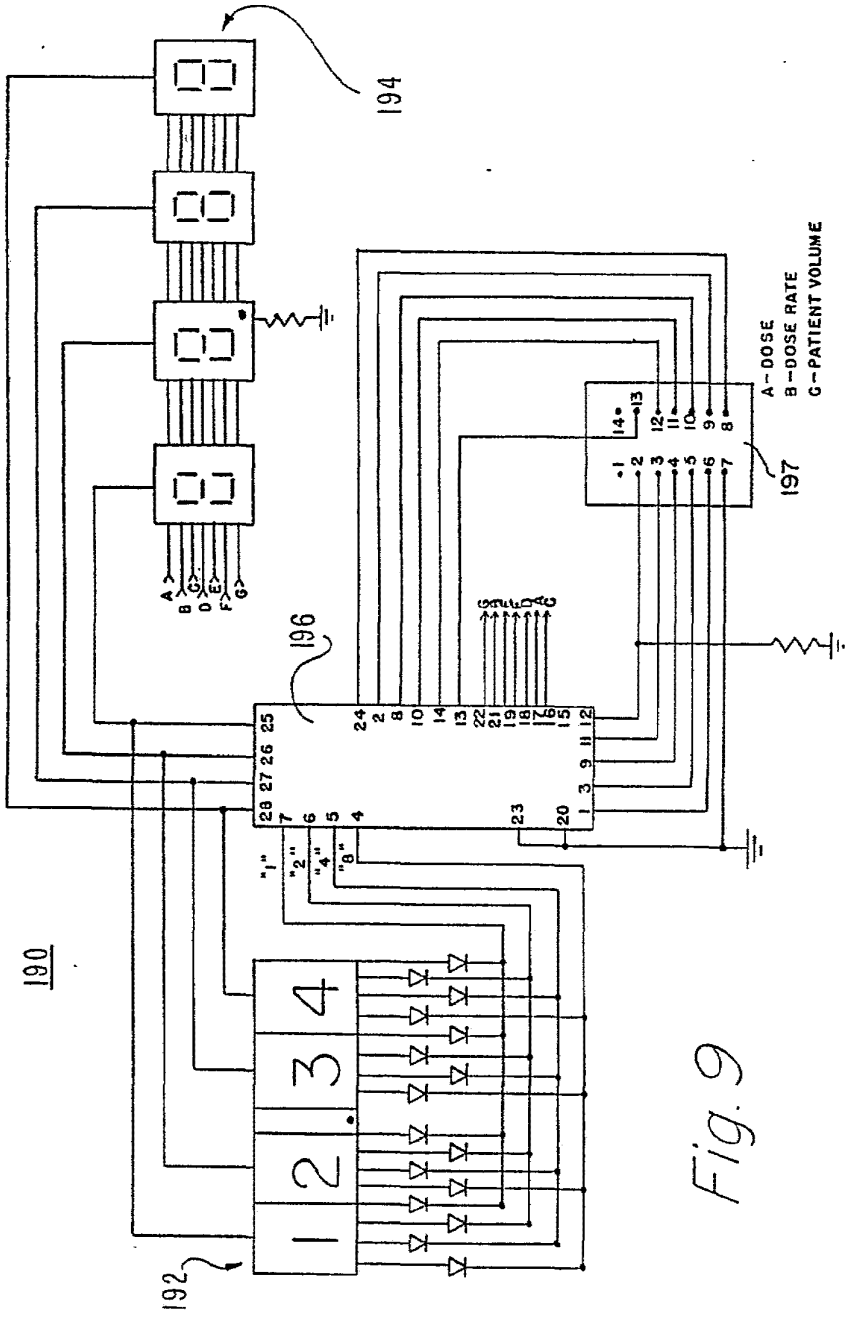
194
196
197
190
192
A-DOSE
B-DOSE RATE
C-PATIENT VOLUME
"1"
"2"
"4"
"8"
1
2
3
4

Fig. 9

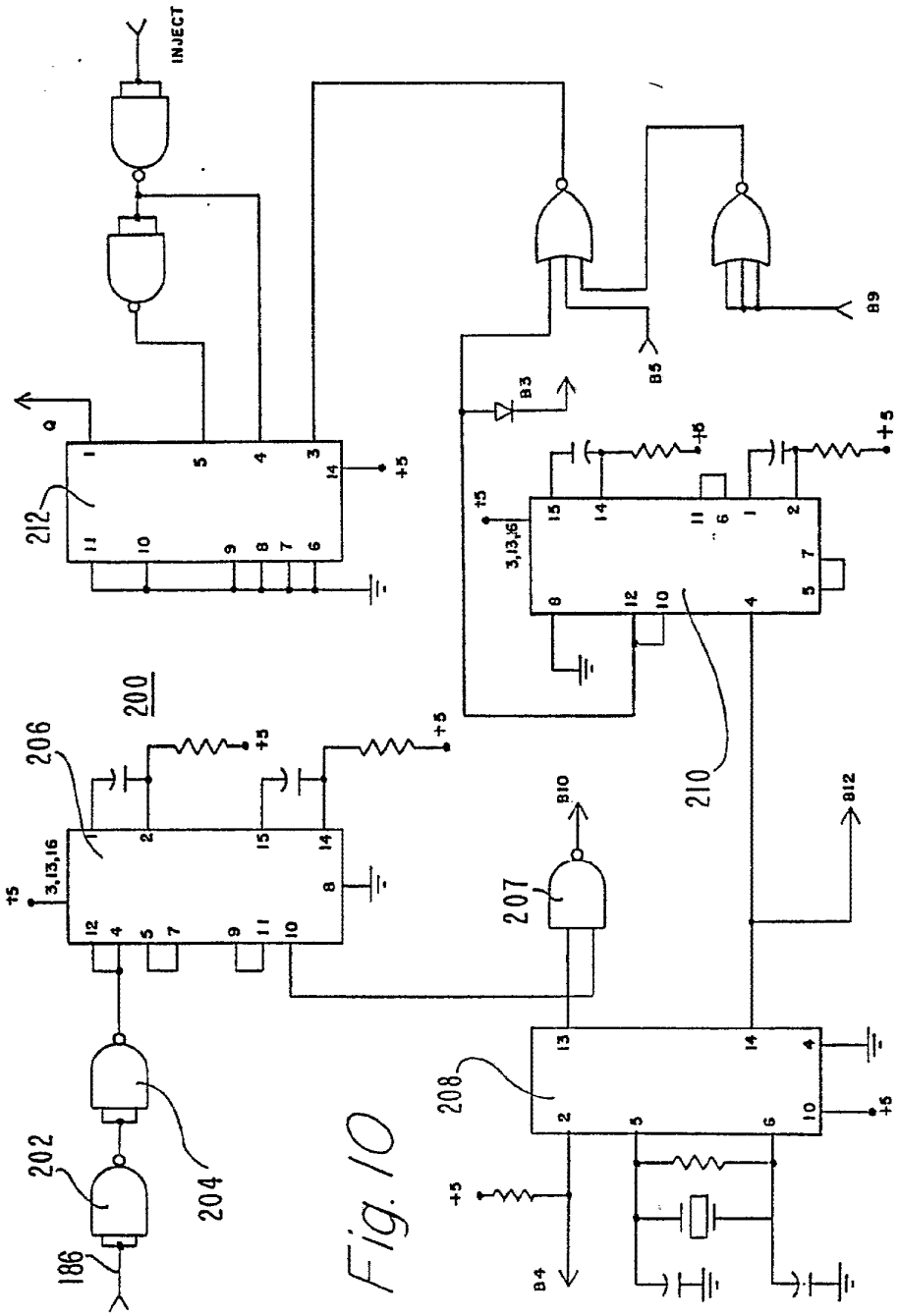
INJECT
200
206
212
210
207
208
202
204
186
B3
B5
B9
B10
B12
B4
+5
+15
3,13,16

Fig. 10

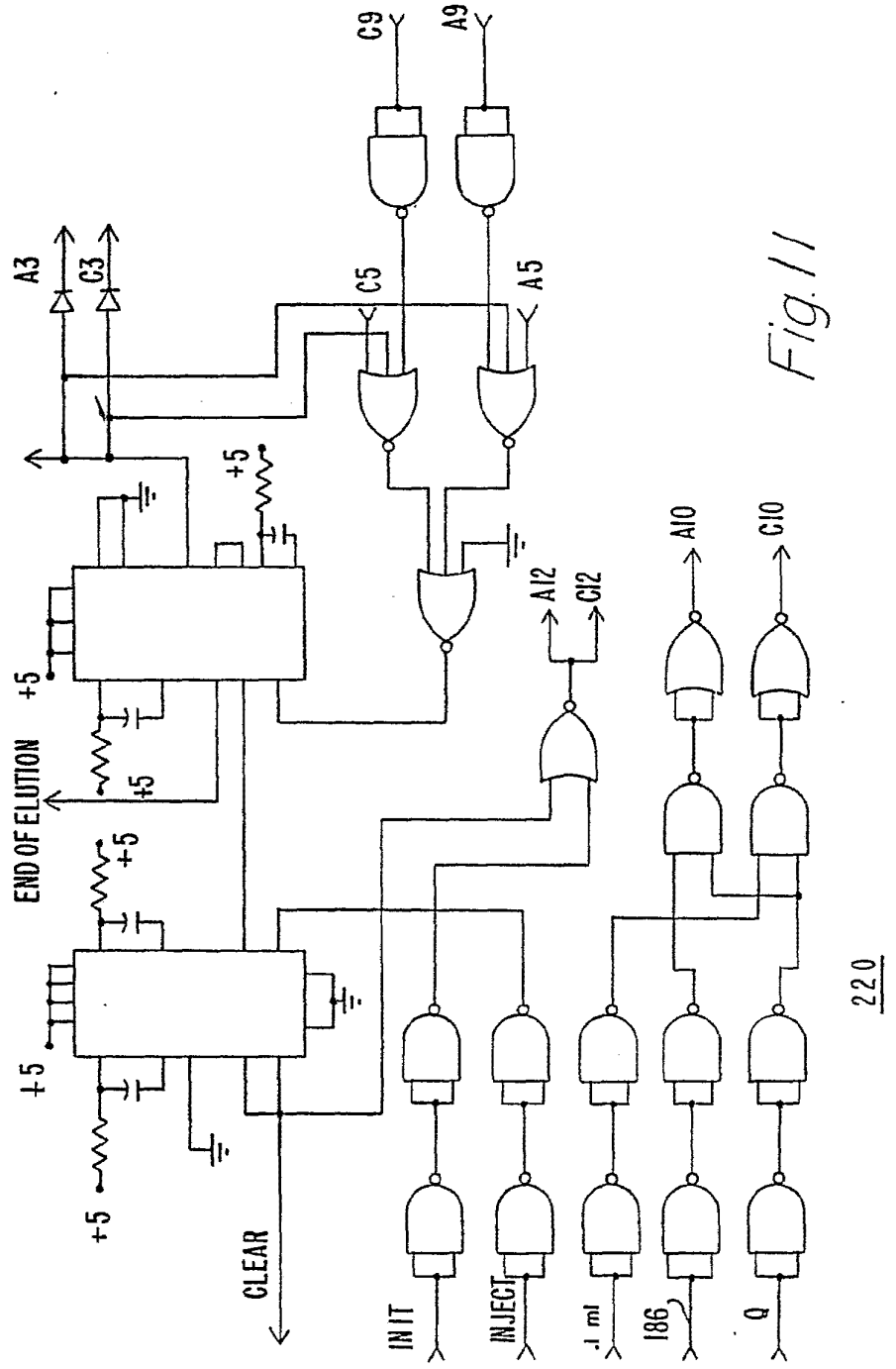
C9
A9
A3
C3
C5
A5
+5
A12
CI2
A10
C10
END OF ELUTION
CLEAR
INIT
INJECT
.1 ml
186
Q
220

Fig. 11

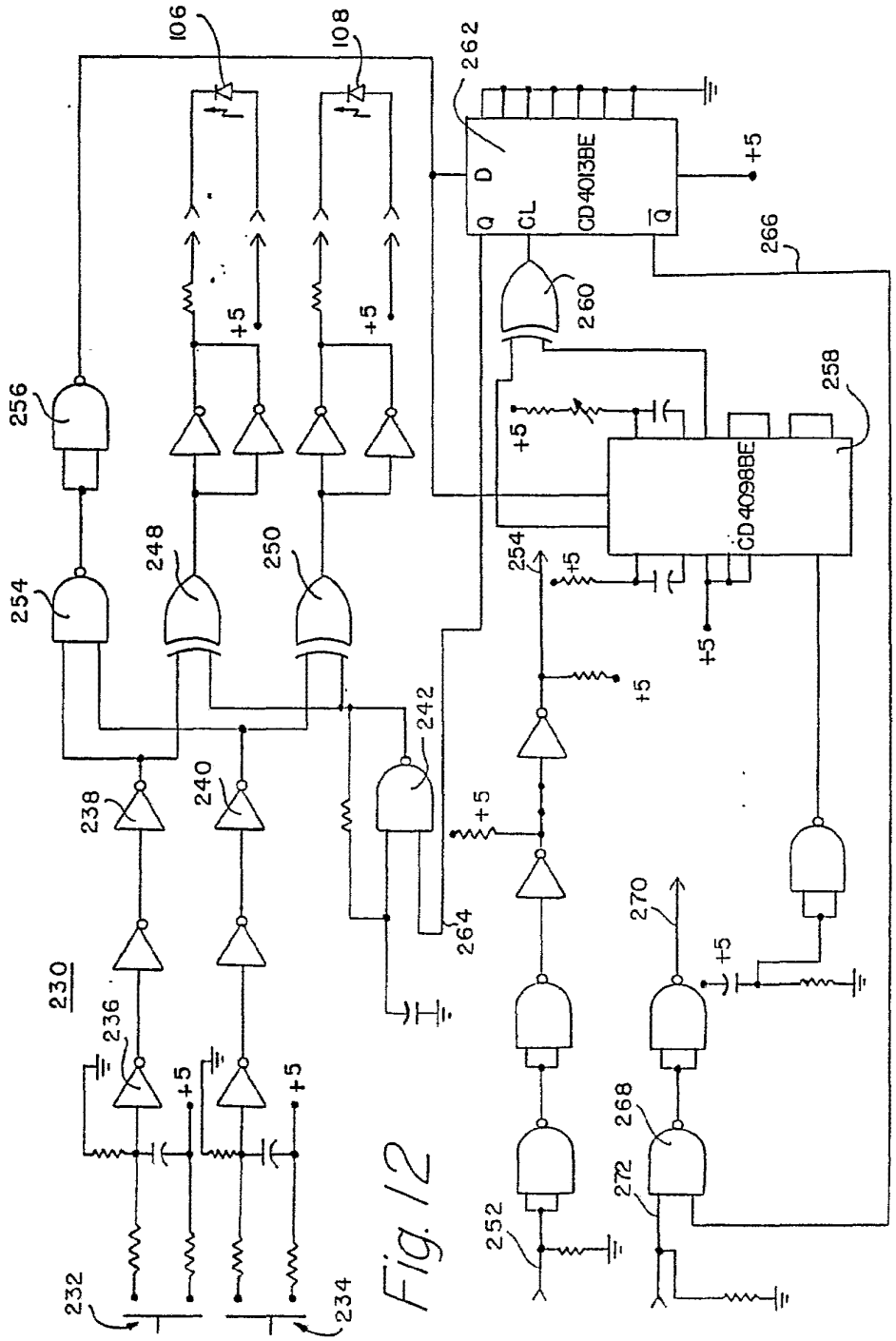
106
108
262
CD4013BE
D
Q
CL
Q
+5
266
260
258
CD4098BE
256
254
248
250
242
238
240
230
236
232
234
264
270
268
272
252

Fig. 12

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(60) **Références à d'autres documents nationaux apparentés :**

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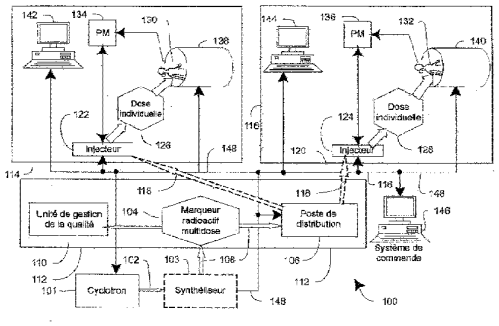
(74) **Mandataire(s) :** CASALONGA ET JOSSE.

(54) SYSTEMES, PROCEDES ET APPAREILS DE PERFUSION DE PRODUITS RADIOPHARMACEUTIQUES.

(57) Systèmes, appareils et procédés à l'aide desquels un système d'injection (122 ou 124) automatise un procédé d'injection d'une dose individuelle (126 ou 128) prise sur une dose multiple (104) d'un marqueur radioactif. Dans certaines formes de réalisation, le système d'injection (122 ou 124) comprend un premier système d'étalonnage de dose qui reçoit un flacon multidose de marqueur radioactif, un deuxième système d'étalonnage de dose, une pompe à perfusion et une aiguille intraveineuse. Dans certaines formes de réalisations, le premier système d'étalonnage de dose et le flacon multidose ont une forme correspondante. Dans certaines formes de réalisation, le premier système d'étalonnage de dose comporte un bras pneumatique qui reçoit le flacon multidose.



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SYSTEMES, PROCEDES ET APPAREILS DE PERFUSION DE PRODUITS RADIOPHARMACEUTIQUES

La présente invention concerne d'une façon générale la tomographie par émission de positons, et plus particulièrement des injecteurs.

Dans les systèmes de commande de tomographie par émission de positons selon la technique antérieure, une dose individuelle d'un marqueur radioactif prédosé est administrée à un patient. Le marqueur radioactif prédosé individuel est préparé par un fournisseur de marqueurs radioactifs (couramment appelé une radiopharmacie). Le plus fréquemment, on utilise un cyclotron pour préparer le marqueur radioactif. Le marqueur radioactif est livré à un établissement médical qui administre le marqueur radioactif prédosé individuel en tant que produit radiopharmaceutique. Le marqueur radioactif prédosé individuel est préparé par le fournisseur de marqueurs radioactifs conformément à une prescription établie par un médecin. La prescription comprend une quantité donnée de radioactivité à un moment à venir et une date de l'administration prescrite d'un volume connu d'un liquide injectable dans un sujet vivant.

Le procédé classique de production de marqueur radioactif dans un cyclotron, mis en œuvre par un fournisseur de marqueurs radioactifs, est le suivant : le fournisseur de marqueurs radioactifs irradie une matière cible dans le cyclotron à l'aide d'un faisceau de protons ou de deutons pour produire une quantité voulue de radioactivité dans la matière cible. Le degré d'irradiation est prévu pour satisfaire le besoin en radioactivité au moment à venir et à la date prescrits. La matière cible irradiée est un isotope radioactif. On peut citer comme exemples d'isotopes radioactifs produits par un cyclotron l'azote-13, le fluor-18, le carbone-11 et l'oxygène-15. Souvent, des composés sont liés à l'isotope radioactif pour produire des marqueurs radioactifs tels que le fluorodésoxyglucose (FDG) qui est produit à l'aide de fluor-18. Parmi les autres marqueurs radioactifs figurent l'ammoniac à azote-13 utilisé pour le myocarde, les marqueurs au carbone-11 couramment employés en neurologie et l'oxygène-15 gazeux ainsi que des marqueurs dérivés de celui-ci, couramment employés en cas de problème de circulation sanguine. Le FDG est de loin le marqueur radioactif le plus couramment employé et a une période de

109 minutes, ce qui permet sa distribution depuis une radiopharmacie centralisée vers de multiples sites d'imagerie.

Le fournisseur de marqueurs radioactifs emballe ordinairement le marqueur radioactif dans un flacon individuel contenant une dose, comme dans le cas du FDG. Ensuite, le flacon contenant une dose individuelle est conditionné dans un conteneur individuel à blindage de plomb. Chaque conteneur à blindage de plomb pèse environ 23 à 27 kg. Ordinairement, le fournisseur de marqueurs radioactifs prépare chaque jour, pour chaque établissement médical, un certain nombre de flacons individuels contenant une dose. Chacun des flacons contenant une dose est conditionné dans un conteneur individuel. De ce fait, un certain nombre de conteneurs pesant de 23 à 27 kg sont livrés quotidiennement à chaque établissement médical. En outre, pour faire face à des changements imprévus dans les besoins en marqueurs radioactifs d'un établissement médical, ainsi que pour répondre à d'autres besoins logistiques, ordinairement deux livraisons ou plus de flacons individuels contenant une dose dans des conteneurs individuels sont réalisées chaque jour. Les deux livraisons ou plus sont ordinairement réalisées tôt le matin avant 7 heures et en fin de matinée entre 10 heures et 11 heures, ou selon les souhaits de l'établissement médical. Les frais impliqués par la préparation de flacons de doses individuelles, le conditionnement et le transport, deux fois par jour, des lourds conteneurs sont très élevés.

De plus, lorsque le produit radiopharmaceutique est administré au patient, l'opérateur pratiquant la tomographie est exposé à la radioactivité. L'opérateur pratiquant la tomographie raccorde une tubulure d'injection intraveineuse (IV) dans le conteneur de produit radiopharmaceutique, insère dans le patient une aiguille montée à l'autre extrémité de l'IV, commence l'injection de l'isotope radioactif via l'IV, surveille le déroulement de l'injection et met fin à l'injection, en restant constamment auprès du patient et de l'IV contenant le produit radiopharmaceutique. Le fait de se tenir tout près de la source de radioactivité occasionne de nombreuses expositions à de faibles doses de radioactivité qui peuvent être préjudiciables à la santé de l'opérateur pratiquant la tomographie par émission de positons.

La gestion de la qualité quant à la quantité de radionucléides et à la pureté chimique du lot en vrac est ordinairement réalisée manuellement par le fournisseur. Du fait des aspects manuels de la gestion de la qualité, les critères de gestion de la qualité sont subjectifs. En outre, les systèmes classiques peuvent être lents, ce qui nécessite que le radioisotope doit être produit à un niveau de radioactivité plus élevé afin d'avoir au moment de l'injection la quantité de radioactivité requise.

Un certain nombre de radioisotopes ont une période tellement courte que le radioisotope doit être produit par un cyclotron à proximité immédiate de l'établissement médical. L'ammoniac à azote-13 a une période de 10 minutes et l'oxygène-15 a une période de 2,1 minutes. En raison de leur courte période, l'ammoniac à azote-13 et l'oxygène-15 nécessitent une production tout près du site de l'établissement médical. Par conséquent, l'utilisation d'ammoniac à azote-13 et d'oxygène-15 pour la TEP est limitée aux sites qui ont un accès immédiat à leur production.

Plus généralement, les systèmes classiques ont un déroulement séquentiel et par étape. Les principales fonctions, comme la production du marqueur radioactif et l'injection du produit radiopharmaceutique, la collecte de données cliniques suivant un protocole d'imagerie spécifique, sont gérées par des organismes séparés, par du personnel différent, souvent avec un certain manque de coordination et de liens.

Pour les raisons évoquées ci-dessus et pour d'autres raisons mentionnées plus loin, qui apparaîtront aux spécialistes de la technique à la lecture de la présente description et après compréhension de celle-ci, il y a dans la technique un besoin de réduire le nombre de flacons de doses individuelles et de conteneurs blindés que les fournisseurs de radioisotope préparent et livrent chaque jour à chaque établissement médical. Il est également nécessaire de réduire le nombre de voyages de livraison qu'un fournisseur de marqueurs radioactifs effectue quotidiennement vers chaque établissement médical. De plus, il est nécessaire de réduire l'exposition des personnes, par exemple les opérateurs de TEP, à la radioactivité pendant les étapes manuelles d'administration d'un produit radiopharmaceutique à des patients. Il est également nécessaire d'améliorer la gestion de la qualité de l'administration des produits radiopharmaceutiques aux patients. De plus, il est nécessaire de réduire la gestion et le contrôle sans liens des fonctions de préparation et d'injection de radioisotope dans des patients. En outre, il est nécessaire de disposer d'un procédé commode pour produire et administrer sur place un produit radiopharmaceutique tel que l'ammoniac à azote-13 en vue d'examens cardiologiques.

Une solution est apportée aux inconvénients, défauts et problèmes évoqués ci-dessus, ce que l'on comprendra à la lecture et à l'étude de la description ci-après.

Selon un premier aspect, un système comprend un réseau local d'entreprise coopérant avec un ou plusieurs systèmes d'imagerie de tomographie par émission de positons. Le système comprend également un poste de distribution qui sert à recevoir

une partie ou un flacon de plusieurs doses d'un produit radiopharmaceutique. Le poste de distribution sert à distribuer des parties du produit radiopharmaceutique à un ou plusieurs systèmes d'imagerie de tomographie par émission de positons. Le poste de distribution coopère également avec le réseau local d'entreprise. Le poste de distribution adminstre un produit radiopharmaceutique aux patients dont une image est ensuite réalisée à l'aide des systèmes d'imagerie de tomographie par émission de positons. Le poste de distribution permet de distribuer aux patients une partie en plusieurs doses du produit radiopharmaceutique, ce qui permet des économies d'échelle et constitue un moyen commode de distribution du produit radiopharmaceutique.

Dans un autre exemple, le système comprend également une unité de gestion de la qualité. L'unité de gestion de la qualité sert à contrôler la pureté radiochimique et isotopique du produit radiopharmaceutique distribué par le poste de distribution. L'unité de gestion de la qualité coopère avec le réseau local d'entreprise et coopère avec le poste de distribution.

Dans encore un autre exemple, un appareil de synthèse de produit chimique coopère entre un dispositif de production de radioisotope (par exemple un cyclotron, un accélérateur linéaire ou un générateur de radioisotopes) et le poste de distribution. Le dispositif de synthèse reçoit un radioisotope du dispositif de production de radioisotope, lie le radioisotope à un composé biologique et transfert dans le poste de distribution le marqueur radioactif ainsi obtenu.

Dans encore un autre exemple, l'appareil comprend un système de commande qui coopère avec le réseau local d'entreprise, pour recevoir des informations de bilan de l'un quelconque des dispositifs du système, et envoyer des instructions à l'un quelconque des dispositifs du système tels que le/les systèmes d'imagerie de tomographie par émission de positons, le poste de distribution, le dispositif de synthèse de produit chimique et l'unité de gestion de la qualité. Le système de commande détermine une quantité de radioactivité et une quantité de radioisotope à produire et envoie en conséquence des instructions au dispositif de production de radioisotope.

Dans certains exemples, un système d'imagerie de tomographie par émission de positons comprend un système d'injection, un moniteur physiologique coopérant avec l'injecteur et un scanner de tomographie par émission de positons coopérant avec le moniteur physiologique et le système d'injection. Le système d'injection sert à recevoir de multiples doses du produit pharmaceutique et sert à

injecter des doses individuelles du produit radiopharmaceutique dans un patient, à lancer une tomodensitométrie à un instant prédéfini suivant un protocole clinique spécifique prédéfini. Le système d'injecteur est également apte à injecter d'autres produits pharmaceutiques définis dans le protocole.

L'invention sera mieux comprise à l'étude de la description détaillée d'un mode de réalisation pris à titre d'exemple non limitatif et illustré par les dessins annexés, sur lesquels :

la Fig. 1 est un schéma présentant une vue générale d'une forme de réalisation au niveau du système ;

la Fig. 2 est un schéma de principe d'un appareil pour injecter une ou plusieurs doses individuelles d'un produit radiopharmaceutique à partir d'une dose multiple du produit radiopharmaceutique ;

la Fig. 3 est un schéma de principe d'un poste de distribution selon une forme de réalisation ;

la Fig. 4 est un schéma de principe d'un système d'injection automatisée pour médications de TEP selon une forme de réalisation ;

la Fig. 5 est un schéma de principe d'un système médical d'administration de produit radiopharmaceutique selon une forme de réalisation ;

la Fig. 6 est un schéma de principe d'un système médical d'administration de produit radiopharmaceutique selon une forme de réalisation ;

la Fig. 7 est un organigramme d'une forme de réalisation d'un procédé de fonctionnement d'une forme de réalisation du système d'injection ;

la Fig. 8 est un organigramme d'une forme de réalisation d'un procédé de préparation d'un système d'injection à utiliser par plusieurs patients ;

la Fig. 9 est un organigramme d'une forme de réalisation d'un procédé de préparation d'un système d'injection pour chaque patient individuel ;

la Fig. 10 est un organigramme d'une forme de réalisation d'un procédé d'administration d'une injection à l'aide du système d'injection de la Fig. 4 pour chaque patient individuel ;

la Fig. 11 est un organigramme d'un procédé exécuté par un système de commande selon une forme de réalisation ; et

la Fig. 12 est un schéma de principe de l'environnement matériel et opérationnel dans lequel peuvent être mises en œuvre différentes formes de réalisation.

Dans la description détaillée qui suit, il est fait référence aux dessins annexés qui font partie de celle-ci et sur lesquels sont représentées à titre d'illustration des formes de réalisation spécifiques pouvant être mises en œuvre. Ces formes de réalisation sont décrites d'une manière suffisamment détaillée pour permettre aux spécialistes de la technique de mettre en œuvre les formes de réalisation.

La description détaillée est divisée en cinq chapitres. Dans le premier chapitre, une vue générale au niveau du système est présentée. Dans le deuxième chapitre, un appareil selon une forme de réalisation est proposé. Dans le troisième chapitre, des procédés selon des formes de réalisation sont présentés. Dans le quatrième chapitre est décrit l'environnement matériel et opérationnel en liaison avec lequel peuvent être mises en œuvre des formes de réalisation. Dans le cinquième chapitre est présentée une conclusion de la description détaillée.

Présentation générale au niveau du système

La Fig. 1 est un schéma de principe qui présente une vue générale, au niveau du système, d'un système médical 100 d'administration de produit radiopharmaceutique. Le système médical 100 d'administration de produit radiopharmaceutique est un système intégré pour la production, la gestion de la qualité et la distribution de produits radiopharmaceutiques médicaux en imagerie de tomographie par émission de positons (TEP).

Le système 100 comprend un cyclotron 101. Le cyclotron 101 irradie une matière cible à l'aide d'un rayonnement en produisant un radioisotope 102. De multiples doses du radioisotope 102 sont produites par le cyclotron 101. On peut citer comme autres exemples de dispositifs produisant des radioisotopes les accélérateurs linéaires (LINIAC) et les générateurs de radioisotopes. Du rubidium 82 est produit par un générateur de radioisotopes. Dans certaines formes de réalisation, le radioisotope 102 est chimiquement lié à un composé biologique dans un dispositif de synthèse 103 de produit chimique, en produisant un marqueur radioactif 104.

La partie du radioisotope 102 ou du marqueur radioactif 104 représentant plusieurs doses est transférée dans un poste de distribution 106. Dans les formes de réalisation où le marqueur radioactif 104 ou le radioisotope 102 a une courte période (par exemple le carbone-11, l'oxygène-15 et l'azote-13), le transfert s'effectue par l'intermédiaire d'une conduite assurant une protection contre la radioactivité, par

exemple une conduite 108 à blindage de plomb, comme représenté sur la Fig. 1. Dans les formes de réalisation où le marqueur radioactif 104 ou le radioisotope 102 a une période plus longue (par exemple le fluor-18), le transfert peut s'effectuer en plaçant dans un réservoir la partie de radioisotope 102 ou de marqueur radioactif 104 représentant plusieurs doses et en transportant le réservoir jusqu'au poste de distribution 106 et en vidant le contenu du réservoir dans le poste de distribution 106. Quelle que soit la manière dont la matière est transportée, la partie de radioisotope 102 ou de marqueur radioactif 104 représentant plusieurs doses est stockée dans le poste de distribution 106.

Dans certaines formes de réalisation, le système 100 comprend également une unité de gestion de la qualité (QC) 110 qui contrôle la quantité de radioactivité et d'autres mesures qualitatives et quantitatives de la partie de radioisotope représentant plusieurs doses qui est stockée dans le poste de distribution 106. La QC 110 permet de vérifier la pureté des radionucléides et des produits chimiques, à savoir la qualité du radioisotope en ce qui concerne la quantité de radioactivité de l'isotope voulue et la pureté chimique du marqueur radioactif. Dans certaines formes de réalisation de contrôle par gestion de la qualité, une analyse et une vérification sont effectuées à intervalles particuliers dans le temps ou pour des lots de production particuliers ou pour un échantillon représentatif d'un marqueur radioactif produit en vrac. Les intervalles de temps et les lots peuvent être prédéterminés et modifiés par un opérateur. De ce fait, la QC 110 permet l'exécution des fonctions de gestion de qualité par un processus automatisé qui est plus efficace, assure moins d'exposition professionnelle et est plus fiable que les systèmes classiques. Ainsi, le système 100 améliore la gestion de la qualité de l'administration de produits radiopharmaceutiques à des patients. Dans un système qui produit et distribue de l'ammoniac à azote-13, la QC 110 peut être encore présente mais peut n'être utilisée que pour certaines productions prédéterminées.

Dans certaines formes de réalisation, la QC 110 comprend un dispositif de chromatographie en phase liquide à haute performance (HPLC) et/ou un détecteur de NaI. Dans certaines formes de réalisation, la QC 110 comprend aussi un filtre pour la partie de radioisotope représentant plusieurs doses qui est stockée dans le poste de distribution 106. De la sorte, la QC 110 assure des fonctions de gestion de la qualité et de filtrage qui sont automatisées, ce qui est plus commode et plus fiable que les systèmes selon la technique antérieure.

Dans la forme de réalisation illustrée sur la Fig. 1, la QC 110 échantillonne le marqueur radioactif 104 représentant plusieurs doses délivrées par le poste de distribution 106. Dans d'autres formes de réalisation, la QC 110 échantillonne un marqueur radioactif 104 représentant plusieurs doses, provenant d'une cible dans le cyclotron 101. Dans certaines autres formes de réalisation, la QC 110 estime la quantité de radioactivité dans le marqueur radioactif 104 par un calcul reposant sur la période du marqueur radioactif 104 et le temps écoulé depuis la production du marqueur radioactif 104.

Dans certaines formes de réalisation, le système 100 comprend un ou plusieurs écrans 112 de protection radiologique qui entourent des parties radioactives du système. L'écran 112 de protection radiologique comprend ordinairement du plomb. L'écran 112 de protection radiologique protège toutes les personnes contre les rayonnements, et, en particulier, l'écran 112 de protection radiologique protège le personnel qui fait fonctionner le cyclotron 101, le poste de distribution 106.

Depuis le poste de distribution 106, des parties du marqueur radioactif 104 représentant plusieurs doses sont distribuées à un ou plusieurs systèmes d'imagerie TEP 114 et 116. Dans certaines formes de réalisation, le transfert ou le transport des parties du marqueur radioactif 104 représentant plusieurs doses vers les systèmes d'imagerie TEP 114 ou 116 s'effectue par l'intermédiaire d'une conduite, 118 ou 120, par exemple une conduite à blindage de plomb qui protège de la radioactivité. Dans d'autres formes de réalisation, les parties du marqueur radioactif 104 représentant plusieurs doses sont transférées ou transportées en plaçant dans un réservoir la partie du marqueur radioactif 104 représentant plusieurs doses et en transportant le réservoir jusqu'aux systèmes d'imagerie TEP 114 et 116.

Chacun des systèmes d'imagerie TEP 114 et 116 comporte respectivement un système d'injecteur 122 et 124. Une mise en œuvre des systèmes d'injection 122 ou 124 est examiné plus en détail ci-après en référence à la Fig. 4. Les systèmes d'injection 122 et 124 extraient des doses individuelles 126 et 128 d'une préparation radiopharmaceutique et injectent ou administrent la dose dans des sujets vivants, respectivement 130 et 132. Dans certaines formes de réalisation, les sujets vivants 130 et 132 sont des patients humains. Ainsi, le système 100 permet la distribution du marqueur radioactif 104 représentant plusieurs doses sous la forme de doses individuelles 126 et 128. En comparaison des systèmes selon la technique antérieure qui nécessitent une irradiation et une expédition de nombreuses doses individuelles de produit radiopharmaceutique, la préparation et l'expédition d'une partie de

marqueur radioactif 104 représentant plusieurs doses par le système 100 sont plus commodes. Le système 100 permet également un processus plus automatisé qui est plus fiable que les systèmes classiques nécessitant davantage d'interventions humaines. En outre, le système 100 réduit les expositions indésirables du personnel aux rayonnements.

Dans certaines formes de réalisation, des dispositifs de surveillance physiologique (PM) 134 et 136 coopèrent respectivement avec les systèmes d'injection 122 et 124 et avec les sujets vivants 130 et 132. Les PM 134 et 136 surveillent un certain nombre de mesures de la santé du sujet vivant, comme la pression sanguine et l'activité cardiaque, représentée par un électrocardiogramme (ECG). Les PM 134 et 136 détectent des anomalies dans les mesures de la santé du sujet vivant et signalent les anomalies au système de commande ainsi qu'au personnel médical.

Chaque système d'imagerie de TEP 114 et 116 comporte également respectivement un tomographe 138 et 140. Chaque système d'imagerie de TEP peut comporter un ou plusieurs tomographes.

Les sujets vivants 130 et 132 sont placés à l'intérieur des tomographes 138 et 140 après ou pendant l'injection des produits radiopharmaceutiques 126 et 128 pour détecter la radioactivité des produits radiopharmaceutiques injectés 126 et 128 respectivement chez les sujets vivants 130 et 132.

Un ordinateur à interface graphique (GUI) 142, 144 est situé dans les systèmes d'imagerie TEP 114 et 116. Un opérateur de TEP fait fonctionner la GUI 142, 144 d'ordinateur afin de commander, de gérer et de superviser tout le processus de TEP, dont les activités du système d'injection, comme la distribution et l'injection de la dose individuelle de produit radiopharmaceutique 126, 128 dans le sujet vivant 130, 132 et l'examen du sujet vivant à l'aide d'un protocole clinique approprié. Une forme de réalisation d'ordinateur 142 ou 144 est constituée par l'ordinateur 1202 de la Fig. 12.

Dans certaines formes de réalisation, l'ordinateur 142, 144 reçoit des PM 134 et 136 un avis signalant des anomalies dans les mesures de la santé du sujet vivant, et il demande par conséquent aux systèmes d'injection respectivement 122 et 124 d'arrêter l'injection ou de prendre une autre mesure correctrice appropriée. Dans encore d'autres formes de réalisation, l'ordinateur 142, 144 demande au tomographe 138 ou 140 de lancer une opération de tomographie dans un délai approprié après l'injection par le système d'injection, respectivement 122 ou 124. Dans encore

d'autres formes de réalisation, un seul système d'injection est commandé par son interface utilisateur autonome et sert à injecter une quantité donnée de radioactivité dans des patients qui sont examinés soit successivement sur un seul tomographe, soit en parallèle sur de multiples tomographes.

Les parties des systèmes d'imagerie TEP 114 ou 116 sont appelées postes de dosage. Un premier poste de dosage sur la Fig. 1 comporte un système d'injection 122, un PM 134 et un ordinateur 142. Un autre poste de dosage sur la Fig. 1 comporte le système d'injection 124, le PM 136 et l'ordinateur 144.

Dans certaines formes de réalisation, le système 100 comprend un système de commande 146. Le système de commande 146 sert à recevoir des informations de bilan des dispositifs de TEP, et envoie des instructions aux dispositifs de TEP tels que le cyclotron 101, le poste de distribution 106, le dispositif de gestion de la qualité 110, les systèmes d'injection 122 et 124, les moniteurs physiologiques 130 et 136, les tomographes 138 et 140 et les ordinateurs 142 et 144. Dans certaines formes de réalisation, un programme informatique enregistré dans le système de commande 146 sert à calculer des quantités de marqueur radioactif 104 représentant plusieurs doses, à transporter jusqu'au système d'injection 124, d'après des variables de commande spécifiques du site. Une forme de réalisation de l'ordinateur 146 est constituée par l'ordinateur 1202 de la Fig. 12.

Dans certaines autres formes de réalisation, les variables de commande comprennent la distance et le temps de transfert entre le tomographe 138 ou 140 et un cyclotron 101 qui produit de l'ammoniac à azote-13. Dans ces formes de réalisation, le système 100 constitue un procédé commode pour produire et administrer sur place un produit radiopharmaceutique constitué par de l'ammoniac à azote-13 pour des études cardiologiques.

Dans encore d'autres formes de réalisation, un programme informatique enregistré dans le système de commande 146 stocke des données de production et de dosage. Ainsi, le système 100 permet un stockage plus centralisé d'archives lors de la préparation, de la livraison, du contrôle et de l'injection de marqueurs radioactifs pour des patients, ce qui réduit la gestion sans liens de ces fonctions, contrairement aux systèmes selon la technique antérieure.

Dans encore une autre forme de réalisation, des données décrivant des descripteurs de haut niveau d'un ou plusieurs sujets vivants à traiter par le système 100 sont extraites d'un tomographe de TEP 138 ou 140 ou d'un autre dispositif. Un autre exemple des autres dispositifs consiste en un système d'information sur les

patients au sein de l'établissement médical. Les données sont reçues par le système de commande 146. Les descripteurs de haut niveau comprennent la dose prescrite pour chaque sujet vivant et le temps d'injection prévu pour le sujet vivant. Dans encore d'autres formes de réalisation, les données comprennent le type de produit radiopharmaceutique (par exemple, de l'oxygène-15), une équation paramétrique prédéfinie et/ou un protocole clinique suivi dans la procédure médicale.

D'après ces données, l'activité requise de la dose de marqueur radioactif est calculée et comparée avec l'activité totale disponible dans la partie du marqueur radioactif 104 représentant plusieurs doses. En cas de manque, le système 100 avise l'opérateur. Si le cyclotron 101 est géré par un fournisseur extérieur de radioisotopes, le fournisseur est avisé par une liaison Internet ou autre moyen électronique. Le fournisseur est informé de l'activité requise de la dose supplémentaire et du temps nécessaire à l'administration des marqueurs radioactifs supplémentaires.

Le système 100 permet des économies d'échelle rentables.

Une économie d'échelle est assurée par l'utilisation de plusieurs systèmes d'imagerie TEP pour chaque poste de distribution 106, l'unité de gestion de la qualité 110 et chaque système de commande 146.

Dans certaines formes de réalisation, le système de commande 146 est un système informatique, comme représenté sur la Fig. 12. Dans certaines formes de réalisation, le système de commande 146 coopère avec les dispositifs de TEP par un réseau local d'entreprise (LAN) 148. Des liaisons de communication du LAN peuvent être réalisées soit par des câblages physiques, soit par une liaison radioélectrique. Les liaisons de communication entre le LAN 148 et les systèmes d'imagerie de TEP 114 et 116 et le cyclotron sont assurées par l'intermédiaire d'interfaces LAN bien connues dans la technique. Dans certaines formes de réalisation, les dispositifs de surveillance physiologiques 134 et 136 coopèrent également directement avec le LAN 148. Dans des formes de réalisation où le cyclotron 120, les dispositifs situés à l'intérieur de l'écran 112 de protection radiologique, et/ou les systèmes de tomographie 114 et 116 se trouvent dans des établissements différents, les liaisons de communication par LAN entre ces parties du système sont des réseaux étendus. A la place d'un LAN 148, les dispositifs du système 100 peuvent coopérer par une liaison de communication directe.

Dans certaines formes de réalisation, le système de commande 146 gère le processus de production du marqueur radioactif 104 et de livraison du radioisotope en fonction des besoins immédiats d'un système d'imagerie de TEP. Le système de

commande 146 est apte à recevoir des informations décrivant une quantité d'une dose individuelle requise 126 ou 128, à envoyer les instructions au cyclotron 101 pour produire la quantité individuelle du radioisotope, à envoyer des instructions au poste de distribution pour distribuer la quantité individuelle du radioisotope au système d'imagerie de TEP demandeur. Dans certaines formes de réalisation, la demande est lancée par un opérateur de l'interface graphique d'un ordinateur 142 ou 144 dans un système d'imagerie de TEP 114 ou 116. Dans certaines formes de réalisation, le système de commande 146 est avisé par les PM 134 et 136 en cas d'anomalie dans les mesures de la santé du sujet vivant, et il demande par conséquent aux systèmes d'injection, respectivement 122 et 124, d'arrêter l'injection. Dans encore certaines autres formes de réalisation, lorsque la QC 110 indique que la qualité est en deçà de critères minimaux acceptables, le système de commande 146 fournit à l'opérateur du système de commande 146 des indications de la qualité non acceptable et demande aux systèmes de purger l'appareil contenant le marqueur radioactif.

Dans encore d'autres formes de réalisation, le système de commande 146 demande au tomographe 138 ou 140 de lancer une opération de tomographie dans un délai approprié après l'injection par le système d'injection, respectivement 122 ou 124. Dans encore d'autres formes de réalisation, le tomographe 138 ou 140 suit un ensemble prédéfini de stratégie d'acquisition en fonction du marqueur radioactif et du protocole clinique utilisés. Dans certaines formes de réalisation, les stratégies d'acquisition comprennent le démarrage d'une tomographie après un laps de temps prédéfini suivant l'injection du marqueur radioactif, l'introduction d'un agent d'induction d'efforts suivie de l'injection d'un marqueur radioactif et de la réalisation d'une nouvelle image après un laps de temps prédéfini.

En outre, dans certaines formes de réalisation, des parties du système 100 sont montées à l'intérieur d'une structure mobile, avec ou sans roues, pour constituer un système médical portatif ou déplaçable 100 d'administration de produit radiopharmaceutique pour la préparation et l'injection de produits radiopharmaceutiques à partir de multiples doses du produit radiopharmaceutique. Dans un exemple, l'écran de protection radiologique 112 est monté sur une structure ayant des roues de façon que les parties du système présentes dans l'écran de protection radiologique et qui sont radioactives soient plus facilement déplacées d'un endroit à un autre.

