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.

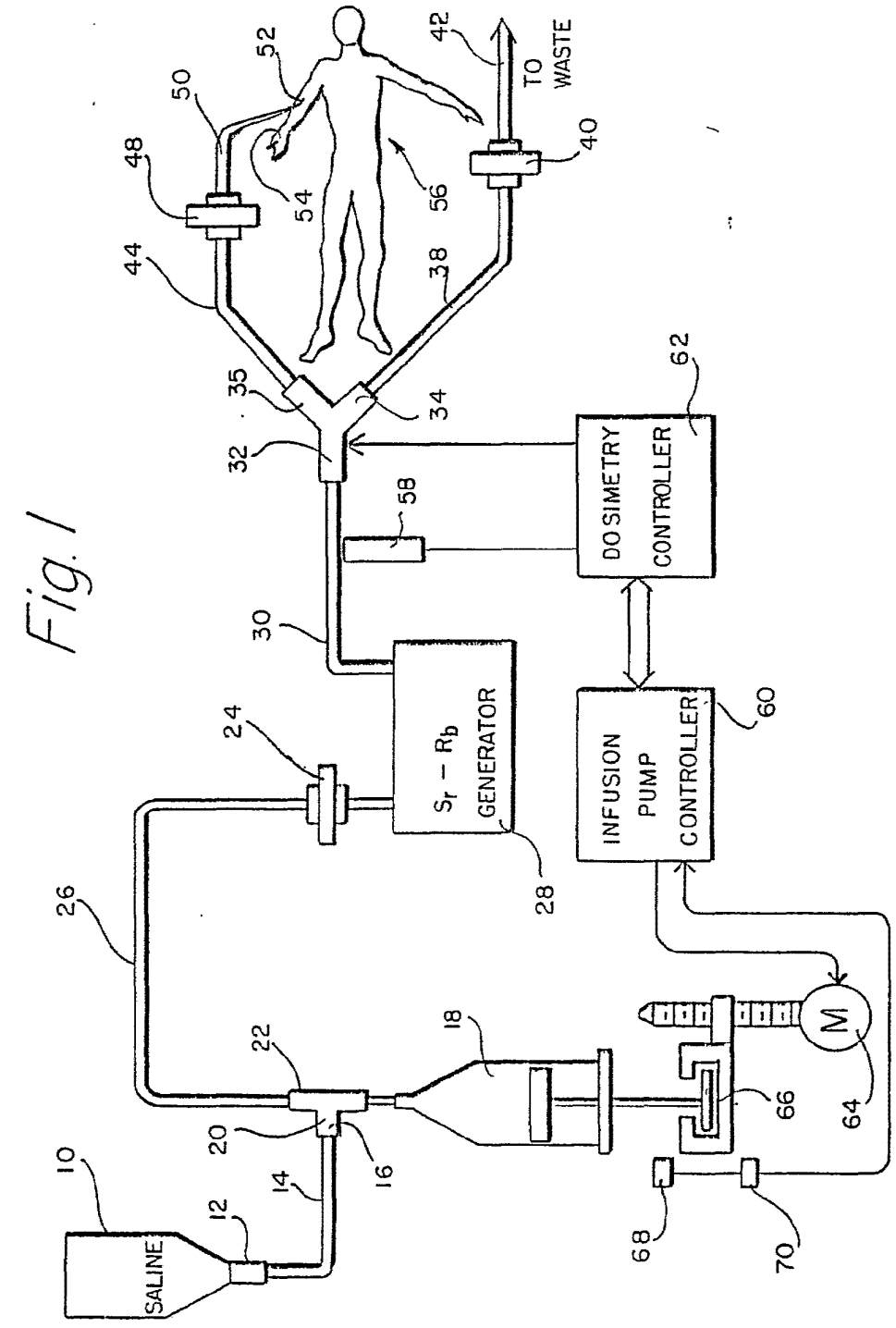
TO WASTE
42
40
52
50
48
54
56
44
38
35
34
32
62
DOSIMETRY CONTROLLER
58
30
$S_r - R_b$ GENERATOR
28
24
INFUSION PUMP CONTROLLER
60
26
M
64
66
18
22
20
16
14
10
12
SALINE
68
70