La vue générale, au niveau du système, du fonctionnement d'une forme de réalisation a été décrite dans le présent chapitre de la description détaillée. Le système 100 est un système intégré pour la production, la gestion de la qualité, la distribution et l'imagerie à l'aide de produits radiopharmaceutiques de TEP. Le système 100 réduit la gestion sans liens des fonctions de préparation et d'injection de radioisotopes chez des sujets vivants. Le système 100 constitue un système de commande entier qui considère comme un seul problème les difficultés cliniques de l'administration d'isotopes radioactifs à des sujets vivants, et il permet, d'une manière automatisée, un programme intégré de production, de distribution, de gestion de qualité, d'injection et d'acquisition de données. En outre, il constitue une manière automatisée d'administrer des protocoles d'imagerie TEP successifs par exemple dans le cas de l'imagerie TEP cardiaque de repos-effort.

Bien que le système 100 ne soit pas limité à un cyclotron particulier 101, à la partie de marqueur radioactif 104 représentant plusieurs doses, au poste de distribution 106, à la partie individuelle de produit pharmaceutique 126 et 128, aux systèmes d'imagerie TEP 114 et 116, à l'écran 112, au dispositif de gestion de la qualité 110, aux systèmes d'injection 122 et 124, aux moniteurs physiologiques 134 et 136, aux tomographes 138 et 140, aux ordinateurs 142 et 144, au système de commande 146 et au LAN 148, des organes simplifiés ont été décrits pour plus de clarté.

Appareil selon une forme de réalisation

Dans le chapitre précédent, une vue générale au niveau du système du fonctionnement d'une forme de réalisation a été décrite. Dans le présent chapitre, l'appareil selon une telle forme de réalisation est décrit en référence à une série de schémas de principe. La description de l'appareil permet à un spécialiste de la technique de réaliser et d'utiliser l'appareil.

La Fig. 2 est un schéma de principe d'un appareil 200 pour injecter une ou plusieurs doses individuelles 126 ou 128 d'un produit radiopharmaceutique à partir d'une dose multiple du produit radiopharmaceutique. L'appareil 200 comprend un dispositif d'extraction 202. L'extrémité inférieure du dispositif d'extraction 202 est placée dans une dose multiple du produit radiopharmaceutique. Une dose individuelle 126 ou 128 est retirée de la dose multiple du produit radiopharmaceutique par le dispositif d'extraction 202, par aspiration ou mise en dépression. L'extraction d'une dose individuelle 126 ou 128 d'un produit

radiopharmaceutique à partir d'une dose multiple du produit radiopharmaceutique réduit le nombre de flacons de doses individuelles et de conteneurs blindés que les fournisseurs de radioisotopes préparent et livrent quotidiennement à chaque établissement médical. L'extraction d'une dose individuelle 126 ou 128 réduit également le nombre de trajets de livraison parcourus chaque jour par un fournisseur de marqueurs radioactifs vers chaque établissement médical. La Fig. 2 représente un exemple de dispositif d'extraction 202 qui est un système d'administration de médicament.

Le dispositif d'extraction 202 coopère avec un dispositif d'injection intraveineuse 204 comportant une aiguille à injection intraveineuse. Le dispositif d'extraction 202 est raccordé par l'intermédiaire d'une tubulure de perfusion intraveineuse 206. La tubulure permet un raccordement par l'intermédiaire duquel des liquides peuvent être transférés, transportés et/ou distribués. Dans certaines formes de réalisation, la tubulure 206 est une conduite à blindage de plomb qui réduit l'exposition des personnes, par exemple les opérateurs de TEP, à la radioactivité pendant les étapes manuelles d'administration d'un produit radiopharmaceutique à des patients. La dose individuelle du produit radiopharmaceutique est distribuée par l'intermédiaire de la tubulure 206 et injectée dans un sujet vivant à l'aide du dispositif d'injection intraveineuse 204.

Ainsi, l'appareil 200 permet de distribuer des doses individuelles 126 ou 128 d'un produit radiopharmaceutique à partir d'une dose multiple du produit radiopharmaceutique et de les injecter dans un sujet vivant au sein du même établissement médical. L'appareil 200 constitue également un moyen pour préparer et distribuer des doses individuelles 126 ou 128 d'un produit radiopharmaceutique qui est plus commode que les systèmes selon la technique antérieure qui nécessitent une irradiation et une expédition de chaque dose individuelle de produit raadiopharmaceutique.

La Fig. 3 est un schéma de principe d'un système d'étalonnage 300 de doses selon une forme de réalisation. Le système d'étalonnage 300 de doses permet de distribuer une dose multiple de produit radiopharmaceutique sous la forme d'une ou de plusieurs doses individuelles. Une dose multiple d'un produit radiopharmaceutique est une quantité d'un marqueur radioactif 104, soumise à un contrôle de qualité, qui est calculée d'une manière convenable pour assurer de la radioactivité pour plus d'une dose de radioactivité. Une dose individuelle d'un produit radiopharmaceutique est une quantité d'un produit radiopharmaceutique

calculée de manière adéquate pour assurer la radioactivité pour une dose de radioactivité.

Le système d'étalonnage 300 de doses contient un réservoir 302 destiné à recevoir une dose multiple d'un produit radiopharmaceutique, comme sur la Fig. 1. Le réservoir 302 est logé dans une cavité du système d'étalonnage 300 de dose. Le réservoir 302 est également appelé flacon multidose. Un dispositif mécanique de tenue 304, tel qu'un bras de transport, tient le réservoir 302 à l'intérieur du poste de distribution. Dans certaines formes de réalisation, le dispositif mécanique de tenue 304 est monté à l'intérieur de la cavité du système d'étalonnage 300 de dose. Le flacon multidose 302 du système 300 réduit le nombre de flacons de doses individuelles qu'un fournisseur de marqueurs radioactifs doit livrer quotidiennement à un établissement médical, ce qui réduit à son tour le nombre de trajets de livraison qu'un fournisseur de marqueurs radioactifs doit effectuer chaque jour vers chaque établissement médical.

Le système d'étalonnage 300 de doses extrait des doses individuelles 126 ou 128 de produit radiopharmaceutique du réservoir 302, à l'aide d'un dispositif d'extraction 202. Le dispositif d'extraction 202 est monté sur le système d'étalonnage 300 de doses, par exemple en étant monté à l'intérieur de la cavité du système d'étalonnage 300 de doses. La dose individuelle 126 ou 128 de produit radiopharmaceutique est distribuée à un ou plusieurs systèmes d'imagerie TEP 112 et 114, comme sur la Fig. 1. Ainsi, le système d'étalonnage 300 de doses permet de distribuer à partir du réservoir 302 une dose multiple de produit radiopharmaceutique sous la forme d'une ou plusieurs doses individuelles. Le système d'étalonnage 300 de doses constitue un moyen de préparation et de distribution de doses individuelles 126 ou 128 de produit radiopharmaceutique qui est plus commode que les systèmes selon la technique antérieure qui nécessitent une irradiation et une expédition de nombreuses doses individuelles de produit radiopharmaceutique.

La Fig. 4 est un schéma de principe d'un système d'injection automatisé pour médications de TEP 400 selon une forme de réalisation. Le système d'injection 400 est une forme de réalisation des systèmes d'injection 122 et 124.

Le système 400 permet de distribuer à partir d'un flacon multidose 302 une dose individuelle d'un produit radiopharmaceutique 126 ou 128. Le flacon multidose 302 est livré par un fournisseur de marqueurs radioactifs sur le site du système 400 dans un conteneur d'expédition 402 à blindage de plomb. Le flacon multidose 302 du système 400 réduit le nombre de flacons de doses individuelles que le fournisseur de

marqueurs radioactifs doit livrer quotidiennement à un établissement médical, ce qui réduit à son tour le nombre de trajets de livraison que le fournisseur de marqueurs radioactifs doit effectuer chaque jour vers chaque établissement médical.

Le conteneur d'expédition 402 est mis dans une position fixe sous un système d'étalonnage 404 de doses à blindage de plomb (ce système est également appelé chambre d'ionisation) et le couvercle 306 sur le dessus du flacon multidose 302 est retiré. Le couvercle 406 sur le dessus du flacon peut être retiré manuellement ou par un moyen mécanique automatisé. On peut citer comme exemple de moyen automatisé un moyen dans lequel un bras pneumatique 304 descend dans le conteneur d'expédition 402 et se fixe au flacon multidose 302. Le flacon multidose 302 est soulevé hors du conteneur d'expédition 402 pour être placé dans le système d'étalonnage 404 de doses et une aiguille 408 est automatiquement insérée dans le flacon multidose 302. Une dose individuelle 126 ou 128 est extraite de la dose multiple du produit radiopharmaceutique par le dispositif d'extraction 202, par aspiration ou mise en dépression. Ainsi, le système 400 permet la distribution d'une partie d'une dose multiple de produit radiopharmaceutique sous la forme de doses individuelles 126 ou 128. Le système 400 constitue un moyen de préparation et d'injection d'une dose individuelle d'un produit radiopharmaceutique qui est plus commode que les systèmes selon la technique antérieure qui nécessitent l'irradiation et l'expédition de nombreuses doses individuelles de produit radiopharmaceutique. Le système 400 permet de grandes économies d'échelle dans la préparation et la distribution de doses de produits radiopharmaceutiques.

Le moyen d'extraction 302 extrait une quantité de produit radiopharmaceutique qui est calculée de manière adéquate pour constituer une dose individuelle du produit radiopharmaceutique 126 ou 128. La quantité de la dose individuelle 126 ou 128 est calculée en fonction du type de produit radiopharmaceutique, de la période radioactive du produit radiopharmaceutique, d'une équation paramétrique prédéfinie, du protocole clinique suivi, de la durée prévue de l'injection dans un sujet vivant 124 et de descripteurs de haut niveau du sujet vivant, comme le poids, le sexe et les dimensions physiques du sujet vivant.

Les organes du système 400 ont des dimensions et des formes prédéfinies qui sont conçues pour s'harmoniser physiquement les unes avec les autres. Dans un premier exemple, le flacon multidose 302 et le conteneur d'expédition blindé 402 ont des dimensions et des formes prédéfinies qui sont conçues pour qu'ils s'harmonisent physiquement l'un avec l'autre. Dans un autre exemple, le flacon multidose 302 et le

système d'étalonnage 404 à blindage de plomb ont des dimensions et des formes prédéfinies qui permettent leur harmonisation physique l'un avec l'autre. Ces formes intégrées permettent aux organes de s'assembler l'un l'autre dans le respect de tolérances données pour réduire les fuites de matière radioactives et pour permettre des manœuvres automatisées comme la sortie du flacon multidose 302 du récipient d'expédition blindé 402 par un bras de transport et son installation dans le système d'étalonnage 404 de doses. Dans certaines formes de réalisation, les dimensions et formes prédéfinies sont spécifiées par un fournisseur de marqueurs radioactifs et sont exclusives pour ce fournisseur de marqueurs radioactifs. Le fait d'avoir des organes de dimensions et de formes prédéfinies incite fortement un établissement médical à rester fidèle au fournisseur de marqueurs radioactifs si le flacon multidose 302 et le conteneur d'expédition blindé 402 risquent de ne pas avoir des dimensions et des formes physiquement compatibles avec le système d'étalonnage 404 de doses dans la mesure où le système d'étalonnage 404 de doses risque de ne pas recevoir le flacon multidose 302.

Dans certaines formes de réalisation, le moyen d'extraction 202 coopère par l'intermédiaire d'une tubulure intraveineuse 206 avec un dispositif qui régule l'écoulement de multiples liquides, par exemple un robinet d'arrêt 410 à trois voies commandé par un solénoïde ou un autre type de vanne à plusieurs orifices. Le robinet d'arrêt 410 coopère également avec un réservoir d'un autre produit pharmaceutique liquide, par exemple une poche d'administration intraveineuse de chlorure de sodium (NaCl) à concentration appropriée 412, couramment appelé solution saline. La dose individuelle 126 ou 128 est mélangée au NaCl 412 par le robinet d'arrêt 410. Le mélange est pompé à partir du robinet d'arrêt 410, à l'aide d'un pompe 414 telle qu'une pompe péristaltique.

Dans certaines formes de réalisation, un deuxième réservoir 416 d'un deuxième étalonneur 418 de doses reçoit le mélange à partir de la pompe péristaltique 414. Dans certaines formes de réalisation, le réservoir 416 est un flacon qui possède un fond en "V" et est appelé flacon de patient. Le mélange passe à travers un filtre 415, par exemple un filtre pour marqueurs radioactifs de 0,22 micromètres, et est stocké dans le deuxième réservoir 416. Dans certaines formes de réalisation, une pompe à perfusion coopère avec la pompe péristaltique 414 plutôt qu'au réservoir 416 d'un deuxième étalonneur 418 de doses. Dans certaines formes de réalisation, l'étalonneur de doses comprend une chambre d'ionisation qui mesure la quantité de radioactivité du mélange. La mesure de la radioactivité permet de vérifier

que la radioactivité de chaque dose individuelle est adéquate juste avant l'injection et à proximité immédiate du site d'injection.

Le mélange est pompé vers le sujet vivant par un système de perfusion 420 tel qu'une pompe à perfusion, par l'intermédiaire d'un deuxième dispositif qui régule l'écoule de multiples liquides, par exemple un deuxième robinet d'arrêt 422 à trois voies commandé par un solénoïde. Le robinet d'arrêt 422 coopère également avec un réservoir d'un autre produit pharmaceutique liquide tel qu'une poche d'administration intraveineuse contenant un produit pharmaceutique non radiologique 424 tel qu'un agent pharmacologique d'effort. On peut citer comme exemples d'agents d'effort utilisés dans les examens du myocarde par perfusion le dipyridamole et l'adénosine. Dans certaines formes de réalisation, un réceptacle pour produits usés 426 coopère avec la tubulure d'injection intraveineuse 206 entre le dispositif qui régule l'écoulement de multiples liquides 422 et la pompe à perfusion 420.

La pompe à perfusion 420 envoie par pompage le mélange dans le sujet vivant 124 par l'intermédiaire d'un dispositif d'injection 204 par voie intraveineuse, en administrant ainsi une dose individuelle 126 ou 128 d'un produit radiopharmaceutique à un sujet vivant 124 à partir d'une dose multiple 104 du produit radiopharmaceutique. Dans diverses formes de réalisation, le produit radiopharmaceutique est également mélangé à d'autres produits pharmaceutiques tels que la solution saline 412 et/ou un produit pharmaceutique 424, ce qui assure donc une certaine souplesse de configuration pour permettre diverses applications médicales.

Dans certaines formes de réalisation du système 400, un dosimètre vérifie la quantité de la dose individuelle 126 ou 128 du produit radiopharmaceutique. Le dosimètre peut coopérer soit avec la tubulure intraveineuse 206 soit avec la tubulure intraveineuse 428. La tubulure intraveineuse est également appelée tubulure de patient. Dans d'autres formes de réalisation, le système 400 comprend également un ou plusieurs étalonneurs supplémentaires 404 de doses. Le/les étalonneurs supplémentaires 404 de doses permettent au système d'injecter un ou plusieurs produits radiopharmaceutiques autres que le produit radiopharmaceutique du système d'étalonnage 404 de dose.

Afin de protéger les sujets vivants contre l'exposition aux produits pharmaceutiques et aux microorganismes de sujets vivants qui ont utilisé précédemment le système 400, de nombreux organes du système sont remplacés à chaque utilisation. Les organes remplacés après chaque utilisation du système sont

tous les éléments jetables situés entre le filtre 415 et le sujet vivant 124. Les éléments jetables comprennent la tubulure intraveineuse 428 et le dispositif d'injection intraveineuse 204.

Un exemple du fonctionnement du système 400 est décrit en détail en référence au procédé 800 de la Fig. 8.

La Fig. 5 est un schéma de principe d'un système médical d'administration de produit radiopharmaceutique selon une forme de réalisation 500. Le système médical 500 d'administration de produit radiopharmaceutique est un système intégré pour la production, la gestion de la qualité et l'injection de doses individuelles d'un produit radiopharmaceutique en imagerie de tomographie par émission de positons (TEP).

Dans le système 500, une cible 502 de cyclotron produit un isotope radioactif tel que l'ammoniac à azote-13. Dans les formes de réalisation à ammoniac à azote-13, la matière formant cible placée dans la cible 502 de cyclotron peut être soit un mélange d'alcool éthylique à concentration molaire appropriée dans de l'eau à forte résistivité, du méthane en surpression sur de l'eau ou simplement de l'eau, subissant ensuite une réduction d'anions à l'aide d'un alliage de DeVarda. En outre, la cible 502 de cyclotron a une cavité d'un volume compris entre environ 0,5 millilitres et moins d'une dizaine de millilitres.

Une pompe 503 reçoit le radioisotope et dépose le radioisotope dans un réservoir de stockage 504. Le radioisotope est amené à circuler à l'intérieur du réservoir de stockage 504.

Ultérieurement, la pompe reçoit le radioisotope du réservoir de stockage 504. La pompe reçoit aussi éventuellement une solution de rinçage 506. La pompe 503 renvoie également les produits usés dans le réservoir 508. Les produits usés sont les parties supplémentaires non nécessaires du radioisotope et/ou de la solution de rinçage 506.

Les organes du système 500 qui produisent le mélange contenant le radioisotope, comme la pompe 503, la cible 502 de cyclotron, le réservoir 504 de radioisotope, la solution de rinçage 506 et le réservoir 508 de produits usés sont tous situés dans la même salle 509 qu'un cyclotron. Les autres organes du système 500 peuvent être situés dans le même bâtiment que la salle 509 du cyclotron ou dans un bâtiment voisin du même complexe médical.

Dans certaines formes de réalisation, le mélange d'ammoniac à azote-13 ou d'un autre radioisotope et de la solution de rinçage 506 sort de la pompe 503 pour

entrer dans un filtre 415, par exemple un filtre de 0,22 micromètres pour marqueurs radioactifs.

Le mélange entre dans un système d'étalonnage 404 de dose. Le système d'étalonnage 404 de dose extrait une dose individuelle 126 ou 128 du mélange. La dose individuelle entre dans un dispositif de perfusion tel qu'un pousse-seringue 512 ou une pompe à perfusion. Dans certaines formes de réalisation, de l'eau stérile à injecter à partir du réservoir 514 et/ou un agent d'effort issu d'un réservoir 516 d'agent d'effort entrent également dans le pousse-seringue 512. L'eau sert à rincer les conduites 206. Depuis le pousse-seringue, le mélange de la dose individuelle, de l'eau et de l'agent d'effort pénètre dans un dispositif d'injection intraveineuse 204 comportant une aiguille d'injection intraveineuse, passe par une tubulure intraveineuse pour être injecté dans un sujet vivant. Ainsi, le système d'étalonnage 404 de dose permet l'administration d'une dose multiple d'un produit radiopharmaceutique à un ou plusieurs sujets vivants sous la forme de doses individuelles, éventuellement avec un agent d'effort, de l'eau stérile et une solution de rinçage. Le système d'étalonnage 404 de dose réduit le nombre de flacons de doses individuelles qu'un fournisseur de marqueurs radioactifs doit livrer chaque jour à un établissement médical, ce qui réduit à son tour le nombre de trajets de livraison qu'un fournisseur de marqueurs radioactifs doit effectuer quotidiennement vers chaque établissement médical.

Les produits usés issus du pousse-seringue 512 entrent également dans un réservoir 518 de produits usés. La qualité du mélange constituant une dose est contrôlée par l'unité de gestion de la qualité 110. La tubulure intraveineuse 506 sert, dans le système 500, à transporter les liquides et les mélanges.

Le système 500 peut être placé, en partie ou dans sa totalité, sur une table 520 ou monté sur une structure de support. En outre, des parties du système 500 peuvent également être montées à l'intérieur d'une structure mobile munie de roues afin de constituer un système médical portatif 500 d'administration de produit radiopharmaceutique pour préparer et injecter des doses individuelles d'un produit radiopharmaceutique à partir de multiples doses du produit radiopharmaceutique.

Le système 500 constitue un procédé commode pour produire et administrer sur place un marqueur radioactif tel que de l'ammoniac à azote-13.

La Fig. 6 est un schéma de principe d'un système médical d'administration de produit radiopharmaceutique selon une forme de réalisation 600. Le système médical 600 d'administration de produit radiopharmaceutique est un système intégré

pour la production, la gestion de la qualité et l'injection de doses individuelles d'un produit radiopharmaceutique en imagerie de tomographie par émission de positons (PET).

Dans le système 600, une cible 502 d'un cyclotron produit un radioisotope tel que de l'ammoniac à azote-13. Dans les formes de réalisation à ammoniac à azote-13, la matière formant cible placée dans la cible 502 du cyclotron pour produire de l'ammoniac à azote-13 peut être soit un mélange d'alcool éthylique à concentration molaire appropriée dans de l'eau à forte résistivité, du méthane en surpression sur de l'eau ou simplement de l'eau, soumis ensuite à une réduction d'anions à l'aide d'un alliage de DeVarda. En outre, la cible 502 du cyclotron a une cavité d'un volume compris entre 0,5 millilitres et moins d'une dizaine de millilitres.

Une pompe 503 reçoit le radioisotope et dépose le radioisotope dans un réservoir de stockage 504. Le radioisotope est amené à circuler à l'intérieur du réservoir de stockage 504.

Ultérieurement, la pompe reçoit le radioisotope du réservoir de stockage 504. La pompe reçoit également éventuellement une solution de rinçage 506. La pompe 503 renvoie également des liquides usés dans le réservoir 508. Les liquides usés sont les parties supplémentaires inutiles du radioisotope et/ou de la solution de rinçage 506.

Dans certaines formes de réalisation, le mélange du radioisotope et de la solution de rinçage passe de la pompe 503 à un filtre 415, par exemple un filtre de 0,22 micromètres pour marqueurs radioactifs. La qualité du mélange est contrôlée par l'unité de gestion de la qualité 110.

Le mélange entre dans un système d'étalonnage 404 de dose. Le système d'étalonnage 404 de dose extrait une dose individuelle 126 ou 128 du mélange par l'intermédiaire d'un dispositif d'extraction 102, par aspiration ou mise en dépression. Ainsi, le système 600 permet la distribution d'une dose multiple d'un produit radiopharmaceutique sous la forme de doses individuelles 126 ou 128. Le système 600 constitue un moyen de préparation et d'injection d'une dose individuelle d'un produit radiopharmaceutique qui est plus commode que les systèmes selon la technique antérieure nécessitant l'irradiation et l'expédition de nombreuses doses individuelles de produit radiopharmaceutique. Le système 600 permet de grandes économies d'échelle dans la préparation et la distribution de doses de produits radiopharmaceutiques. Le flacon multidose 302 du système 600 réduit le nombre de flacons de doses individuelles qu'un fournisseur de marqueurs radioactifs doit livrer

quotidiennement à un établissement médical, ce qui réduit à son tour le nombre de trajets de livraison qu'un fournisseur de marqueurs radioactifs doit effectuer chaque jour vers chaque établissement médical.

Le moyen d'extraction 302 extrait une quantité de produit radiopharmaceutique qui est calculée de manière adéquate pour réaliser une dose individuelle du produit radiopharmaceutique 126 ou 128. La quantité de la dose individuelle 126 ou 128 est calculée en fonction de la période radioactive du produit radiopharmaceutique, de la durée prévue de l'injection dans un sujet vivant 124 et du poids du sujet vivant 124.

Dans certaines formes de réalisation, le moyen d'extraction 202 coopère, par l'intermédiaire d'une tubulure d'injection intraveineuse 206, avec un dispositif qui régule l'écoulement de multiples liquides, par exemple un robinet d'arrêt 410 à trois voies commandé par un solénoïde, ou un autre type de vanne à plusieurs orifices. Le robinet d'arrêt 410 coopère également avec un réservoir d'un autre produit pharmaceutique liquide, par exemple une poche d'administration intraveineuse de chlorure de sodium (NaCl) 412, couramment appelé solution saline. La dose individuelle 126 ou 128 est mélangée avec le NaCl 412 par le robinet d'arrêt 410. Le mélange est pompé depuis le robinet d'arrêt 410 par une pompe péristaltique 414.

Dans certaines formes de réalisation, un deuxième réservoir 416 présent dans un deuxième étalonneur 418 de dose reçoit le mélange venant de la pompe péristaltique 414. Le mélange est stocké dans le deuxième réservoir 416. Dans certaines formes de réalisation, une pompe à perfusion coopère avec la pompe péristaltique 414 plutôt qu'avec le réservoir 416 dans un deuxième étalonneur 418 de dose.

Le mélange est pompé vers le sujet vivant par une pompe à perfusion 420, par l'intermédiaire d'un deuxième dispositif qui régule l'écoulement de multiples liquides, par exemple un deuxième robinet d'arrêt 422 à trois voies commandé par un solénoïde. Le robinet d'arrêt 422 coopère aussi avec un réservoir d'un autre produit pharmaceutique liquide, par exemple une poche d'administration intraveineuse contenant un produit pharmaceutique 424. Dans certaines formes de réalisation, un réceptacle pour produits usés 426 coopère avec la tubulure d'injection intraveineuse 206 entre le dispositif qui régule l'écoulement de multiples liquides 422 et la pompe à perfusion 420.

La pompe à perfusion 420 envoie le mélange dans le sujet vivant 124 par l'intermédiaire d'un dispositif d'injection intraveineuse 204 comportant une aiguille

d'injection intraveineuse, en administrant ainsi une dose individuelle 126 ou 128 d'un produit radiopharmaceutique à un sujet vivant 124 à partir d'une multiple dose 104 du produit radiopharmaceutique. Dans diverses formes de réalisation, le produit radiopharmaceutique est également mélangé à d'autres produits pharmaceutiques tels que le NaCl 412 et/ou un produit pharmaceutique 424, ce qui assure une certaine souplesse des configurations pour permettre diverses applications médicales.

Procédés de mise en œuvre d'une forme de réalisation

Dans les chapitres précédents, une vue générale du fonctionnement d'une forme de réalisation au niveau du système a été présentée et des formes de réalisation d'appareils ont été décrites. Dans le présent chapitre, les procédés particuliers mis en œuvre par les opérateurs de TEP et le système de commande 146 d'une telle forme de réalisation sont décrits en référence à une série d'organigrammes. Le fait de décrire les procédés en référence à un organigramme permet à un spécialiste de la technique d'élaborer des procédures manuelles ou des instructions informatiques.

La Fig. 7 est un organigramme d'une forme de réalisation d'un procédé 700 de mise en œuvre de l'appareil 400. Le procédé 700 est mis en œuvre par un opérateur de TEP. Ordinairement, le procédé 700 est exécuté une fois pour chaque journée de fonctionnement d'un système de tomographie par TEP.

Lors de l'étape 702, décrite plus en détail en référence à la Fig. 8, un opérateur de TEP prépare le système 400 en vue de son utilisation par un certain nombre de patients. Ensuite, le système 400 est préparé de manière répétée, à l'étape 704, pour chaque patient individuel, de la manière décrite à propos de la Fig. 9, et l'injection pour chaque patient est administrée, à l'étape 706, comme décrit en référence à la Fig. 10.

Ensuite, dans certaines formes de réalisation, un fournisseur de marqueurs radioactifs fournissant le produit radiopharmaceutique est avisé du nombre de doses et de l'activité totale utilisée pour la journée et des besoins pour le lendemain.

La Fig. 8 est un organigramme d'une forme de réalisation d'un procédé 800 de préparation du système d'injection 400 en vue de son utilisation par un certain nombre de patients. Le procédé 800 est une forme de réalisation de l'étape 702 de la Fig. 7.

Selon le procédé 800, le système informatique 142 ou 144 est mis en marche, à l'étape 802.

Le procédé 800 comprend également la fourniture, à l'étape 804, d'un flacon multidose 302 de radioisotope au système 400. Le flacon multidose 302 est levé, à l'étape 806, jusque dans le système d'étalonnage 404 de dose.

La Fig. 9 est un organigramme d'une forme de réalisation du procédé 900 de préparation d'un système d'injection 400 pour chaque patient individuel. Le procédé 900 est une forme de réalisation de l'étape 704 de la Fig. 7. Les étapes du procédé 900 servent à installer des éléments jetables neufs.

Le procédé 900 comprend l'installation 902 d'un flacon 416 de patient propre, stérile et apyrogène dans l'étalonneur 418 de dose. Le procédé 900 comprend également le raccordement 904 d'une aiguille de sortie à une conduite 206 venant de la pompe péristaltique 414. L'aiguille de sortie est insérée en 906 ou placée au fond du flacon 416. Ensuite, l'opérateur de TEP place, à l'étape 908, le flacon 416 dans l'étalonneur 418 de dose.

Le procédé 900 comprend également l'installation 910 d'un robinet d'arrêt neuf 422. Une tubulure intraveineuse neuve 428 est également installée, à l'étape 912, à travers le robinet d'arrêt neuf 422 en introduisant la tubulure intraveineuse 428 dans une première entrée du robinet d'arrêt 410 à trois voies. Une tubulure intraveineuse neuve 204 est également installée, à l'étape 914. Une tubulure intraveineuse provenant d'une poche de solution saline ou d'une poche d'un autre produit pharmaceutique 412 est fixée, à l'étape 916, à une deuxième entrée du robinet d'arrêt 410 à trois voies.

Ainsi, dans le procédé 900, un flacon 416, une tubulure intraveineuse 428, un robinet d'arrêt 422 et une tubulure intraveineuse 204 neufs sont utilisés pour chaque patient.

Ensuite, le système 400 est prêt pour commencer à administrer une dose individuelle à un patient.

La Fig. 10 est un organigramme d'une forme de réalisation d'un procédé 1000 d'administration d'une injection à l'aide du système d'injection 400 pour chaque patient individuel. Le procédé 1000 est une forme de réalisation de l'étape 706 de la Fig. 7.

Le procédé 1000 comprend l'extraction 1002 d'une dose individuelle d'un produit radiopharmaceutique à partir d'un flacon multidose 302. Le produit radiopharmaceutique est envoyé par pompage, via un robinet d'arrêt 410 à trois voies, dans un flacon 416 de patient situé dans l'étalonneur 418 de dose d'un patient.

Lorsque la quantité requise de radioactivité est présente dans le flacon 416 du patient, une comparaison est faite pour vérifier, à l'étape 1004, que la quantité de radioactivité dans le flacon 416 du patient est égale à la quantité de radioactivité qui a été évacuée du flacon multidose 302. Dans l'affirmative, une solution saline supplémentaire est ajoutée, à l'étape 1006, dans le flacon 416 du patient via le robinet d'arrêt 410 à trois voies et la poche 412 de solution saline.

La dose destinée au patient est enregistrée par le système 142 ou 144 et la dose enregistrée qui est enregistrée sur les systèmes informatiques est vérifiée, à l'étape 1008, avec le flacon du patient par l'opérateur de TEP. L'activité initiale de la dose destinée au patient à un instant initial est enregistrée, à l'étape 1010.

Une injection 1012 est alors réalisée dans le patient à un débit donné. On notera que, si le marqueur radioactif est du FDG, l'injection est réalisée dans une salle séparée, environ une heure avant la tomographie.

Lorsque le flacon de produit radioactif est vide, l'entrée du robinet d'arrêt 422 à trois voies du patient est mise en position de solution saline pour permettre au flux de chasser ou de purger, à l'étape 1014, les substances radioactives présentes dans la tubulure 428 du patient. Après un laps de temps donné, la perfusion de solution saline est terminée et la tubulure 428 du patient est retirée, le robinet d'arrêt 422 et la tubulure de solution saline sont débranchés, à l'étape 1016.

La tubulure de solution saline, la tubulure 428 du patient et le robinet d'arrêt 422 sont mis, à l'étape 1018, dans l'étalonneur 418 de dose de patient et l'activité résiduelle dans l'étalonneur 418 de dose du patient à cet instant final est mesurée, à l'étape 1020. L'activité initiale de la dose et l'activité résiduelle, ainsi que les repères chronologiques correspondants, sont transmis, à l'étape 1022, au tomographe de TEP par le système d'injection 400.

Le fait de décrire le procédé ci-après en référence à un organigramme permet à un spécialiste de la technique d'élaborer des programmes, des microprogrammes ou du matériel informatique, dont les instructions pour mettre en œuvre les procédés sur des clients informatisés et/ou des serveurs appropriés en exécutant les instructions fournies par des supports lisibles par un ordinateur. De même, les procédés exécutés par des programmes, microprogrammes ou matériels informatiques sont également composés d'instructions exécutables par un ordinateur.

La Fig. 11 est un organigramme d'un procédé 1100 exécuté par le système de commande 146 selon une forme de réalisation. Le procédé sert à gérer l'isotope radioactif dans le système 1100. Le procédé 1100 est mis en œuvre par un

programme exécuté sur ou par un microprogramme ou un matériel qui fait partie d'un ordinateur tel que l'ordinateur 1202 de la Fig. 12.

Le procédé 1100 comprend la réception 1102 d'informations décrivant une quantité requise de radioactivité, le type de radioisotope, la durée prévue de l'injection du radioisotope, des descripteurs de niveau élevé du patient et l'identification du système d'imagerie TEP à l'origine de la demande. Ensuite, le procédé comprend la détermination 1104 d'une quantité de matière formant cible à utiliser pendant le processus d'irradiation, et une quantité de radioactivité du radioisotope à produire pendant l'irradiation. La détermination 1104 est calculée d'après les informations descriptives. Ensuite, le procédé comprend l'envoi 1106 d'instructions à une cible dans le cyclotron 101 pour produire la quantité requise du radioisotope. Après cela, le procédé comprend l'envoi 1108 d'instructions au poste de distribution 106 pour distribuer la quantité du radioisotope au système d'imagerie TEP demandeur. Le procédé 1100 réduit la gestion et la commande sans liens des fonctions de préparation et d'injection de radioisotopes dans des sujets vivants en gérant les radioisotopes à l'aide du système de commande 146. Un effet technique du procédé 1100 est que la préparation et l'injection de radioisotopes dans des sujets vivants sont gérées et commandées par des processus informatisés.

Dans certaines formes de réalisation, le procédé 1100 est mis en œuvre sous la forme d'un signal de données informatiques sous la forme d'une onde porteuse, qui représente une suite d'instructions qui, lorsqu'elles sont exécutées par un processeur, comme le processeur 1204 de la Fig. 12, amènent le processeur à exécuter le procédé correspondant. Dans d'autres formes de réalisation, le procédé 1100 est mis en œuvre sous la forme d'un support accessible par un ordinateur, contenant des instructions exécutables permettant de demander à un processeur tel que le processeur 1204 de la Fig. 12 d'exécuter le procédé correspondant. Dans diverses formes de réalisation, le support est un support magnétique, un support électronique ou un support optique.

Le procédé 1100 peut être mis en œuvre sous la forme de circuits matériels d'un ordinateur ou sous la forme d'un programme lisible par un ordinateur, ou sous la forme d'une combinaison des deux. Dans une autre forme de réalisation, le procédé 1100 est mis en œuvre dans un système de prestations de services d'applications (ASP).

Plus particulièrement, dans la forme de réalisation à programme lisible par un ordinateur, les programmes peuvent avoir une structure par objets utilisant un langage à objets tel que Java, Smalltalk ou C++, et les programmes peuvent avoir

une structure adaptée à des procédures, utilisant un langage de procédure tel que COBOL ou C. Les composants logiciels communiquent par l'un quelconque d'un certain nombre de moyens bien connus des spécialistes de la technique, comme les interfaces de programmes d'applications (API) ou les techniques de communication entre processus telles que l'appel de procédure à distance (RPC), l'architecture CORBA, la spécification COM de modèle d'objet composant, la spécification DCOM de modèle d'objet composant distribué, la spécification DSOM de modèle d'objet système réparti et le protocole RMI d'invocation à distance de méthodes.

Environnement matériel et d'exploitation

La Fig. 12 est un schéma de principe de l'environnement matériel et d'exploitation 1200 dans lequel peuvent être mises en œuvre différentes formes de réalisation. La description de la Fig. 12 donne une idée générale du matériel informatique et d'un environnement informatique approprié en liaison avec lequel peuvent être mises en œuvre certaines formes de réalisation. Les formes de réalisation sont décrites en fonction d'un ordinateur exécutant des instructions exécutables par un ordinateur. Cependant, certaines formes de réalisation peuvent être mises en œuvre entièrement dans du matériel informatique dans lequel les instructions exécutables par un ordinateur sont exécutées dans la mémoire morte. Certaines formes de réalisation peuvent également être mises en œuvre dans des environnements informatiques client/serveur où des dispositifs distants qui exécutent des tâches sont en liaison par l'intermédiaire d'un réseau de communications. Des modules de programmes peuvent se trouver dans des dispositifs de mémorisation locaux et distants dans un environnement de traitement distribué.

L'ordinateur 1202 comprend un processeur 1204, commercialisé par Intel, Motorola, Cyrix et autres. L'ordinateur 1202 est une forme de réalisation de l'ordinateur 142, 144 ou 146 de la Fig. 1.

L'ordinateur 1202 comprend également une mémoire vive (RAM) 1206, une mémoire morte (ROM) 1208 et une ou plusieurs mémoires externes 1210, et un bus système 1212, qui fait coopérer divers organes du système avec le processeur 1204. Les mémoires 1206, 1208 et les mémoires externes, 1210, sont des supports du type accessibles par un ordinateur. Les mémoires externes 1210 sont plus spécifiquement des types de supports rémanents accessibles par un ordinateur et peuvent contenir un ou plusieurs lecteurs de disques durs, lecteurs de disquettes, lecteurs de disques

optiques et lecteurs de chargeurs à bandes. Le processeur 1204 exécute des programmes informatiques enregistrés sur les supports accessibles par ordinateur.

L'ordinateur 1202 peut être relié à l'Internet 1214 via un dispositif de communication 1216. La connexion à l'Internet 1214 est bien connue dans la technique. Dans une première forme de réalisation, un dispositif de communication 1216 est constitué par un modem qui réagit à des pilotes de communication pour se connecter à l'Internet par ce qu'on appelle dans la technique un "accès à ligne commutée". Dans une autre forme de réalisation, un dispositif de communication 1216 est constitué par un Ethernet® ou une carte de réseau physique similaire connectée à un réseau local (LAN) lui-même connecté à l'Internet par ce qu'on appelle dans la technique une "connexion directe" (par exemple, une ligne T1, etc.).

Un utilisateur saisit des instructions et des informations sur l'ordinateur 1202 par l'intermédiaire de dispositifs de saisie tels qu'un clavier 1218 ou un dispositif de pointage 1220. Le clavier 1218 permet d'entrer dans l'ordinateur 1202 des informations sous forme de texte, comme on le sait dans la technique, et les formes de réalisation ne sont limitées à aucun type de clavier particulier. Le dispositif de pointage 1220 permet de commander le pointeur affiche à l'écran, grâce à une interface graphique (GUI) de systèmes d'exploitation tels que les versions de Microsoft Windows®. Les formes de réalisation ne se limitent à aucun dispositif de pointage particulier 1220. Ces dispositifs de pointage comprennent les souris, les pavés de touches, les boules roulantes, les télécommandes et les ergots de pointage. D'autres dispositifs de saisie (non représentés) peuvent être constitués par un microphone, un manche à balai, une poignée de jeu, une antenne parabolique, un scanner ou autre.

Dans certaines formes de réalisation, l'ordinateur 1202 coopère avec un dispositif d'affichage 1222. Le dispositif d'affichage 1222 est connecté au bus système 1212. Le dispositif d'affichage 1222 permet d'afficher des informations, dont des informations informatisées, vidéo et autres, pour permettre leur examen par un utilisateur de l'ordinateur. Les formes de réalisation ne se limitent à aucun dispositif d'affichage particulier 1222. Ces dispositifs d'affichage peuvent être constitués par des afficheurs (écrans) à tube cathodique ainsi que par des écrans plats tels que des écrans à cristaux liquides. En plus d'un écran, les ordinateurs comportent ordinairement d'autres périphériques d'entrée/sortie tels que des imprimantes (non représentées). Des enceintes acoustiques 1224 et 1226 permettent une sortie audio de

signaux. Les enceintes acoustiques 1224 et 1226 sont elles aussi connectées au bus système 1212.

L'ordinateur 1202 comprend également un système d'exploitation (non représenté) stocké sur les supports accessibles par ordinateur, la mémoire vive 1206, la mémoire morte 1208 et la mémoire externe 1210, et qui est exécuté par le processeur 1204. On peut citer comme exemples de systèmes d'exploitation Microsoft Windows®, Apple MacOS®, Linux®, UNIX®. Cependant, le système d'exploitation ne se limite pas à un système particulier et la structure et l'utilisation de tels systèmes d'exploitation sont bien connues dans la technique.

L'ordinateur 1202 peut fonctionner à l'aide d'au moins un système d'exploitation pour avoir une interface graphique (GUI) comportant un pointeur commandable par l'utilisateur. L'ordinateur 1202 peut avoir au moins un programme d'application de navigation sur la toile, exécuté au sein d'au moins un système d'exploitation, pour permettre aux utilisateurs de l'ordinateur 1202 d'accéder à des pages de sites intranet ou Internet atteintes grâce à des adresses URL. On peut citer comme exemples de programmes de navigation Netscape Navigator® et Microsoft Internet Explorer®.

L'ordinateur 1202 peut fonctionner dans un environnement en réseau utilisant des connexions logiques à un ou plusieurs ordinateurs distants, par exemple l'ordinateur distant 1228. Ces connexions logiques sont réalisées par un dispositif de communication couplé à l'ordinateur 1202 ou faisant partie de l'ordinateur 1202. Les formes de réalisation ne se limitent à aucun type de dispositif de communications particulier. L'ordinateur distant 1228 peut être un autre ordinateur, un serveur, un routeur, un PC en réseau, un client, un dispositif homologue ou autre nœud d'un réseau commun. Les connexions logiques illustrées sur la Fig. 12 comprennent un réseau local d'entreprise (LAN) 1230 et un réseau étendu (WAN) 1232. De tels environnements en réseau sont courants dans les bureaux, les réseaux informatiques d'entreprise, les intranets et l'Internet.

Lorsqu'on les utilise dans un environnement en réseau LAN, l'ordinateur 1202 et l'ordinateur distant 1228 sont connectés à un réseau local 1230 par des interfaces ou une carte réseau 1232, qui constituent un type de dispositif de communications 1216. L'ordinateur distant 1228 comporte également un dispositif 1234 de réseau. Utilisés dans un environnement en réseau WAN classique, l'ordinateur 1202 et l'ordinateur distant 1228 communiquent avec un WAN 1236 par l'intermédiaire de modems (non représentés). Le modem, qui peut être interne ou

externe, est connecté au bus système 1212. Dans un environnement en réseau, les modules de programmes indiqués concernant l'ordinateur 1202, ou des parties de ceux-ci, peuvent être enregistrées dans l'ordinateur distant 1228.

L'ordinateur 1202 comprend également une alimentation électrique 1238. L'alimentation électrique peut être une pile. Dans certaines formes de réalisation, l'ordinateur 1202 coopère également avec un dispositif de réseau 1240 de zones de mémoire (SAN) qui est un réseau très rapide connectant de multiples dispositifs de stockage de façon que les multiples dispositifs de stockage soient accessibles sur tous les serveurs d'un LAN tels que le LAN 1230 ou d'un WAN tel que le WAN 1236.

Les formes de réalisation de 1200 fonctionnent dans un environnement de fonctionnement multitraitement, multifile d'un ordinateur.

Conclusion

On a décrit un système de distribution de produit radiopharmaceutique. Bien que des formes de réalisation spécifiques aient été illustrées et décrites ici, les spécialistes ordinaires de la technique comprendront que n'importe quel agencement conçu pour parvenir au même but peut être substitué aux formes de réalisation spécifiques présentées. La présente demande est destinée à couvrir les éventuelles adaptations ou variantes. Par exemple, un spécialiste ordinaire de la technique comprendra que des mises en œuvre peuvent être réalisées dans un environnement pour procédures ou pour objets ou tout autre environnement assurant les relations nécessaires.

La terminologie utilisée dans la présente demande est destinée à couvrir tous les environnements médicaux, de technologie à objets, de base de données et de communication et d'autres technologies assurant la même fonctionnalité que celle décrite ici.

REVENDICATIONS

1. Système automatisé comprenant :

au moins un injecteur (122 ou 124) de produit radiopharmaceutique comprenant :

un dispositif d'extraction (202) pour extraire une dose individuelle (126 ou 128) de produit radiopharmaceutique d'une dose multiple (104) d'un produit radiopharmaceutique ;

un système d'étalonnage (300) de dose coopérant avec le dispositif d'extraction (202) pour recevoir la dose individuelle (126 ou 128) du produit radiopharmaceutique ;

une pompe à perfusion (420) coopérant avec le système d'étalonnage (300) de dose, pour prélever par pompage la dose individuelle (126 ou 128) du produit radiopharmaceutique dans le système d'étalonnage (300) de dose; et

un dispositif d'injection intraveineuse, par exemple une aiguille intraveineuse (204), coopérant avec la pompe à perfusion (420) pour injecter la dose individuelle (126 ou 128) du produit radiopharmaceutique dans un sujet vivant.

2. Système selon la revendication 1, comprenant en outre

une tubulure (206) à blindage de protection radiologique, pour transférer la dose individuelle du produit radiopharmaceutique, ayant une première extrémité et une deuxième extrémité, la première extrémité coopérant avec le dispositif d'extraction.

3. Système selon la revendication 1 ou 2, dans lequel le système d'étalonnage (300) de dose comprend un dispositif de tenue (304) monté à l'intérieur d'un injecteur (404) pour tenir un réservoir (302) de doses multiples (104) du produit radiopharmaceutique, et dans lequel le dispositif d'extraction (202) est monté à l'intérieur de l'injecteur (404).

4. Système selon la revendication 3, dans lequel le système d'étalonnage (300) de dose coopère en outre avec le dispositif d'injection intraveineuse (204).

5. Système selon la revendication 3 ou 4, dans lequel que le système d'étalonnage (300) de dose comporte en outre un cylindre pneumatique (304) pour lever et abaisser le réservoir (302) afin de l'introduire dans le poste de distribution (106) et de le sortir du poste de distribution (106).

6. Système selon l'une quelconque des revendications 3 à 5, dans lequel le dispositif de tenue (304) est un bras de transport (304) adapté pour tenir un flacon

multidose (302) d'une forme correspondant à celle du bras de transport (304) et un conteneur d'expédition (402) pour le flacon multidose (302).

7. Système selon la revendication 1, comprenant en outre :

une salle (509) de cyclotron pour produire un produit radiopharmaceutique ;

une tubulure (206) pour transporter le produit radiopharmaceutique de la salle (509) de cyclotron au système d'étalonnage (404) de dose ; et

un dispositif de perfusion (512) pour recevoir du système d'étalonnage (404) de dose la dose individuelle (126 ou 128) du marqueur radioactif (104), via la tubulure (206) ; et

un dispositif de perfusion (512) pour recevoir la dose individuelle (126 ou 128) produit radiopharmaceutique du système d'étalonnage (404) de dose par la tubulure (206).

8. Procédé pour préparer un système d'injection (122 ou 124), comprenant les étapes consistant à :

installer (902) un flacon (416) de patient dans un système d'étalonnage (418) de dose du système d'injection (400), le flacon de patient étant stérile et apyrogène ;

monter (904) une aiguille de sortie sur une tubulure venant d'une pompe péristaltique (414) du système d'injection ;

insérer (906) l'aiguille de sortie au fond du flacon (416) de patient ;

placer (908) le flacon (416) de patient dans le système d'étalonnage (418) de dose ;

installer (910) un robinet d'arrêt (422) dans le système d'injection (400) ;

installer (912) une tubulure intraveineuse (428) à travers le robinet d'arrêt (422) ;

installer (914) une aiguille intraveineuse (204) dans le système d'injection (400) ; et

fixer (916) une poche de solution saline (412) au robinet d'arrêt (422).

9. Procédé selon la revendication 8, comprenant en outre les étapes consistant à :

mettre en marche (802) un système informatique (1200) ;

fournir (804) un flacon multidose (302) d'un produit radiopharmaceutique (104) au système d'injection (122 ou 124) commandé par le système informatique (1200) ; et

lever (806) le flacon multidose (302) jusque dans un système d'étalonnage (300) de dose du système d'injection (122 ou 124).

10. Procédé (1000) de préparation d'un produit radiopharmaceutique destiné à être injecté à un patient en utilisant un système d'injection (400), le procédé comprenant les étapes consistant à :

extraire (1002) d'un flacon multidose (302) un dose individuelle (126 ou 128) d'un produit radiopharmaceutique (104) ;

vérifier (1004) que la quantité de radioactivité dans le flacon (416) de patient est égale à la quantité de radioactivité qui a été évacuée du flacon multidose (302) ; et

ajouter (1006) une solution saline provenant d'une poche (412) de solution saline et d'une conduite de solution saline dans le flacon (416) de patient via un deuxième robinet d'arrêt (410) à trois voies.

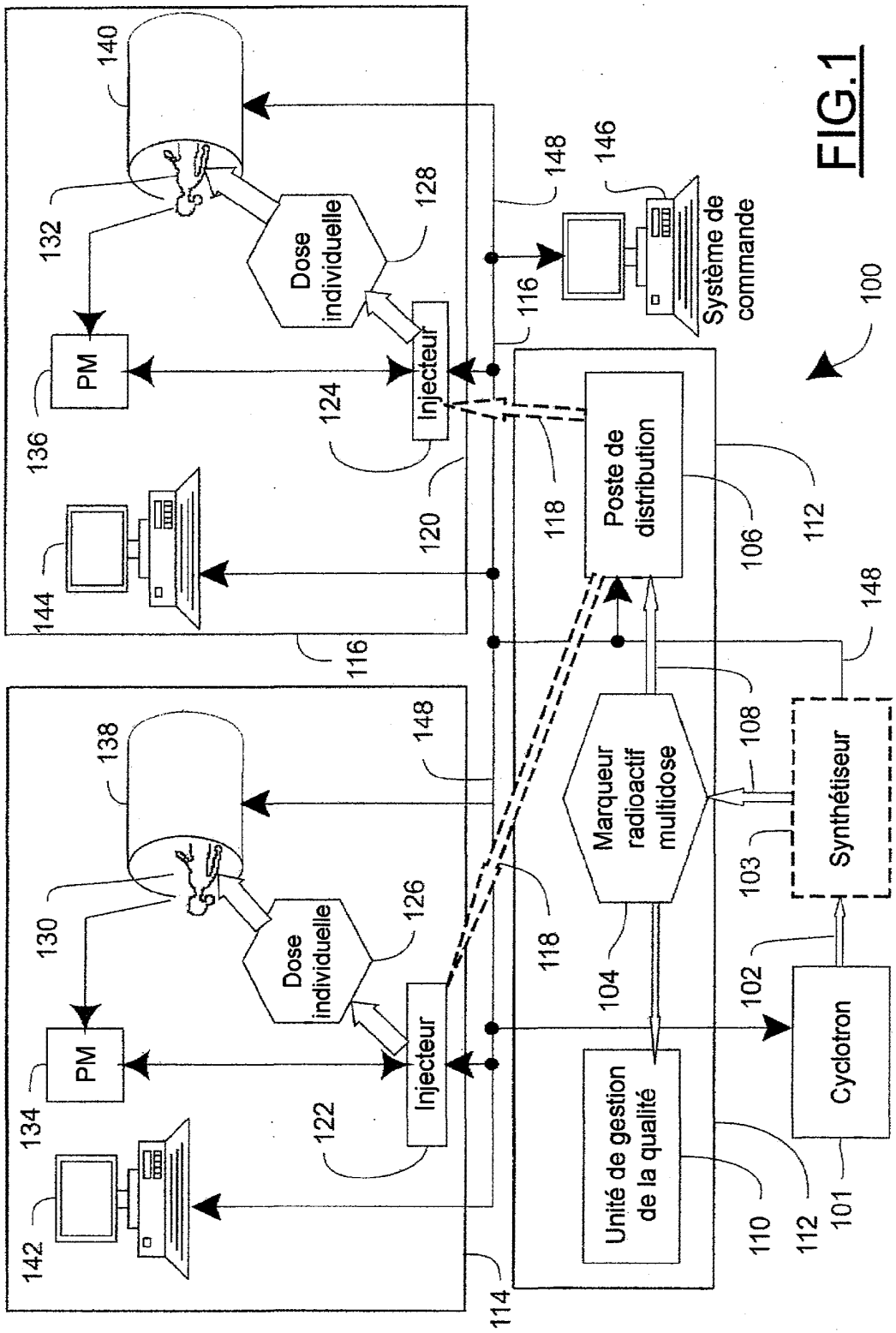

140
132
Dose individuelle
128
148
146
Système de commande
116
100
PM
136
124
Injecteur
120
118
Poste de distribution
106
112
144
116
148
138
Marqueur radioactif multidose
108
Synthétiseur
103
130
Dose individuelle
126
118
104
102
PM
134
122
Injecteur
Cyclotron
Unité de gestion de la qualité
110
112
101
142
114

FIG.1

FIG.2

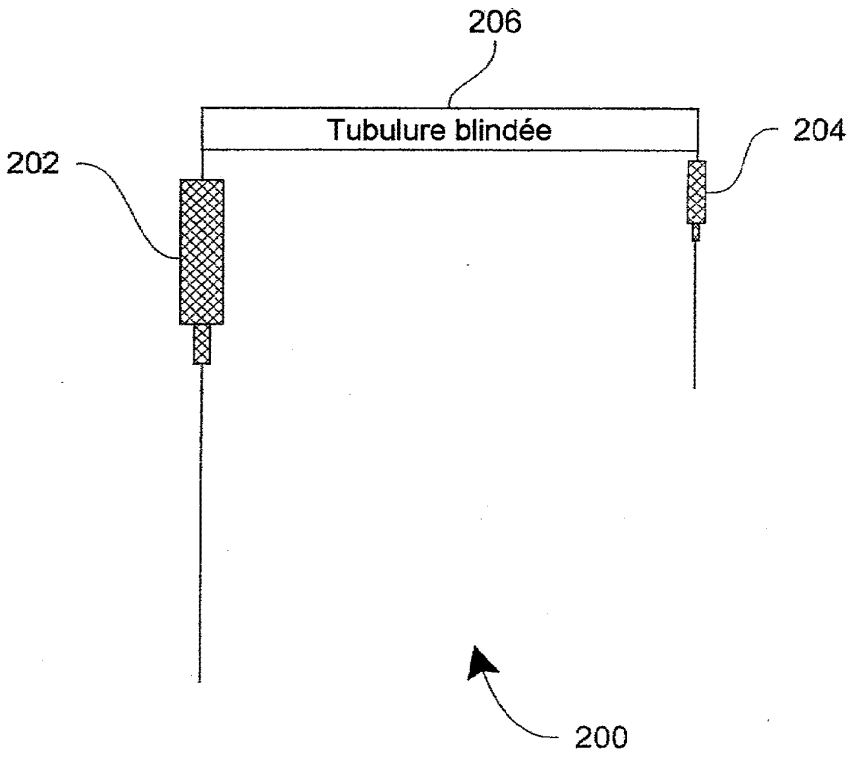
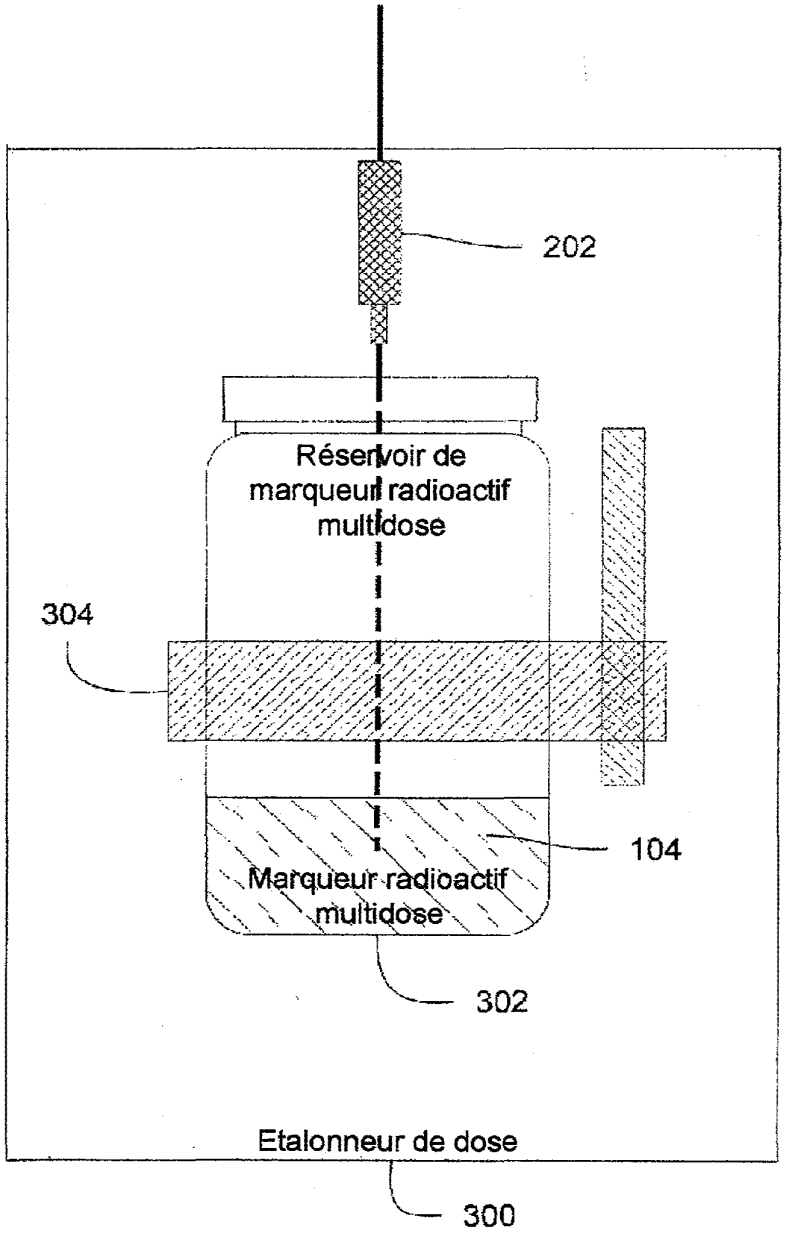


FIG.3


202
Réservoir de marqueur radioactif multidose
304
104
Marqueur radioactif multidose
302
Etalonneur de dose
300

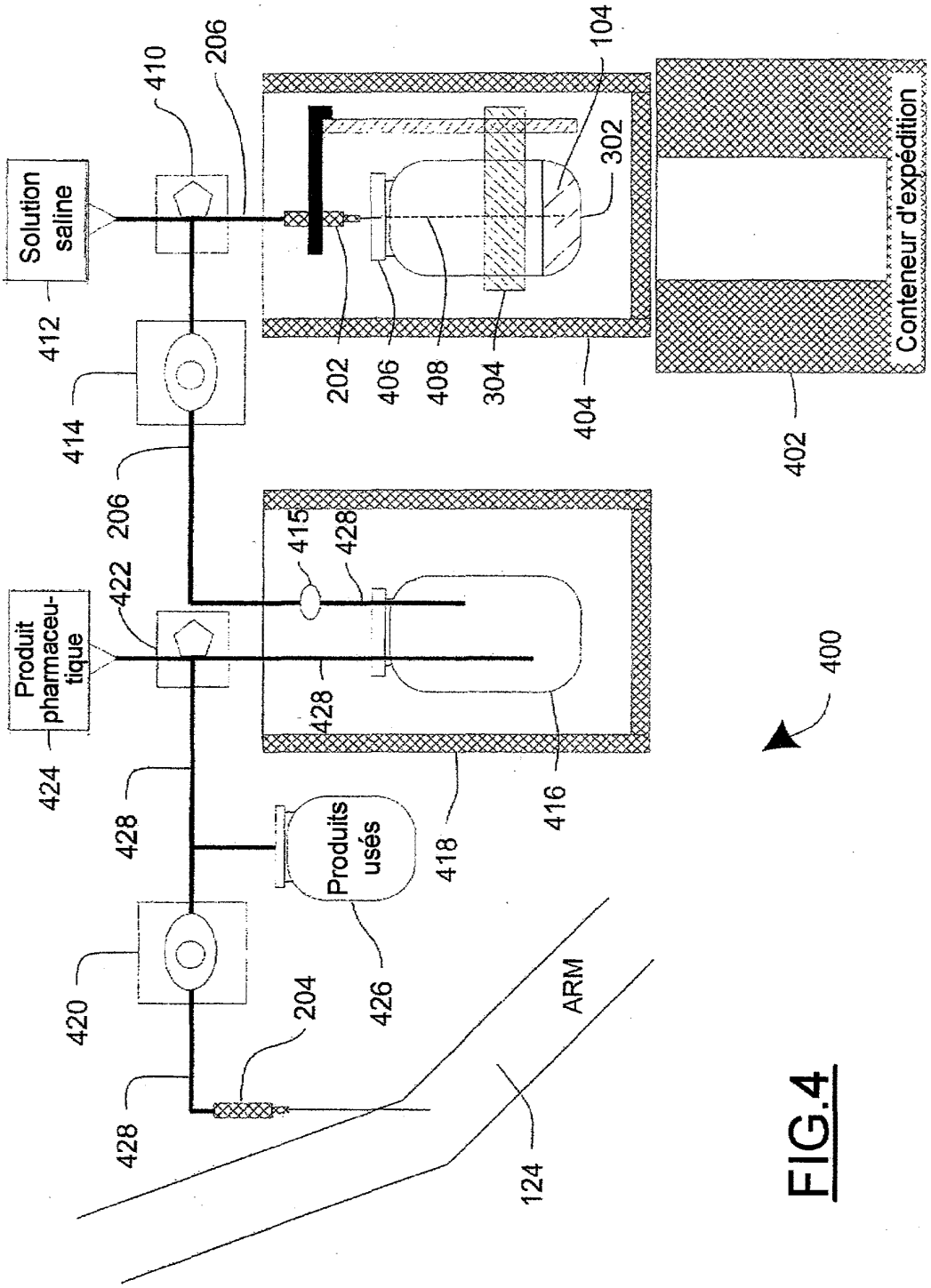

Solution saline
Produit pharmaceutique
Produits usés
Conteneur d'expédition
ARM
400
402
404
410
412
414
416
418
420
422
424
426
428
104
124
202
204
206
302
304
406
408
415

FIG.4

FIG.5

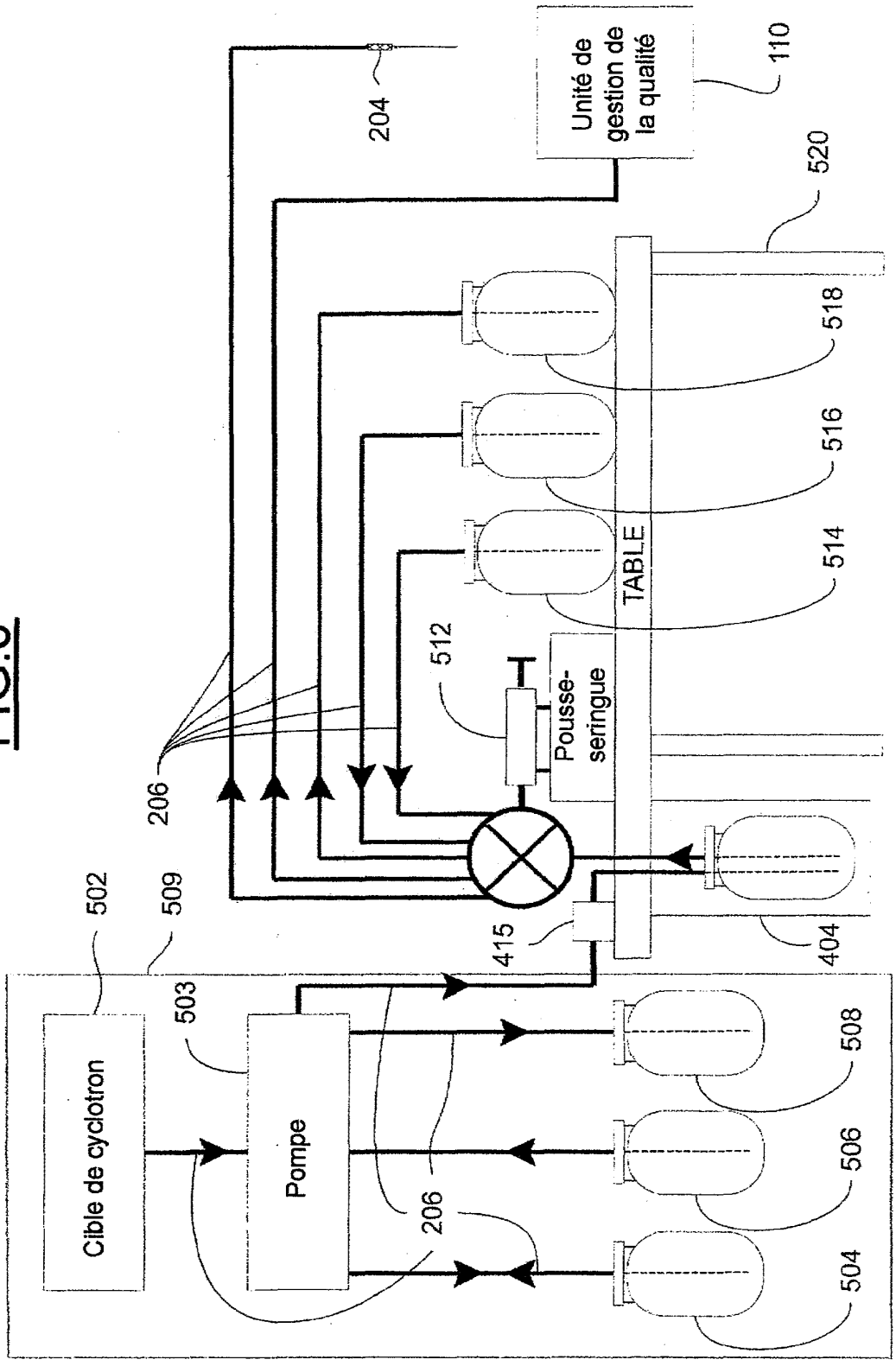

Unité de gestion de la qualité
110
204
520
518
516
514
TABLE
512
Pousse-seringue
206
502
509
503
415
404
Cible de cyclotron
Pompe
508
506
504
206

FIG.6

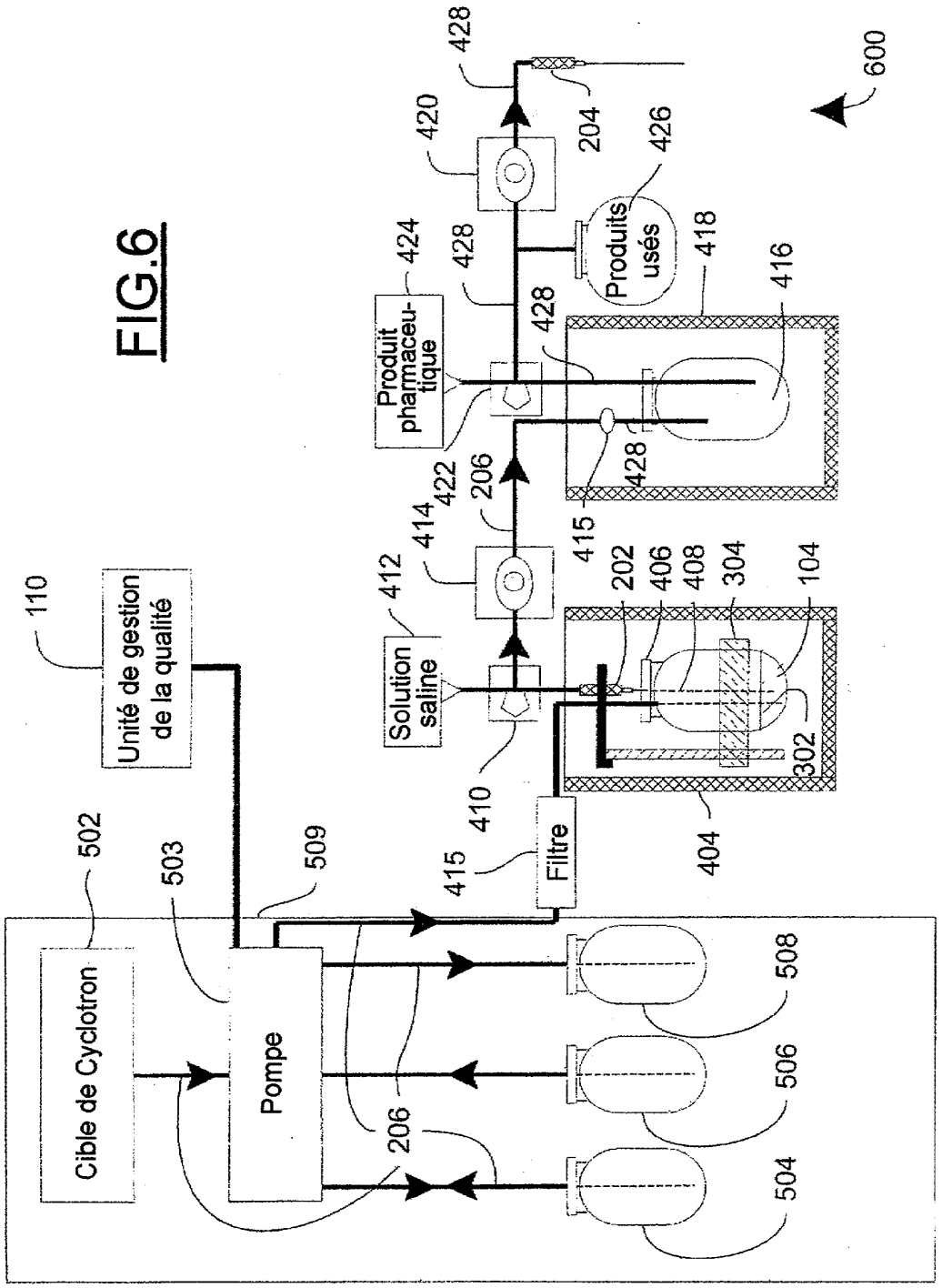

600
110
Unité de gestion de la qualité
502
Cible de Cyclotron
503
Pompe
509
206
508
506
504
415
410
Filtre
404
412
Solution saline
414
422
206
202
406
408
304
104
302
415
428
204
420
426
Produits usés
418
416
424
Produit pharmaceutique
428
428
428

FIG.7

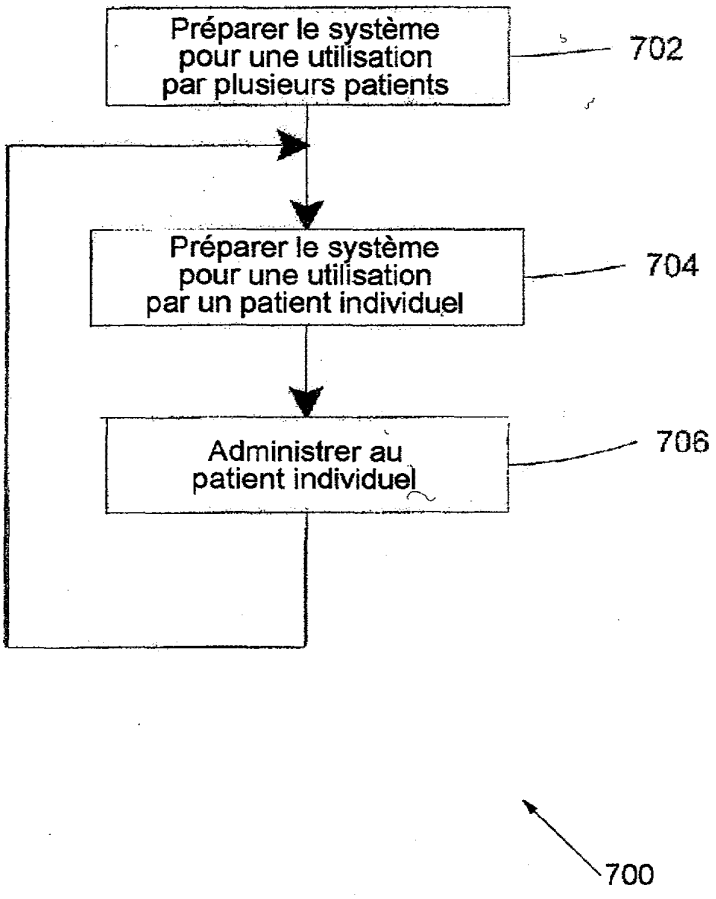

Préparer le système pour une utilisation par plusieurs patients
702
Préparer le système pour une utilisation par un patient individuel
704
Administrer au patient individuel
706
700

FIG.8

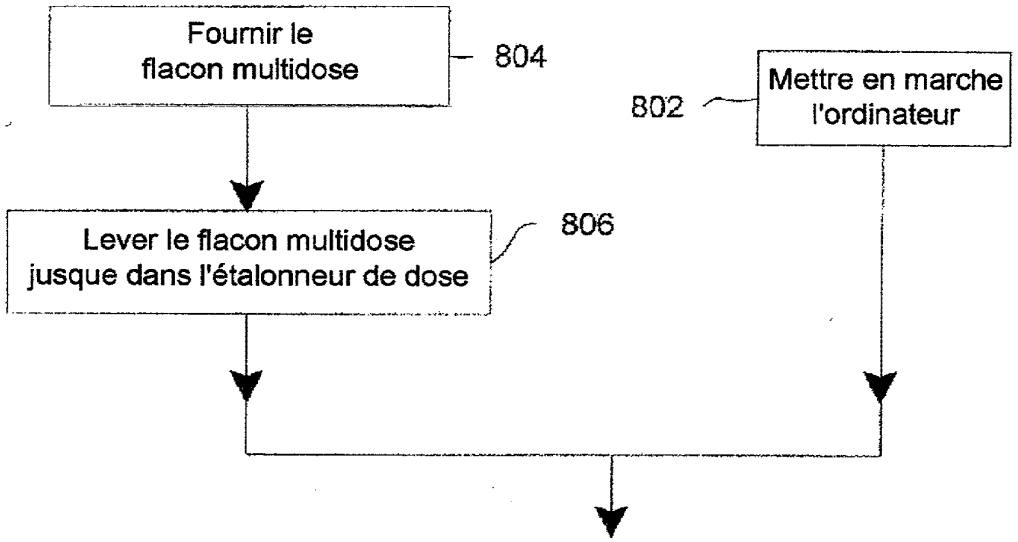

Fournir le flacon multidose
804
Mettre en marche l'ordinateur
802
Lever le flacon multidose jusque dans l'étalonneur de dose
806
800

FIG.9

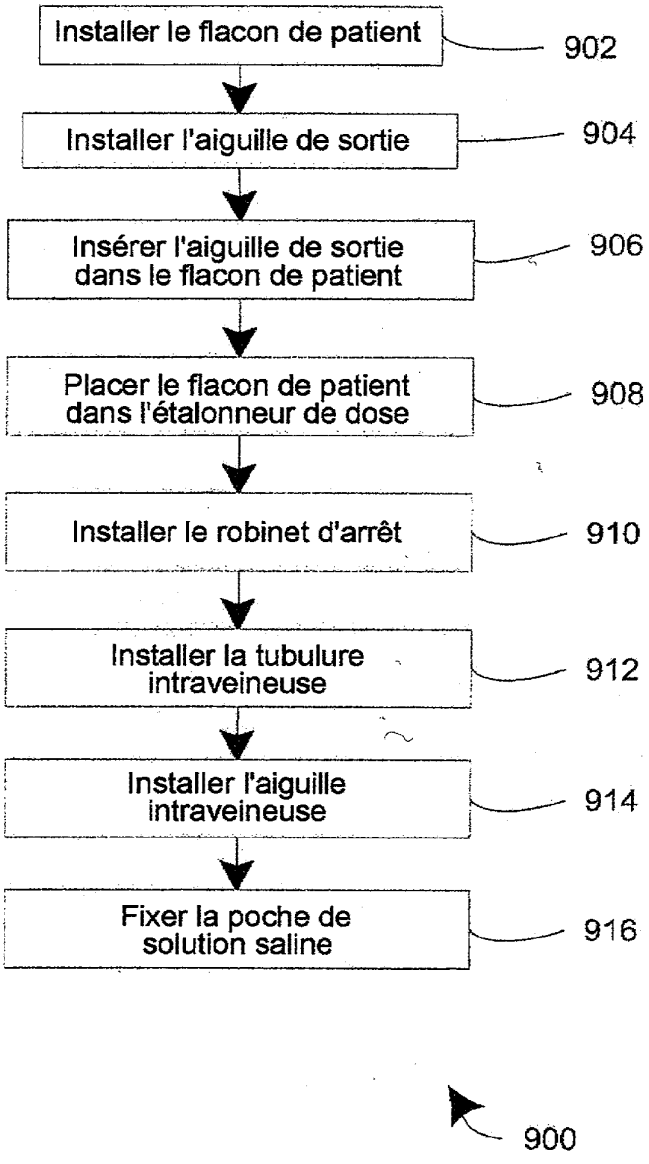

Installer le flacon de patient
902
Installer l'aiguille de sortie
904
Insérer l'aiguille de sortie dans le flacon de patient
906
Placer le flacon de patient dans l'étalonneur de dose
908
Installer le robinet d'arrêt
910
Installer la tubulure intraveineuse
912
Installer l'aiguille intraveineuse
914
Fixer la poche de solution saline
916
900

FIG.10

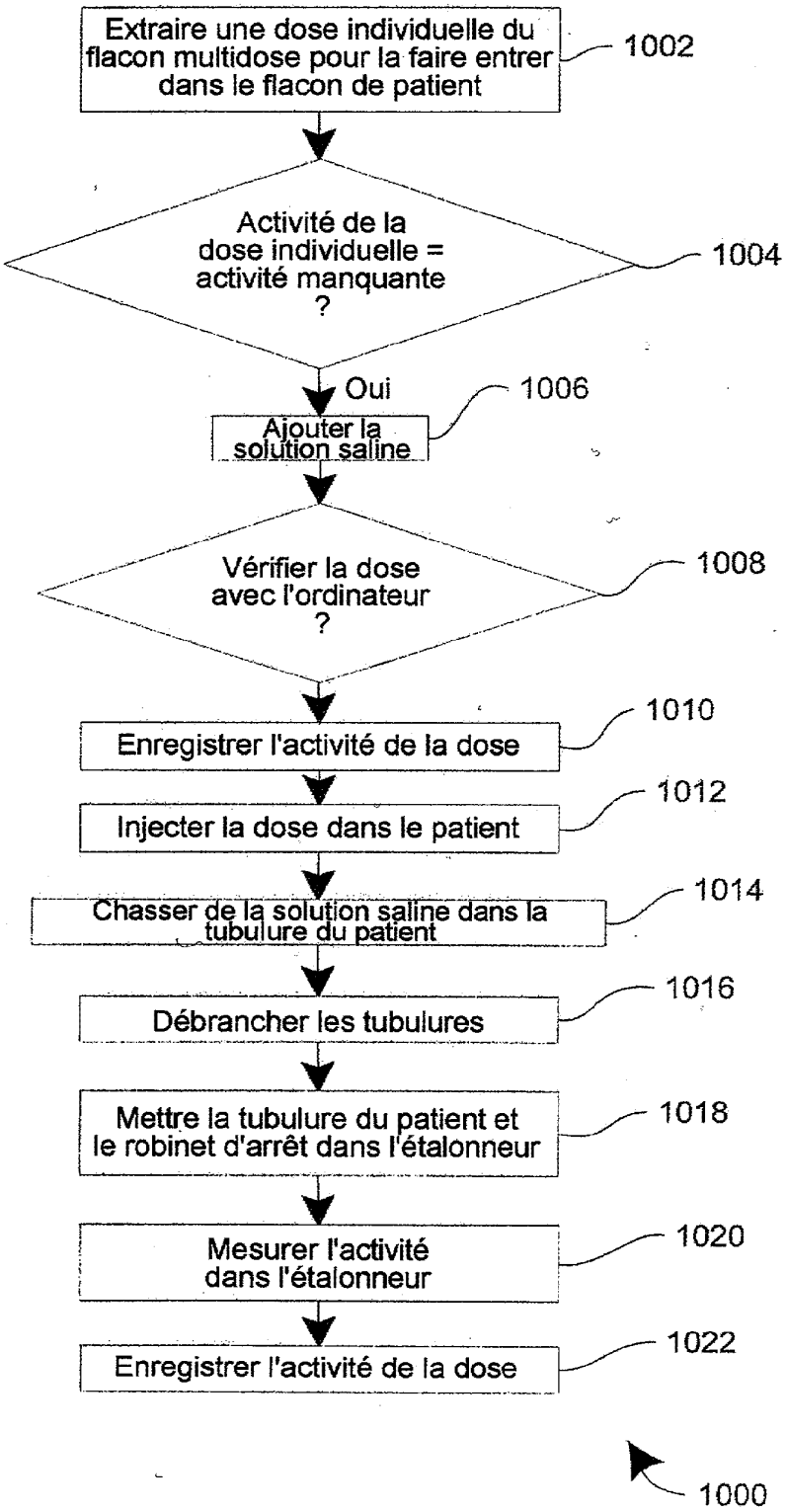
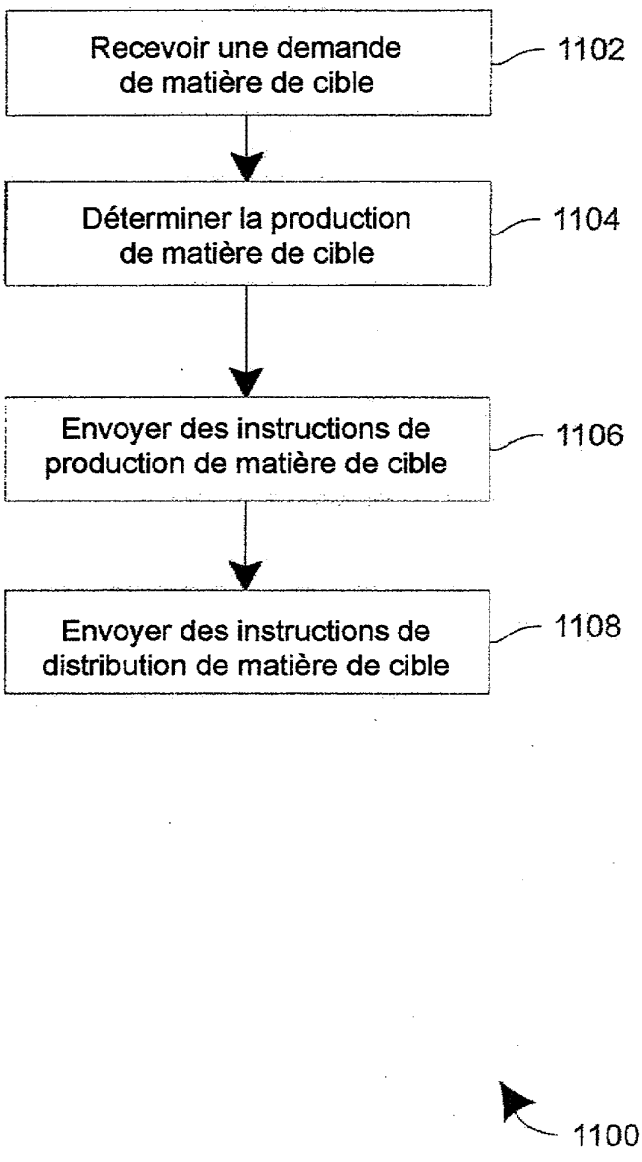

Extraire une dose individuelle du flacon multidose pour la faire entrer dans le flacon de patient
1002
Activité de la dose individuelle = activité manquante ?
1004
Oui
1006
Ajouter la solution saline
Vérifier la dose avec l'ordinateur ?
1008
Enregistrer l'activité de la dose
1010
Injecter la dose dans le patient
1012
Chasser de la solution saline dans la tubulure du patient
1014
Débrancher les tubulures
1016
Mettre la tubulure du patient et le robinet d'arrêt dans l'étalonneur
1018
Mesurer l'activité dans l'étalonneur
1020
Enregistrer l'activité de la dose
1022
1000

FIG.11


Recevoir une demande de matière de cible
1102
Déterminer la production de matière de cible
1104
Envoyer des instructions de production de matière de cible
1106
Envoyer des instructions de distribution de matière de cible
1108
1100

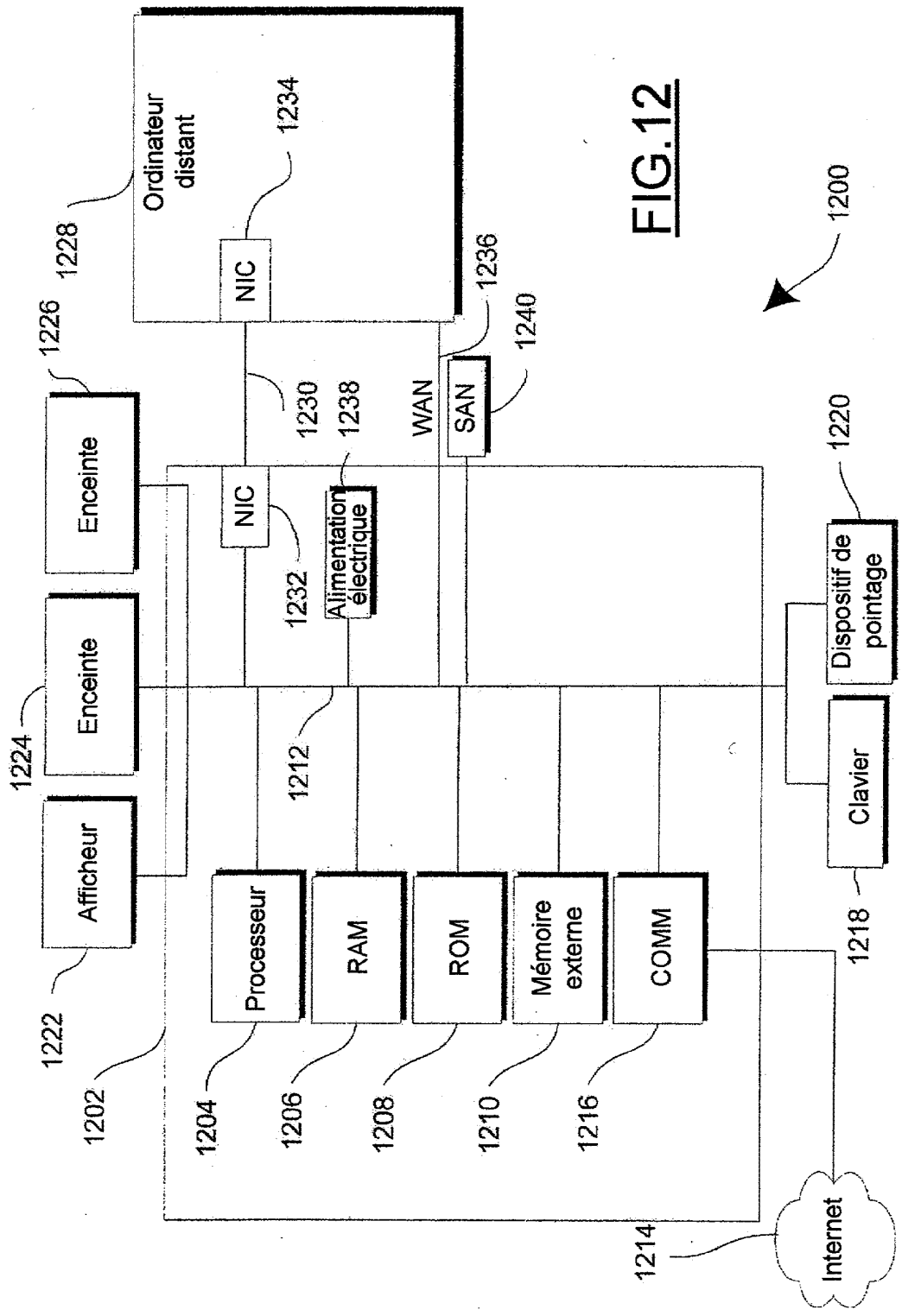

Ordinateur distant
1228
1234
NIC
1236
1240
WAN
SAN
1226
1230
1238
Enceinte
NIC
Alimentation électrique
1232
1220
Dispositif de pointage
1224
Enceinte
1212
Clavier
1218
Afficheur
1222
Processeur
RAM
ROM
Mémoire externe
COMM
1202
1204
1206
1208
1210
1216
1214
Internet
1200

FIG.12

Automatic injection system for radiopharmaceutical products, comprises an injector connected to an extractor that selects a dose of a radiopharmaceutical product

Patent number: FR2867084 (A1)

Publication date: 2005-09-09

Inventor(s): JACKSON MARK ALAN; DHAWALE PARITOSH JAYANT; LARA HERMAN RODRIGO; BRUSSERMANN MICHAEL; KETZSCHER ULRICH

Applicant(s): GEN ELECTRIC [US]

Classification:

- international: ***G21H5/02; A61B6/00; A61B6/03; A61K51/00; A61M5/158; A61M5/168; A61M5/178; A61M36/06; A61M36/12; G01T1/161; G21F5/015; G21F5/018; G21F5/14; G21G4/08;*** *A61M5/00;* **G21H5/00; A61B6/00; A61B6/03; A61K51/00; A61M5/14; A61M5/168; A61M5/178; A61M36/00; G01T1/00; G21F5/00; G21G4/00;** A61M5/00; (IPC1-7): A61M36/06; A61B6/00; A61B6/03; G21F5/015; G21F5/14

- european: G21G4/08; G21F5/018; G21H5/02

Application number: FR20050001689 20050218

Priority number(s): US20040792683 20040302

Also published as:

US2008242915 (A1)

JP2005326398 (A)

DE102005010154 (A1)

Cited documents:

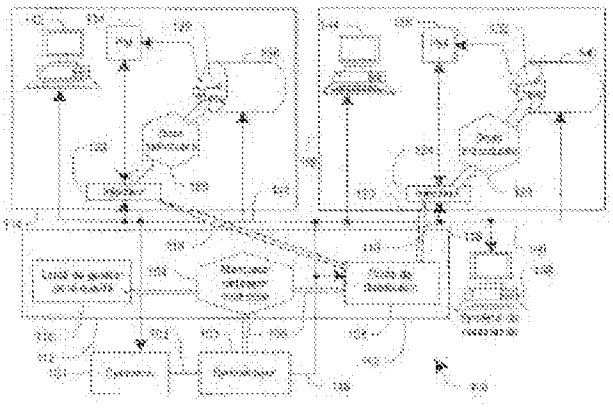
US2003004463 (A1)

EP0310148 (A2)

US5885216 (A)

Abstract of **FR 2867084 (A1)**

An automatic injection system comprises an injector (122, 124) connected to an extractor that selects an individual dose (126, 128) of a radiopharmaceutical product from a multiple dose unit (104). - An automatic injection system comprises an injector (122, 124) connected to an extractor that selects an individual dose (126, 128) of a radiopharmaceutical product from a multiple dose unit (104). It has a calibration system that co-operates with the extractor, and a perfusion pump co-operates with the calibration system and an intravenous needle to inject the selected individual dose into a live subject.