Fig. 1

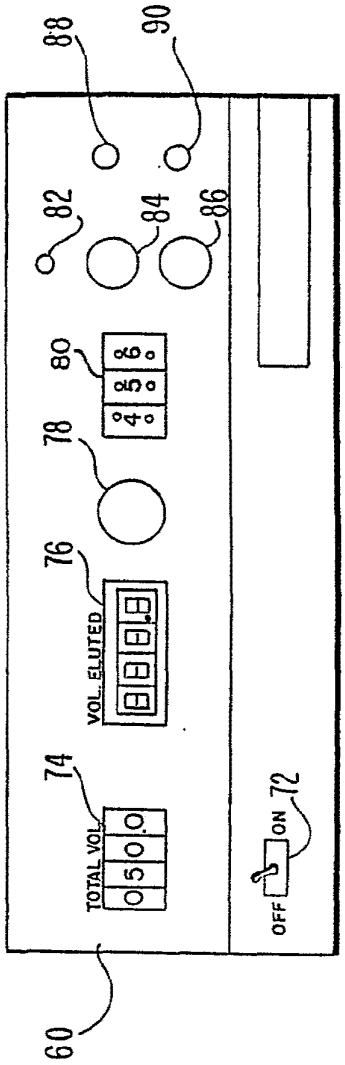
88
90
82
84
86
80
78
76
74
TOTAL VOL
VOL. ELUTED
ON
OFF
72
60

Fig. 2

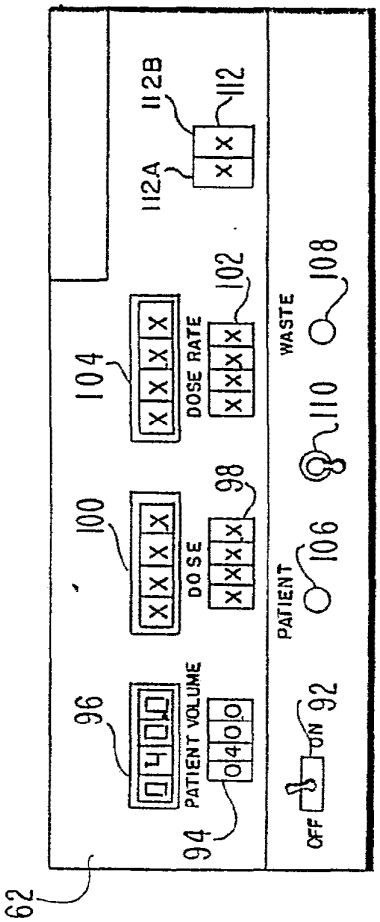
112B
112A
112
104
DOSE RATE
102
108
WASTE
110
100
DOSE
98
PATIENT
106
96
PATIENT VOLUME
94
ON
92
OFF
62

Fig. 3

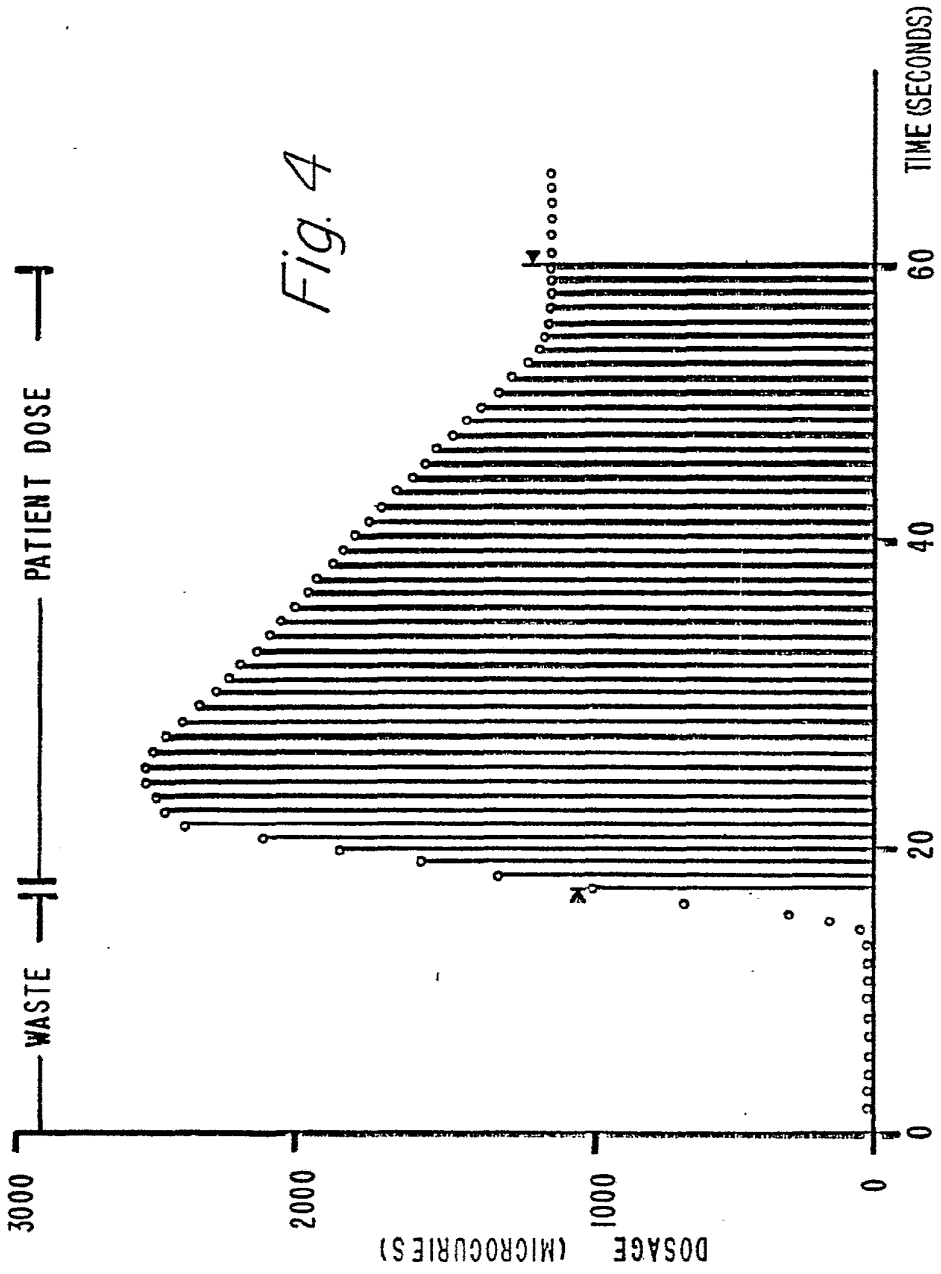
WASTE
PATIENT DOSE
3000
2000
1000
0
DOSAGE (MICROCURIES)
0
20
40
60
TIME (SECONDS)