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(22)出願日　平成17年5月25日 (2005.5.25)

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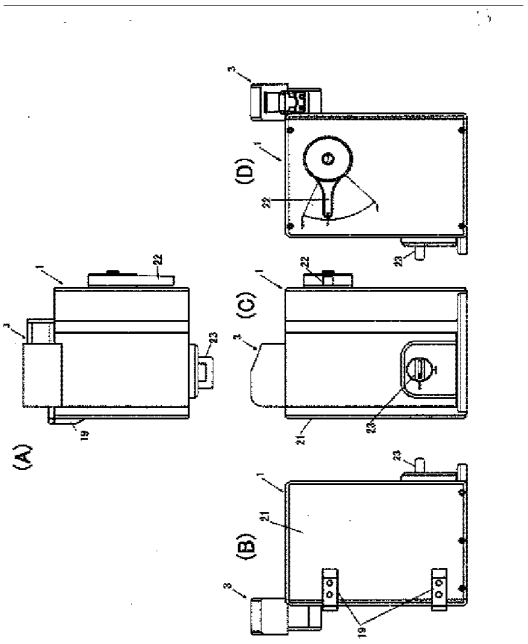
(54)【発明の名称】放射性薬剤吸引装置

(57)【要約】
【課題】液状放射性医薬剤をバイアルからシリンジへ吸引する際に、吸引を行う医療従事者が被曝しないように遮蔽材を有する放射性薬剤吸引装置に関し、被曝の可能性をより減らし、針先がバイアルのガラス壁を損傷する懸念をなくし、手作業の際に針で指を傷つけにくく、装置をコンパクトにできるようにする。
【解決手段】遮蔽キャビネット１とシリンジ用遮蔽器３とを別に設け、別々に開閉する。薬剤針９及びエア針１１を昇降させる昇降機構１５は、穿刺された薬剤針９の針先がガラス壁に接触しても衝撃を与えないバネを備える。薬剤針９及びエア針１１を取り付けるホルダー部が、遮蔽キャビネット１の開かれた側へ所定距離移動できる引出機構を有する。バイアル５を傾けて収納するための収納部は、傾斜を有し、薬剤針９及びエア針１１の降下した針先が、バイアル５の傾いた底部の隅にセットされる。
【選択図】図1



【特許請求の範囲】
【請求項1】
放射線を遮蔽する遮蔽材を全面に有し開閉可能で内部に液状放射性医薬剤を充填されたバイアルを収納できる遮蔽キャビネットと、前記遮蔽キャビネットの内部に設けられ、前記バイアルの上部のゴム栓に穿刺される薬剤針と、これらの薬剤針を、遮蔽キャビネットの外部からの力により、前記ゴム栓に向かって針の方向に沿って昇降させる昇降機構と、前記遮蔽キャビネットの内部に収納されるシリンジに連通し前記薬剤針に連通するチューブと、遮蔽キャビネットの外部からの力により、前記シリンジのプランジャを引いて吸引を行う吸引動作機構と、を有することを特徴とする放射性薬剤吸引装置。
【請求項2】
放射線を遮蔽する遮蔽材を全面に有し開閉可能で内部に液状放射性医薬剤を充填されたバイアルを収納できる遮蔽キャビネットと、前記遮蔽キャビネットの内部に設けられ、前記バイアルの上部のゴム栓に穿刺される薬剤針と、これらの薬剤針を、遮蔽キャビネットの外部からの力により、前記ゴム栓に向かって針の方向に沿って昇降させる昇降機構と、前記遮蔽キャビネットの外部に一体的に設けられ、放射線を遮蔽する遮蔽材を全面に有し開閉可能で内部に液状放射性医薬剤を吸引するためのシリンジを収納できるシリンジ用遮蔽器と、このシリンジに連通し前記シリンジ用遮蔽器及び前記遮蔽キャビネットを貫通して前記薬剤針に連通するチューブと、を有することを特徴とする放射性薬剤吸引装置。
【請求項3】
放射線を遮蔽する遮蔽材を全面に有し開閉可能で内部に液状放射性医薬剤を充填されたバイアルを収納できる遮蔽キャビネットと、前記遮蔽キャビネットの内部に設けられ、前記バイアルの上部のゴム栓に穿刺される薬剤針及びエア針と、これらの薬剤針及びエア針を、遮蔽キャビネットの外部からの力により、前記ゴム栓に向かって針の方向に沿って昇降させる昇降機構と、前記遮蔽キャビネットの外部に一体的に設けられ、放射線を遮蔽する遮蔽材を全面に有し開閉可能で内部に液状放射性医薬剤を吸引するためのシリンジを収納できるシリンジ用遮蔽器と、このシリンジに連通し前記シリンジ用遮蔽器及び前記遮蔽キャビネットを貫通して前記薬剤針に連通するチューブと、を有することを特徴とする放射性薬剤吸引装置。
【請求項4】
前記昇降機構は、穿刺された薬剤針の針先がガラス壁に接触しても衝撃を与えないバネを備えた衝撃緩和機構を有することを特徴とする請求項１、２、又は３に記載の放射性薬剤吸引装置。
【請求項5】
前記昇降機構は、薬剤針又はエア針を取り付けるホルダー部を有し、このホルダー部が、前記遮蔽キャビネットの開かれた側へ所定距離引き出すことができる引出機構を有することを特徴とする請求項１、２、３、又は４に記載の放射性薬剤吸引装置。
【請求項6】
前記昇降機構は、薬剤針又はエア針を取り付けるホルダー部のうち、直接に針のハブに接触するクランプ部分が、プラスチック製又はアルミ製であることを特徴とする請求項１、２、３、４、又は５に記載の放射性薬剤吸引装置。
【請求項7】
前記昇降機構は、遮蔽キャビネットの外部に設けられた駆動レバーと、遮蔽キャビネットの内部に設けられ前記駆動レバーに連動して回動する駆動アームと、この駆動アームにより押されて昇降する薬剤針スライダ又はエア針スライダと、前記薬剤針スライダをガイドする薬剤針スライドレールと、前記エア針スライダをガイドするエア針スライドレールと、薬剤針スライダ及びエア針スライダのうち一方に固定され他方を略水平方向にガイドし昇降動作を同期させる接続レールと、を有して構成されることを特徴とする請求項２、３、４、５、又は６に記載の放射性薬剤吸引装置。
【請求項8】

前記遮蔽キャビネットの内部で前記バイアルを傾けて収納するための収納部は、傾斜を有し、前記薬剤針又はエア針の降下した針先が、前記バイアルの傾いた底部の隅にセットされるように位置することを特徴とする請求項１、２、３、４、５、６、又は７に記載の放射性薬剤吸引装置。

【請求項9】

前記遮蔽キャビネットは、箱状をなし、左右側面の一方又は両方に開閉扉を有し、前面を含む前面部分と背面を含む背面部分が分割されており、互いに前後方向にスライド可能なスライド機構を有し、前面部分と背面部分の一方に前記バイアルが収納され、他方に前記昇降機構を有することを特徴とする請求項１、２、３、４、５、６、７、又は８に記載の

【発明の詳細な説明】

【技術分野】

【0001】

本発明は、液状放射性医薬剤をバイアル（バイアル瓶のこと）からシリンジ（注射器のこと）へ吸引する際に、吸引を行う医療従事者が被曝しないように遮蔽材を有する放射性薬剤吸引装置の構造に関する。

【背景技術】

【0002】

前記液状放射性医薬剤としては、例えば、ＰＥＴ（陽電子放射断層診断法）用の放射性薬剤であるＦＤＧ（フッ素化したブドウ糖誘導体）、ＳＰＥＣＴ（単光子放出コンピュータ断層撮影法）放射性医薬品などがある。

【0003】

このような液状放射性医薬剤をバイアルからディスポーザブルシリンジなどに取り出す時、医療従事者が指先に被曝しないように、鉛又はタンブステンなどの遮蔽材の外側から手動又は自動的に操作により、薬剤針がバイアル上部ゴム栓中央部に手動又は自動的に穿刺し、バイアルからシリンジにより薬液を吸引し、人体に谷に自動的に供給する装置を、出願人は既に出願している（下記特許文献１）。

【0004】

この装置は、遮蔽材で覆われた大きなキャビネットの中に、遮蔽材付きのバイアル入りのコンテナと、このバイアルの上部のゴム栓に穿刺する薬剤針およびエア針と、薬剤針にチューブで連通するシリンジと、を備える。そして、薬剤針およびエア針を同軸でサーボモーターにより自動的にバイアルに穿刺し、吸引を行うものである。

【特許文献1】特願平２００４－１９７９８２　このような装置を一部改良して、液状放射性医薬剤をバイアル（バイアル瓶のこと）からシリンジ（注射器のこと）へ吸引する際に、吸引を行う医療従事者が被曝しないように遮蔽材を有する放射性薬剤吸引装置を製造することが考えられる。

【発明の開示】

【発明が解決しようとする課題】

【0005】

発明が解決しようとする課題は、前記特許文献１の装置を一部改良して、液状放射性医薬剤をバイアルからシリンジへ吸引する際に、吸引を行う医療従事者が被曝しないように遮蔽材を有する放射性薬剤吸引装置を提供することにある。

そして、仮にそのようにして製造した装置であっても、遮蔽材で覆われた大きなキャビネットへバイアル入りのコンテナやシリンジを、手作業でセットする必要がある。その際、ＦＤＧのようにエネルギーの大きい放射性医薬品を取り扱うときに、被曝の可能性が残されていた。

【0006】

すなわち、これまでの鉛又はタングステンシールド付きのシリンジ、及び鉛又はタングステンなどの遮蔽材付きのバイアル入りのコンテナを用いても、バイアル上部からとシリンジ上部からの放射能の漏洩のため、医療従事者への指先被曝の可能性は残される。

（１）特に、１本のバイアルから液状放射性医薬剤を数本のシリンジへ吸収する際に、

シリンジを交換するために何度もキャビネットを開けなければならず、そのたびごとに、被曝の可能性が発生する。

（２）また、バイアル内の液状放射性医薬剤を残さず吸引するには、手動又は自動によりバイアルへ穿刺する薬剤針の針先が、バイアルの底部ぎりぎりに位置しなければならない。しかし、手作業に伴う誤差により、針先がバイアルの底部に当たりガラス壁を損傷する懸念がある。

【0007】

（３）また、手作業により薬剤針およびエア針をセットする際には、指を傷つけないように、セットが終わった後に針カバーを外すことが望ましい。しかし、医療現場の限られたスペースの事情から、装置はコンパクトであることが望ましく、装置内部のスペースは狭く、セット後に針カバーを外しにくいため、指を傷つけやすい状況があった。

【0008】

（４）また、装置をコンパクトにしようとすると、装置内部での手作業が困難になった。

この発明は、以上の問題点を解決するために、被曝の可能性をより減らし、針先がバイアルのガラス壁を損傷する懸念をなくし、手作業の際に針で指を傷つけにくく、装置をコンパクトにできる放射性薬剤吸引装置を提供することを目的とする。

【課題を解決するための手段】

【0009】

以上の課題を解決するために、第一発明は、放射線を遮蔽する遮蔽材を全面に有し開閉可能で内部に液状放射性医薬剤を充填されたバイアルを収納できる遮蔽キャビネットと、前記遮蔽キャビネットの内部に設けられ、前記バイアルの上部のゴム栓に穿刺される薬剤針と、これらの薬剤針を、遮蔽キャビネットの外部からの力により、前記ゴム栓に向かって針の方向に沿って昇降させる昇降機構と、前記遮蔽キャビネットの内部に収納されるシリンジに連通し前記薬剤針に連通するチューブと、遮蔽キャビネットの外部からの力により、前記プランジャを引いて吸引を行う吸引動作機構と、を有することを特徴とする放射性薬剤吸引装置である。

第二発明は、放射線を遮蔽する遮蔽材を全面に有し開閉可能で内部に液状放射性医薬剤を充填されたバイアルを収納できる遮蔽キャビネットと、前記遮蔽キャビネットの内部に設けられ、前記バイアルの上部のゴム栓に穿刺される薬剤針と、これらの薬剤針を、遮蔽キャビネットの外部からの力により、前記ゴム栓に向かって針の方向に沿って昇降させる昇降機構と、前記遮蔽キャビネットの外部に一体的に設けられ、放射線を遮蔽する遮蔽材を全面に有し開閉可能で内部に液状放射性医薬剤を吸引するためのシリンジを収納できるシリンジ用遮蔽器と、このシリンジに連通し前記シリンジ用遮蔽器及び前記遮蔽キャビネットを貫通して前記薬剤針に連通するチューブと、を有することを特徴とする放射性薬剤吸引装置である。

【0010】

第三発明は、放射線を遮蔽する遮蔽材を全面に有し開閉可能で内部に液状放射性医薬剤を充填されたバイアルを収納できる遮蔽キャビネットと、前記遮蔽キャビネットの内部に設けられ、前記バイアルの上部のゴム栓に穿刺される薬剤針９及びエア針と、これらの薬剤針９及びエア針を、遮蔽キャビネットの外部からの力により、前記ゴム栓に向かって針の方向に沿って昇降させる昇降機構と、前記遮蔽キャビネットの外部に一体的に設けられ、放射線を遮蔽する遮蔽材を全面に有し開閉可能で内部に液状放射性医薬剤を吸引するためのシリンジを収納できるシリンジ用遮蔽器と、このシリンジに連通し前記シリンジ用遮蔽器及び前記遮蔽キャビネットを貫通して前記薬剤針に連通するチューブと、を有することを特徴とする放射性薬剤吸引装置である。

【0011】

第四発明は、さらに、前記昇降機構は、穿刺された薬剤針の針先がガラス壁に接触しても衝撃を与えないバネを備えた衝撃緩和機構を有することを特徴とする放射性薬剤吸引装置である。

第五発明は、さらに、前記昇降機構は、薬剤針９及びエア針を取り付けるホルダー部を有し、このホルダー部が、前記遮蔽キャビネットの開かれた側へ所定距離引き出すことができる引出機構を有することを特徴とする放射性薬剤吸引装置である。

【0012】

第六発明は、さらに、前記昇降機構は、薬剤針９及びエア針を取り付けるホルダー部のうち、直接に針のハブに接触するクランプ部分が、プラスチック製又はアルミ製であることを特徴とする放射性薬剤吸引装置である。

第七発明は、さらに、前記昇降機構は、遮蔽キャビネットの外部に設けられた駆動レバーと、遮蔽キャビネットの内部に設けられ前記駆動レバーに連動して回動する駆動アームと、この駆動アームにより押されて昇降する薬剤針スライダ又はエア針スライダと、前記薬剤針スライダをガイドする薬剤針スライドレールと、前記エア針スライダをガイドするエア針スライドレールと、薬剤針スライダ及びエア針スライダのうち一方に固定され他方を略水平方向にガイドし昇降動作を同期させる接続レールと、を有して構成されることを特徴とする放射性薬剤吸引装置である。

【0013】

第八発明は、さらに、前記遮蔽キャビネットの内部で前記バイアルを傾けて収納するための収納部は、傾斜を有し、前記薬剤針９及びエア針の降下した針先が、前記バイアルの傾いた底部の隅にセットされるように位置することを特徴とする放射性薬剤吸引装置である。

【0014】

第九発明は、さらに、前記遮蔽キャビネットは、箱状をなし、左右側面の一方又は両方に開閉扉を有し、前面を含む前面部分と背面を含む背面部分が分割されており、互いに前後方向にスライド可能なスライド機構を有し、前面部分と背面部分の一方に前記バイアルが収納され、他方に前記昇降機構を有することを特徴とする放射性薬剤吸引装置である。

【発明の効果】

【0015】

第一、第二、第三、第四、第五、第六、第七、第八、又は第九発明によれば、液状放射性医薬剤をバイアルからシリンジへ吸引する際に、吸引を行う医療従事者が被曝しないで済む。

第二、第三、第四、第五、第六、第七、第八、又は第九発明によれば、遮蔽キャビネットとシリンジ用遮蔽器とを別に設けるので、１本のバイアルから液状放射性医薬剤を数本のシリンジへ吸収する際であっても、シリンジを交換するためにシリンジ用遮蔽器のみを開閉すればよく、遮蔽キャビネットは開ける必要がない。よって、その分、被曝の可能性が減少する。

【0016】

第四、第五、第六、第七、第八、又は第九発明によれば、さらに、バネを備えた緩和機構の働きで、針先がバイアルの底部に当たってもガラス壁を損傷する懸念がない。このため、針先がバイアルの底部ぎりぎりに位置でき、バイアル内の液状放射性医薬剤を残さず吸引できる。

【0017】

第五、第六、第七、第八、又は第九発明によれば、さらに、薬剤針又はエア針を取り付けるホルダー部が、遮蔽キャビネットの開かれた側へ所定距離引き出すことができるので、これらの針のセットが容易であり、また、セット後に針カバーを外しやすい。よって、指を傷つけにくい。

【0018】

第六、第七、第八、又は第九発明によれば、さらに、ホルダー部のうちの直接に針のハブに接触するクランプ部分が、プラスチック製又はアルミ製であることから、他の金属製である場合などに比べ、針を締め付ける十分な締付力が得られ、よってクランプ部分、ひいてはホルダー部構造を簡略にでき、結果的に装置をコンパクトにできる。

【0019】

第七、第八、又は第九発明によれば、さらに、薬剤針９及びエア針を同期して昇降させる昇降機構の構造が簡略にでき、結果的に装置をコンパクトにできる。

第八、又は第九発明によれば、さらに、バイアルを傾けて収納することで、液状放射性医薬剤を傾いた底部の隅に集めることができ、残さず吸引できる。

第九発明によれば、さらに、遮蔽キャビネットが前後方向にスライド可能なスライド機構を有し、このスライド可能な前面部分と背面部分の一方にバイアルが収納され、他方に昇降機構を有することで、手作業時にバイアルと昇降機構を離し作業スペースを拡げることができ、結果的に装置をコンパクトにできる。

【発明を実施するための最良の形態】

【0020】

この発明の実施形態を、図１～図１０に示す。

（（装置概要））

この実施形態の放射性薬剤吸引装置は、遮蔽キャビネット１とシリンジ用遮蔽器３が別々に設けられ（図１）、互いに独立して開閉可能である。そして、遮蔽キャビネット１は、放射線を遮蔽する遮蔽材を全面に有し、開閉可能で、内部に液状放射性医薬剤を充填されたバイアル５（図３）を収納できる。シリンジ用遮蔽器３は、遮蔽キャビネット１の外部に一体的に設けられ、放射線を遮蔽する遮蔽材を全面に有し、開閉可能で、内部に液状放射性医薬剤を吸引するためのシリンジ７（図９）を収納できる。

【0021】

薬剤針９及びエア針１１は、遮蔽キャビネット１の内部に設けられ、バイアル５の上部のゴム栓１３（図３）に穿刺される。これらの薬剤針９及びエア針１１を、昇降機構１５の働きで、遮蔽キャビネット１の外部からの力により、ゴム栓１３に向かって針の方向に沿って昇降させる。

【0022】

吸引を行うシリンジ7はチューブ１７の一端に連通し、このチューブ１７（図7、図９、図１０）は、シリンジ用遮蔽器及び遮蔽キャビネット１を貫通して、薬剤針９に連通する。

（（装置外観））

図１に、この実施形態に係る装置全体の概要を示す。

図１のうち（Ａ）は平面図、（Ｂ）は左側面図、（Ｃ）は正面図、（Ｄ）は右側面図である。

液状放射性医薬剤を充填されたバイアル５（図３）を収納できる箱状の遮蔽キャビネット１と、液状放射性医薬剤を吸引するためのシリンジ７（図９）を収納できるシリンジ用遮蔽器３とが別々に設けられる。それぞれが独立して開閉可能である。

遮蔽キャビネット１の外部の左側面には、ヒンジ１９を介して開閉扉２１が設けられる。遮蔽キャビネット１の外部の正面には、開閉扉２１のロックを行う開閉レバー２３が取り付けられる。また、遮蔽キャビネット１の外部の右側面には、装置内部の昇降機構１５を駆動させる手動式の駆動レバー２２が設けられる。遮蔽キャビネット１の外部に一体的にシリンジ用遮蔽器３が設けられている。

【0023】

（放射線遮蔽材）

遮蔽キャビネット１及びシリンジ用遮蔽器３の全面は、遮蔽材で覆われている。遮蔽材の材質としてはタングステン、タングステン合金、鉛、鉛ガラス、タンタル、ビスマス等が用いられる。

【0024】

特に、鉛は加工が容易なため、用いられるが、生理食塩水の接触により腐食・汚染が見られるため、使用に際し、ステンレス、プラスチック、ゴム、塗料、めっき等により被覆することが望ましい。また、一部の面を内部が観察できるように鉛ガラス、鉛含有アクリル樹脂板を用いることができる。さらに、一部をのぞき窓にすることもできる。

【0025】

遮蔽材の厚さは使用する放射性薬剤の種類にもよるが、一般的に5～30ｍｍ、好ましくは10～20ｍｍが用いられる。

【0026】

（開閉扉２１）

装置の左側面には、遮蔽材からなる開閉扉２１が設けられており、薬剤針９およびエア針１１の取り付け作業にあたっては、この開閉扉２１を開いて作業を行う。

【0027】

（スライド機構）

遮蔽キャビネット１は、箱状をなし、前記したように左側面に開閉扉２１を有するが、さらに、図２に示すように、前面を含む前面部分２５と背面を含む背面部分２７が分割されており、背面部分２７が装置用架台２９に固定しており、この背面部分２７に対して、前面部分２５が前後方向にスライド可能なスライド機構３１を有する。前面部分２５の上部と下部にスライダー３３Ａ、３３Ｂが形成され、背面部分２７の上部と下部に、このスライダー３３Ａ、３３Ｂをガイドするスライドガイド３５Ａ、３５Ｂが形成される。

【0028】

前面部分２５にバイアル入りのコンテナ３７が収納され、背面部分２７に前記昇降機構１５を有する。

作業時には、作業者は装置の前面に立ち、前面部分２５をスライド機構３１により手前に引き出すことで、左右側面が大きく開放される。また、バイアル入りのコンテナ３７と、昇降機構１５とを離し、両者の間に作業スペースＳを拡げることができる。この状態で、作業者は、左右の手により、遮蔽材付きのバイアル入りのコンテナ３７を、収納部トレイ３９に置くなどの作業を行う。

【0029】

（放射性薬剤）

ここで用いられる液状の放射性薬液とはＰＥＴ（陽電子断層診断法：Positron Emission Tomography）検査用の短寿命核種を含むＦＤＧ（フッ素１８で標識された製剤：［18F］-2-deoxy-2-fluoro-D-glucose）、ＦＤＰＡ（フッ素18で標識された製剤：6-［18F］-fluoro-3,4-dihydroxy-phenyl-L-alanine）、ＦＤＡ（6-［18F］-fluoro-dopamine）等があるが、主に、［18F］-2-deoxy-2-fluoro-D-glucoseが使用される。他に、９９ｍＴｃ、１２３Ｉ、１３１Ｉ、２０１Ｔｌ、６７Ｇａ、５１Ｃｒ等のSPECT(単光子放出コンピュータ断層撮影法：Single Photon Emission Computed Tomography）用放射性同位元素核種からなる治療用および検査用注射液にも適用できる。

【0030】

（（昇降機構１５））

図３～図６において、昇降機構１５を説明する。

（概略）

この昇降機構１５は、遮蔽キャビネット１の外部に設けられた駆動レバー２２と同軸に、遮蔽キャビネット１の内部に駆動アーム４１が設けられる。よって、手動により駆動レバー２２が回動されると、駆動アーム４１も連動して回動する。この駆動アーム４１により押されて昇降する薬剤針スライダ４３は、鉛直方向に配置される薬剤針スライドレール４５によって昇降方向にガイドされる。

【0031】

そして、エア針スライダ４７は、傾斜して配置されるエア針スライドレール４９によって斜めの昇降方向にガイドされる。薬剤針スライダ４３に固定された水平な接続レール５１が、エア針スライダ水平方向にガイドする。これにより、二つのスライダの昇降動作を同期させる。

【0032】

エア針スライダ４７を斜めに昇降させることで、二つの針を、バイアル５の上部の狭い面積のゴム栓１３に、正確に穿刺させることができる。

【0033】
（機構の詳細）
図３（Ａ）に示すように、昇降機構１５を構成する外部の駆動レバー２２は、遮蔽キャビネット１を貫通する駆動シャフト５３により、遮蔽キャビネット１の内部の駆動アーム４１と同軸に連通される。図４、図５図６に示すように、薬剤針スライドレール４５は、２本の平行レールからなる。エア針スライドレール４９は、１本のレールからなる。薬剤針スライダ４３及びエア針スライダ４７は、リニアベアリングが装着されていて、それぞれのレール４５，４９の上を滑らかに移動するようになっている。
【0034】
接続レール５１の片端は、薬剤針スライダ４３に固定されており、エア針スライダ４７にはリニアベアリングが装着されていて、エア針スライダ４７がこの接続レール５１の上を滑らかに移動できるようになっている。
駆動アーム４１の先端には、長孔５５が形成され、この長孔５５に薬剤針スライダ４３に形成されたピン５７が挿入されている。
【0035】
また駆動アーム４１にはアームスプリング５９の下端が連結され、アームスプリング５９の上端は装置本体に連結されている。よって、アームスプリング５９は駆動アーム４１を常に上方へ引っ張る。そして、アームスプリング下端が、駆動アーム４１の回動に伴い、回動軸６３を越える際には引き伸ばされ、超えてしまうと縮む。
【0036】
（動作）
図１（Ｄ）に示すように、駆動レバー２２を「針上位置」より「針下位置」の方向に回動して下げると、駆動アーム４１はこの回動と連動して回動し、長孔５５がピン５７を、上下方向に押し、よって、薬剤針スライダ４３を下方に押し下げる（図４（Ｅ）、図５（Ｂ））。一方、エア針スライダ４７も薬剤針スライダ４３に固定されている接続レール５１により、薬剤針ライダ同様に下方に押し下げられる。薬剤針スライダ４３、及びエア針スライダ４７が下方に押し下げられることにより、それぞれのスライダに取り付けてある薬剤針９及びエア針１１は、同期して、バイアル５のゴムに同時に穿刺される。また、駆動レバー２２を元の「針上位置」に戻すことにより、これらの針をバイアル５から抜くことができる。
【0037】
また、アームスプリング５９の働きにより、駆動レバー２２及び駆動アーム４１が水平位置を境に上方にある場合、すなわち、アームスプリング５９が図で示す垂直軸Ａより左側にある場合は、駆動アーム４１を上方の「針（上）位置」に、移動するように作動する。逆に駆動レバー２２及び駆動アーム４１が水平位置を境に下方にある場合、すなわち、アームスプリング５９が垂直軸Ａより右側にある場合は、駆動アーム４１を下方の「針（下）位置」に移動するように作動する。
【0038】
これにより駆動レバー２２の動きに節度をあたえることができ、また、バイアル５に穿刺された薬剤針９は、このアームスプリング５９の作用により適正な力でバイアル５の底部に押しつけられる。
【0039】
（（収納部トレイ３９の傾斜））
図２、図３に示すように、バイアル５の入った遮蔽材付きのコンテナ３７を、収納する収納部トレイ３９は、所定角度傾斜させる。この傾斜角度は使用するバイアル５の容量にもよるが一般的に10～25°、好ましくは15～20°である。これにより、薬剤針９が穿刺されたときに針先が、傾いたバイアル瓶の底部の低端部に位置し、バイアル５中の薬剤のほとんどを吸引することができる。
【0040】
（（衝撃緩和機構及び引出機構））

図７、図８において、薬剤針９及びエア針１１のそれぞれに設けられる衝撃緩和機構及び引出機構を説明する。図は、例として、薬剤針９ものを示す。

針９、１１は、針ロックレバー６７によって開閉する針ホルダ６９によって取り付けられる。この針ホルダ６９が針９、１１に実際に接触する部分はクランプ７１と呼ばれ、この実施形態では、このクランプ７１はプラスチック製が用いられる。

すなわち、針９、１１は、チューブ１７が接続される針９、１１のハブ７３の部分を針接続コネクタ７５に通される。この針接続コネクタ７５が針ホルダ６９のクランプ７１の縦孔７７に通される。すなわち、クランプ７１はU字状で左右の爪７９を有し、U字の基部は、爪７９側が開放した縦孔７７になっている。

【0041】

この縦孔７７の内部には窓が形成され、非円断面を有する押圧軸８１の一部が露出する。非円断面は、例えば丸棒（ステンレス材）の一部が面取りされて得られる。押圧軸８１は針ロックレバー６７に固定される。針ロックレバー６７の回動により、押圧軸８１が軸周りに回動すると、非円断面の面取りされていない面が露出することで、この面が針接続コネクタ７５を押圧しロックがなされる。

【0042】

針ホルダ６９は、横長の部材で、四角断面を有し、対応する四角断面の挿入穴８３を有する針ホルダベース８５に引き出し可能に挿入される。針ホルダベース８５の側面には位置決めプランジャ８７と、周り止めピン８８とが設けられ、これらの先端が針ホルダ６９の側面に形成された図示しない位置決め穴に嵌合し、引出後に戻された位置へ位置決めする。

【0043】

針ホルダ６９の後端は、ピン結合８９によって、水平シャフト９１に結合される。この水平シャフト９１は、針ホルダ取付アーム９３の一部に固定される。すなわち、針ホルダ取付アーム９３は、水平に形成されるコの字形状を有し、このコの字の中央奥に、水平シャフト９１が固定される。これにより、コの字の上下の辺部は、横長の針ホルダ６９の上下に位置する。

【0044】

針ホルダ取付アーム９３のコの字の上辺部９５には、押圧スプリング９７が設けられ、押圧スプリング９７の下端が針ホルダ６９の先端の上面を、下方向に弾性的に押圧する。これにより、針先に上向きに衝撃が働いたときに、衝撃を緩和することができる。そして、コの字の下辺部９９には、上向きの調整ネジ１０１が設けられて、調整ネジ１０１の先端が針ホルダ６９の先端の下面を上方に押し上る。調整ネジ１０１によってこの押し上げ量を調整することで、押圧スプリング９７の押圧力が調整される。

【0045】

（引出機構の動作）

針９、１１を取り付ける時は、針ホルダ６９を持ち手前に引くと、針ホルダ６９が水平方向にスライド移動し、引き出される。針ホルダ６９のセット位置及び針交換時位置は、位置決めプランジャ８７により保持される。

【0046】

そして、針ホルダ６９を手前に引き出した状態で、薬剤針９又はエア針１１を針カバーが付いたまま取り付ける。この取付が終わった後、さらには、遮蔽材付きのバイアル入りのコンテナ３７の収納が終わった後に、針カバーを外し、針ホルダ６９を押して元に戻す。

【0047】

このように、針カバーを外すことなく薬剤針９又はエア針１１を取り付けることができるので、安全（針刺し防止）・衛生（手の接触防止）に優れている。

すなわち、針ホルダ６９を、遮蔽キャビネット１の開かれた手前側へ所定距離引き出すことができるので、十分な作業スペースがある場所でこれらの針９、１１のセットを容易に行うことができ、また、セット後に図示しない針カバーを外しやすい。

仮に、引き出すことができないときは、針先とバイアル５などとの間に十分なスペースがないので、セット後には図示しない針カバーを外すことができず、したがって予め針カバーを外した状態で２本の針９、１１を取り付ける作業を行わなければならず、誤って手に針９、１１が刺さったり、針９、１１に手が触れたりして衛生上の問題があった。この実施形態によれば、これらの問題を解決できる。

【0048】

（緩衝機構の動作）

駆動アーム４１にはアームスプリング５９が取り付けられているため、薬剤針９がバイアル５底部に接触しても衝撃的な負荷がかからないようになっているが、それ以外にも、この押圧スプリング９７により衝撃緩和がなされる。

【0049】

すなわち、針ホルダ６９は、針ホルダ取付アーム９３の押圧スプリング９７により下方向に押圧されている。そして、針９、１１がバイアル５内に穿刺され、バイアル５の底部に接しているが、さらに下方に力が加わった場合、底部への強い接触が起き、針先に上向きの衝撃が働くことがあるが、押圧スプリング９７により図中のストロークＳＬの分だけ移動し、その衝撃を緩和することができる。

【0050】

（クランプ７１の材質）

薬剤針９およびエア針部のハブ７３に接触して固定するクランプ７１は、針９、１１のハブ73の部分が接触する部分は締め付けが十分になるようにプラスチック製部品又はアルミ製部品が貼り付けられる。もっとも、クランプ７１の表面のみをプラスチックで被覆する方法でもよい。

【0051】

すなわち、薬剤用ビン針およびエア針部のハブ７３を固定するクランプ７１は針９、１１が接触する部分は締め付けが十分になるようにステンレス材、アルミ材が用いられる。また、これらのステンレス材、アルミ材にプラスチック製部品が貼り付けられるか、クランプ７１をプラスチックで被覆する方法が用いられる。使用されるプラスチックとしてはポリアセタール、ナイロン、ABS等のエンジニアリングプラスチック、天然ゴム、BR,SBR,NBR、シリコーン等のゴム類およびポリオレフィン系、ポリスチレン系、塩ビ系、ポリエステル系、ポリアミド系、ポリウレタン系等の熱可塑性エラストマーが用いられる。中でもポリアセタールが比較的しっかりとクランプできるため好ましい。

【0052】

（（シリンジ用遮蔽器３））

図９、図１０において、シリンジ７を収納するシリンジ用遮蔽器３を説明する。

（シリンジ７）

図９に示すように、この実施形態で使用されるシリンジ７は、１回の使用毎に回収されるディスポーザブルシリンジ７で、それ自体がある程度、放射線を遮蔽する遮蔽材を有する。すなわち、シリンジ７は、液状放射性医薬剤を吸引し溜める部分１０５が、タングステン製の遮蔽材を有するシリンジシールド１０７を備える。シリンジシールド１０７の中央には鉛ガラス１０９が設けられ液状放射性医薬剤が観察できる。後方には、プランジャ８７を備え、前方には、三方活栓１１１が接続されている。三方活栓１１１はチューブ１７に連通され薬剤針９に接続される。

【0053】

（遮蔽容器）

図１０に示すように、シリンジ７を収納するシリンジ用遮蔽器３は、前方にはシリンジ７の三方活栓１１１を挿入して覆う略箱状の前方シールド１１３が設けられる。プラスチック製の三方活栓１１１内の液状放射性医薬剤による被曝を避けることができる。前方シールド１１３の後方はシリンジ７のシリンジシールド１０７に接する。シリンジシールド１０７の後方には、プランジャ８７を上下左右から開閉可能に覆うプランジャシールド上面、下面、左面、右面１１５Ａ、１１５Ｂ、１１５Ｃ、１１５Ｄが接する。プランジャシ

ールドの後方の開口には、プランジャシールド後面１１７が後付される。プランジャシールド後面１１７の働きにより、シリンジ７のフランジ部およびプランジャーヘッド部１２１からの放射線による被曝を避けることができる。

【0054】

プランジャシールド後面１１７の中央には、プランジャ８７を延長するプランジャシャフト１２３が貫通する。

すなわち、プランジャ８７の後端は、プランジャシャフト１２３の先端に設けられたプランジャホルダー１２５により保持される。プランジャシャフト１２３の中央には、シャフトロック１２７が設けられて、プランジャシールド後面１１７に対する位置決めがなされ、後端には、プランジャノブ１２９が設けられる。このプランジャノブ１２９を引いて吸引を行う。

【0055】

これらのシールドを形成する遮蔽材の材質はタングステンが望ましいが、タングステン合金、鉛、鉛ガラス１０９、タンタル、ビスマス等が用いられる。これらは、生理食塩液の接触および空気酸化による腐食・汚染が見られるため、使用に際し、ステンレス、プラスチック、ゴム、塗料、めっき等により被覆することが望ましい。

【0056】

（（流路とチューブ１７））

液状放射性医薬剤の流路は、装置上部に配置されたシリンジ用遮蔽器３のシールド内で、シリンジ７先端の三方活栓１１１に連通されたエクステンションチューブ１７を通って針ホルダ６９に固定された薬剤針９のハブ７３に接続される。

【0057】

シリンジ７先端の三方活栓１１１の他方は、図示しない生理食塩液用ディスポーザブルシリンジ７を取り付けることができ、流路の洗浄および流路の液充填に用いることができる。さらに、三方活栓１１１のもう一方のノズルは、別のエクステンションチューブ１７を接続することができ、薬剤用シリンジ内の薬剤を他へ注入することができる。

【0058】

エクステンションチューブ１７の材質としてのポリ塩化ビニル製（ＰＶＣ）は、その優れた物性により（特に，輸液ポンプ等の機器との併用等によるチューブ１７に大きな負荷がかかる場合においては，チューブ１７の潰れによる閉塞や引っ張りによる破断といった不具合を生じにくく、ひいてはこれらの不具合の結果生じる投薬上の問題や失血等の危険性が低い医療用具として）、国内外において医療の場で広く使用されているため、好ましい。

【0059】

一方，ＰＶＣは、その特性である優れた柔軟性を保持するために、材質中に可塑剤が添加されており、この可塑剤としてＤＥＨＰ：フタル酸ジ-2-エチルヘキシルが、多く用いられているが、接触する溶媒中に溶出することが知られている。そのため、可塑剤としてトリメリット酸トリス（２－エチルヘキシル）：ＴＯＴＭ、アジピン酸ジオクチル：ＤＯＡを用いたものが、好ましい。また、ＰＶＣは各接続部との接着が優れているため、好ましい。

【0060】

ＰＶＣ以外のチューブ用材質としては、ポリブタジエン、軟質ポリエチレン、ポリウレタン、シリコーンゴム、熱可塑性エラストマー等が用いられる。

（（装置用架台２９））

装置は全面が遮蔽材により覆われ、重量があり容易に移動できないため、移動可能なキャスター付きの架台１３３に置くか、装置自体にキャスターを取り付け、医療機関に搬送し、院内における移動しやすいようにすることも可能である。

【0061】

（（手動動作））

この装置は以下のように操作して使用する。

1)バイアル５中の薬剤を吸引するためのディスポーザブルシリンジ７は、装置上部に一体的に設けられたシリンジ用遮蔽器３内に収納する。
2）遮蔽キャビネット１のスライド機構３１を働かせて、前面部を手前に引き出す。
3)左側面の開閉扉２１を開ける。
4）遮蔽キャビネット１内部で、エクステンションチューブ１７に薬剤針９を取り付ける。
5)その薬剤針９を薬剤針用ホルダーに取り付け、針カバーをはずす。
6)エア針１１をホルダーに取り付け、針カバーをはずす。
7）シリンジ用遮蔽器３を開け、中にあるエクステンションチューブ１７の他端を、ディスポーザブルシリンジ７の三方活栓１１１に取り付ける。
8）シリンジ用遮蔽器３を閉じる。
9)遮蔽材を有するコンテナ３７に収められ放射性薬剤又は医薬品の入ったバイアル５を、遮蔽材付きの収納部トレイ３９にセットする。
10)コンテナ３７のフタを開ける。
11）遮蔽キャビネット１のスライド機構３１を働かせて、前面部を押して、元に戻す。
12）遮蔽キャビネット１の右側面に付いた駆動レバー２２を「針（上）位置」から「針（下）位置」の方向に下げ、薬剤針９およびエア針１１をバイアル５に穿刺する。
13）シリンジ用遮蔽器装のプランジャノブ１２９を引いて、バイアル５内の薬剤を吸引する。
14)右側面に付いた駆動レバー２２を元に戻す。
（自動動作）
12)および14)をサーボモーター、コントローラー付きの駆動ユニットを用いて自動で操作を行うことができる。それ以外は手動動作と同様である。
【0062】
（（実施形態の効果））
以上の実施形態によれば、遮蔽キャビネット１とシリンジ用遮蔽器３とを別に設けるので、１本のバイアル５から薬剤を数本のシリンジ７へ分けて吸収する際であっても、シリンジ７を交換する際にシリンジ用遮蔽器３のみを開閉すればよく、遮蔽キャビネット１は開ける必要がない。よって、その分、被曝の可能性が減少する。
【0063】
さらに、バネを備えた緩和機構の働きで、針先がバイアル５の底部に当たってもガラス壁を損傷する懸念がない。このため、針先がバイアル５の底部ぎりぎりに接して位置でき、バイアル５内の薬剤を残さず吸引できる。
さらに、薬剤針９及びエア針１１のハブ73の部分を取り付ける針ホルダ６９が、遮蔽キャビネット１の開かれた側へ所定距離引き出すことができるので、これらの針９、１１を取り付けるセットが容易であり、また、セット後に針カバーを外しやすい。よって、指を傷つけにくい。
【0064】
さらに、針ホルダ６９のうちの直接に針９、１１のハブ73の部分に接触するクランプ７１が、全てあるいは表面的にプラスチック製又はアルミ製であることから、全て他の金属製である場合に比べ、針９、１１を締め付ける十分な締付力が得られる。よって締付力をうるためにクランプ部分、ひいてはホルダー部構造を複雑にする必要がなく、結果的に装置をコンパクトにできる。
【0065】
さらに、薬剤針９及びエア針１１を同期して昇降させる昇降機構１５の構造が簡略にでき、結果的に装置をコンパクトにできる。
さらに、収納部トレイ３９を傾斜させることで、バイアル５を傾けて収納でき、薬剤を傾いた底部の隅に集めることができ、残さず吸引できる。
さらに、遮蔽キャビネット１が前後方向にスライド可能なスライド機構３１を有し、このスライド可能な前面部分２５と背面部分２７の一方にバイアル５が収納され、他方に昇降機構１５を有することで、手作業時にバイアル５と昇降機構１５を離し、これによって

作業スペースを拡げることができ、装置がコンパクトでも作業が可能になる。結果的に装置をよりコンパクトにできる。

【0066】

「他の実施形態」

以上の実施形態では、遮蔽キャビネット１の外部から手動により、ゴム栓１３に向かって針９、１１の方向に沿って昇降させる昇降機構１５を駆動するものであったが、他の実施形態では、昇降機構１５を駆動するサーボモーターなどを設け、自動化することも容易に行える。

【0067】

以上の実施形態では、遮蔽キャビネット１の左側面に開閉扉２１を有するものであったが、他の実施形態では、右側面に有するものでも良いし、左右側面の両方に開閉扉２１を有するものでも良い。

以上の実施形態では、スライド機構３１によって離される前面部分２５と背面部分２７のうち、前面部分２５にバイアル５が収納され、背面部分２７に前記昇降機構１５を有するものであったが、他の実施形態ではこの関係は逆でも良い。

【0068】

以上の実施形態では、駆動アーム４１により直接に押されて昇降するのは薬剤針スライダ４３であり、接続レール５１を介して間接的にエア針スライダ４７が押されて昇降するものであったが、他の実施形態では、この関係は逆にして、直接に押されて昇降するのはエア針スライダ４７であり、間接的に押されて昇降するのが薬剤針スライダ４３とすることができる。

【0069】

以上の実施形態では、二つの針９、１１の昇降動作を同期させる接続レール５１は、薬剤針スライダ４３に固定され、エア針スライダ４７をガイドするものであったが、他の実施形態では、接続レール５１は、エアスライダに固定され、薬剤針スライダ４３をガイドするものであっても良い。

【0070】

以上の実施形態では、吸引装置は、薬剤針９及びエア針１１を有するものであったが、他の実施形態では、薬剤針９のみとすることも可能である。すなわち、バイアル５に薬剤針９を挿入後、ディスポシリンジにより約４～５ｍｌのエアを、エクステンションチューブ１７を介してバイアル５に投入すると、バイアル５内が加圧となるため、エア針１１を設けなくても、自然にバイアル５中の薬液がディスポシリンジに抜き出される。

以上の実施形態では、遮蔽キャビネット１の外部に別に設けられたシリンジ用遮蔽器３にシリンジ７を収納するものであったが、他の実施形態ではシリンジ用遮蔽器３を設けず、遮蔽キャビネット１の内部にシリンジを収納することもできる。この場合には、遮蔽キャビネット１の外部からの力により、内部のシリンジ７のプランジャ８７を引いて吸引を行う吸引動作機構を設ける。

【図面の簡単な説明】

【0071】

【図1】装置全体の外観図で、（Ａ）は平面図、（Ｂ）は左側面図、（Ｃ）は正面図、（Ｄ）は右側面図である。

【図2】装置の開閉扉を取り除いて内部を示す左側面図で、（Ａ）はスライド機構により前面部分が引き出された状態を示す図、（Ｂ）はスライド機構により前面部分がもとに戻された状態を示す図である。

【図3】は装置の壁を取り除いて内部の昇降機構を示すもので、（Ａ）は正面図、（Ｂ）は左側面図、（Ｃ）は（Ｂ）において昇降機構により針が穿刺された状態を示す図である。

【図4】は図３の装置の壁を取り除いて内部の昇降機構を示すもので、（Ｄ）は右側面図、（Ｅ）は（Ｄ）において昇降機構により針が穿刺された状態を示す図である。

【図5】は図４の装置の外の駆動レバーと内部の昇降機構との関係を示す透視図で、（Ａ

）は駆動レバーを上げた状態を示す図、（Ｂ）は駆動レバーを下げた状態を示す図である。

【図6】は図５の要部を拡大して示す図である。

【図7】図３（Ａ）の薬剤針又はエア針のそれぞれに設けられる衝撃緩和機構及び引出機構の拡大図を示すもので、（Ａ）は側面図、（Ｂ）は断面側面図、（Ｃ）は平面図、（Ｄ）は（Ａ）の一部を引き出した状態を示す図である。

【図8】は図７の（Ｄ）の要部をさらに詳しく示すもので、（Ｅ）は一部を断面にした図、（Ｆ）は（Ｅ）の平面図、（Ｇ）は（Ｅ）のロックを解除した状態の図、（Ｈ）は（Ｇ）の平面図である。

【図9】は図１のシリンジ用遮蔽器に収納されるシリンジを示すもので、（Ａ）は水平断面図、（Ｂ）は縦断面図である。

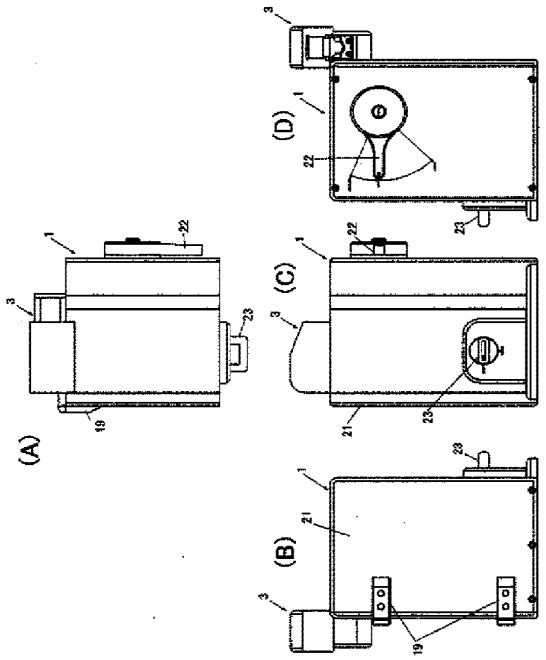
【図10】は図１のシリンジ用遮蔽器にシリンジが収納された状態を示す水平断面図である。

【符号の説明】

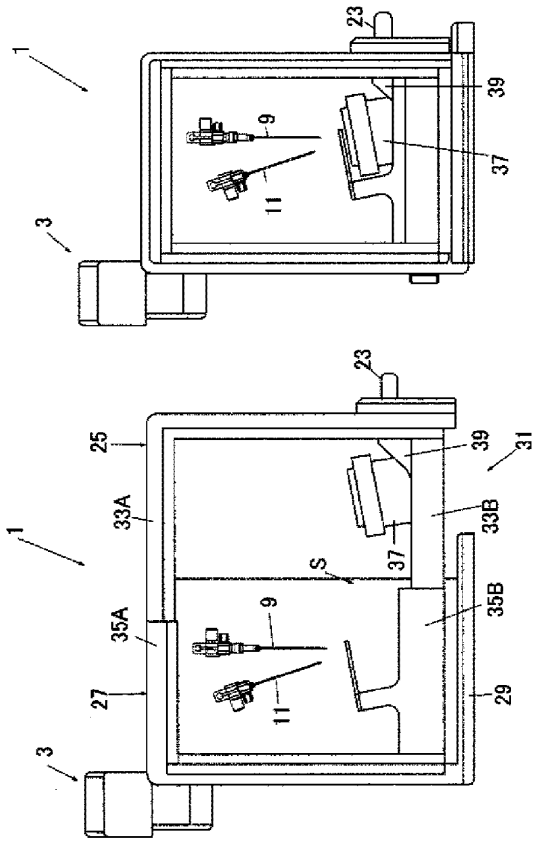
【0072】

１…遮蔽キャビネット、３…シリンジ用遮蔽器、５…バイアル、７…シリンジ、９…薬剤針、１１…エア針、１３…ゴム栓、１５…昇降機構、１７…チューブ、１９…ヒンジ、２１…開閉扉、２２・・駆動レバー、２３…開閉レバー、２５…前面部分、２７…背面部分、２９…装置用架台、３１…スライド機構、３３…スライダー、３５…スライドガイド、３７…コンテナ、３９…収納部トレイ、４１…駆動アーム、４３…薬剤針スライダ、４５…薬剤針スライドレール、４７…エア針スライダ、４９…エア針スライドレール、５１…接続レール、５３…駆動シャフト、５５…長孔、５７…ピン、５９…アームスプリング、６１…装置本体、６３…回動軸、６５…針、６７…針ロックレバー、６９…針ホルダ、７１…クランプ、７３…ハブ、７５…針接続コネク、７７…縦孔、７９…爪、８１…押圧軸、８３…挿入穴、８５…針ホルダベース、８７…プランジャ、８９…ピン結合、９１…水平シャフト、９３…針ホルダ取付アーム、９５…上辺部、９７…押圧スプリング、９９…下辺部、１０１…調整ネジ、１０５…部分、１０７…シリンジシールド、１０９…鉛ガラス、１１１…三方活栓、１１３…前方シールド、１１５…右面、１１７…プランジャシールド後面、１１９…フランジ部、１２１…プランジャーヘッド部、１２３…プランジャシャフト、１２５…プランジャホルダー、１２７…シャフトロック、１２９…プランジャノブ、１３３…架台。

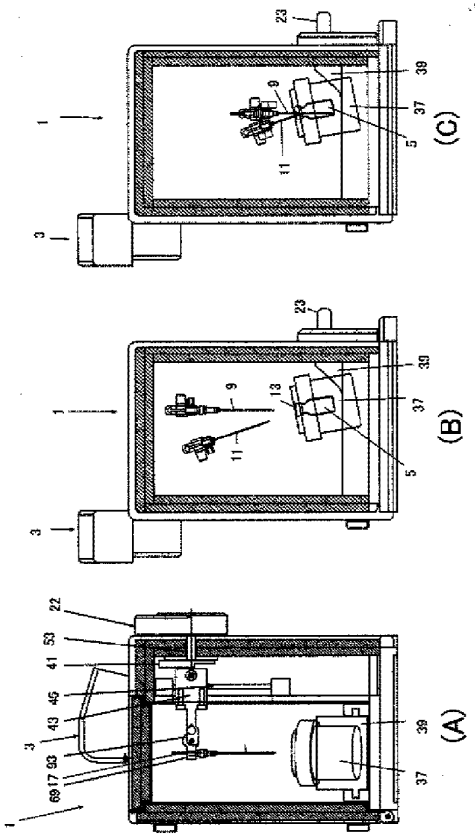
【図1】



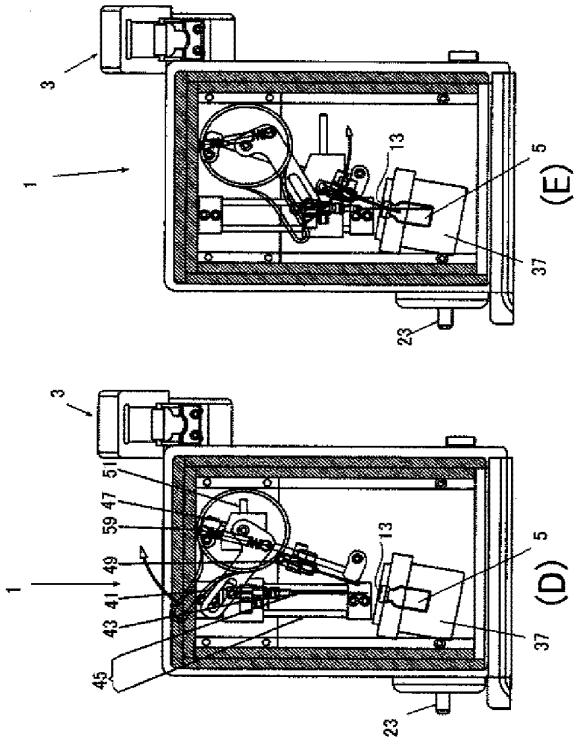
【図2】



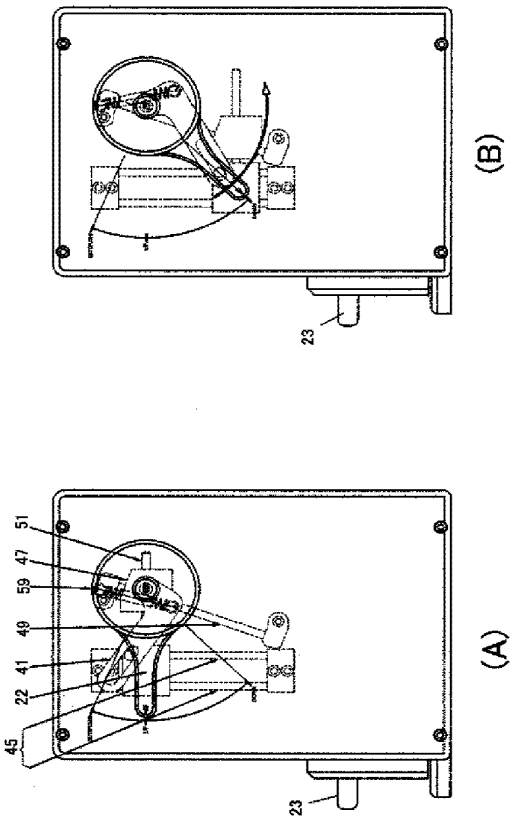
【図3】



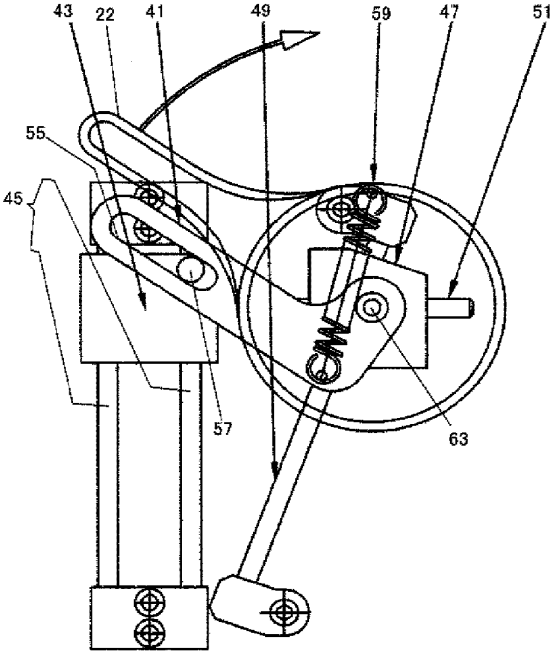
【図4】



【図5】


(B)
23
(A)
51
47
59
49
41
22
45
23

【図6】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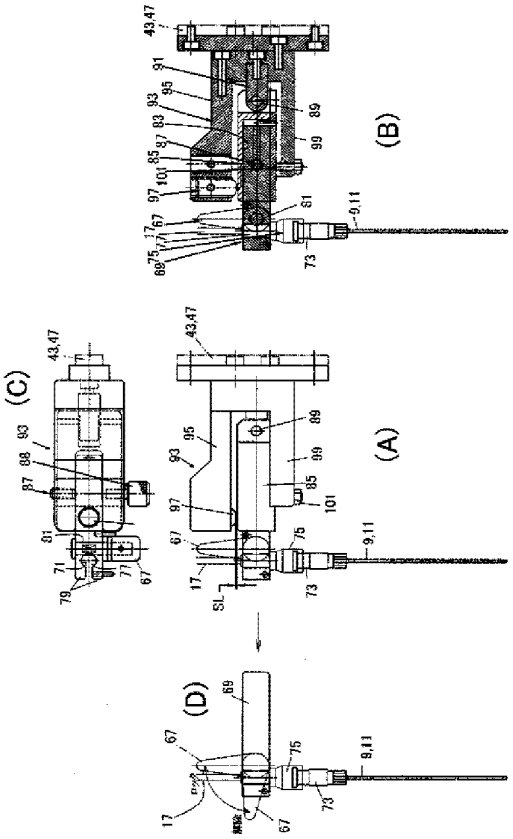
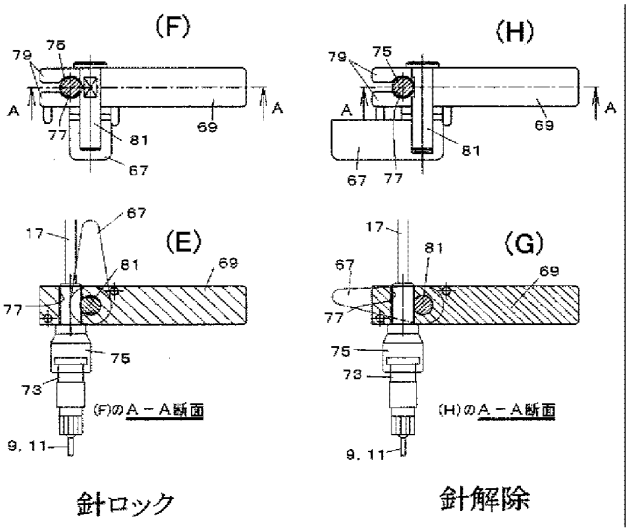
57
63

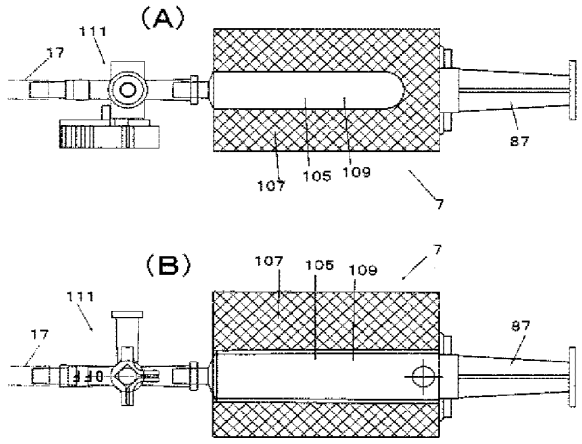
【図7】


43,47
(B)
(C)
(A)
(D)

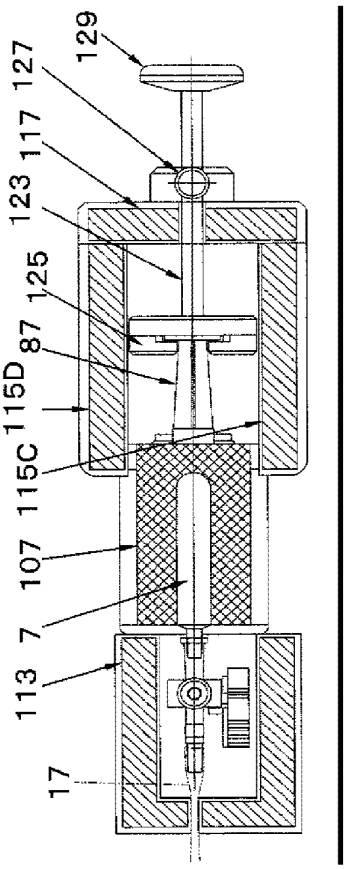
【図8】


(F)
(H)
(E)
(G)
(F)のA－A断面
(H)のA－A断面
針ロック
針解除

【図9】


(A)
111
17
87
107
105
109
7
(B)
107
105
109
7
111
17
87

【図10】


129
127
117
123
125
87
115D
115C
107
7
113
17

Patent Abstracts of Japan

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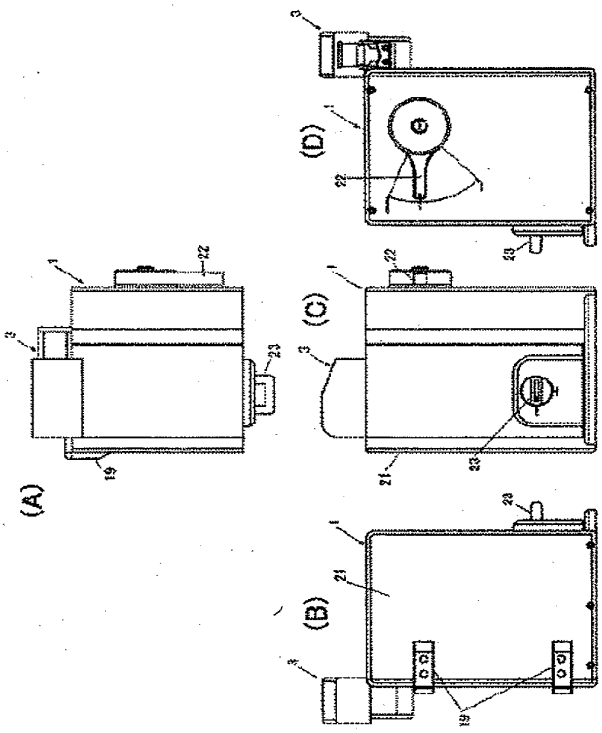
APPLICANT : SD GIKEN:KK;

INVENTOR : SAITO KAZUHIRO;

INT.CL. : A61J 1/00 (2006.01)

TITLE : RADIOPHARMACEUTICALS SUCKING DEVICE



ABSTRACT : PROBLEM TO BE SOLVED: To reduce the possibility of exposure of a medical staff, to eliminate the risk of damage of a glass wall of a vial with a needle tip, to prevent injury of fingers of the medical staff during the manual operation, and to make a device compact on a radiopharmaceuticals sucking device with a shielding material to prevent the medical staff in charge of sucking a liquid radiopharmaceuticals in the vial into a syringe from being exposed to radiation.

SOLUTION: A shielding cabinet 1 and a shield 3 for the syringe are separately disposed to be independently opened/closed. A lifting mechanism 15 for lifting a pharmaceuticals needle 9 and an air needle 11 has a spring not to apply the impact to the vial even if the tip of the punctured pharmaceuticals needle 9 touches the glass wall. A holder part to which the pharmaceuticals needle 9 and the air needle 11 are attached has a drawer mechanism capable of being moved by a prescribed distance to the side where the shielding cabinet 1 is opened. A storage part for storing the inclined vial 5 has inclination, and the lowered tips of the pharmaceuticals needle 9 and the air needle 11 are set in corners of the inclined bottom of the vial 5.

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（P2000－350783A）
(43)公開日　平成12年12月19日(2000.12.19)

(51)Int.Cl.[7]		識別記号	FI			テーマコード*(参考)
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	5/00	３２０		5/00	３２０	
		３３０			３３０	
Ｇ２１Ｇ	4/08		Ｇ２１Ｇ	4/08		

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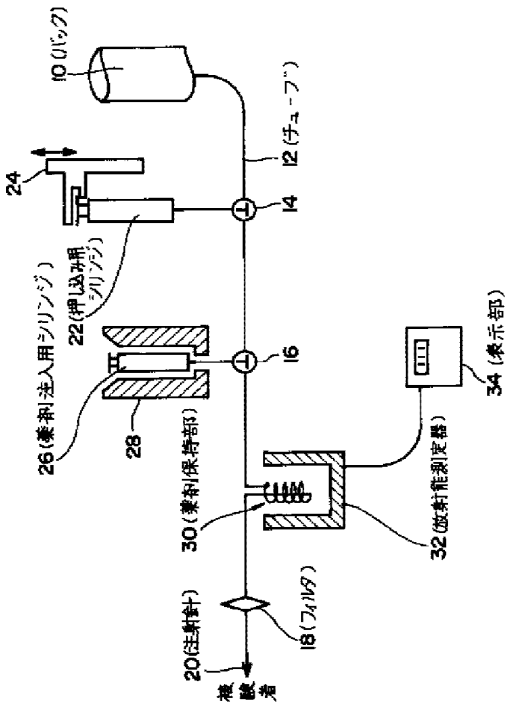
弁理士　高矢　諭　（外２名）

最終頁に続く

(54)【発明の名称】　放射性液体の注入方法及び装置

(57)【要約】
【課題】　放射性薬剤取扱者の被爆量を減少させつつ、投与量を、簡単、且つ、正確に測定する。
【解決手段】　注入直前に、放射性液体の全量を一時的に、放射線遮蔽された液体保持部３０に収容し、該液体保持部３０に収容された放射性液体の放射能量を測定した後、該放射性液体の全量を人体に注入する。



【特許請求の範囲】
【請求項１】放射性液体を人体に注入するための放射性液体の注入方法において、
注入直前に、放射性液体の全量を一時的に、放射線遮蔽された液体保持部に収容し、
該液体保持部に収容された放射性液体の放射能量を測定した後、
該放射性液体の全量を人体に注入することを特徴とする放射性液体の注入方法。
【請求項２】放射性液体を人体に注入するための放射性液体の注入装置において、
注入直前の放射性液体の全量を一時的に収容可能な液体保持部と、
該液体保持部を遮蔽する放射線遮蔽手段と、
該液体保持部に収容された放射性液体の放射能量を測定する放射能測定手段と、
放射能測定後の放射性液体の全量を人体に注入するための液体押し込み手段と、
を備えたことを特徴とする放射性液体の注入装置。
【請求項３】請求項２において、更に、前記液体保持部に放射性液体を送入するための放射性液体送入手段を遮蔽する放射線遮蔽手段を備えたことを特徴とする放射性液体の注入装置。
【請求項４】請求項２又は３に記載の手段が、全て、移動可能な台車に搭載されていることを特徴とする放射性液体の注入装置。
【発明の詳細な説明】
【０００１】
【発明の属する技術分野】本発明は、放射性液体の注入方法及び装置に係り、特に、半減期の短い、放射性の強い核種で標識された放射性医薬品を被験者に投与する際に用いるのに好適な、放射性液体を人体に注入するための放射性液体の注入方法及び装置に関する。
【０００２】
【従来の技術】病院の検査室等において、半減期が短い、放射性の強い核種で標識された放射性医薬品を被験者に投与する場合、取扱者の放射線被爆を防止すると共に、所定の投与量を、正確に、一定速度で投与する機構が必要となり、自動化・遠隔化装置が必要である。そのため、被験者に放射線医薬品を自動投与する装置として、ＭＲ造影剤注入装置や放射性医薬品自動注入装置等が実用化されている。
【０００３】これらの注入装置は、基本的に、薬液を一定量充填されたシリンジと、被験者までのチューブ、該チューブを注射用蒸留水又は生理食塩水で充填したり、薬液全量を投与するための最後の押し込み注入用のシリンジ、及び、液流れを切り換えるための自動又は手動バルブ、一定速度で投与するための動作機構、コントローラ等から構成されている。
【０００４】このような注入装置を用いて、短寿命核種（例えば、ポジトロン放出核種として、15Oは２分、11Cは２０分、18Fは１１０分の半減期を持つ）で標識された15O－水あるいは11C－メチオニンあるいは18F－ＦＤＧ（フルオロデオキシグルコース）等の薬剤を被験者に投与する場合、従来は、、投与前に、薬剤をシリンジに入れた状態で放射能量を測定し、投与後、再度シリンジ内に残留した放射能量を測定し、投与した時間（基準時間）での放射能量を放射能減衰補正して求めることで、被験者に投与された放射能量を測定していた。
【０００５】通常、薬液のバイアルは、濃度が既知であり、希望する放射能量を得るには、計算で求めた、決められた容量を吸引することになる。この場合、バイアルでなくても、別装置から一定量の薬液を注入することも可能である。いずれにしても、一定量吸入したシリンジは、正確に測定する必要があるため、通常、鉛容器に入れた状態からシリンジを取出し、測定後、再度鉛容器に入れて、検査室被験者の場所に運搬し、装置に取り付け、投与終了後、シリンジに残留する放射能量を再度測定して、投与量を求めていた。
【０００６】
【発明が解決しようとする課題】従って、投与前と投与後の２回、放射能量を正確に測定する必要があり、手間がかかって面倒であるだけでなく、シリンジに含まれる放射能量を測定するときに、測定者は被爆されることになる。しかも、投与後にシリンジを測定することで、被爆し、投与液が身体に付着する危険もあった。
【０００７】本発明は、前記従来の問題点を解決するべくなされたもので、短寿命核種で標識された放射性医薬品や放射性化合物の投与量を、取扱者の放射線被爆量を減少させて、簡単且つ正確に測定することを課題とする。
【０００８】
【課題を解決するための手段】本発明は、放射性液体を人体に注入するための放射性液体の注入方法において、注入直前に、放射性液体の全量を一時的に、放射線遮蔽された液体保持部に収容し、該液体保持部に収容された放射性液体の放射能量を測定した後、該放射性液体の全量を人体に注入するようにして、前記課題を解決したものである。
【０００９】本発明は、又、放射性液体を人体に注入するための放射性液体の注入装置において、注入直前の放射性液体の全量を一時的に収容可能な液体保持部と、該液体保持部を遮蔽する放射線遮蔽手段と、該液体保持部に収容された放射性液体の放射能量を測定する放射能測定手段と、放射能測定後の放射性液体の全量を人体に注入するための液体押し込み手段とを備えることにより、前記課題を解決したものである。
【００１０】更に、前記液体保持部に放射性液体を送入するための放射性液体送入手段を遮蔽する放射線遮蔽手段を備えたものである。

【００１１】又、前記手段を、全て、移動可能な台車に搭載したものである。

【００１２】

【発明の実施の形態】以下図面を参照して、本発明の実施形態を詳細に説明する。

【００１３】本発明の基本的な構成に対応する第１実施形態を図１に示す。

【００１４】本実施形態は、生理食塩水又は注射用蒸留水が入れられたバック１０と、後端に該バック１０が接続され、途中に、バック１０側から順に、２個の三方活栓付バルブ１４、１６とフィルタ１８が配設され、先端に注射針２０が接続されたチューブ１２と、前記三方活栓付バルブ１４を介して、該チューブ１２内の生理食塩水又は注射用蒸留水を押し込むための、例えば超音波モータによるサーボアクチュエータ２４付の押し込み用シリンジ２２と、前記三方活栓付バルブ１６を介して、前記チューブ１２内に放射性薬剤を注入するための、例えば鉛製のシールド容器２８内に収容された、例えば超音波モータによるサーボアクチュエータ付又は手動の放射性薬剤注入用シリンジ２６とを備えた注入装置において、前記薬剤注入用シリンジ２６とフィルタ１８の間に、注入直前の放射性薬剤の全量を一時的に収容可能な、例えばコイル状の薬剤保持部３０と、該薬剤保持部３０に収容された放射性薬剤の放射能量を測定するための、表示部３４を有する放射能測定器３２を設け、該放射能測定器３２により薬剤保持部３０に収容された放射性薬剤の放射能を測定した後、該放射性薬剤の全量を、前記押し込み用シリンジ２２により被験者に注入するようにしたものである。

【００１５】前記薬剤注入用シリンジ２６は、先端（図では下端）が開放されているシールド容器２８に格納され、該シールド容器２８内に収容されたままの状態で、装置に着脱可能とされている。この薬剤注入用シリンジ２６内の薬液は、バルブ１６の切換えによって、自動又は手動で、全量がチューブ１２内に押し込まれ、チューブ１２の途中に設けられたコイル状の薬剤保持部３０に向けて全量が投入される。更に、バルブ１６とコイル状の薬剤保持部３０の入口に残る薬液は、押し込み用シリンジ２２で注射用蒸留水又は生理食塩水を定められた量吐出して、薬液全量を薬剤保持部３０に押し込む。

【００１６】前記薬剤保持部３０は、前記薬剤注入用シリンダ２６により薬液の全量が投入された状態で、薬液が被験者に到達しないコイル容量を確保しておく。

【００１７】前記放射能測定器３２としては、正確に測定するためには、ウェル型ドーズ（放射線量）キャリブレータが好適である。しかしながら、目的によっては、ＮａＩシンチレーション検出器、あるいは、ＧＭ検出器等、簡易検出器を用いて、値をレートメータや放射線カウンタ等で検出する方法も有効である。

【００１８】以下、本実施形態の作用を説明する。

【００１９】装置に取り付けた後、薬剤注入用シリンジ２６を軽く押し込み、予め計算された量を吐出して、薬液全量を薬剤保持部３０に押し込む。更に、バルブ１６とコイル状の薬剤保持部３０の入口に残る薬液は、押し込み用シリンジ２２で注射用蒸留水又は生理食塩水を定められた量吐出して、薬液全量を薬剤保持部３０に押し込む。

【００２０】次に、被験者にチューブ１２先端の注射針２０を取り付ける。

【００２１】検査準備が整ってから、放射能測定器３２で正確な放射能量を測定し、押し込み用シリンジ２２で、注射用蒸留水又は生理食塩水を流して、薬剤保持部３０に保持されていた放射性薬剤の全量を被験者に投与する。

【００２２】投与後、次の投与準備に取り掛かる。この時、全量が投与されているので、従来とは異なり、投与に使用した薬剤注入用シリンジ２６の放射能残留量を測定する必要がない。

【００２３】次に、実際の病院で用いるのに適した具体的な第２実施形態について詳細に説明する。

【００２４】本実施形態は、図２（正面から見た縦断面図）、図３（上面から見た横断面図）、図４（図２の右側から見た縦断面図）及び図５（要部の背面図）に示す如く、前記第１実施形態と同様のバック１０、チューブ１２、三方活栓付バルブ１４、１６、フィルタ１８、押し込み用シリンジ２２、薬剤注入用シリンジ２６、薬剤保持部３０、放射能測定器３２を、全て、固定キャスタ４２、ブレーキ付自在キャスタ４４及び取手４６を備えたワゴン４０に搭載して、病院内での移動を容易としたものである。

【００２５】図において、５０は、図３に示す矢印Ａの範囲で揺動可能なバック１０用のスタンド、５２は、フィルタ１０用の固定台、５４は、前記押し込み用シリンジ２２を保持するためのシリンジホルダ、５６は、先端が例えばタングステン製のシールド容器２８によって遮蔽された前記薬剤注入用シリンジ２６を保持するためのシリンジホルダ、５８は、該薬剤注入用シリンジ２６を、図３の矢印Ｂに示す如く、駆動するためのサーボアクチュエータ、６０は、前記薬剤保持部３０を構成するチューブ巻取用パイプ、６２は、前記放射能測定器３２を構成するドーズキャリブレータ、６４は、そのシールド、６６は、図２の背面側にパネルが固定された、ドーズキャリブレータ６２のコントローラ、６８は、同じく図２の背面側に設けられた、図３の矢印Ｃに示す如く引出し可能な、パネル引出式の操作盤、７０は、ワゴン４０の下方に配設された主制御盤、７２は、該主制御盤７０の上方に設けられた副制御盤、７４は、ワゴン４０上部の前記チューブ１２、三方活栓付バルブ１４、１６、フィルタ１８、薬剤注入用シリンジ２６等を遮蔽するための、矢印Ｄに示す如く、水平方向にスライド可能な、

例えば厚さ１０ｍｍの鉛製上蓋７６を有する、例えば厚さ２０ｍｍの鉛シールド、７８は、前記チューブ１２の出口側に設けられた、放射性薬剤の通過を確認するための放射線センサ、８０は排液用ボトル、８２は、そのホルダ、８４は、押し込み用シリンダ２２を収容するためのケース、８６は、その、透明な塩化ビニール製の扉、８８は、バッファ液廃棄用スタンドである。

【００２６】本実施形態を使用するに際しては、まず、放射性液体を含んだ薬剤注入用シリンジ２６を、スライド可能な鉛シールド７４の上扉７６を開いてセットする。

【００２７】上扉７６を閉じて完全な遮蔽状態とした後、サーボアクチュエータ５８を駆動して、放射性液体の全量を、チューブ巻取用パイプ６０に巻き取られた薬剤保持部３０に送り込む。更に、バルブ１６とコイル状の薬剤保持部３０の入口に残る薬液は、押し込み用シリンジ２２で注射用蒸留水又は生理食塩水を定められた量吐出して、薬液全量を薬剤保持部３０に押し込む。

【００２８】次いで、パイプ６０を、矢印Ｅに示す如く、下げて、ドーズキャリブレータ６２内に入れた状態で、放射能量を測定する。

【００２９】放射能量測定後の放射性薬剤は、サーボアチュエータ２４により駆動される押し込み用シリンジ２２によって、追い出（フラッシング）され、全量が被験者に送られる。

【００３０】本実施形態においては、この際、放射線センサ７８によって放射性薬剤の通過が確認される。なお、この放射線センサ７８は省略することも可能である。

【００３１】本実施形態においては、操作を自動化し、放射性液体の通過部分を、ほぼ完全にシールドしているので、被爆低減効果が高い。特に、接液部のフィルタ、チューブ、三方活栓付バルブ、シリンジは、全て滅菌済みのデスポーザブルを使用することができ、無菌の保持が簡単にできる。又、ラインの交換も容易にできる。

【００３２】なお、短寿命でない放射性医薬品については、それほど被爆防止の必要性は有しないので、正確な測定は困難ではないが、本発明を適用できることは明らかである。

【００３３】

【発明の効果】本発明によれば、取扱者の放射線被曝量を減少させ、投与量を簡単且つ正確に測定することが可能となる。

【図面の簡単な説明】

【図１】本発明の基本的な構成を示す第１実施形態の構成図

【図２】本発明の具体的な構成例である第２実施形態を示す、正面から見た縦断面図

【図３】同じく上面から見た横断面図

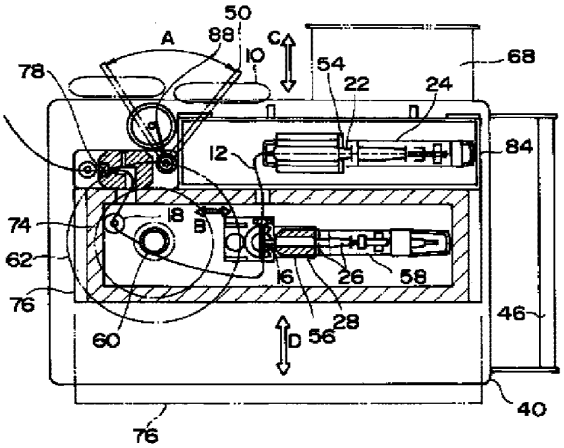
【図４】同じく右側面から見た縦断面図

【図５】同じく要部の背面図

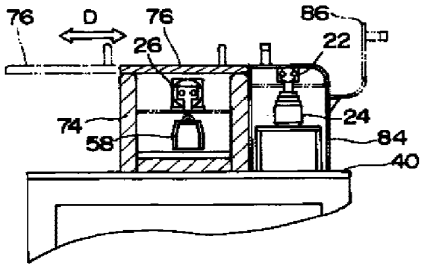
【符号の説明】

１０…バック
１２…チューブ
１４、１６…三方活栓付バルブ
１８…フィルタ
２０…注射針
２２…押し込み用シリンジ
２６…放射性薬剤注入用シリンジ
３０…薬剤保持部
３２…放射能測定器
４０…ワゴン
６０…チューブ巻取パイプ
６２…ドーズキャリブレータ
２８、６４、７４、７６…シールド

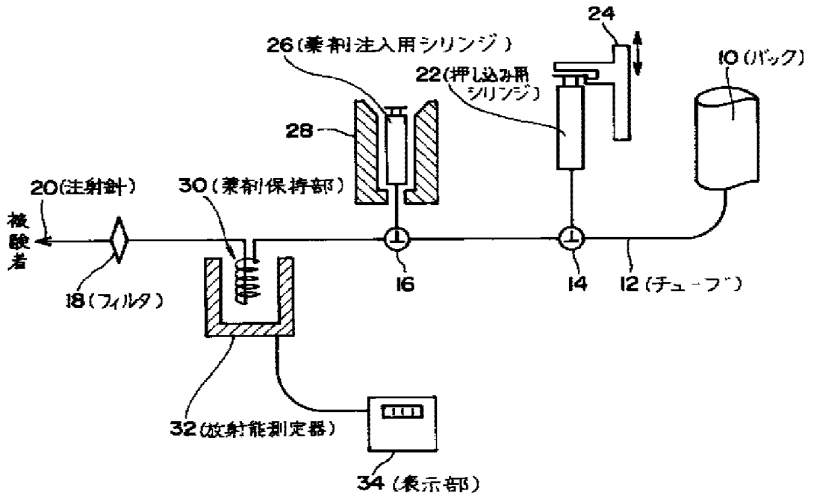
【図３】



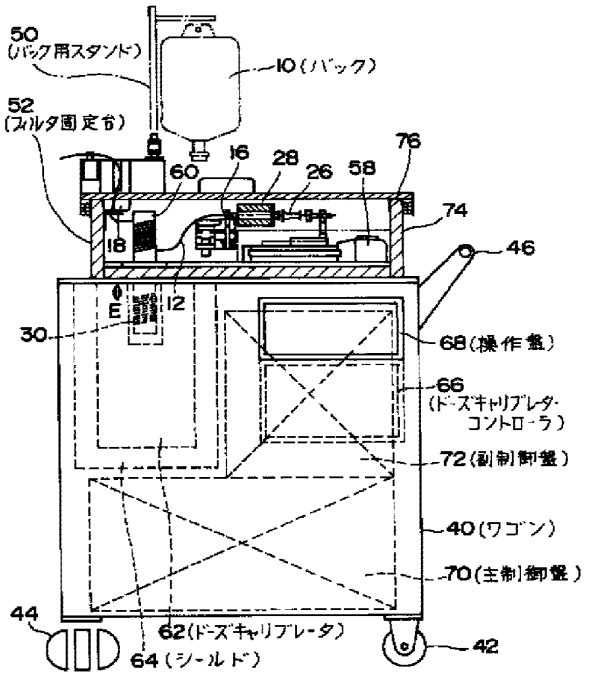
【図４】



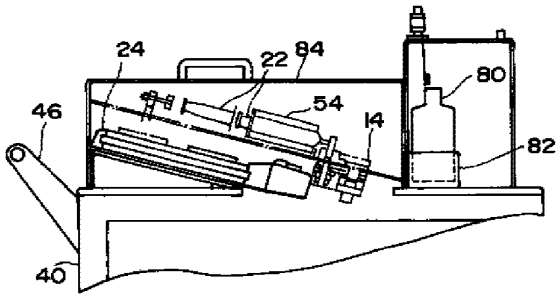
【図1】



【図2】



【図5】



フロントページの続き

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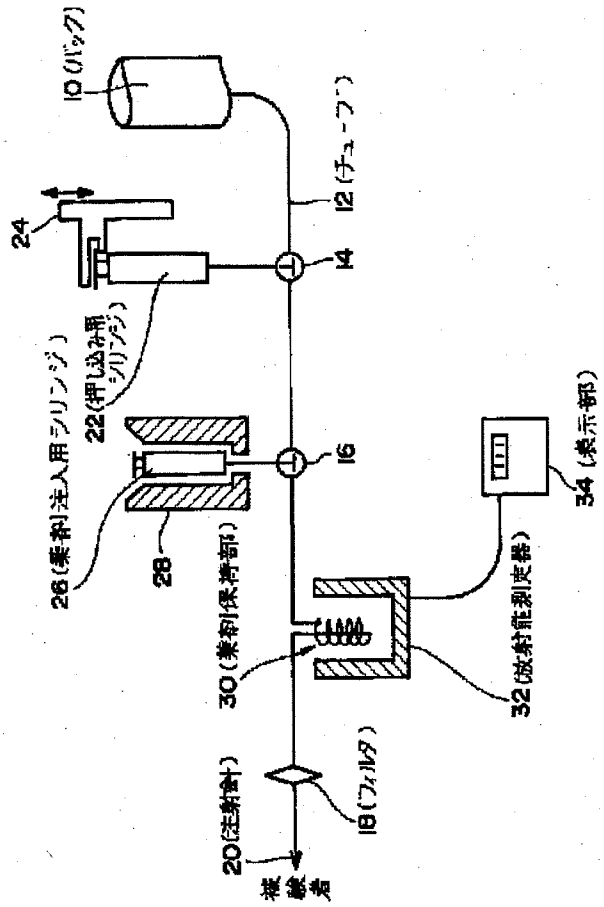
TITLE : INJECTION METHOD AND APPARATUS OF RADIOACTIVE LIQUID



ABSTRACT : PROBLEM TO BE SOLVED: To reduce exposure quantity to a handling person and measure the dose simply and accurately by temporarily keeping the whole radioactive liquid in a radiation shielding liquid retainer immediately before injection, measuring the radiation dose, then injecting the whole quantity into a human body.

SOLUTION: A medicine liquid of a precalculated quantity is pushed in a medicine retainer 30 by lightly pushing a medicine injecting cylinder 26. And, the medicine liquid remaining in a valve 16 and the inlet of a coil-form medicine retainer 30 is pushed in the medicine retainer 30 by quantitative discharge of distilled water for injection or saline by a pushing cylinder 22. Thereby the whole quantity is pushed in the retainer 30. Then, inspection preparation is arranged by attaching an injection needle 20 at the tip of a tube 12 to a subject, and the radiation dose is measured by a radioactivity measuring instrument 32. Then the total radioactive medicine is administered to the subject by feeding distilled water for injection or saline with the pushing cylinder 22. Thus accurate administration is possible with reduced exposure quantity to a handling person.

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Warnings:					
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4	Foreign Reference	WO2006129301A2.pdf	8063321 ca5d9340c1342351071eb4c9a28f631424ab8dac	no	152
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5	Foreign Reference	WO2008037939A2.pdf	930500 5a5a97f3d408d70cb7716dcbdd4e6f91e3cd74d6	no	18
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6	Foreign Reference	WO2008082966A2.pdf	6042906 e68c5721046494ae068a4203d7fd457dbdc5dba2	no	158
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8	Foreign Reference	EP0310148A2.pdf	940420 d65761328c609b56b84279ae9a8fbcc9784b741a	no	20
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12	Foreign Reference	JP2006325826Abstract.pdf	205713 f3bac4c407c20dc79a9f509eed83cf2af3d8ccc2	no	1
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	3737
Examiner Name	
Attorney Docket Number	56782.1.7

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	3774036		1973-11-20	Gerhart	
	2	3997784		1976-12-14	Picunko, et al.	
	3	4286169		1981-08-25	Rossem	
	4	4625118		1986-11-25	Kriwetz et al.	
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	Attorney Docket Number	56782.1.7

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	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3737
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	1	2006007750	WO	A1	2006-01-26	UNIVERSITÄT ZÜRICH		☐

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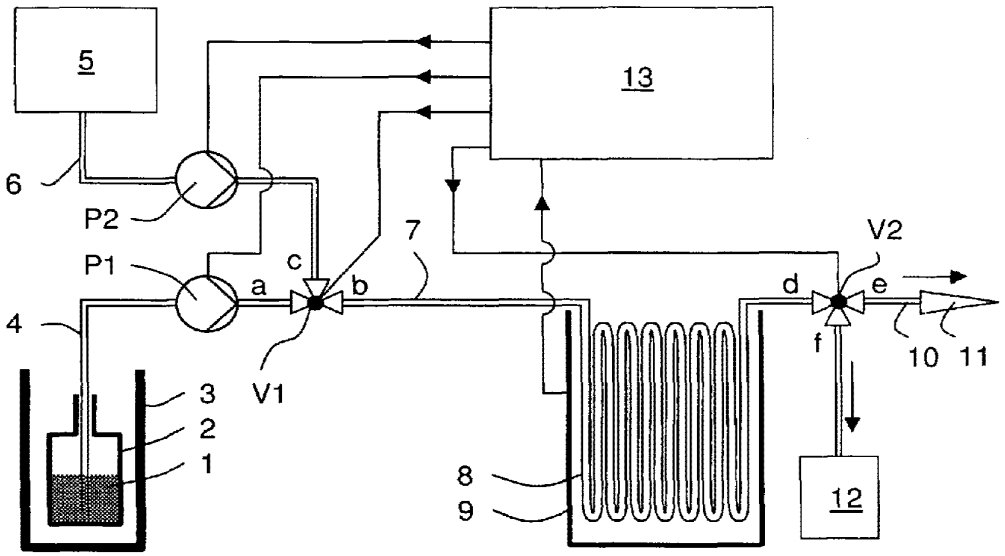
(54) Title: METHOD AND DEVICE FOR ACCURATE DISPENSING OF RADIOACTIVITY



(57) Abstract: A device and a method for accurate and remote dispensing of a radioactive liquid are disclosed. A source of a radioactive liquid (1) and a source of a flushing liquid (5) are selectively connected to a fluid delivery path (7, 8, 10) by way of valve means (V1). An activity metering unit (9) is operable to determine a level of radioactivity in a metering section (8) of the fluid delivery path downstream from the valve means (V1). The device is operated by transporting a first amount of radioactive liquid (1) to the metering section (8), using the activity metering unit (9) to measure a reference level of radioactivity, calculating a second amount of the radioactive liquid still to be delivered such that the first and second amounts of radioactive liquid together have some predetermined level of radioactivity, and delivering the first and second amounts of radioactive liquid to the destination (11).

WO 2006/007750 A1

Method and device for accurate dispensing of radioactivity

Background of the invention

The present invention relates to a device and a method for dispensing a radioactive liquid to a destination. In particular, the invention relates to the problem of accurately dispensing a well-determined dose of radioactivity, e.g., for injection to a living body.

In a number of medical applications, it is necessary to deliver a radiopharmaceutical containing a radionuclide to a patient. Due to the ionizing radiation emitted by the radionuclide, such pharmaceuticals pose a danger to both the patient and the personnel administering the radiopharmaceutical if not handled properly.

Examples for diagnostic uses of radiopharmaceuticals include positron emission tomography (PET) and single-photon emission computerized tomography (SPECT). In these methods, a patient is injected a dose of a radiopharmaceutical which can be absorbed by certain cells in the brain or in other organs. The concentration of the accumulated radiopharmaceutical in a specific body part will often depend on factors of diagnostic interest, such as cell metabolism or other physiological or biochemical processes. Thus, such processes can be imaged in a non-invasive fashion by determining the spatio-temporal distribution of radioactivity within the body part of interest. In PET, this is achieved by monitoring pairs of temporally coincident gamma rays emitted in opposite directions resulting from the annihilation of positrons, which are emitted through beta-plus decays of the (proton-rich) radionuclide. The most common radionuclides (radioisotopes) for use

with PET are ^{15}O, ^{18}F, ^{11}C, ^{13}N and ^{82}Rb. Radiopharmaceuticals of interest for PET include, but are not limited to, substances like [^{15}O]-H_2O, [^{18}F]-fluorodeoxyglucose ([^{18}F]-FDG), [^{18}F]-fluoromisonidazole ([^{18}F]-FMISO), [^{11}C]-labeled amino acids, [^{13}N]-ammonia etc.