Fig. 4

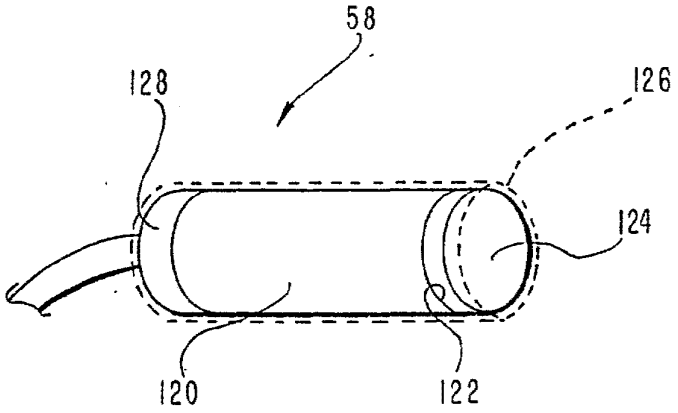
58
128
126
124
120
122

Fig. 5

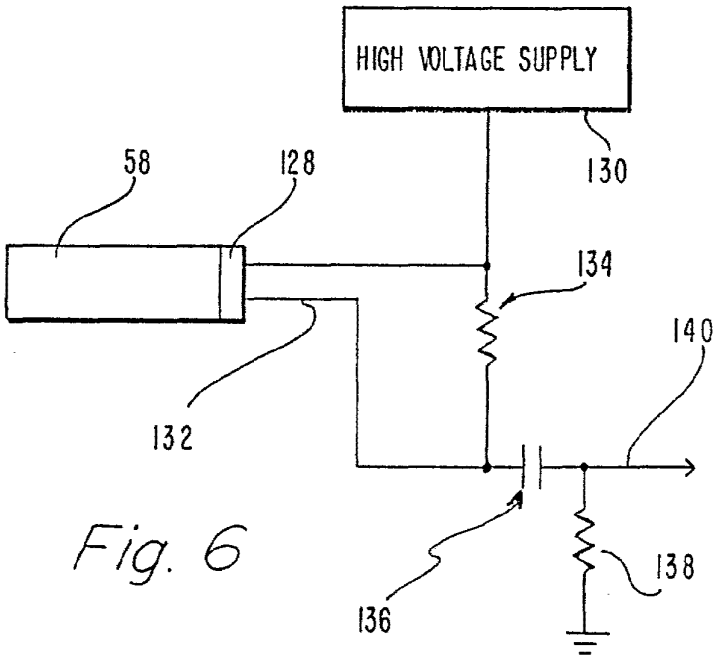
HIGH VOLTAGE SUPPLY
130
58
128
134
140
132
136
138

Fig. 6

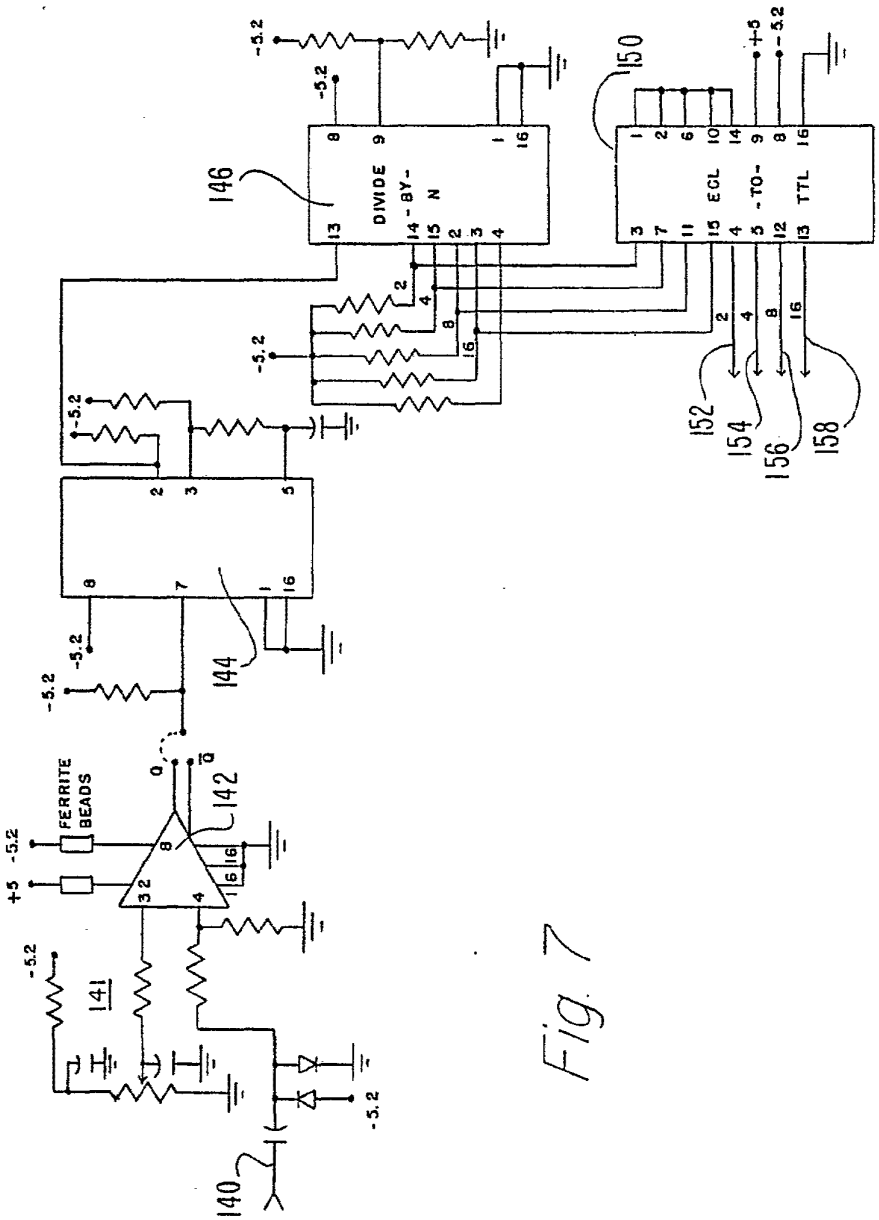
-5.2
146
DIVIDE
-BY-
N
150
ECL
-TO-
TTL
+5
152
154
156
158
144
142
FERRITE
BEADS
141
140