The most common therapeutic uses of radiopharmaceuticals are the ^{131}I therapies in thyroid diseases.

In these applications, it is desirable to administer an exactly determined dose of radiopharmaceutical to the body. Often the radiopharmaceutical is delivered in a vial from which it has to be dispensed into individual patient doses. In many centers this is a manual process done by the technical personnel. Since the concentration of the radiopharmaceutical in the vial can be very high, the manual dispensing is associated with considerable radiation burden to the hands. Furthermore the accuracy of the manual dispensing is limited and dependent on the experience of the person in charge.

As an example, U.S. patent No. 4,410,108 discloses a syringe shield equipped with a radiation detector. A liquid radiopharmaceutical is drawn from a vial into the barrel of a syringe placed within the syringe shield, while the level of radioactivity within the barrel is monitored by the radiation detector. In this way, an aliquot of the radiopharmaceutical having exactly the required dose of radioactivity can be drawn into the syringe. Subsequently, the syringe with its shield is manually removed from the vial, and the radiopharmaceutical is injected to the patient. This device is unsatisfactory in requiring manual transfer of the syringe after it has been filled with the radiopharmaceutical, as this may expose the personnel handling the syringe to ionizing radiation. Although the half-life of the radiopharmaceutical is usually rather short and the applied dosages are themselves not harmful, constant and repeated exposure over an extended period of time can be harmful.

A number of techniques have been proposed to reduce exposure by minimizing the time of exposure of personnel, by maintaining distance between personnel and the source of radiation, and by shielding personnel from the source of radiation. As

an example, European patent application EP 0 486 283 discloses a system for delivering $H_2{}^{15}O$. A collection bottle is filled with saline, then a fluid stream comprising $H_2{}^{15}O$ is passed through the collection bottle while the activity in this bottle is monitored by a radiation detector. When a desired level of radiation is reached, the liquid in the bottle is transferred to a motor-driven syringe and then injected to the patient body. U.S. patent application publication No. 2003/0004463 also discloses a system for dispensing a radiopharmaceutical in a remote fashion, without the need of manual intervention. The radiopharmaceutical is drawn from a vial into a syringe surrounded by a radiation detector, and the level of radioactivity in the syringe is determined. Through specially adapted tubing and valves, the radiopharmaceutical is subsequently delivered to a patient without the need of moving the syringe to another location.

While these systems obviate the need of manual handling of a syringe, they tend to be imprecise in situations where small amounts of radioactive liquid, possibly with a very high concentration of activity, need to be handled, due to the presence of dead volumes. By the way of example, the radiopharmaceutical may come in a vial at an activity concentration of 2 GBq/ml (one billion Becquerels per milliliter). If the required activity for injection to the patient is, say, 100 MBq, a volume of just 50 microliters needs to be transferred from the vial to the patient. Such small amounts of liquid are difficult to handle with the systems of the prior art.

U.S. patents No. 4,562,829 and 4,585,009 disclose strontium-rubidium infusion systems equipped with an in-line radiation detector. A radiopharmaceutical exiting a strontium-rubidium generator flows past the radiation detector, which monitors the activity of the radiopharmaceutical in passing. From there, the radiopharmaceutical is either administered to a patient or is sent to waste. In U.S. patent No. 4,409,966, a flow of patient blood is shunted through a radiation detector during injection of the radiopharmaceutical, and the level of radioactivity in the blood is monitored. Also with such systems, it is difficult to administer an exactly determined dose, especially for concentrated radiopharmaceuticals with high specific activities, as the volume of the tubing already may exceed the desired volume to be injected.

Summary of the invention

It is therefore an object of the invention to provide a device which is capable of accurately dispensing a desired level of radioactivity in a liquid, and which may be operated remotely. This object is achieved by a device with the features of claim 1.

Thus, according to the invention, a source of a radioactive liquid and a source of a flushing liquid can be selectively connected to a fluid delivery path by way of valve means. An activity metering unit is operable to determine a level of radioactivity in a metering section of the fluid delivery path downstream from the valve means. In this way, it is possible to provide some amount, even a very small amount, of the radioactive liquid to a section of the fluid delivery path adjacent to the valve means. The flushing liquid can then be used to flush this amount of radioactive liquid to the metering section, where its activity can be determined and further steps to be taken can be decided based on this determination of activity. By use of valve means adapted for remote control (e.g. an electromagnetically or pneumatically operated valve), operation of the inventive device can be performed remotely.

It is a further object of the present invention to provide a method of operation of such a device. This object is achieved by a method with the features of claim 7.

Thus, according to the invention, the device is operated by transporting a first amount of radioactive liquid to the metering section, using the activity metering unit to measure a reference level of radioactivity, calculating a second amount of the radioactive liquid still to be delivered such that the first and second amounts of radioactive liquid together have some predetermined level of radioactivity, and delivering the first and second amounts of radioactive liquid to the destination. In this way, it is possible to deliver an exactly known level of radioactivity to the destination, independent of the activity concentration of the radioactive liquid. Preferably, the first amount of radioactive liquid is between 20% and 80% of the sum of the first and second amounts of radioactive liquid, more preferably between 30% and 70%, most preferably between 40% and 60%. In this way, high precision can be achieved.

In an advantageous embodiment of the inventive device, the device additionally comprises a control unit. The unit receives signals from the activity metering unit and controls operation of the valve means between at least two states. In the first state, the source of radioactive liquid is connected to the fluid delivery path for flow of the radioactive liquid into the fluid delivery path. In the second state, the source of flushing liquid is connected to the fluid delivery path for flow of flushing liquid into the fluid delivery path. If any other actively driven components are present in the device, such as additional valves or pumps, they may also be controlled by the control unit.

Advantageously, second valve means are provided downstream from the metering section for directing flow in the fluid delivery path either to the destination or to a waste reservoir. In this way it is avoided that the destination receives excessive amounts of flushing liquid during operation of the device, and in case of malfunctioning of components of the device, the radioactive liquid can be dumped to the waste reservoir.

Advantageously, a first and/or a second pump are provided for pumping the radioactive liquid or the flushing liquid, respectively, through the first valve means and into the fluid delivery path. Preferably, the first pump and/or the second pump is operable to receive a control signal and to deliver a predetermined volume of liquid based on the control signal. In this way, exactly known amounts (volumes) of the radioactive liquid and/or of the flushing liquid can be dispensed to the fluid delivery path.

The fluid delivery path may comprise a fill-in section extending from the first valve means to the metering section. Advantageously, the metering section is capable of holding a fluid volume which is at least three times, more preferably at least five times the volume of the fill-in section. This enables the metering section to hold at least two, preferably three, fractions of radioactive liquid, each with a volume up to the volume of the fill-in section, plus the flushing liquid required to flush these fractions into the metering section. Thereby, the total activity of two, preferably three,

fractions of radioactive liquid may be determined in a single measurement by the activity metering unit.

Advantageously, the device is adapted for delivering a radiopharmaceutical for injection to a living body (i.e., for delivering the radiopharmaceutical to an injection needle). This encompasses, among other things, the use of compatible materials, which must be resistant to the radiopharmaceutical and the flushing liquid (usually saline solution in this case), and which must be able to withstand sterilization procedures. Such materials are well known.

As used herein, the term "pharmaceutical" refers to any substance to be injected or otherwise delivered into the body (either human or animal) in a medical procedure and includes, but is not limited to, substances used in imaging procedures and therapeutic substances. The term "radiopharmaceutical" refers to any pharmaceutical emitting ionising radiation by radioactive decay.

Further advantageous embodiments of the invention are laid down in the dependent claims. In particular, the inventive method may comprise an additional initialization procedure, in which an offset amount of radioactive liquid is transported to the metering section, an offset level of radioactivity is determined, and the predetermined level of radioactivity for the main procedure is determined from this offset level and a desired level of radioactivity to be dispensed.

Brief description of the drawings

The invention will be described in more detail in connection with an exemplary embodiment illustrated in the drawings, in which

Fig. 1 shows a schematic and simplified illustration of a device according to the present invention;

Fig. 2 shows a schematic and simplified illustration of a dose calibrator;

Fig. 3A and 3B show simplified illustrations of a pinch valve;

Fig. 4 illustrates a first state of operation of the device of Fig. 1;

Fig. 5 illustrates a second state of operation of the device of Fig. 1;

Fig. 6 illustrates a third state of operation of the device of Fig. 1;

Fig. 7 illustrates a fourth state of operation of the device of Fig. 1;

Fig. 8 illustrates a fifth state of operation of the device of Fig. 1;

Fig. 9 shows a flow diagram of a process according to the present invention; and

Fig. 10 illustrates the levels of activities measured in various stages of the process of Fig. 9.

Detailed description of the invention

Fig. 1 shows, in a highly schematic manner, a device for dispensing a radioactive liquid according to a preferred embodiment of the present invention. The device is designed for dispensing a radiopharmaceutical for injection to a patient.

The radiopharmaceutical 1 is provided in a vial 2. In order to protect the surroundings from radioactivity originating from the vial 2, the vial 2 is placed inside a shield 3. Suitable vials and shields for various kinds of radiopharmaceuticals are well known in the art and are available commercially.

A section 4 of tubing, comprising a needle at its end for puncturing a septum closing off vial 2, extends from the inside of vial 2 through a first peristaltic precision pump P1 and to a first three-way pinch valve V1. At its first port "a", the valve V1 is connected to the section 4 of tubing from the vial 2; at its second port "b", it is connected to a section of tubing 7 extending from the valve V1 to an activity metering unit 9 (in the following shortly called a "dose calibrator"). The third port "c" is connected to a section 6 of tubing leading from a saline reservoir 5 through a second peristaltic precision pump P2 to the valve V1. The valve V1 is operable to connect port "a" with port "b" or to connect port "c" with port "b".

Fig. 3A and 3B illustrate, in a highly schematic manner, the mode of operation of the pinch valve V1 as advantageously used in the present embodiment. A sliding element 31 can be moved up or down, pressing either on an upper or on a lower section of flexible tubing which is passed through the pinch valve. Thereby, either port "c" or port "a" is closed off from port "b", and the other port is connected to port "b". The sliding element 31 may, e.g., be operated electromechanically or

pneumatically. A similar pinch valve is used as valve V2. Such pinch valves are advantageous because no moving parts get into contact with the liquid within the tubing. Thus the valve cannot get contaminated by radioactive liquid possibly present in the tubing.

The pumps P1 and P2 are preferably peristaltic precision pumps. In a peristaltic pump, a section of flexible tubing is passed through the pump unit. Fluid is forced along the tubing by waves of contraction produced mechanically on the flexible tubing. Peristaltic pumps offer the advantage that the liquid is always contained in the tubing, and no moving parts get into contact with the liquid to be delivered. Thus the pump itself cannot be contaminated by radioactive liquid present in the tubing. By the use of peristaltic pumps and pinch valves, the connections from the saline reservoir 5 to the metering section 7 and from the vial 2 to the metering section 7 may consist of a single piece of flexible tubing each, which can be easily replaced in regular intervals to avoid cross-contamination, without the need to replace the much more expensive pump and valve assemblies themselves.

The section 7 of tubing may be called a "fill-in section". This fill-in section 7 is connected to a section 8 of tubing placed inside the dose calibrator 9, section 8 being called a "metering section". The metering section 8 is relatively long, providing a volume of at least five times the volume of the fill-in section, by having a meander-like shape or, preferably, a coil shape as illustrated for a metering section 8' in Fig. 2. A coil shape is preferred in practice because it minimizes pressure losses during fluid flow. The meander-like shape has been chosen in Figs. 1 and 3-7 for illustrative purposes.

The tubing exits the dose calibrator 9 and connects to the first port "d" of a second three-way valve V2. The second port "e" of this valve is connected to a section 10 of tubing leading to an injection needle 11, only crudely symbolized by a triangle in Fig. 1. The third port "f" of valve V2 leads to a waste reservoir 12. The waste reservoir 12 is preferably shielded, as radioactivity may enter in operation.

The dose calibrator 9 is connected to a controller 13 and provides signals to the

controller 13 which are indicative of the level of activity within the dose calibrator 9. The outputs of the controller 13 are connected to the pumps P1 and P2 as well as to the valves V1 and V2 for control of these.

A method of operation of the device is illustrated in Figs. 4 to 8 and symbolized in a flow diagram in Fig. 9. Operation can generally be divided into five phases: in an initialisation phase 910, the device is brought into a well-defined initial state. In a calibration phase 920, steps are performed for calibrating the radioactivity in vial 2. In a delivery phase 930, the radiopharmaceutical is delivered to the destination. In a step 940, it is decided whether another injection shall be performed. If yes, operation will continue again with the calibration phase 920; if not, a shutdown phase 950 will follow.

Before starting the operation, the operator will have to determine two quantities: the desired activity Ar to be injected to the patient, and the estimated concentration of activity in the vial (activity per unit of volume, e.g., expressed in MBq/ml), Cv. These data are provided to the controller 13. Operation then starts with the initialisation period 910.

The initialisation period 910 comprises the following steps:

Step 911 (Initial filling of radiopharmaceutical to point C): In a first step, the complete tubing is filled with saline, thereby excluding air from the tubing system. For this, valve V1 is switched into a state connecting ports "c" and "b", while valve V2 connects "d" and "e". Pump P2 flushes saline up to point B (cf. Fig. 4). Then the tubing section 4 is inserted into a vial containing saline. Valve V1 is brought into a state connecting ports "a" and "b", while valve V2 still connects "d" and "e". Pump P1 now flushes saline until the tubing is completely filled with saline from point A (cf. Fig. 4) to the destination beyond valve V2, and air is thus completely purged from the system. The tubing section 4 is then inserted into the vial 2 containing the radiopharmaceutical. Valve V1 is brought into a state connecting ports "a" and "b", while valve V2 connects ports "d" and "f". Pump P1 is operated to pump radiopharmaceutical 1 from inlet point A and past point B at valve V1 to some point C in the fill-in section 7. The volume of radiopharmaceutical between points B and C in

the fill-in section 7 does not need to be known exactly; it suffices to ensure that the section of tubing from A to B is filled completely with radiopharmaceutical, and that the activity in the volume between B and C is not larger than the desired end activity Ar. The situation at the end of step 911 is illustrated in Fig. 4, where the volume of radiopharmaceutical between points B and C is designated by reference number 21.

Step 912 (Flushing of offset volume to dose calibrator): Valve V1 is now switched to a state in which it connects ports "c" and "b". Pump P2 is operated to pump saline from the saline reservoir 5 towards valve V1. The volume to be pumped is slightly larger than the volume in the fill-in section 7 of the tubing, i.e. slightly larger than the volume between points B and D. This volume need not be known exactly. Thereby, the "offset volume" 21 is moved into the metering section 8. The situation at the end of this step is illustrated in Fig. 5.

Step 913 (Initial determination of activity): The activity of volume 21 in the metering section 8 is measured by the dose calibrator 9 (measurement M1). This activity will be called the "offset activity" A1. The controller 13 now calculates the missing activity Am required to reach a total activity of Ar: Am = Ar – A1. This is illustrated in Fig. 10 in the leftmost column. From this and the estimated concentration of activity in the vial, Cv, the estimated missing volume Va1 still to be delivered is calculated: Va1 = Am / Cv. It is important to note that this calculation is still based on the estimate of the concentration of activity in the vial, and the result cannot be expected to be highly accurate. It is further important to note that no knowledge about the offset volume 21 is required in this calculation.

This step concludes initialisation 910. In the following calibration phase 920, the following steps are performed:

Step 921 (Filling of radiopharmaceutical to point C'): Valve V1 is switched to a state in which it connects ports "a" and "b". Pump P1 is operated to pump a volume Vc' through valve V1, filling the fill-in section to point C'. This situation is illustrated in Fig. 6, where this volume is designated by reference number 22. Volume

Vc' is chosen to be approximately half of the estimated missing volume Va1: Vc' ≈ Va1 / 2. It is important to note that volume Vc' is known exactly in system internal units. The exact nature of these units depends on the type of pump used, e.g., the units could be pump revolutions, pump cycles etc. If a volume flow meter is placed in-line with the pump, the units provided by the flow meter can be used as system internal units. Depending on the type of pump and the type of tubing, the resolution of volume in this step can be very small, and even small volumes can be delivered accurately.

Step 922 (Flushing of volume Vc' to dose calibrator): Valve V1 is switched to connect ports "c" and "b". Pump P2 is operated to pump slightly more than the volume between points B and D of saline through valve V1. Thereby, volume 22 (= Vc') of radiopharmaceutical is moved into the metering section 8. The situation at the end of this step is illustrated in Fig. 7.

Step 923 (Calibration of activity): The activity in the metering section 8 is measured by the dose calibrator 9 (measurement M2). This activity level will be called A2. It corresponds to the sum of the offset activity A1 and the activity of the volume Vc', which will be called the "reference activity" Ac'. This is illustrated in the second column of Fig. 10. Now the activity concentration in the vial in system internal units, Cs, is calculated: Cs = Ac' / Vc' = (A2 – A1) / Vc'. The system is now calibrated in system internal units.

Step 924 (Determination of volume Vc''): The activity Ac'' still required to reach a total activity of Ar is determined: Ac'' = Ar – A2. From this, the volume Vc'' still to be delivered is calculated in system internal units: Vc'' = Ac'' / Cs = (Ar – A2) / Cs = (Ar – A2) / (A2 – A1) * Vc'.

This completes the calibration phase 920. In the following delivery phase 930, the following steps are performed:

Step 931 (Filling of radiopharmaceutical to point C''): Valve V1 is switched to a state in which it connects ports "a" and "b". Pump P1 is operated to pump the vol-

ume Vc'' through valve V1, filling the fill-in section to point C''. This situation is illustrated in Fig. 8, where this volume is designated by reference number 23.

Step 932 (Flushing of volume Vc'' to dose calibrator): Valve V1 is switched to connect ports "c" and "b". Pump P2 is operated to pump slightly more than the volume between points B and D of saline through valve V1. Thereby, volume 23 (= Vc'') of radiopharmaceutical is moved into the metering section 8. Optionally, the total activity in the metering section is now measured (optional measurement M3, see right column of Fig. 10). It should correspond exactly to the total desired activity Ar, provided that the volume of the metering section is large enough to hold all three volumes 21, 22 and 23 within this section. The latter condition is can always be fulfilled if the volume of the metering section 8 is at least five times the volume of the fill-in section 7. If a significant discrepancy is detected, the system is stopped.

Step 933 (Delivery to injection needle): Valve V2 is switched to connect ports "d" and "e". Pump P2 is operated to pump at least the volume of the metering section 8, plus the volume of the tubing from the metering section to the injection needle and of the injection needle itself, of saline through valve V1. Thereby, all liquid in the metering section 8 is flushed to the patient, and exactly the required dose of radioactivity is delivered to the patient.

This completes the delivery phase 930. If another injection of the same radiopharmaceutical (to the same or a different patient) is required, operation continues by repeating the calibration and delivery phases 920 and 930. Otherwise, operation stops by a suitable shutdown procedure, which may involve additional cycles of flushing with saline.

When repeating calibration phase 930, no additional initialisation as in phase 910 is necessary, since the metering section 8 has been flushed with saline, and the radiopharmaceutical extends exactly to point B. No activity is present in the metering section 8. Therefore, in the above calculations, A1 can be set to zero in this case, and Am is set to Ar. No further changes are necessary. The three-phase

procedure with phases 910, 920 and 930 now simplifies to a two-phase procedure with phases 920 and 930 only.

It will be appreciated that the device of the present invention and the associated method of operation provide a number of inherent safety features. Specifically, there is a high degree of redundancy in the operation of the device, such that even in case of failure of one component, such as a pump or a valve, it is impossible that more than the desired dose will be delivered to the patient. Specifically, by its design the system will only allow the dose present within the metering section 8 to be delivered to the patient. This is because during the actual delivery of the radiopharmaceutical there is no connection between the vial 2 and the fluid delivery line. The discrete nature of the sequential measurements of activity within the metering section 8 is another feature which increases safety: In step 932, the activity in the metering section 8 is actually known beforehand, and measurement M3 just serves to confirm that the right amount of activity is present in the metering section 8. If significant discrepancies are detected between the expected result and the actual measurement, operation will be stopped immediately, and an alarm will be given.

It will also be appreciated that, in normal operation, no radiopharmaceutical will enter the waste reservoir 12. Thus, generation of radioactive waste is minimized.

A device according to the present invention in the embodiment of Fig. 1 has been set up and tested in practice. The device was assembled from standard components available commercially. For the tubing sections 4 and 6, flexible tubing made from silicone with an inner diameter of 1.52 mm was used. The pumps P1 and P2 were peristaltic precision pumps (P1: Ismatec™ ISM 596B, P2: Arcomed™ Volumed™ mVp 5000). The valves V1 and V2 were electrically operated pinch valves available from Bio-Chem Valve Inc. The metering section 8' of tubing had a coil shape with nine windings and a diameter of 3.5 cm, made from fluoroethylene-propylene. A Veenstra VDC 405 dose calibrator was used as activity metering unit/dose calibrator 9. The complete assembly was shielded by a 5 cm lead shield. As a controller 13, a standard personal computer (Compaq Armada E500)

equipped with a standard interface card was used. The control algorithm was implemented in LabVIEW™, available from National Instruments™.

This embodiment is especially suitable for the use with radiopharmaceuticals typically used in PET and SPECT applications. The device has been used to deliver radiopharmaceuticals with activity concentrations as high as 1000 MBq/ml to patients, with an absolute precision of as good as 100 microliters and a relative precision of better than 2 % of the total activity delivered to the patient.

From the above description, it is clear that numerous variations of the described device and method are possible, and the invention is in no way limited to the above examples.

While the method has been described in a way that the volume of the metering section 8 of tubing is large enough to hold at the same time all volumes of radiopharmaceutical to be injected together, the method can readily be adapted for use with a dose calibrator which measures only one of these volumes at a time. In this case, the activities A1, Ac' and, optionally, Ac'' are measured directly and sequentially and need not be calculated. Both variants of the method have in common that the activity of a precisely known volume (in some arbitrary units) is measured, enabling determination of the activity concentration of the radiopharmaceutical.

The method can be extended to take into account the decrease of activity during the dispensing procedure, in a straightforward manner by calculating the decay during the (predetermined) time needed for the dispensing procedure.

The inventive device and method are not only useful for delivering a radiopharmaceutical to a human or animal body, but also in other applications, also of a non-medical nature, in which a precisely known amount of activity is to be delivered to some destination. Accordingly, many variations of the types of tubing, valves, pumps etc. are possible. Specifically, other pump types than peristaltic pumps may be used. In fact, while the use of pumps is preferred, pumps may be omitted if the vial 2, the saline reservoir 5 or both are placed "top-down" in a position higher than

valves V1, V2 and the destination 16. Fluid flow is then effected by gravity alone. Instead of pumps, flow meters should then be provided, yielding volume information to the controller 13.

Different types of valves than the above-described two-way pinch valves may be used. Specifically, it may be advantageous to provide, as valve V1, a valve which can be switched to a third state such that liquid can flow between ports "a" and "c". In this way, the sections of tubing between points A and B may be flushed with saline from reservoir 5, without the need of inserting a vial with saline instead of the vial with the radiopharmaceutical during initialisation.

Any suitable activity detector may be used as a dose calibrator 9. Such detectors include standard Geiger-Müller counters, scintillating counters etc., which should be calibrated to yield a sufficiently precise measure of the actual activity in the metering section 8.

Additional safety measures may be taken, such as providing bubble detectors in the fluid delivery path which stop operation immediately if bubbles are detected. Bubble detectors are well known in the art.

List of reference signs

P1	first pump
P2	second pump
V1	first valve
V2	second valve
a, b, c	connections of first valve
d, e, f	connection of second valve
A	inlet of radiopharmaceutial
B, C, C', C''	reference points
D	start of metering section
E	end of metering section

M1, M2, M3 measurements

A1, A2, Ar, Am, Ac', Ac" activities

1	radiopharmaceutical
2	vial
3	shield
4	tubing
5	saline container
6	tubing
7	tubing
8, 8'	metering section
9	dose calibrator
10	tubing
11	injection needle
12	waste
13	controller
21, 22, 23	volumes of radiopharmaceutical
31	sliding element

Claims

1. Device for dispensing a radioactive liquid (1) to a destination (11), comprising

   - first valve means (V1);

   - a fluid delivery path (7, 8, 10) for fluid flow from said first valve means (V1) to said destination (11); and

   - an activity metering unit (9) operable to determine a level of radioactivity within a metering section (8) of said fluid delivery path (7, 8, 10); wherein said first valve means (V1) are adapted for selectively connecting a source (2) of said radioactive liquid (1) and a source of a flushing liquid (5) to said fluid delivery path (7, 8, 10) upstream of said metering section (8).

2. Device according to claim 1, characterized in that said first valve means (V1) are adapted for remote operation and that said device further comprises a control unit (13) receiving signals from said activity metering unit (9) and controlling operation of said first valve means (V1) between at least the following states:

   - a state in which said source (2) of radioactive liquid (1) is connected to said fluid delivery path (7, 8, 10); and

   - a state in which said source of flushing liquid (5) is connected to said fluid delivery path (7, 8, 10).

3. Device according to claim 1 or 2, characterized in that said device further comprises second valve means (V2) for selectively connecting said fluid delivery path (7, 8, 10) downstream from said metering section (8) to said destination (11) or to a waste reservoir (12).

4. Device according to one of claims 1 to 3, characterized in that said device further comprises a first pump (P1) for pumping said radioactive liquid (1) from its source (2) toward said first valve means (V1) and/or a second pump (P2) for pumping said flushing liquid from its source (5) toward said first valve means (V1).

5. Device according to one of claims 1 to 4, characterized in that said fluid delivery path comprises a fill-in section (7) extending from said first valve means (V1) to said metering section (8), and that said metering section (8) is capable of holding a fluid volume (D-E) which is at least three times the volume (B-D) of said fill-in section (7).

6. Device according to one of claims 1 to 5, characterized in that said device is adapted for delivering a radiopharmaceutical to an injection needle for injection of liquid into a human or animal body.

7. Method of operation of a device according to claim 1, comprising the steps of

- transporting a first amount (22) of said radioactive liquid to said metering section (8) of said fluid delivery path (7, 8, 10);
- with said activity metering unit (9), measuring a reference level of radioactivity (A2) present in said metering section (8);
- - from said reference level of radioactivity (A2), calculating a second amount (23) of said radioactive liquid still to be delivered such that said first and second amounts of radioactive liquid together have a predetermined level of radioactivity (Am); and
- delivering at least said first and second amounts of radioactive liquid (1) to said destination (11).

8 Method according to claim 7, characterized in that said first amount of ra-

dioactive liquid is between 20% and 80% of the sum of the first and second amounts of radioactive liquids.

9. Method according to claim 7 or 8, characterized in that said step of transporting said first amount of said radioactive liquid comprises:

- operating said first valve means to connect said source (2) of radioactive liquid (1) to said fluid delivery path (7, 8, 10);
- allowing said first amount of radioactive liquid (1) to flow from said first valve means (1) into said fluid delivery path (7, 8, 10);
- operating said first valve means to connect said source of flushing liquid (5) to said fluid delivery path (7, 8, 10); and
- allowing flushing liquid (5) to flow into said fluid delivery path (7, 8, 10), whereby said first amount of radioactive liquid is moved into said metering section (8) of said fluid delivery path (7, 8, 10).

10. Method according to one of claims 7 to 9, characterized in that said step of delivering said first and second amounts of said radioactive liquid (1) comprises:

- operating said first valve means to connect said source (2) of radioactive liquid (1) to said fluid delivery path (7, 8, 10);
- allowing said second amount of radioactive liquid (1) to flow from said first valve means (1) into said fluid delivery path (7, 8, 10);
- operating said first valve means to connect said source of flushing liquid (5) to said fluid delivery path (7, 8, 10); and
- allowing flushing liquid (5) to flow into said fluid delivery path (7, 8, 10), whereby said first and second amounts of radioactive liquid are moved to said destination (11).

11. Method according to one of claims 7 to 10, additionally comprising the fol-

lowing steps:

- before transporting said first amount (22) of radioactive liquid (1) to said metering section (8), transporting an offset amount (21) of said radioactive liquid (1) to said metering section (8);
- with said activity metering unit (9), measuring an offset level of radioactivity (A1) of said offset amount (21) of radioactive liquid;
- from said offset level of radioactivity (A1) and a desired level of radioactivity to be dispensed (Ar), calculating said predetermined level of radioactivity (Am); and
- delivering said offset amount (21) of radioactive liquid to said destination.

12. Method according to one of claims 7 to 11, wherein said radioactive liquid is a liquid comprising a radiopharmaceutical and wherein said destination is an injection needle for injection of liquid into a human or animal body.

13. Method of operation of a device to deliver a radioactive liquid to a destination (11), comprising:

- determining a predetermined level of radioactivity (Am) to be delivered to said destination (11);
- transporting a first amount (22) of said radioactive liquid to a metering section (8) of a fluid delivery path (7, 8, 10) for fluid flow to said destination (11), said metering section (8) having a metering unit (9) in operative connection therewith and being operable to determine a level of radioactivity within the metering section (8), the first amount (22) of said radioactive liquid having a reference level of radioactivity (A2) less than the predetermined level of radioactivity (Am);
- with said activity metering unit (9), measuring the reference level of radioactivity (A2) present in said metering section (8);
- from said reference level of radioactivity (A2), calculating a second

amount (23) of said radioactive liquid still to be delivered such that first and second amounts of radioactive liquid together have the predetermined level of radioactivity (Am); and

- delivering at least said first and second amounts of radioactive liquid (1) collectively from said fluid delivery path (7, 8, 10) to said destination (11).

14. System for dispensing a radioactive liquid (1) to a destination (11), comprising:

- a first valve (V1) adapted for remote operation;

- a fluid delivery path (7, 8, 10) for fluid flow from said first valve (V1) to said destination (11);

- an activity metering unit (9) operable to determine a level of radioactivity within a metering section (8) of said fluid delivery path (7, 8, 10); wherein said first valve (V1) is adapted for selectively being placed in one of at least two states: a first state in which a source (2) of said radioactive liquid (1) is connected to said fluid delivery path (7, 8, 10) upstream of said metering section (8) and a second state in which a source of a flushing liquid (5) is connected to said fluid delivery path (7, 8, 10) upstream of said metering section (8); and

- a control unit (13) adapted to receive signals from said activity metering unit (9) and control operation of said first valve (V1) between the first state and the second state; said control unit being adapted to:

i. place said first valve (V1) in the first state to transport a first amount (22) of said radioactive liquid through said first valve (V1), the first amount (22) of said radioactive liquid having a level of radioactivity less than a predetermined level of radioactivity (Am) input into said control unit (13);

ii. place said first valve (V1) in the second state to transport an amount of flushing liquid (5) through said first valve (V1) to transport said first amount of said radioactive liquid to said metering section (8) of said fluid delivery

path (7, 8, 10);

iii. receive a signal from said activity metering unit (9) of a measured reference level of radioactivity (A2) present in said metering section;

iv. calculate from said reference level of radioactivity (A2) a second amount (23) of said radioactive liquid still to be delivered such that said first and second amounts of radioactive liquid together have a predetermined level of radioactivity (Am) input into said control unit (13);

v. place said first valve (V1) in said first state and transport through said first valve (V1) said second amount (23) of said radioactive liquid;

vi. place said first valve (V1) in said second state to transport an amount of flushing liquid (5) through valve (V1) to transport said second amount (23) of said radioactive liquid to said metering section (8) of said fluid delivery path (7, 8, 10) while maintaining said first amount (22) of said radioactive liquid in said metering section (8); and

vii. place said first valve (V1) in said second state and transport through said first valve (V1) sufficient flushing liquid to deliver at least said first and second amounts of radioactive liquid (1) through said fluid delivery path (7, 8, 10) to said destination (11).

15. System for dispensing a radioactive liquid (1) to a destination (11), comprising:

- a source of a radioactive liquid (1);
- a source of a flushing liquid (5);
- a fluid delivery path (7, 8, 10) for fluid flow of said radioactive liquid and said flushing fluid to said destination (11), the fluid delivery path including a metering section (8);
- an activity metering unit (9) operable to determine a level of radioactivity within said metering section (8) of said fluid delivery path (7, 8, 10); and
- a control unit (13) adapted to receive signals from said activity meter-

ing unit (9) and control flow of said radioactive liquid and said flushing fluid through said fluid delivery path (7, 8, 10); said control unit being further adapted to:

i. transport a first amount (22) of said radioactive liquid having a level of radioactivity less than a predetermined level of radioactivity (Am) to said metering section (8) of said fluid delivery path (7, 8, 10);

ii. receive a signal from said activity metering unit (9) of a measured reference level of radioactivity (A2) present in said metering section;

iii. calculate from said reference level of radioactivity (A2) a second amount (23) of said radioactive liquid still to be delivered such that first and second amounts of radioactive liquid together have a predetermined level of radioactivity (Am) input into said control unit (13);

iv. transport said second amount (23) of said radioactive liquid to said metering section (8) of said fluid delivery path (7, 8, 10) while maintaining said first amount (22) of said radioactive liquid in said metering section (8); and

v. transport sufficient flushing fluid through said fluid delivery path (7, 8, 10) to deliver at least said first and second amounts of radioactive liquid (1) through said fluid delivery path (7, 8, 10) to said destination (11).

16. Method of delivering a radioactive liquid to a destination (11), comprising:

- determining a level of radioactivity (Am) to be delivered to said destination (11);

- transporting a first amount (22) of said radioactive liquid having a level of radioactivity less than the determined level of radioactivity (Am) to a metering section (8) of a fluid delivery path (7, 8, 10), said metering section (8) having an activity metering unit (9) in operative connection therewith to measure radioactivity in said metering section (8);

- measuring a reference level of radioactivity (A2) present in said metering section (8);

- calculating from said reference level of radioactivity (A2) a second amount (23) of said radioactive liquid still to be delivered such that first and second amounts of radioactive liquid together have the predetermined level of radioactivity (Am);

- transporting said second amount (23) of said radioactive liquid to said metering section (8) of said fluid delivery path (7, 8, 10) while maintaining said first amount (22) of said radioactive liquid in said metering section (8); and

- delivering said first amount and said second amount of radioactive liquid (1) through said fluid delivery path (7, 8, 10) to said destination (11).

17. Method of delivering a radioactive liquid to a destination (11), comprising:

- determining a level of radioactivity (Am) to be delivered to said destination (11);

- estimating a concentration of activity (Cv) in a source of radioactive liquid (1);

- transporting from said source of radioactive liquid (1) a first amount (21) of said radioactive liquid having a level of radioactivity, based upon the estimated concentration of activity (Cv), less than the determined level of radioactivity (Am) to a metering section (8) of a fluid delivery path (7, 8, 10), said metering section (8) having an activity metering unit (9) in operative connection therewith to measure radioactivity in said metering section (8);

- measuring a level of radioactivity (A1) present in said metering section (8);

- based upon the estimated concentration of activity (Cv), transporting a second amount (22) of said radioactive liquid having a reference level of activity (Ac') such that the total activity (A2) of said first amount (21) and said second amount (22) is less than the determined level of radioactivity (Am) to said metering section (8);

- measuring a level of radioactivity (A2) present in said metering section (8);

- based upon the measured level of radioactivity (A2), calculating the concentration of radioactivity (Cs) in said source of radioactive liquid (5);

- based upon the calculated concentration of activity (Cs), transporting a third amount (23) of said radioactive liquid having a level of activity (Ac'') such that the total activity of said first amount (21), said second amount (22) and said third amount (23) is the determined level of radioactivity (Am) to said metering section (8); and

- delivering said first amount, said second amount and said third amount of said radioactive liquid (1) through said fluid delivery path (7, 8, 10) to said destination (11).

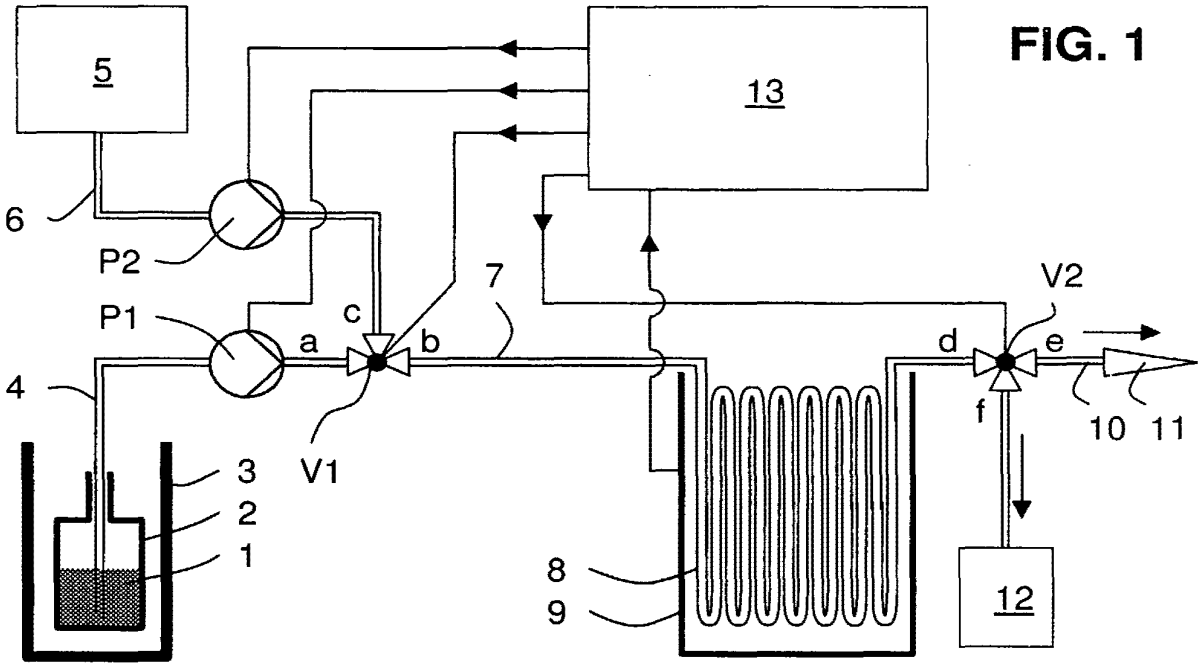


FIG. 1

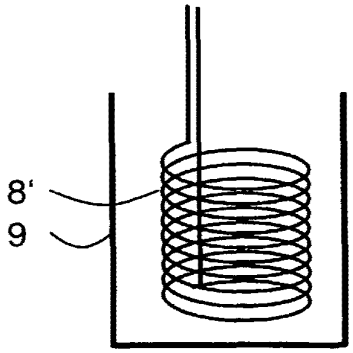


FIG. 2

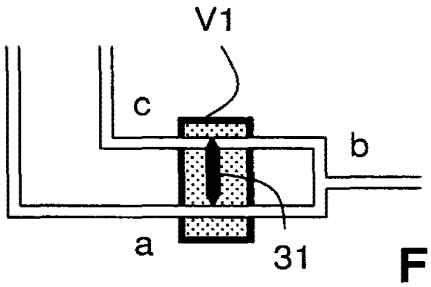


FIG. 3A

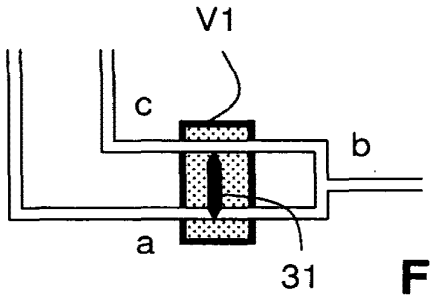


FIG. 3B

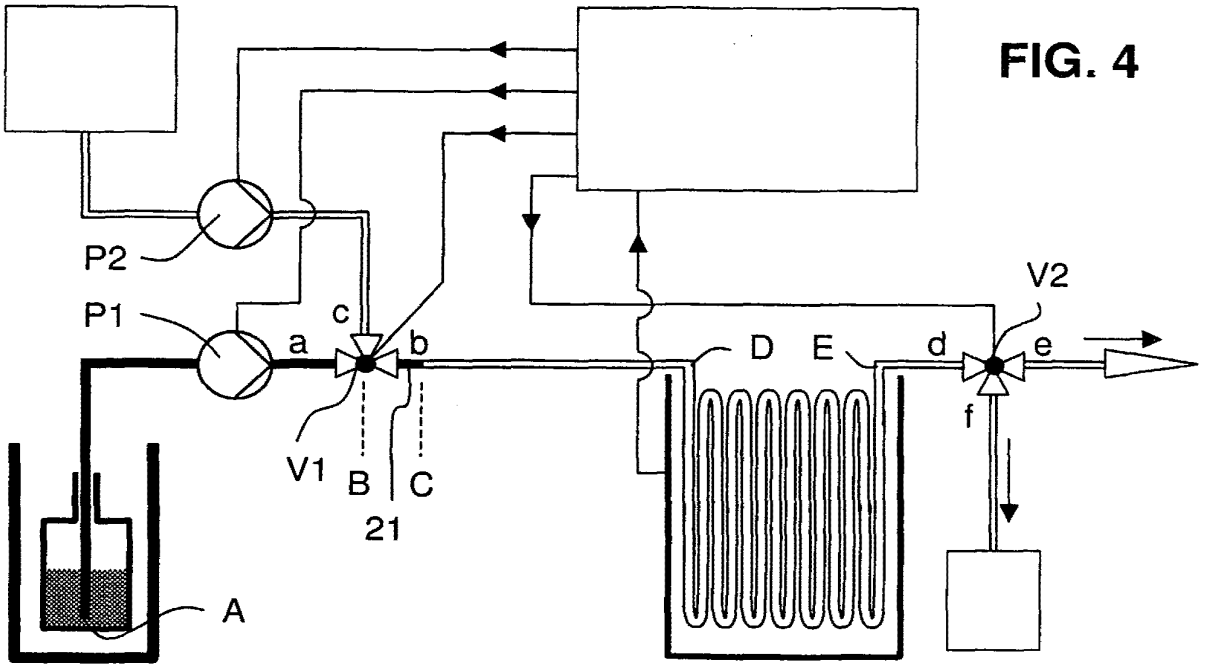


FIG. 4

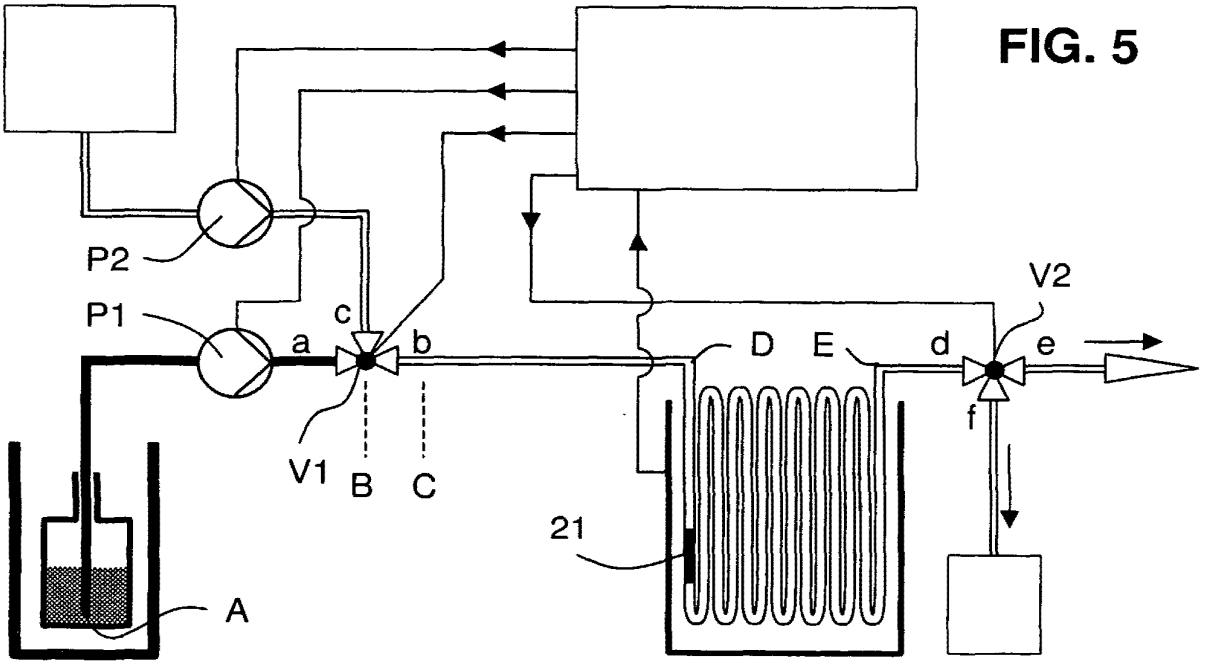


FIG. 5

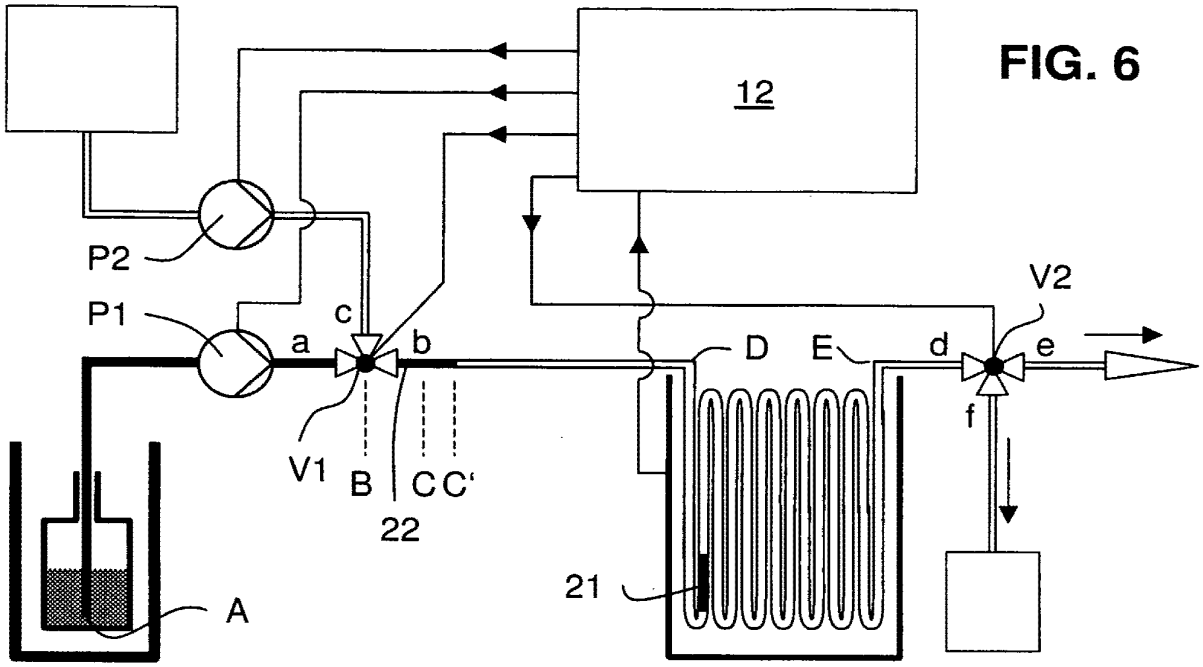
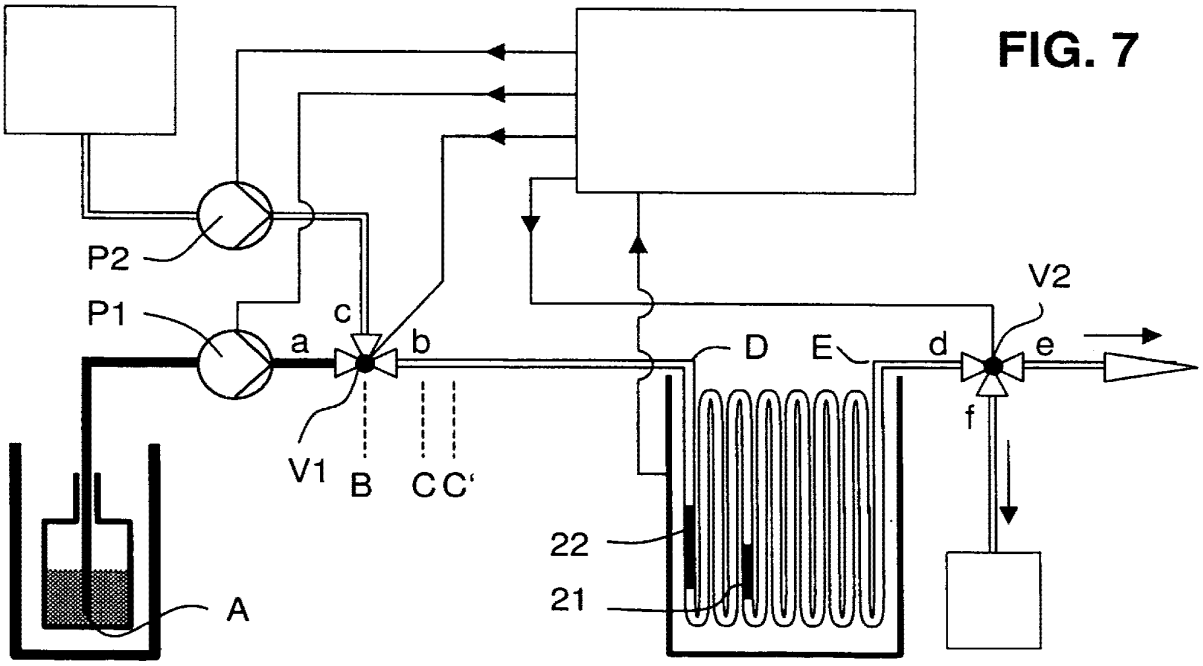