Fig. 7

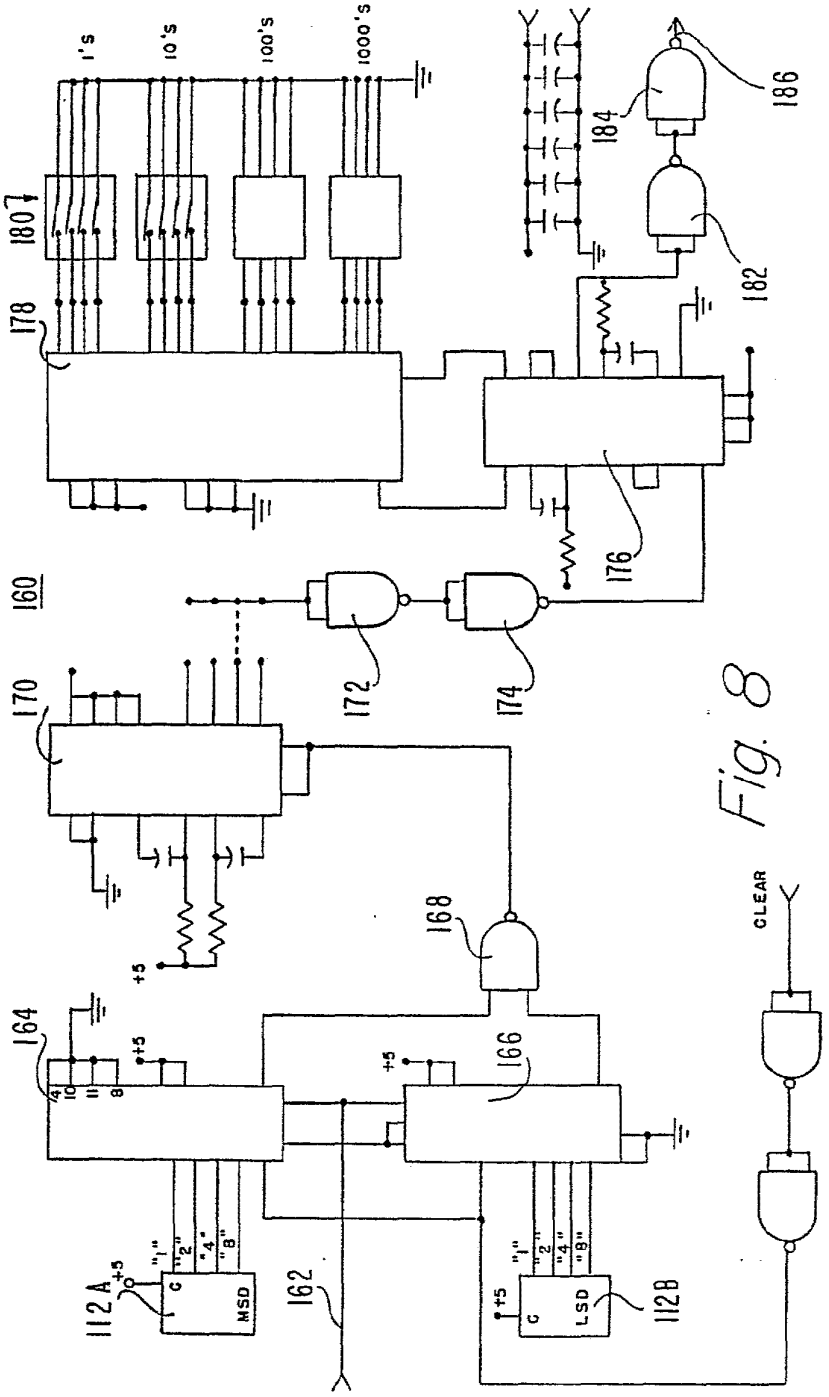
1's
10's
100's
1000's
180
178
184
186
182
176
160
172
174
170
168
164
166
+5
CLEAR
"1"
"2"
"4"
"8"
MSD
LSD
112A
112B
162