12
P2
P1
a
c
b
V1
B
C
C'
22
A
D
E
d
e
V2
f
21

FIG. 6


P2
P1
a
c
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V1
B
C
C'
A
D
E
d
e
V2
f
22
21

FIG. 7

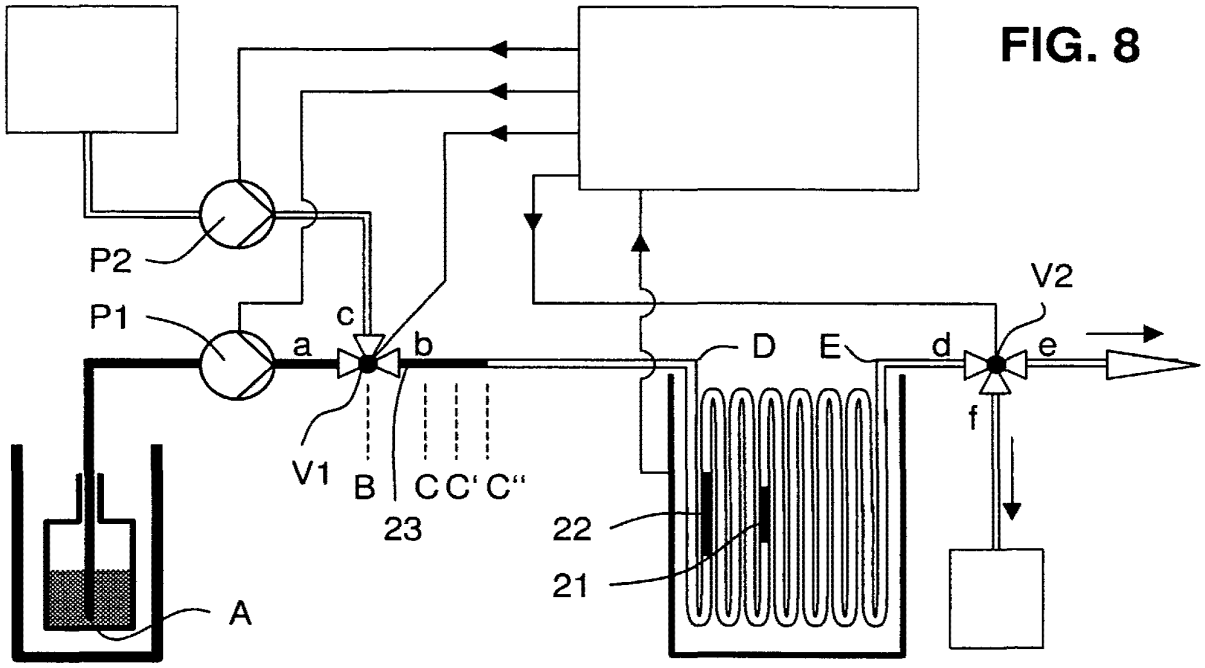

FIG. 8

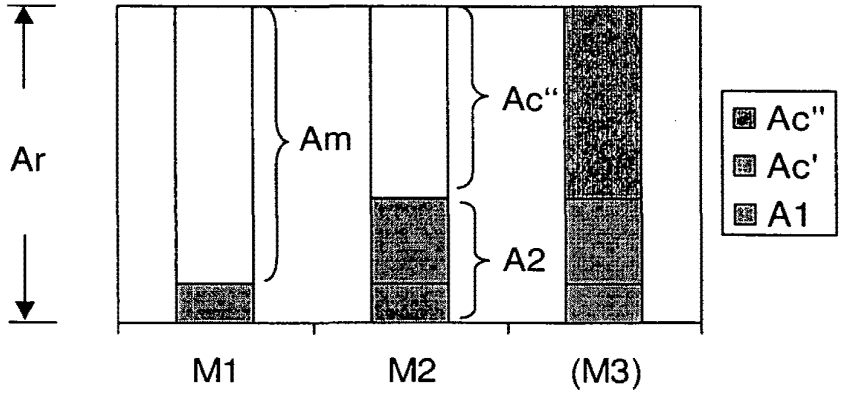

FIG. 10

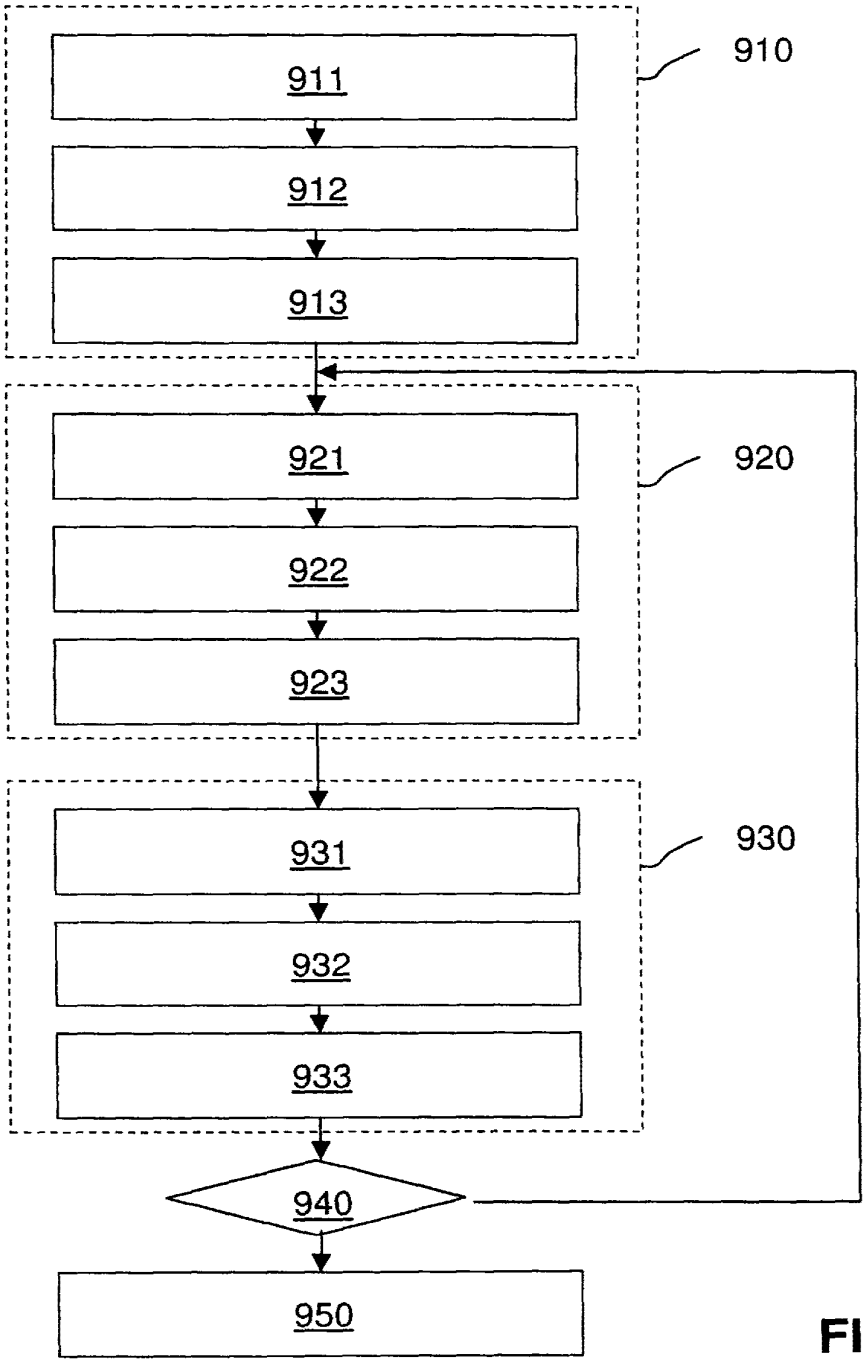

FIG. 9

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CH2005/000403

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M5/14 A61M5/00 A61M5/172

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PATENT ABSTRACTS OF JAPAN vol. 2003, no. 02, 5 February 2003 (2003-02-05) -& JP 2002 306609 A (SUMITOMO HEAVY IND LTD), 22 October 2002 (2002-10-22) the whole document	1-6,14, 15
X	PATENT ABSTRACTS OF JAPAN vol. 2000, no. 15, 6 April 2001 (2001-04-06) -& JP 2000 350783 A (SUMITOMO HEAVY IND LTD), 19 December 2000 (2000-12-19) the whole document	1-6,14, 15
A	EP 0 486 283 A (UEMURA, KAZUO; THE JAPAN STEEL WORKS, LTD) 20 May 1992 (1992-05-20) the whole document	1-6,14, 15

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"P" document published prior to the international filing date but later than the priority date claimed

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 September 2005	15/09/2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Schultz, O

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CH2005/000403

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 562 829 A (BERGNER ET AL) 7 January 1986 (1986-01-07) the whole document	1-6,14, 15
A	US 2003/004463 A1 (REILLY DAVID M ET AL) 2 January 2003 (2003-01-02) the whole document	1-6,14, 15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CH2005/000403

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 7-13,16,17
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CH2005/000403

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
JP 2002306609 A	22-10-2002	NONE	
JP 2000350783 A	19-12-2000	NONE	
EP 0486283 A	20-05-1992	CA 2055297 A1	14-05-1992
		EP 0486283 A2	20-05-1992
		US 5223434 A	29-06-1993
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		AU 4186285 A	07-11-1985
		CA 1250504 A1	28-02-1989
		DE 3581653 D1	14-03-1991
		EP 0160303 A2	06-11-1985
		JP 2568169 B2	25-12-1996
		JP 60241454 A	30-11-1985
US 2003004463 A1	02-01-2003	US 2004260143 A1	23-12-2004
		US 2003216609 A1	20-11-2003

Electronic Acknowledgement Receipt

EFS ID:	5704892
Application Number:	12137364
International Application Number:	
Confirmation Number:	7377
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Customer Number:	22859
Filer:	Elisabeth Lacy Belden
Filer Authorized By:	
Attorney Docket Number:	56782.1.7
Receipt Date:	15-JUL-2009
Filing Date:	11-JUN-2008
Time Stamp:	15:56:05
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Filed (SB/08)	56782_1_7_IDS4.pdf	999553 69b81729bf3d340ad734cf1cbd876bc2c66405b3	no	6

Warnings:	
Information:	

2	Foreign Reference	56782_1_WO2006007750A1.pdf	751592 c114731a4f363285ed3917e90e312715e5fe75fa	no	35

Warnings:	
Information:	
Total Files Size (in bytes):	1751145

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New International Application Filed with the USPTO as a Receiving Office

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PTO/SB/08a (03-08)
Approved for use through 06/30/2008. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	2628
Examiner Name	
Attorney Docket Number	56782.1.7

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	1	2007071022	WO	A1	2007-06-28	Robert A. Dekemp		☐
	2	2007104133	WO	A1	2007-09-20	Robert A. Dekemp		☐

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	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	2628
	Examiner Name	
	Attorney Docket Number	56782.1.7

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
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Examiner Signature		Date Considered	

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	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	2628
	Examiner Name	
	Attorney Docket Number	56782.1.7

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Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

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☐ See attached certification statement.

☐ Fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ None

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Elisabeth Lacy Belden/	Date (YYYY-MM-DD)	2009-05-20
Name/Print	Elisabeth Lacy Belden	Registration Number	50,751

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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
28 June 2007 (28.06.2007)

PCT

(10) International Publication Number
WO 2007/071022 A1

(51) International Patent Classification:
B01D 15/42 (2006.01) *B01J 20/34* (2006.01)

(21) International Application Number:
PCT/CA2006/002043

(22) International Filing Date:
14 December 2006 (14.12.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
11/312,368 21 December 2005 (21.12.2005) US

(71) Applicant *(for all designated States except US)*: **OTTAWA HEART INSTITUTE RESEARCH CORPORATION** [CA/CA]; 40 Ruskin Street, Ottawa, Ontario K1Y 4W7 (CA).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **DEKEMP, Robert, A.** [CA/CA]; 92 Ross Avenue, Ottawa, Ontario K1Y 0N5 (CA).

(74) Agent: **OGILVY RENAULT LLP/S.E.N.C.R.L., s.r.l.**; Suite 1500, 45 O'Connor Street, Ottawa, Ontario K1P 1A4 (CA).

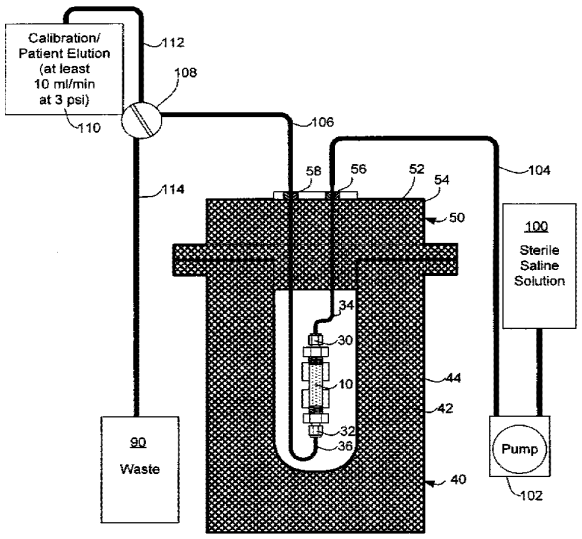
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: A RUBIDIUM GENERATOR FOR CARDIAC PERFUSION IMAGING AND METHOD OF MAKING AND MAINTAINING SAME



(57) Abstract: An $^{82}Sr/^{82}Rb$ generator column is made using a fluid impervious cylindrical container having a cover for closing the container in a fluid tight seal, and further having an inlet for connection of a conduit for delivering a fluid into the container and an outlet for connection of a conduit for conducting the fluid from the container. An ion exchange material fills the container, the ion exchange material being compacted within the container to a density that permits the ion exchange material to be eluted at a rate of at least 5 ml/min at a fluid pressure of 1.5 pounds per square inch (10 kPa). The generator column can be repeatedly recharged with ^{82}Sr. The generator column is compatible with either three-dimensional or two-dimensional positron emission tomography systems.

WO 2007/071022 A1

A RUBIDIUM GENERATOR FOR CARDIAC PERFUSION IMAGING AND METHOD OF MAKING AND MAINTAINING SAME

TECHNICAL FIELD

The present application relates in general to nuclear medicine and, in particular, to a rubidium generator for cardiac perfusion imaging and method of making and maintaining same.

BACKGROUND OF THE INVENTION

As is well known in the art, ^{82}Rb is used as a positron emission tomography (PET) tracer for measurement of myocardial perfusion (blood flow) in a non-invasive manner.

Recent improvements in PET technology have introduced 3-dimensional positron emission tomography (3D PET). Although 3D PET technology may permit more efficient diagnosis and prognosis in patients with suspected coronary artery disease, the sensitivity of 3D PET requires very accurate control of the delivery of ^{82}Rb activity to a patient being assessed.

As is well understood in the art, ^{82}Rb for myocardial perfusion imaging is produced using a strontium-rubidium ($^{82}Sr/^{82}Rb$) generator which is eluted using a sterile saline solution (0.9% Sodium Chloride Injection) to produce an ^{82}Rb eluate ([^{82}Rb] Rubidium Chloride Injection) that is injected into the patient during the PET imaging. Due to the above-noted sensitivity of 3D PET it is desirable to deliver the ^{82}Rb elution to the patient as far away from the patient's heart as can be practically achieved. This

is best accomplished by using a small vein in the patient's hand, for example, as the ^{82}Rb elution injection site. Doing so, however, requires a low pressure, low flow rate elution and precision flow control.

There therefore exists a need for an ^{82}Rb generator that enables low pressure elution and facilitates precision flow control of patient elution injections.

SUMMARY OF THE INVENTION

It is therefore an object of the invention to provide a rubidium generator column that enables low pressure elution and facilitates precision flow control of patient elutions.

The invention therefore provides a method of preparing an $^{82}Sr/^{82}Rb$ generator column for low pressure elution, comprising: filling the generator column with an ion exchange material that tightly binds ^{82}Sr but not ^{82}Rb, and compacting the ion exchange material to a density that permits fluid solutions to be pumped through the generator column at a rate of at least 5 ml/min at a fluid pressure of 1.5 pounds per square inch (10 kPa); conditioning the ion exchange material; and loading the generator column with a solution of ^{82}Sr.

The invention further provides an $^{82}Sr/^{82}Rb$ generator column, comprising: a fluid impervious cylindrical container having a cover for closing the container in a fluid tight seal, and further having an inlet for connection of a conduit for delivering a fluid into the container and an outlet for connection of a conduit for conducting the fluid from the container; and an ion exchange material filling the container, the ion exchange

material being compacted within the container to a density that permits the ion exchange material to be eluted at a rate of at least 5 ml/min at a fluid pressure of 1.5 pounds per square inch (10 kPa).

BRIEF DESCRIPTION OF THE DRAWINGS

Further features and advantages of the present invention will become apparent from the following detailed description, taken in combination with the appended drawings, in which:

Fig. 1 is a schematic diagram illustrating the packing of a generator column in accordance with the invention;

Fig. 2 is a schematic diagram of the generator column shown in Fig. 1 suspended in a shielding body and being loaded with ^{82}Sr;

Fig. 3 is a schematic diagram of the generator column shown in Fig. 1 configured for calibration and patient elutions;

Fig. 4 is a flowchart illustrating the method in accordance with the invention for making the generator columns shown in Figs. 1-3; and

Fig. 5 is a flowchart illustrating principle steps in the use of the generator column shown in Fig. 3.

It will be noted that throughout the appended drawings, like features are identified by like reference numerals.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

The present invention provides an $^{82}Sr/^{82}Rb$ generator column for use in positron emission tomography cardiac perfusion imaging. In accordance with the invention, the generator column is filled with an ion exchange material that tightly binds ^{82}Sr but not ^{82}Rb. The ion exchange material is compacted to a density that permits fluid solutions to be pumped through the generator column at a rate of at least 5 ml/min at a fluid pressure of 1.5 pounds per square inch (10 kPa). After the generator column is packed with the ion exchange material, it is conditioned with a source of excess sodium cations and loaded with a solution of ^{82}Sr. The generator column in accordance with the invention enables low pressure injections using a peristaltic pump and facilitates precision flow control of patient elutions. Advantageously, the generator column in accordance with the invention can also be reloaded with ^{82}Sr a plurality of times. This has distinct advantages. First, residue ^{82}Sr remaining in the column from a previous load is not wasted. Second, the expense of building and conditioning the generator column is distributed over a plurality of ^{82}Sr loads, so the overall cost of using ^{82}Rb for cardiac perfusion imaging is reduced.

Fig. 1 illustrates the packing of an ^{82}Rb generator column 10 using a method in accordance with the invention. As is known in the art, the generator column 10 is constructed from stainless steel hardware components that are commercially available. In the embodiment shown in Fig. 1, a pair of SWAGELOK® reducing adaptors with nuts and ferrules 12, 14 are connected to opposite ends of a stainless tubing 16 that is packed with an ion exchange material 18. In one embodiment of the invention, the ion exchange material 18 is an α-hydrous tin dioxide (

$SnO_2.xH_2O$, where x equals 1-2) wetted with a NH_4OH/NH_4Cl buffer (pH 10).

A 25 micron filter 24 closes a bottom of the cylinder 16 at an outlet end thereof. Likewise, a 25 micron filter 22 closes an inlet end of the cylinder 16 after the cylinder 16 is packed with the ion exchange material 18. A feature of the invention is that, unlike prior art generator columns in which the ion exchange material is tightly packed so that high pressure elution is required, the ion exchange material 18 is packed only to a density that permits fluid solutions to be pumped through the generator column at a rate of at least 5 ml/min at a fluid pressure of 1.5 pounds per square inch (10 kPa). As shown in Fig. 1, a simple and practical way of accomplishing the required packing of the ion exchange material 18 is to repeatedly strike a side of the generator column 10 with an instrument 26, such as a laboratory wrench, with a force that exerts about 0.1 Joule. Experience has shown that between 50 and 100 strikes are required to achieve the required density of the ion exchange material 18.

After packing of the generator column 10 is complete, a funnel 20 that was used to introduce the ion exchange material 18 into the cylinder 16 is removed and the ion exchange material is leveled with the top of the cylinder 16. The ion exchange material packed into the generator column 10 has a density of not more than 3 g/cm^3 in the packed state. The filter 22 is then placed on top of cylinder 16 and the SWAGELOK adapter, nut and ferrule 12 is secured to the top of the cylinder in a manner well known in the art. As will be understood by those skilled in the art, the generator column 10 in accordance with the invention is constructed under sterile conditions using

sterile components and may be pressure tested for leaks after assembly.

Fig. 2 is a cross-sectional view of the generator column 10 suspended in a shielding body 40. The shielding body 40 is made from a dense shielding material 42, such as lead, tungsten or depleted uranium optionally encased in a stainless steel shell 44. The shielding body 42 includes a shielding lid 50 having apertures through which extend an inlet line 34 and outlet line 36. The inlet line 34 is connected to an inlet end 30 of the generator column 10. The outlet line 36 is connected to an outlet end 32 of the generator column 10. The inlet and outlet lines are connected to external tubing lines 60, 62 using Luer fittings 56 and 58. The shielding lid 50 is likewise constructed of a shielding material 52 such as lead, tungsten or depleted uranium encased in a stainless steel shell 54.

After the generator column 10 is packed with ion exchange material 18, as explained above with reference to Fig. 1, the generator column 10 must be loaded with ^{82}Sr before patient elutions can begin. As schematically illustrated in Fig. 2, in one embodiment a syringe pump 80 is used to deliver ^{82}Sr from a supply 70 through an inlet tube 60 to the generator column 10. The ^{82}Sr is bound by the ion exchange material 18 in the generator column 10. Waste fluid is evacuated through the outlet tube 36 and outlet line 62 to a shielded waste container 90, in a manner known in the art.

Fig. 3 is a schematic diagram of the generator column 10 configured for daily use as an ^{82}Rb source for cardiac perfusion imaging. A source of sterile saline solution 100 is connected to a saline supply tube 104. The sterile

saline solution 100 is pumped through the saline supply tube 104 by a pump 102. In one embodiment of the invention, the pump 102 is a peristaltic pump. In accordance with an alternate embodiment, the pump 102 is the syringe pump 80 shown in Fig. 2.

As understood by those skilled in the art, the pump 102 is controlled by a control algorithm that regulates a flow rate and volume of the sterile saline solution 100 pumped through the generator column 10 via the inlet tube 104 to provide an ^{82}Rb eluate via an outlet tube 106 connected to a controlled valve 108. The valve 108 directs the eluate through a delivery line 112 for a calibration elution or a patient elution 110, or to a shielded waste container 90. As is further understood by those skilled in the art, control of the system shown in Fig. 3 is complex and not all of the fluid paths and control mechanisms are depicted because elution control is not a subject of this invention.

Fig. 4 is a flowchart illustrating principle steps in constructing the generator column 10 in accordance with the invention. The process begins by preparing the ion exchange material and packing the generator column as explained above with reference to Fig. 1 (step 200). The generator column is then conditioned by saturating the ion exchange material 18 with sodium cations. In one embodiment, this is accomplished by passing 120 ml of 2 M NaCl through the column at a flow rate of 0.5 ml/minute followed by waiting for a period of 12 hours. 500 ml of sterile saline solution is then passed through the column at a flow rate of 10 ml/minute. A nondestructive pH test is performed (step 202) by testing a pH of the initial sterile saline solution passed through the column. This

nondestructive pH test prolongs the life of the generator column 10.

If it is determined (step 204) that the pH of the generator column 10 is not alkaline, the generator column 10 is defective and it is disposed of (step 224). If the saline solution is determined in step 204 to be alkaline, the generator column is loaded with ^{82}Sr (step 206) in a manner well known in the art using the equipment briefly described above with reference to Fig. 3. After the ^{82}Sr is loaded into the generator column 10, the generator column 10 is flushed with 1.0 L of sterile saline solution to clear traces of tin dioxide and any radionuclide impurities. The generator column is then eluted with sterile saline solution and the eluate is tested for: trace metals; sterility; radionuclide purity; pyrogens; and pH (step 208). If all of those tests are passed (step 210) the generator column 10 is ready for use (step 212). If any one of the tests fails, ^{82}Sr is optionally recovered from the generator column 10 (step 222) and the generator column 10 is disposed of (step 224).

During generator use, daily testing is performed for the purpose of patient safety and quality control, as will be described in detail with reference to Fig. 5. As long as all daily tests are passed, the generator column can continue to be used for patient elutions. As understood by those skilled in the art, one of the daily tests is a measure of ^{82}Rb yield. If it is determined in step 214 that one of the daily tests failed, it is further determined whether a reload of the generator column 10 is permitted (step 216). Reloading is permitted if the daily test failed due insufficient ^{82}Rb yield only. If the daily test failed for some other reason the generator column 10

cannot be further used, and the ^{82}Sr is optionally recovered (step 222) before the generator column is disposed of (step 224), as described above. If an ^{82}Sr reload is permitted, it is determined in step 218 whether the number of ^{82}Sr reloads of the generator column 10 has exceeded a predetermined reload limit. A generator column in accordance with the invention can be loaded with ^{82}Sr at least three times before any significant ^{82}Sr breakthrough occurs. If it determined in step 218 that the reload limit has been reached, certain jurisdictions require that the generator column be flushed and the eluate tested for: trace metals; sterility; radionuclide purity; pyrogens; and pH. If it is determined in step 218 that the reload limit has not been reached, the process branches back to step 206 and the generator column is reloaded with ^{82}Sr and steps 208-218 are repeated.

Fig. 5 is a flowchart illustrating principle steps involved in the daily use of the generator column 10 in accordance with the invention. Prior to each day's use of the generator column 10, the generator column 10 is flushed with 50 ml of sterile saline solution (step 300) in order to remove any strontium breakthrough from the generator column 10 into the waste vessel 90. The operator then waits for a predetermined period of time (step 302) before performing a calibration elution (step 304). As is well understood by those skilled in the art, under stable conditions the generator column maintains a $^{82}Sr/^{82}Rb$ equilibrium which is achieved after about 10 minutes. Consequently, the predetermined wait before a calibration elution is performed is at least 10 minutes. After the required wait, the generator column is eluted with about 15 ml of sterile saline solution at a constant flow rate of about 15 ml/minute. The calibration eluate is tested (step

306) for ^{82}Rb yield and ^{82}Sr breakthrough. In step 308 it is determined whether the ^{82}Rb yield is above a predetermined radioactivity limit. As is understood by those skilled in the art, the half life of ^{82}Rb is very short (i.e. 76 seconds). Consequently, in one embodiment the ^{82}Rb yield is measured using a positron counter during the elution, in a manner well known in the art.

In step 310, it is determined whether the ^{82}Sr, ^{85}Sr breakthrough is less than a predetermined breakthrough limit. As is also understood by those skilled in the art, all jurisdictions define a threshold for permissible levels of ^{82}Sr, ^{85}Sr breakthrough. As is further understood by those skilled in the art, the strontium breakthrough is readily determined by testing the radioactivity of the elution after about 20 minutes has elapsed, at which time the amount of residual ^{82}Rb is insignificant and does not distort the test results.

Before daily use begins, a cumulative volume of all fluids flushed and eluted through the generator column 10 is computed. Since the generator column 10 in accordance with the invention is repeatedly reloaded with ^{82}Sr, each generator column is identified by a unique identifier, in one embodiment a serial number. If the user of a generator column 10 does not have the facility to reload the generator column 10, the user must return the generator column 10 to the manufacturer, along with a cumulative total of fluid flushed and eluted through the column during that use. Likewise, when a reloaded column is supplied to a user, a cumulative volume of fluid used to flush and elute the column during all prior reload(s) and use(s) is provided to the user. Control software used to control a volume of fluid used during generator column 10 flushes and

elutions accepts the cumulative volume and stores it. The control software then recomputes the cumulative volume after each subsequent flush or elution of the generator column 10. That computed cumulative volume is compared (step 312) to a predefined volume limit. In accordance with one embodiment of the invention, empirical data has shown that 10 to 30 litres of sterile saline solution 100 can be pumped through the generator column 10 before significant ^{82}Sr breakthrough is experienced, so the volume limit may be set between 10 and 30 litres.

If each of the tests 308-312 is successfully passed, patient elutions (step 314) may be performed in a manner well known in the art. After each elution, it is necessary to wait a predetermined period of time, about 5 to 10 minutes, (step 316) to permit ^{82}Rb to regenerate. After each elution, the cumulative volume is recomputed by adding to the cumulative volume a volume of fluid pumped through the generator column 10 during the patient elution. Then it is determined whether the control system date has changed, i.e. a new day has begun (step 318). If not, the cumulative volume is compared to the predetermined volume limit. If the volume limit has been exceeded, the generator column is disposed of (step 324).

If it is determined in step 318 that the control system date has changed, the generator column 10 must be flushed and re-tested per steps 300-312, as described above. If those tests determine that the ^{82}Rb yield is less than a predetermined limit (step 308) then it is determined in step 320 whether the reload limit has been exceeded and if not the generator column 10 is returned for reload and pre-use testing (step 322). Otherwise, the generator column is disposed of (step 324). It should be

noted that if any of tests 308-312 fail, the generator column 10 may be returned to the manufacturer who determines whether the generator column 10 can be reloaded (step 320) and disposes of the generator column 10 (step 324) if it cannot be reloaded.

The generator column 10 in accordance with the invention reduces the expense of cardiac perfusion imaging while ensuring compatibility with 3D PET imaging systems by enabling low pressure, low flow rate elutions that can be precisely flow controlled. Research has conclusively established that the generator column 10 in accordance with the invention remains sterile and pyrogen-free for a period of at least six months when used in accordance with the procedures and limits described above.

Although the invention has been explained with reference to 3D PET imaging systems, it should be understood that the generator column 10 is equally compatible with 2D PET imaging systems and provides the same advantages of low cost, precise flow control, low pressure and low flow elution and a long service life.

The embodiment(s) of the invention described above is(are) intended to be exemplary only. The scope of the invention is therefore intended to be limited solely by the scope of the appended claims.

Claims:

1. A method of preparing a $^{82}Sr/^{82}Rb$ generator column for low pressure elution, comprising:

filling the generator column with an ion exchange material that tightly binds ^{82}Sr but not ^{82}Rb, and compacting the ion exchange material to a density that permits at least 5 ml/min of fluid solution to be pumped through the generator column at a fluid pressure of 1.5 pounds per square inch (10 kPa);

conditioning the ion exchange material; and

loading the generator column with a solution of ^{82}Sr.

2. The method as claimed in claim 1 wherein compacting the ion exchange material comprises compacting the ion exchange material to a density of not more than 3 g/cm^3.

3. The method as claimed in claim 2 wherein compacting the ion exchange material comprises repeatedly striking the generator column with a controlled force.

4. The method as claimed in claim 2 wherein repeatedly striking the generator column comprises repeatedly delivering a controlled force that transfers about 0.1 Joule to the generator column.

5. The method as claimed in claim 3 further comprising repeatedly striking the generator column to deliver the controlled force between 50 and 100 times in order to compact the ion exchange material.

6. The method as claimed in claim 1 wherein conditioning the ion exchange material comprises eluting the material with a source of sodium ions and subsequently flushing the column with a sterile saline solution.

7. The method as claimed in claim 6 further comprising measuring a pH of the sterile saline solution after the generator column has been eluted with the source of sodium ions.

8. The method as claimed in claim 1 further comprising eluting the generator column with a predetermined volume of sterile saline solution and testing the eluate to: determine whether the eluate is free of trace metals; determine whether the eluate is free of radionuclide impurities; measure a pH of the eluate; determine whether the eluate is sterile; and determine whether the eluate is free of pyrogens.

9. The method as claimed in claim 1 further comprising reloading the generator column with ^{82}Sr after the ^{82}Sr has depleted to an extent that an elution of the generator column with the saline solution yields an ^{82}Rb activity that is below a predetermined limit, until a total number of reloads reaches a predetermined radioactivity limit.

10. The method as claimed in claim 1 further comprising, on a daily basis, flushing the generator column with a predetermined volume of sterile saline solution to remove any ^{82}Sr or ^{85}Sr breakthrough.

11. The method as claimed in claim 10 further comprising waiting a predetermined period of time after the flushing, and eluting the generator column with a predetermined volume of sterile saline solution at a constant flow rate to obtain a calibration eluate of ^{82}Rb activity.

12. The method as claimed in claim 11 further comprising measuring a total ^{82}Rb activity of the calibration eluate during the elution for activity calibration.

13. The method as claimed in claim 11 further comprising measuring a radiation activity level of the calibration eluate after a predetermined period of time has elapsed to determine whether a concentration of ^{82}Sr or ^{85}Sr in the test eluate is below a predetermined breakthrough limit.

14. The method as claimed in claim 11 further comprising:

waiting a predetermined period of time after obtaining the calibration eluate, and eluting the generator column with a sterile saline solution to obtain a patient eluate of ^{82}Rb activity; and

computing for each generator column after each flush or elution, a cumulative volume of sterile saline flushed and eluted through the generator column, and disposing of the generator column when the cumulative volume exceeds a predetermined volume limit.

15. An $^{82}Sr/^{82}Rb$ generator column, comprising:

a fluid impervious cylindrical container having a cover for closing the container in a fluid tight

seal, and further having an inlet for connection of a conduit for delivering a fluid into the container and an outlet for connection of a conduit for conducting the fluid from the container; and

an ion exchange material filling the container, the ion exchange material being compacted within the container to a density that permits the ion exchange material to be eluted at a flow rate of at least 5 ml/min at fluid pressure of 1.5 pounds per square inch (10 kPa).

16. The $^{82}Sr/^{82}Rb$ generator column as claimed in claim 15 wherein the ion exchange material comprises α-hydrous tin dioxide.

17. The $^{82}Sr/^{82}Rb$ generator column as claimed in claim 16 wherein a total volume of the α-hydrous tin dioxide in the generator column is about 1.5 cm^3.

18. The $^{82}Sr/^{82}Rb$ generator column as claimed in claim 17 wherein the α-hydrous tin dioxide has a density of about 3 g/cm^3.

19. The $^{82}Sr/^{82}Rb$ generator column as claimed in claim 15 further comprising a particle filter at each of the inlet and the outlet.

20. The $^{82}Sr/^{82}Rb$ generator column as claimed in claim 15 further comprising a peristaltic or syringe pump for flushing and eluting the generator column.

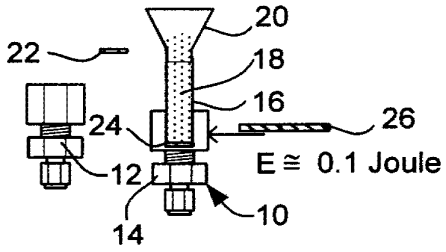

20
22
18
16
24
26
E ≅ 0.1 Joule
12
10
14

FIG. 1

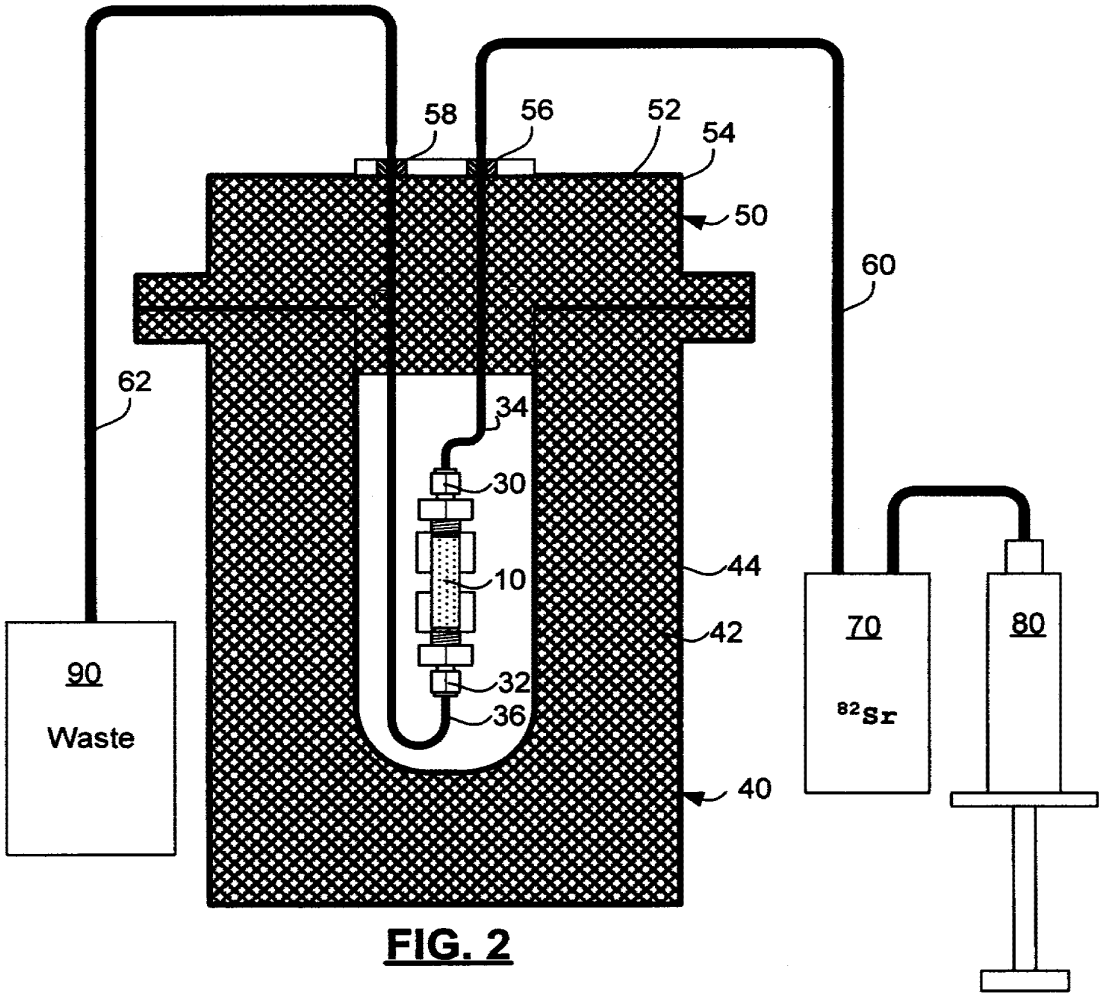

58
56
52
54
50
60
62
34
30
10
44
42
90
Waste
70
80
^{82}Sr
32
36
40

FIG. 2

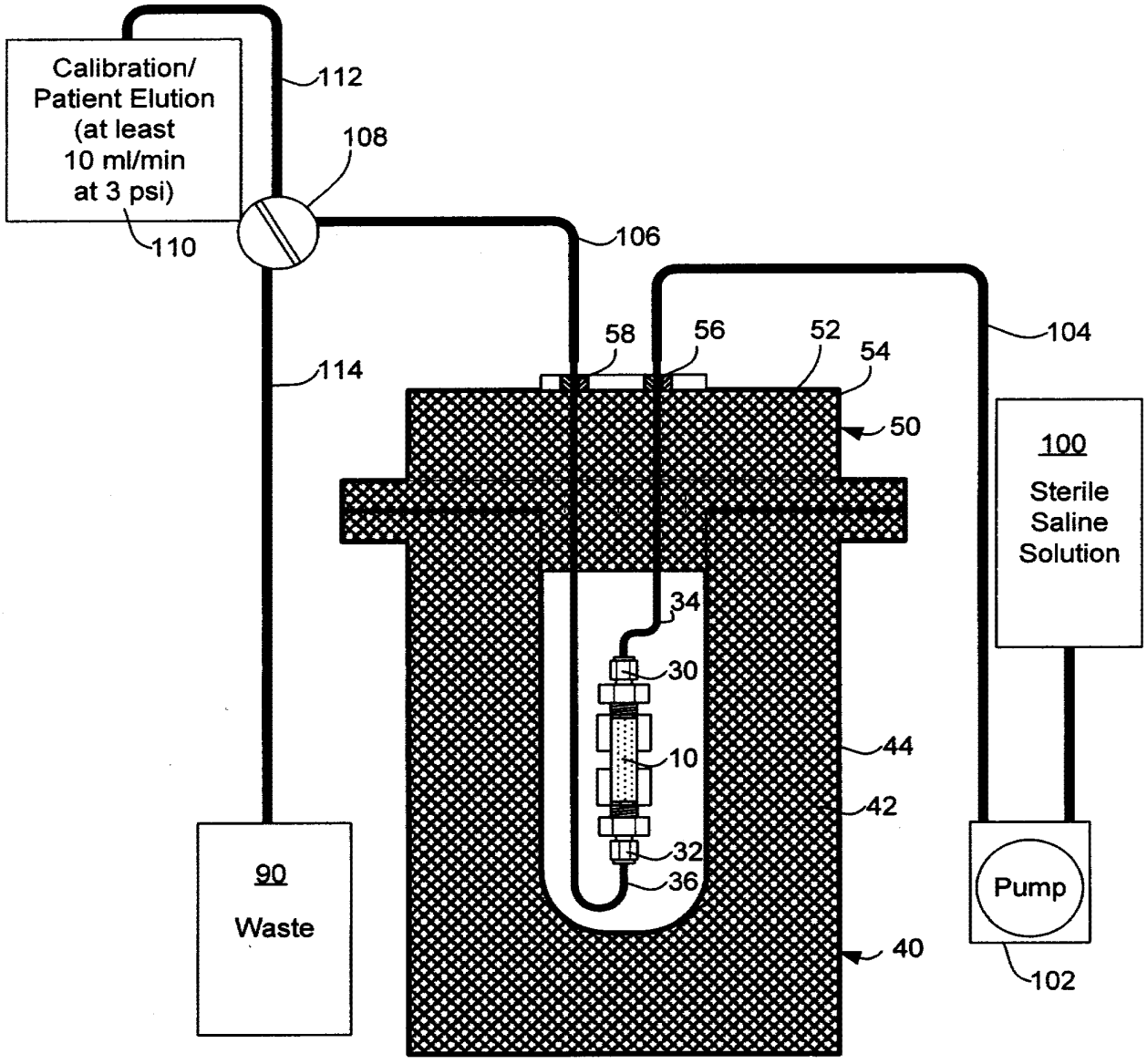

Calibration/
Patient Elution
(at least
10 ml/min
at 3 psi)
110
112
108
106
114
58
56
52
54
104
50
100
Sterile
Saline
Solution
34
30
10
44
42
32
36
90
Waste
Pump
40
102