Fig. 8

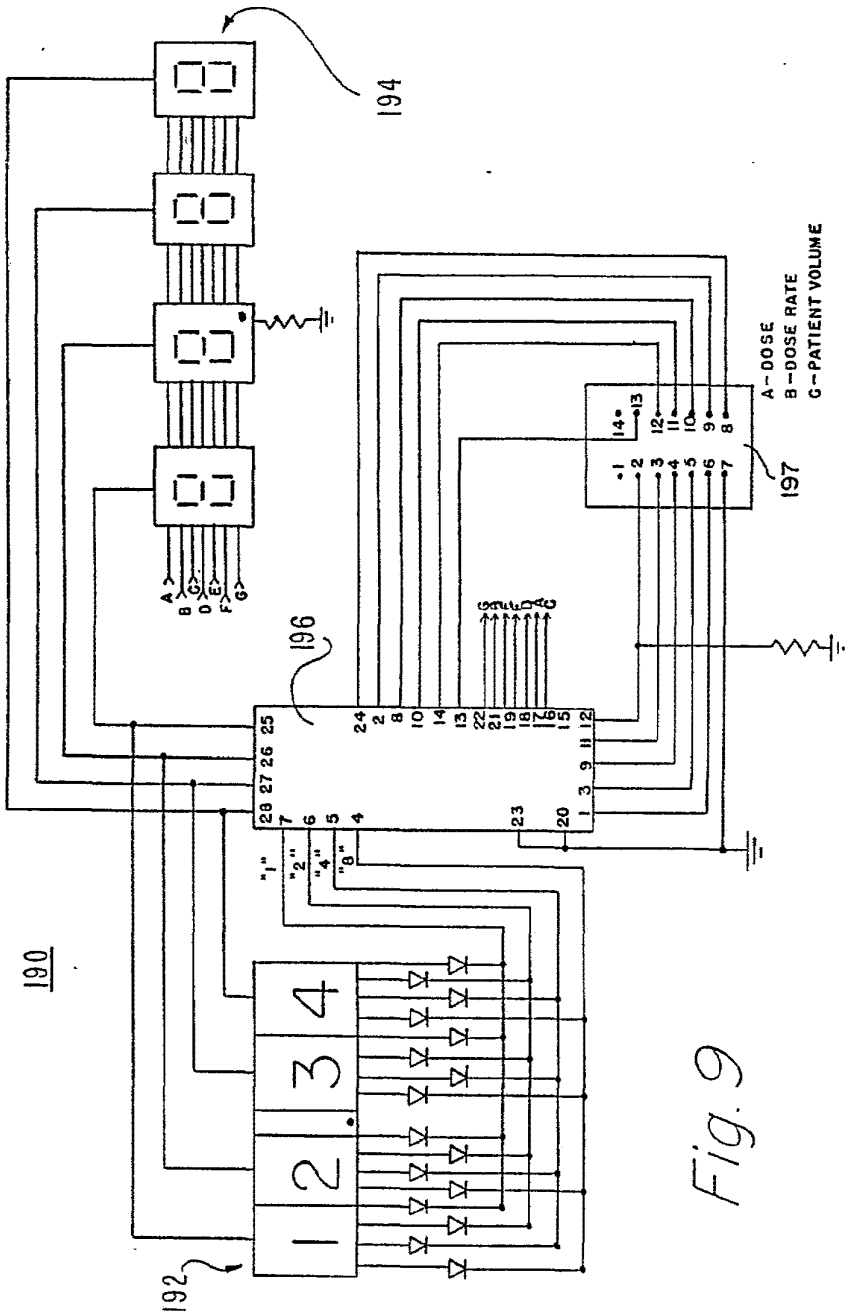
194
196
197
190
192
A-DOSE
B-DOSE RATE
C-PATIENT VOLUME
"1"
"2"
"4"
"8"
1
2
3
4