FIG. 3

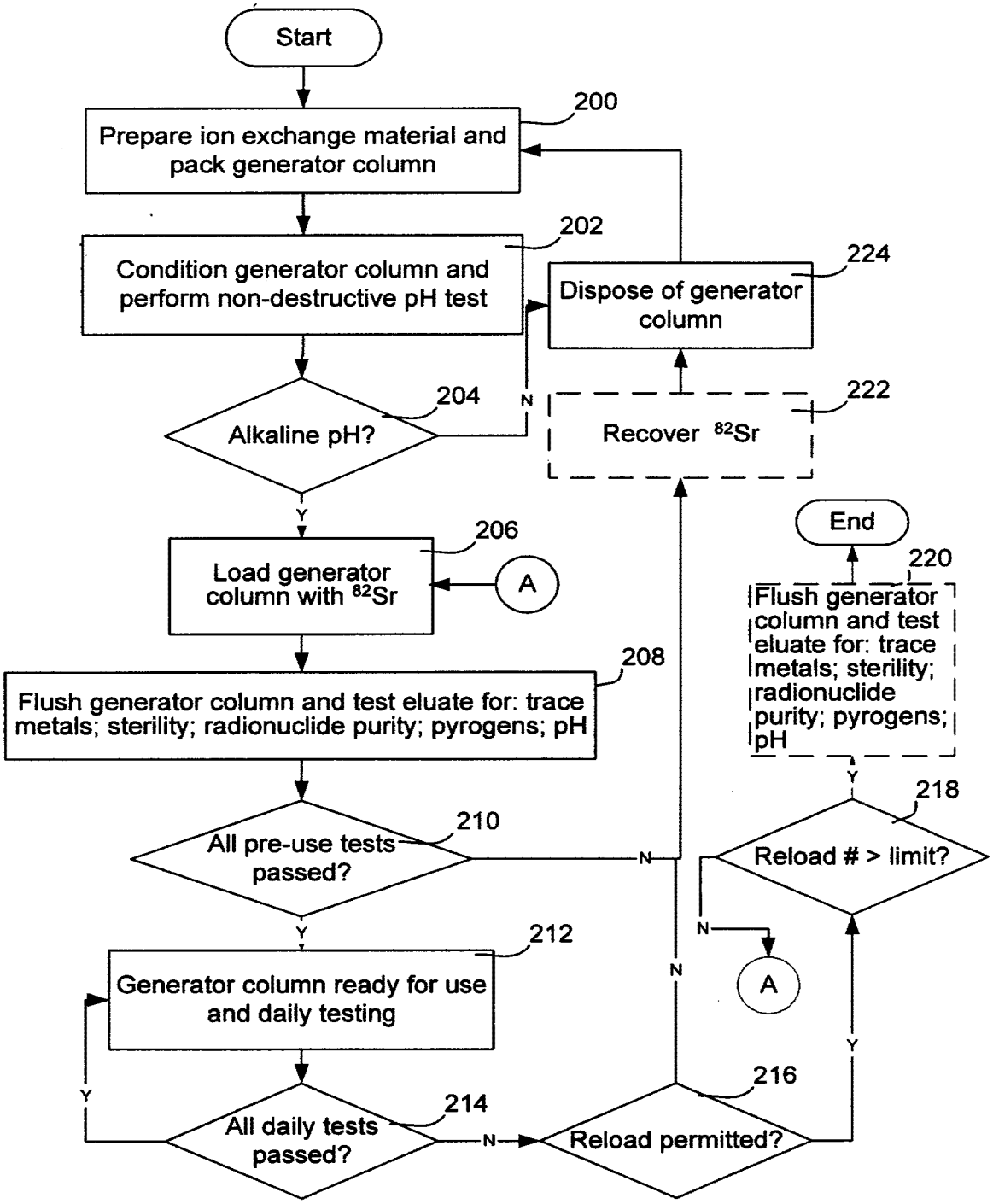

Start
Prepare ion exchange material and pack generator column
200
Condition generator column and perform non-destructive pH test
202
Alkaline pH?
204
N
Y
Dispose of generator column
224
Recover ^{82}Sr
222
Load generator column with ^{82}Sr
206
A
Flush generator column and test eluate for: trace metals; sterility; radionuclide purity; pyrogens; pH
208
All pre-use tests passed?
210
N
Y
Generator column ready for use and daily testing
212
All daily tests passed?
214
N
Y
Reload permitted?
216
N
Y
Reload # > limit?
218
N
A
Y
Flush generator column and test eluate for: trace metals; sterility; radionuclide purity; pyrogens; pH
220
End

FIG. 4

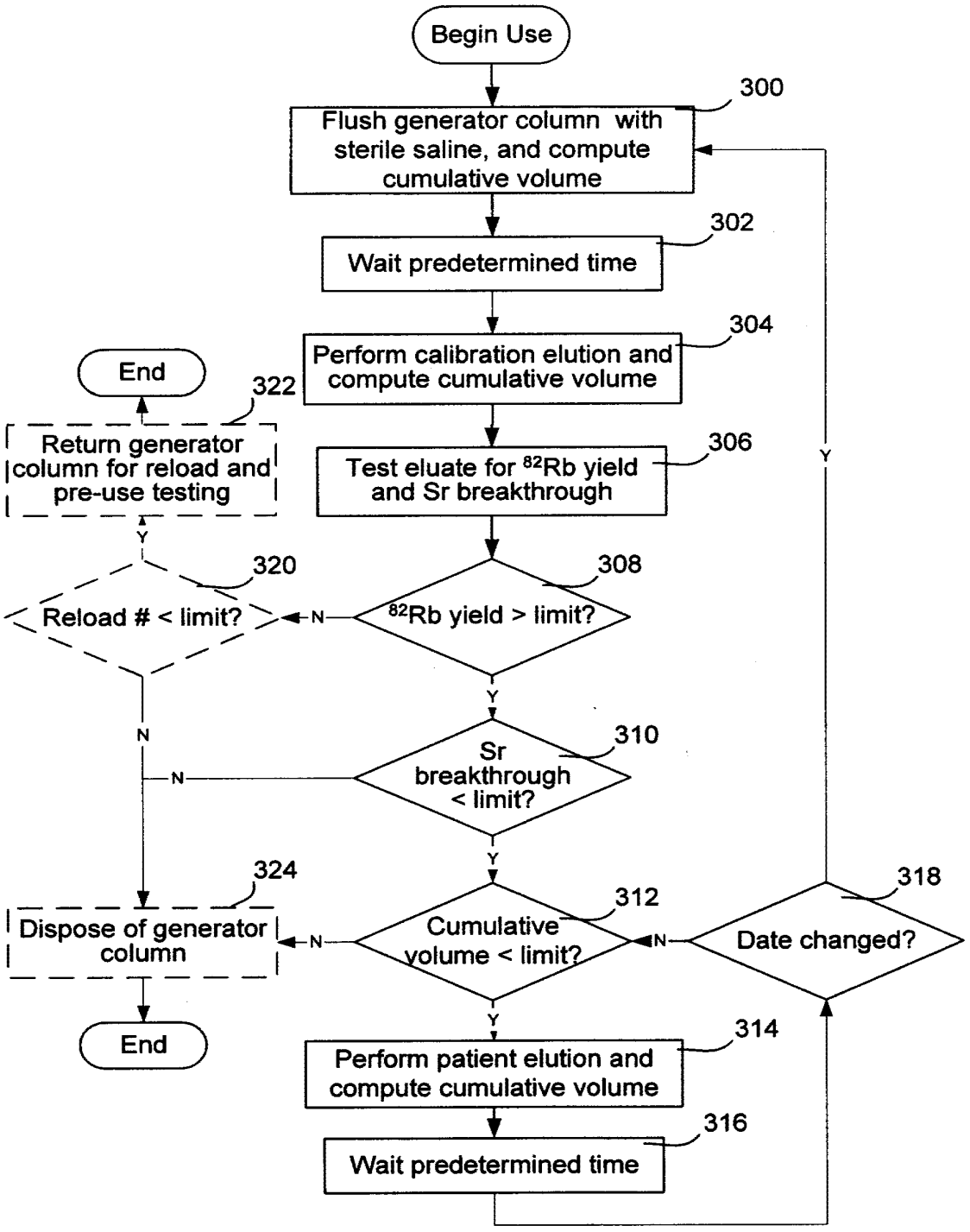

Begin Use
300
Flush generator column with sterile saline, and compute cumulative volume
302
Wait predetermined time
304
Perform calibration elution and compute cumulative volume
306
Test eluate for 82Rb yield and Sr breakthrough
308
82Rb yield > limit?
N
320
Reload # < limit?
Y
322
Return generator column for reload and pre-use testing
End
Y
310
Sr breakthrough < limit?
N
N
Y
312
Cumulative volume < limit?
N
318
Date changed?
Y
324
Dispose of generator column
End
Y
314
Perform patient elution and compute cumulative volume
316
Wait predetermined time

FIG. 5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2006/002043

A. CLASSIFICATION OF SUBJECT MATTER
IPC: ***B01D 15/42*** (2006.01) , ***B01J 20/34*** (2006.01)
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC: ***B01D 15/42*** (2006.01) , ***B01J 20/34*** (2006.01) , B01D 15/20 (2006.01) , B01J 20/28 (2006.01) , A61K 51/00 (2006.01)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
Canadian Patents Database, Delphion, Knovel, Scopus, Internet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ALVAREZ-DIAZ, Teresa M. et al., Manufacture of strontium-82/rubidium-82 generators and quality control of rubidium-82 chloride for myocardial perfusion	1-20
Y	imaging in patients using positron emission tomography, Applied Radiation and Isotopes, vol. 50, no. 6, 1999, pp. 1015-1023 * Whole document *	1-2, 15-20 3-5 6-14
Y	YANO, Y, et al., Rubidium-82 Generators for Imaging Studies, The Journal of Nuclear Medicine, vol. 18, no. 1, 1977, pp. 46-50 * p. 47, col. 1, lines 9-12 *	1-2, 15-20
Y	US 4175037 A (BENNEY, C. H. et al.) 20 November 1979 (20-11-1979) * col. 1, line 64 - col. 2, line 42 *	3-5
Y	US 3935884 A (HAZELTON) 3 February 1976 (03-02-1976) * col. 1, lines 8-11 *	3-5

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 April 2007 (13-04-2007)	17 April 2007 (17-04-2007)

Name and mailing address of the ISA/CA	Authorized officer
Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001-819-953-2476	Pierre Cuerrier 819- 997-4379

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2006/002043

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2845136 A (ROBINSON) 29 July 1958 (29-07-1958) * col. 1, lines 57-63 *	3-5
Y	US 3164980 A (LOYD) 12 January 1965 (12-01-1965) * col. 3, lines 7-9 *	3-5
Y	SCOTT, . P. W. (editor), Gas Chromatography, Proceedings of the third symposium organized by the Society of Analytical Chemistry and the Gas Chromatography Discussion Group of the Hydrocarbon Research Group of the Institute of Petroleum, held at the Assembly Rooms, Edimburgh, 8-10 June 1960, pp. 240-241	3-5
Y	Bracco Diagnostics, CardioGen-82® Rubidium Rb 82 Generator, USA, May 2000 * Whole document *	6-14
Y	YANO, Y, et al., A Precision Flow-Controlled Rb-82 Generator for Bolus or Constant-Infusion Studies of the Heart and Brain, The Journal of Nuclear Medicine, vol. 22, no. 11, 1981, pp. 1006-1010 * Whole document *	6-14
A	Rousseau, Ronald W., Handbook of Separation Process Technology, John Wiley & Sons, 1987, pp. 717-718 * chapter 13.3-2 *	1-20

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/CA2006/002043

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
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		AU3859578 A	07-02-1980
		CA1115551 A1	05-01-1982
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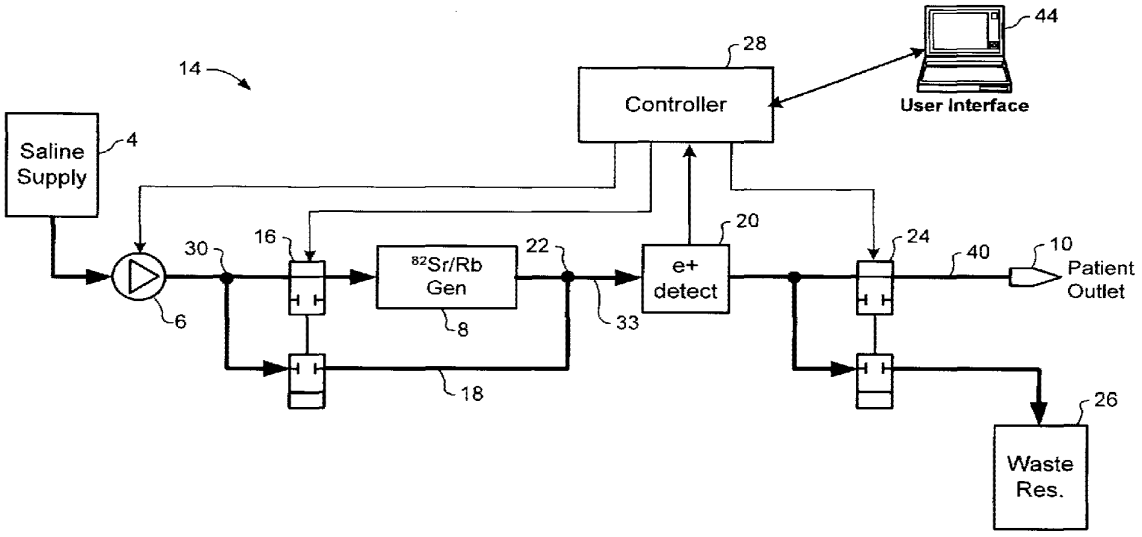
(54) Title: RUBIDIUM ELUTION SYSTEM CONTROL



(57) Abstract: A method of controlling an $^{82}Sr/^{82}Rb$ elution system having a generator valve for proportioning a flow of saline solution between an $^{82}Sr/^{82}Rb$ generator and a bypass line coupled to an outlet of the generator such that saline solution traversing the bypass line will merge with eluted saline solution emerging from the generator to provide an active saline solution. During each elution run, a plurality of successive concentration parameter values are obtained at predetermined intervals. Each concentration parameter value is indicative of a respective instantaneous activity concentration of the active saline solution. Respective error values between each concentration parameter value and a target activity concentration value of the elution run are computed. Error data based on a plurality of the computed error values is accumulated. Between successive elution runs, at least one performance parameter of the elution system is adjusted based on the accumulated error data.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

RUBIDIUM ELUTION SYSTEM CONTROL

FIELD OF THE INVENTION

The present application relates in general to nuclear medicine and, in particular, to a rubidium elution control system.

BACKGROUND OF THE INVENTION

As is well known in the art, Rubidium (^{82}Rb) is used as a positron emission tomography (PET) tracer for non-invasive measurement of myocardial perfusion (blood flow).

Recent improvements in PET technology have introduced 3-dimensional positron emission tomography (3D PET). Although 3D PET technology may permit more efficient diagnosis and prognosis in patients with suspected coronary artery disease, the sensitivity of 3D PET requires very accurate control of the delivery of ^{82}Rb activity to a patient being assessed.

FIGs. 1 and 2 illustrate a conventional rubidium elution system used for myocardial perfusion imaging. As may be seen in FIG. 1, the elution system comprises a reservoir of sterile saline solution (e.g. 0.9% Sodium Chloride Injection), a pump, and a strontium-rubidium ($^{82}Sr/^{82}Rb$) generator. In operation, the pump causes the saline solution to flow from the reservoir 4 and through the generator 8 to elute the ^{82}Rb. The active solution output from the generator 8 is then supplied to a patient (not shown) via a patient outlet 10.

When the system 2 is not in use, the amount of ^{82}Rb within the generator 8 accumulates until a balance is reached between the rate of ^{82}Rb production (that is, ^{82}Sr

decay) and the rate of ^{82}Rb decay. As a result, the ^{82}Rb activity level in the active saline emerging from the generator 8 tends to follow a "bolus" profile 12 shown by the solid line in FIG. 2a. In particular, at the start of an ^{82}Rb elution "run", the activity level rises rapidly and peaks, as accumulated ^{82}Rb is flushed out of the generator 8. Thereafter, the activity level drops back to a substantially constant value. The maximum activity level A_{MAX} (bolus peak) obtained during the run is dependent on the amount of accumulated ^{82}Rb in the generator 8, and thus is generally a function of the system's recent usage history, principally: the current ^{82}Rb production rate; the amount of accumulated ^{82}Rb (if any) remaining at the end of the previous elution run; and the idle time since the previous run. The generally constant level of the bolus tail is dependent on the rate of ^{82}Rb production and the saline flow rate produced by the pump 6.

As is well known in the art, ^{82}Rb is generated by radioactive decay of the ^{82}Sr, and thus the rate of ^{82}Rb production at any particular time is a function of the mass of remaining ^{82}Sr. As will be appreciated, this value will diminish (exponentially) through the useful life of the generator 8. The result is a family of bolus curves, illustrated by the dashed lines of FIG. 2a, mapping the change in elution system performance over the useful life of the generator 8.

Because of the high activity level of ^{82}Rb possible in the generator 8, it is desirable to limit the total activity dosage delivered to the patient during any given elution run. The total elution time required to reach this maximum permissible dose (for any given flow rate) will therefore vary over the life of the ^{82}Sr charge in the

generator 8, as may be seen in FIG. 2b, where the total activity dose, represented by the area under each curve, is equal in both cases.

A limitation of this approach, particularly for 3D PET imaging, is that the delivery of a high activity rate over a short period of time tends to degrade image quality. Low activity rates supplied over a relatively extended period are preferred. As a result, the user is required to estimate the saline flow rate that will obtain the best possible image quality, given the age of the generator and its recent usage history, both of which will affect the bolus peak and tail levels. This estimate must be continuously adjusted throughout the life of the generator 8, as the ^{82}Sr decays.

Accordingly, techniques for controlling an ^{82}Rb elution system that enable a desired activity level to be supplied over a desired period of time, independently of a state of the $^{82}Sr/^{82}Rb$ generator, remain highly desirable.

SUMMARY OF THE INVENTION

Accordingly, an object of the present invention is to provide techniques for controlling an ^{82}Rb elution system.

The present invention therefore provides a method of controlling an $^{82}Sr/^{82}Rb$ elution system having a generator valve for proportioning a flow of saline solution between an $^{82}Sr/^{82}Rb$ generator and a bypass line coupled to an outlet of the generator such that saline solution traversing the bypass line will merge with eluted saline solution emerging from the generator to provide an active saline solution. During each elution run, a plurality of successive concentration parameter values are obtained at

predetermined intervals. Each concentration parameter value is indicative of a respective instantaneous activity concentration of the active saline solution. Respective error values between each concentration parameter value and a target activity concentration value of the elution run are computed. Error data based on a plurality of the computed error values is accumulated. Between successive elution runs, at least one performance parameter of the elution system is adjusted based on the accumulated error data.

BRIEF DESCRIPTION OF THE DRAWINGS

Further features and advantages of the present invention will become apparent from the following detailed description, taken in combination with the appended drawings, in which:

FIG. 1 is a block diagram schematically illustrating principal elements of a conventional Rubidium elution system;

FIGs 2a and 2b are graphs illustrating representative performance of the elution system of FIG. 1;

FIG. 3 is a block diagram schematically illustrating principal elements of a Rubidium elution system in accordance with an embodiment of the present invention;

FIG. 4 illustrates a pinch-type valve arrangement usable in the elution system of FIG. 3;

FIG. 5 schematically illustrates a positron detector usable in the elution system of FIG. 3;

Figs. 6a-6d schematically illustrate respective operating states of the Rubidium elution system of FIG. 3;

FIGs. 7a-7c schematically illustrate a first algorithm for controlling the Rubidium elution system of FIG. 3; and

FIGs. 8a-8c schematically illustrate a second algorithm for controlling the Rubidium elution system of FIG. 3;.

It will be noted that throughout the appended drawings, like features are identified by like reference numerals.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

The present invention provides a Rubidium (^{82}Rb) elution and control system in which the ^{82}Rb activity rate delivered to a patient can be controlled substantially independently of the condition of the ^{82}Sr/^{82}Rb generator. Representative embodiments are described below with reference to FIGs. 3-8.

In the embodiment of FIG. 3, the elution system comprises reservoir 4 of sterile saline solution (e.g. 0.9% Sodium Chloride Injection); a pump 6 for drawing saline from the reservoir 4 at a desired flow rate; a generator valve 16 for proportioning the saline flow between a strontium-rubidium (^{82}Sr/^{82}Rb) generator 8 and a bypass line 18 which circumvents the generator 8; a positron detector 20 located downstream of the merge point 22 at which the generator and bypass flows merge; and a patient valve 24 for controlling supply of active saline to a patient outlet 10 and a waste reservoir 26. A controller 28 is connected to the pump 6, positron detector 20 and valves 16 and 24 to control the elution system 14 in accordance with a desired control algorithm, as will be described in greater detail below.

If desired, the strontium-rubidium ($^{82}Sr/^{82}Rb$) generator 8 may be constructed in accordance with Applicant's co-pending United States Patent Application No. 11/312,368 entitled A Rubidium Generator For Cardiac Perfusion Imaging And Method Of Making And Maintaining Same, filed December 21, 2005. In such cases, the pump 6 may be a low-pressure pump such as a peristaltic pump. However, other types of generator may be used. Similarly, other types of pump may be used, provided only that the pump selected is appropriate for medical applications and is capable of maintaining a desired saline flow rate through the generator.

The generator and patient valves 16, 24 may be constructed in a variety of ways. In principal, the generator valve may be provided as any suitable valve 16 arrangement capable of proportioning saline flow between the generator 8 and the bypass line 18. If desired, the generator valve may be integrated with the branch point 30 at which the saline flow is divided. Alternatively, the generator valve 16 may be positioned downstream of the branch point 30, as shown in FIG. 3. In embodiments in which flexible (e.g. Silicon) tubing is used to convey the saline flow, the generator valve 16 may be provided as one or more conventional "pinch" valves of the type illustrated in FIG. 4. The use of pinch valves is beneficial in that it enables saline flow to be controlled in a readily repeatable manner, and without direct contact between the saline solution and components of the valve. Factors associated with the design of the patient valve 24 are substantially the same as those discussed above for the generator valve 16, with the exception that the saline flow through the patient valve 24 is (or must be assumed to be) carrying radioactive ^{82}Rb. Accordingly, while any suitable

valve design may be selected for the patient valve 24, it is particularly beneficial to avoid direct contact between the active saline solution and valve components. For this reason, pinch valves are preferred for the patient valve 24.

As may be seen in FIG. 5, the positron detector 20 may conveniently be provided as a scintillator 32 disposed immediately adjacent to a feed-line 33 carrying the active saline solution; a photon counter 34 optically coupled to the scintillator 32; and a radiation shield 36 surrounding the scintillator 32 and photon counter 34. The scintillator 32 may be provided by a length of fluorescent optical fiber, which absorbs Beta (e+) radiation generated by ^{82}Rb decay to produce a photon. The photon counter 34 (which may, for example be an H7155 detector manufactured by Hamamatsu) detects incident photons, and generates a detection signal 38 corresponding to each detected photon. The shielding 36, which may be constructed of lead (Pb), serves to shield the scintillator 32 and photon counter 34 from ambient Gamma and Beta radiation. In some embodiments, the radiation shield 36 is approximately ½ inch thick in the vicinity of the scintillation fiber 32, and may extend (in both directions) at least 5-times the feed-line 33 outer diameter from the scintillation fiber 32. This arrangement effectively suppresses ingress of ambient Gamma and Beta radiation along the channel through which the feed-line 33 passes. As a result, spurious photons are suppressed, and the rate at which photons are counted by the photon counter 34 will be proportional to the ^{82}Rb activity concentration of the active saline solution adjacent to the scintillator 32. In the illustrated embodiments, the number of photons detected within a predetermined period of time is counted (e.g. by

the controller 28), and the count value C_{det} is used as an activity parameter which is proportional to the ^{82}Rb activity concentration. If desired, a proportionality constant K between the activity parameter C_{det} and the ^{82}Rb activity concentration can be empirically determined.

In operation, the pump 6 and valves 16, 24 can be controlled to route saline solution through the system 14 in accordance with various modes of operation, as may be seen in FIGs. 6a-6d. Thus, for example, in a "Bypass-to-waste" mode of the system illustrated in FIG. 6a, the generator and patient valves 16, 24 are positioned to route the entire saline flow through the bypass line 18, and into the waste reservoir 26. This mode of operation is suitable for initializing the system 14 immediately prior to beginning an elution run.

FIG. 6b illustrates a "patient line flush" mode of the system 14, in which the generator and patient valves 16, 24 are positioned to route the saline flow through the bypass line 18 and out through the patient outlet 10. This mode of operation may be used prior to an elution run to prime (that is, expel air from) the patient line 40 in preparation for insertion of the patient outlet into, for example, a vein of a patient. At the end of an elution run, this mode may also be used to flush any ^{82}Rb activity remaining within the patient line 40 into the patient, thereby ensuring that the patient receives the entire activity dose required for the PET imaging.

FIG. 6c illustrates a "waiting for threshold" mode of the system 14, in which the generator and patient valves 16, 24 are positioned to route the saline flow through the generator 8, and into the waste reservoir 26. This mode of operation is suitable during the beginning an elution run,

while the ^{82}Rb concentration is increasing from zero, but has not yet reached desired levels. Flushing this leading portion of the ^{82}Rb bolus 12 to the waste reservoir 26 avoids exposing the patient to unnecessary ^{82}Rb activity and allows the total activity dosage delivered to the patient to be closely controlled.

FIG. 6d illustrates an "elution" mode of the system 14, in which the generator valve 16 is actively controlled via a control loop 42 from the positron detector 20 to proportion saline flow through both the generator 8 and the bypass line 18. The generator 8 and bypass saline flows are then recombined (at 22) downstream of the generator 8 to produce an active saline solution having a desired ^{82}Rb activity concentration. The patient valve 24 is positioned to direct the active saline solution to the patient outlet 10.

In the foregoing description, each operating mode is described in terms of the associated steps in performing an elution run to support PET imaging of a patient. However, it will be appreciated that this context is not essential. Thus, for example, one or more of the above operating modes may be used to facilitate calibration of the system, in which case the patient outlet 10 would be connected to a conventional dose calibrator (not shown), rather than a patient.

As will be appreciated from the foregoing discussion, each of the operating modes of the elution system is controlled by the controller unit 28 operating under software control. As a result, it is possible to implement a wide variety of automated processes, as required. Thus, for example, elution runs can be fully automated, based on user-entered target parameters, which allows the user to

avoid unnecessary radiation exposure. Similarly, it is possible to automate desired system calibration and ^{82}Sr break-through detection protocols, which ensures consistency as well as limiting radiation exposure of users. A further benefit of software-based elution system control is that data logs from each elution run can be easily maintained, which assists not only system diagnostics, but can also be used to ensure that the elution parameters (e.g. elution concentration and duration) specified for PET imaging have been satisfied.

As described above, in the "elution" mode of operation (FIG. 6d), the generator valve 16 is actively controlled via a control loop 42 from the positron detector 20 to proportion saline flow through both the generator 8 and the bypass line 18. Recombining the corresponding generator and bypass saline flows downstream of the generator 8 produces an active saline solution having a desired ^{82}Rb activity concentration. Preferably, the control loop 42 is implemented using suitable software executing in the controller 28. Representative algorithms for implementing the control loop 42 are described below with reference to FIGs. 7 and 8.

In the embodiment of FIG. 7, the controller 28 implements a threshold-based control algorithm, in which the generator valve 16 is controlled by comparison of measured activity concentration to a desired activity concentration. If the measured concentration is higher than the desired concentration, the generator valve 16 directs saline flow to the bypass line 18 rather than the generator 8, and vice versa.

In general, the elution run is designed to generate a target ^{82}Rb activity concentration which follows a desired

function in time $C_M(t)$. In the embodiment of FIG. 7, $C_M(t)$ is a square-wave function having a predetermined constant activity concentration C_M and duration (t_2-t_1), as may be seen by the dotted line of FIG. 7b. These parameters may be provided by explicit user input using the user interface 44 (Fig. 3), or calculated from other user-input parameters, such as a total activity dosage and saline flow rate. As will be appreciated, the target activity profile $C_M(t)$ need not be a square-wave function, other profiles may be used, such as a ramp function, if desired.

In some embodiments, the target activity profile $C_M(t)$ may define the desired ^{82}Rb activity concentration at the patient outlet 10. In such cases, an adjusted target profile $C'_M(t)$ may be computed based on the selected flow rate and patient supply line length, to account for expected ^{82}Rb decay (and thus loss of activity) in the patient supply line 40 between the positron detector 20 and the patient outlet 10. This arrangement is advantageous in that it allows a user to specify an amount of activity (either activity concentration or total dose) delivered to the patient, and the control loop 42 will operate to match this specification, taking into account the ^{82}Rb decay within the system 14.

FIG. 7a is a flow chart illustrating a representative threshold-based valve control algorithm which may be used in the embodiment of FIG. 7. For ease of illustration, the flow-chart of FIG. 7a only illustrates the control loop. Process steps and threshold, related to transitioning between various modes of operation are not shown.

In preparation for an elution run, a user enters target parameters for the elution. These parameters may include any three of: total activity dose, target activity

concentration, elution duration, and saline flow rate. From the entered parameters, the remaining parameter can be calculated, and, if desired, an adjusted target profile $C'_M(t)$ obtained (step S2).

At the start of the elution run, the controller 28 opens the generator valve 16 (at time t_0 in FIG. 7b) to place the elution system 14 into the "Waiting for Threshold" mode. During this period, the activity level detected by the positron detector will begin to ramp up following the leading edge of the 'natural' bolus curve 12 (Fig. 2a). During this period, the patient valve 24 remains closed, so that any activity eluted from the generator 8 is passed to the waste reservoir 26. When the detected activity concentration C_{det} exceeds the target value C_M, the controller 28 opens the patient valve 24 (at time t_1 in FIG. 7b), and shifts to the "elution" mode of operation.

During the elution mode, the controller 28 iteratively obtains an updated concentration parameter C_{det} (at S4), which indicates the instantaneous activity concentration at the positron detector. The concentration parameter C_{det} is then compared to the desired concentration C_M. If C_{det} is below the desired concentration C_M (at S6), the generator valve 16 is opened (at S8) so that saline flows through the generator 8 to elute ^{82}Rb activity. If C_{det} is above the desired concentration C_M (at S10), the generator valve 16 is closed (at S12) so that saline flows through the bypass line 18. As may be seen in FIG. 7b, due to delay in response, the result of this operation is a saw-tooth activity concentration profile 46 centered on the target concentration C_M (or C'_M). At the end of the elution run (time t_2 in FIG. 7b), the controller 28 closes the

generator valve 16 and places the elution system 14 into the "Patient line Flush" mode, which terminates elution of ^{82}Rb activity from the generator 8 and flushes any remaining ^{82}Rb activity within the patient line 40 into the patient.

FIG. 7c illustrates the activity concentration profile delivered to the patient as a result of the above-described process. As may be seen from FIG. 7c, no ^{82}Rb activity is delivered to the patient during the "Waiting for Threshold" mode (t_0-t_1). During the "elution" mode (t_1-t_2, the activity concentration 46 follows a saw-tooth pattern centered on the target concentration C_M (or C'_M). Finally, in "Patient line Flush" mode (following t_2) the activity concentration drops rapidly as ^{82}Rb elution is terminated and residual activity is flushed from the patient supply line 40.

As will be appreciated, the accuracy with which the delivered activity concentration follows the target profile $C_M(t)$ is largely dependent on the line volume between the merge point 22 and the positron detector 20. In some cases relatively large excursions from the target profile $C_M(t)$ are acceptable. However the control loop response is such that the difference cannot be reduced past a certain limit. As a result, the "error" between the target profile $C_M(t)$ and the delivered concentration profile 46 (Fig. 7c) cannot be eliminated in the embodiment of FIG. 7. A pulse-width modulation technique which overcomes this limitation is described below with reference to FIG. 8.

The embodiment of FIG. 8 differs from that of FIG. 7 primarily in the manner in which the generator valve 16 is controlled. In the embodiment of FIG. 7, the generator valve 16 is opened or closed based on a comparison between

the detected activity concentration C_{det} and desired activity concentration. By contrast, in the embodiment of FIG. 8, the generator valve is opened and closed continuously at a predetermined frequency. Any desired frequency may be used, depending primarily on the physical properties of the generator valve 16. In some embodiments, a frequency of between 1 and 10 Hz (e.g. 5 Hz) may be used. In order to control the proportioning of saline flow between the generator 8 and the bypass line 18, the duty cycle of the valve 16 is varied. Thus, for example, a duty cycle of "0" may have the effect of directing the entire saline flow through the bypass line 18, and a duty cycle of "100" directs the entire saline flow through the generator 8. A duty cycle between these limits divides the saline flow between the generator 8 and bypass line 18 in accordance with the duty cycle value. The precision with which the saline flow can be divided between the generator 8 and bypass line 18 will be determined by a minimum adjustment step size, which can be a programmable value.

As described above, the amount of ^{82}Rb eluted from the generator 8, for any given flow rate, will depend on the recent usage history of the elution system 14, and the instantaneous production rate of ^{82}Rb within the generator 8. Accordingly, it is possible to improve the accuracy of the elution system 14 by implementing a predictive control algorithm, in which models of the valve 16 and generator performance are used to predict the amount of ^{82}Rb activity that will be eluted from the generator 8 for a given duty cycle setting.

In particular, the generator performance can be modeled to predict the amount of ^{82}Rb activity that will be eluted from the generator for a given flow rate, as will be

described in greater detail below. In some embodiments, a dose calibrator (not shown) is used to measure the generator performance in terms of, for example, ^{82}Rb activity concentration vs. eluted volume. This data can be used to predict eluted ^{82}Rb activity concentration for any given saline flow rate.

In addition, the generator valve response can be modeled to enable a prediction of the flow rate through the generator for any given total saline flow rate (as determined by the pump control setting) and valve duty cycle. In some embodiments, the valve response may be modeled in terms of respective parameters defining upper and lower duty cycle limits Π_{max} and Π_{min}, and a flow ratio vs. duty cycle slope L between the upper and lower limits. With this arrangement, the upper duty cycle limit Π_{max} represents the value beyond which all of the flow is considered to be directed into the generator 8. Conversely, the lower duty cycle limit Π_{min} represents the value below which all of the flow is considered to be directed into the bypass line 18. The flow ratio vs. duty cycle slope L defines the change in the ratio between the respective flows through the generator 8 and the bypass line 18 for duty cycle values lying between the upper and lower limits.

In cases where the valve response is non linear, it may be advantageous to replace the flow ratio vs. duty cycle slope parameter L with one or more parameters defining a mathematical valve response curve.

At the start of the elution run, the controller 28 opens the generator valve 16 (at time t_0 in FIG. 8b) to place the elution system into the "Waiting for Threshold" mode. During this period, the activity level detected by

the positron detector 20 will begin to ramp up following the leading edge of the 'natural' bolus curve 12 (Fig. 2a). During this period, the patient valve 24 remains closed, so that any activity eluted from the generator is passed to the waste reservoir 26. When the detected activity concentration reaches the target concentration C_M (or adjusted target C'_M, as applicable), the controller 28 opens the patient valve 24 (at time t_1 in FIG. 8b), and shifts to the "elution" mode of operation.

During the elution mode, the controller 28 implements a predictive control algorithm in which previously stored generator performance data is used (at S14) to estimate a flow ratio that will yield the target activity concentration C_M (or C'_M) at the positron detector 20, for the selected flow rate of the elution run. This estimated (predicted) flow ratio is then used to control the duty cycle of the generator valve 16. The controller 28 then obtains an updated concentration parameter C_{det} (at S16), which indicates the instantaneous activity concentration at the positron detector 20. The concentration parameter C_{det} is then compared to the target concentration C_M (or C'_M) to obtain an error function ΔC (at S18). Based on the value of the error function ΔC, the duty cycle of the generator valve 16 is adjusted. If $\Delta C<0$ (step S20), the duty cycle is increased (at S22) so that proportionally more saline flows through the generator 8 to elute more ^{82}Rb activity. If $\Delta C>0$ (step S24), the duty cycle is decreased (at S26) so that proportionally more saline flows through the bypass line 18. If neither condition is satisfied the duty cycle is maintained at its current status (S28). As may be seen in FIG. 8b, the result of this operation is a low-error concentration profile 48 that closely matches the target concentration C_M (or C'_M). At the end of the elution run

(time t_2 in FIG. 8b), the controller 28 closes the generator valve 16 (that is, reduces the duty cycle to "0") and places the elution system 14 into the "Patient line Flush" mode, which terminates elution of ^{82}Rb activity from the generator 8 and flushes any remaining ^{82}Rb activity within the patient line 40 into the patient.

FIG. 8c illustrates the activity concentration profile 48 delivered to the patient as a result of the above-described process. As may be seen from FIG. 8c, no ^{82}Rb activity is delivered to the patient during the "Waiting for Threshold" mode (t_0-t_1). During the "elution" mode (t_1-t_2), the activity concentration closely follows the target concentration C_M (or C'_M). Finally, in "Patient line Flush" mode (following t_2) the activity concentration drops rapidly as ^{82}Rb elution is terminated and residual activity is flushed from the patient supply line 40.

In practice, the above-described predictive control algorithm has been found to produce an ^{82}Rb activity concentration that closely matches the desired target profile $C_M(t)$, except during the first few seconds of the elution, where significant prediction errors may occur. In cases where all of the activity from the generator must be eluted to reach the requested total dosage, this error must be tolerated. However, in other cases it is possible to eliminate the error by delaying the start of the "elution" mode of operation. Thus, for example, during the "waiting for threshold", mode, the detected activity level C_{det} can be monitored and compared to a threshold (e.g. 90% of the target concentration C_M). When the threshold level is reached, the generator valve control loop 42 begins operating as described above with reference to FIGs. 8a and 8b, but the patient valve 24 remains closed so that active

solution continues to be routed to the waste reservoir 26. After a predetermined delay, the patient valve 24 opens to begin supplying active saline solution to the patient outlet 10. The duration of the delay may be calculated based on the relative activity of the elution. For example, in elutions in which the target activity concentration C_M is less than 10% of the maximum concentration that the generator 8 can produce, a delay of about 10 seconds may be used. Conversely, for elutions in which the target activity concentration C_M is more than about 70% of the maximum concentration that the generator 8 can produce, no delay may be required. For elutions in which the target activity concentration lies between these two limits, an intermediate delay may be calculated.

As described above, the predictive control algorithm uses stored generator performance data to model the generator performance and thereby enable prediction of a valve flow ratio (or, equivalently duty cycle) that will yield the target activity concentration C_M (or C'_M) at the positron detector 20. One way of obtaining the generator performance data is to calibrate the elution system 14 by performing a predefined elution run with the patient outlet 10 connected to a conventional dose calibrator (e.g. a Capintec CRC-15). Such a calibration elution run enables the dose calibrator to be used to measure the generator performance in terms of, for example, ^{82}Rb activity concentration vs. eluted volume. This data can be used to predict eluted ^{82}Rb activity concentration, for any given saline flow rate, with an accuracy that that will gradually decline with time elapsed since the calibration run. Repeating the calibration run at regular intervals (e.g. once per day) allows the generator performance data to be updated to track changes in the generator performance as

the generator 8 ages, and thereby enable accurate flow ratio prediction between successive calibration runs. If desired, calibration elutions can be scheduled to run automatically, for example as part of a daily protocol, which ensures system accuracy and at the same time limiting the potential for human error.

Preferably, calibration elution runs are performed at the same flow rate (e.g. 15ml/min), and over the same duration (e.g. 1 minute). This enables the known half-life of the ^{82}Rb (76 seconds) to be used to predict the decay time of activity detected by the dose calibrator. A difference between the predicted and actual decay times indicates breakthrough of ^{82}Sr. Accordingly, ^{82}Sr breakthrough can be automatically detected as part of a scheduled system calibration protocol, by sampling the activity level in the dose calibrator at regular intervals throughout the duration of each calibration elution run, and for a predetermined period following completion of the calibration run. The resulting calibration data tracks the activity level within the dose calibrator, as both a function of time and active saline solution volume. Calibration data collected during the elution enables prediction of the ^{82}Rb decay curve after the elution has stopped. Comparison between this predicted decay curve and the calibration data collected after the elution enables detection of ^{82}Sr breakthrough.

The calibration data collected during the elution can also be used to calculate the proportionality constant K between the activity parameter C_{det} and the ^{82}Rb activity concentration. In particular, the instantaneous activity detected by the dose calibrator during the calibration elution is the convolution of the activity concentration

and the well known ^{82}Rb decay curve. Since the saline volumetric flow rate is known, the calibration data collected during the elution can be used to calculate the actual activity concentration of the active saline solution entering the dose calibrator, and thus the proportionality constant K.

In the foregoing description, the predictive control algorithm uses stored generator performance data to predict a valve duty cycle that will yield the target activity concentration C_M (or C'_M) at the positron detector, and this estimate is used to control the generator valve 16. An error ΔC between the detected concentration parameter C_{det} the target activity concentration C_M is then calculated and used to adjust the flow ratio (duty cycle) of the generator valve 16. This error may also be used as data input for a self-tuning algorithm for updating the generator valve response parameters. This functionality is useful for ensuring accuracy of the predictive control algorithm, as well as compensating valve performance changes due, for example, to component aging and wear.

In some embodiments, the self-tuning algorithm uses error data accumulated over a number of elution runs. Thus, for example, during each elution run, desired flow ratios can be calculated (e.g. based on the saline flow rate, target activity concentration C_M and stored generator performance data) and error function ΔC values stored as a function of desired flow ratio. Accumulation of error value vs. flow ratio data over a number of elution runs can then be processed to obtain a slope error ΔL. This error value can then be used to incrementally adjust the flow ratio vs. duty cycle slope parameter L of the value so as to drive the slope error ΔL toward zero.

The upper duty cycle limit Π_{max} may be adjusted based on error data accumulated during elutions in which the predicted activity concentration from the generator cannot satisfy the desired target value C_M. This situation can occur during elution runs conducted toward the end of the useful life of the generator 8, when the ^{82}Rb production rates are at their lowest. When the predicted activity concentration from the generator 8 is less than the desired target value C_M, the predictive control algorithm will operate to set the duty cycle at its upper limit value Π_{max}. In this condition, if the measured concentration parameter C_{det} is less than the target value C_M, the error function value ΔC will be a non-zero value, and the corrective loop (FIG. 8a) will attempt to further increase the duty cycle. If no further increase in the concentration parameter C_{det} occurs (as indicated by a change in the function value ΔC), then the upper limit value Π_{max} may be reduced by a predetermined step size (e.g. 10^{-5}). On the other hand, if operation of the corrective loop does produce an increase in the detected concentration C_{det}, the slope of the error data can be used to increase the upper limit value Π_{max}.

If desired, a similar approach can be used to correct for hysteresis of the valve 16. Hysteresis refers to a system behaving differently depending on the direction of change of an input parameter, usually involving a delayed response. In the case of a bi-state pinch valve of the type illustrated in Fig. 4 the opening and closing latencies may differ. This valve hysteresis manifests itself in the threshold-based elution control algorithm described above with reference to FIG. 7, and appears as a difference between a predicted elution duration (required to achieve a desired eluted activity dose) and the actual elution duration required to obtain that dose.

Accordingly, by monitoring the actual elution time for "total activity dose"-type elution runs, it is possible to calculate a hysteresis factor H, which can be applied to the threshold set point (i.e. the target activity concentration C_M) to compensate the valve hysteresis.

In the foregoing embodiments, the generator valve is controlled as a bi-state valve, which is either "on" to direct all of the saline solution flow into the generator 8; or "off" to direct all of the saline solution flow into the bypass line 18. In the embodiment of FIG. 7, the generator valve 16 is controlled in precisely this manner, in response to a threshold comparison. In the embodiment of FIG. 8, the valve 16 is cycled continuously at a predetermined frequency (e.g. 5Hz) and the duty cycle adjusted to emulate a continuously (or step-wise) variable proportioning valve. Both of these methods of valve control are particularly suited to embodiments in which the valve of FIG. 4, for example, is controlled by a solenoid and a spring. However, it will be appreciated that a continuously variable valve could be used, if desired. For example, the position of the valve of FIG. 4 could be controlled by a servo-motor, in which case accurate proportioning of saline flow between the generator and bypass lines could be obtained without cycling the valve between "on" and "off" states. Clearly, use of different generator valve control techniques would imply corresponding differences in the valve control signal and response parameters. However, based on the teachings provided herein, it is considered that all such modifications will be well within the purview of those of ordinary skill in the art, and therefore are contemplated within the scope of the present invention.

The embodiment(s) of the invention described above is(are) intended to be exemplary only. The scope of the invention is therefore intended to be limited solely by the scope of the appended claims.