Fig. 9

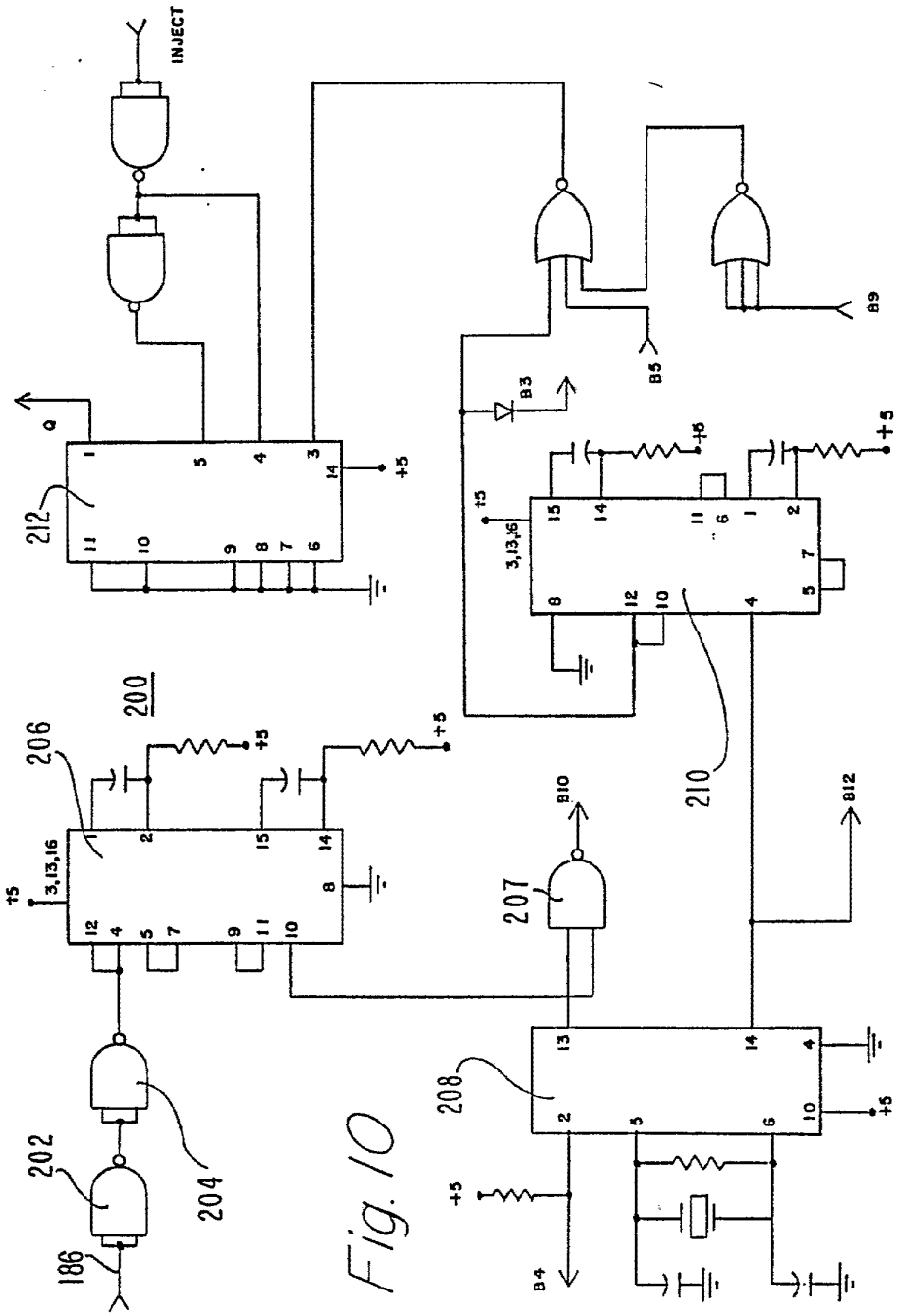
INJECT
200
206
212
202
204
186
207
208
210
B3
B4
B5
B9
B10
B12
+5
+15
3,13,16

Fig. 10

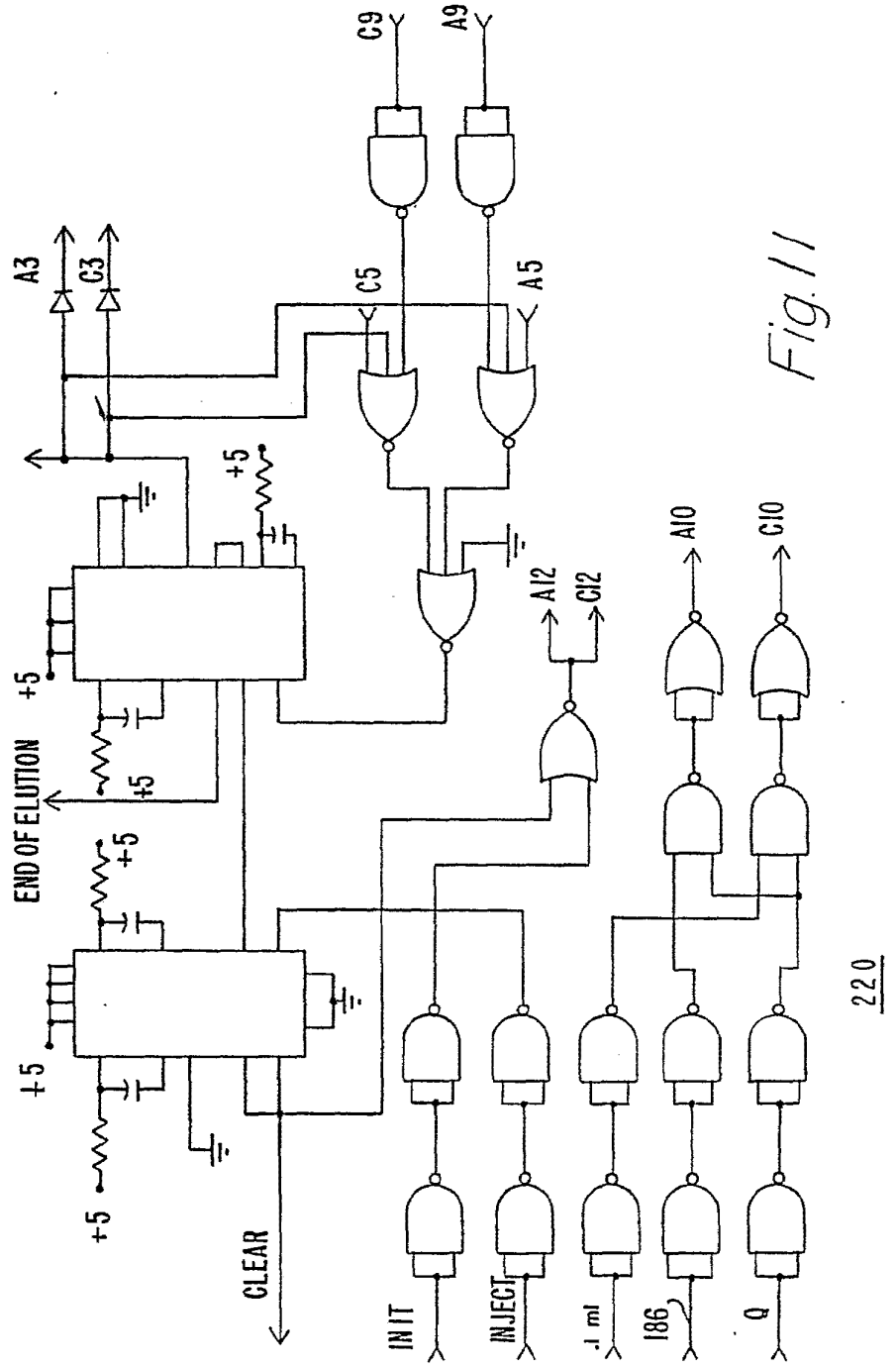
C9
A9
A3
C3
C5
A5
+5
A12
CI2
A10
C10
END OF ELUTION
CLEAR
INIT
INJECT
.1 ml
186
Q
220

Fig. 11

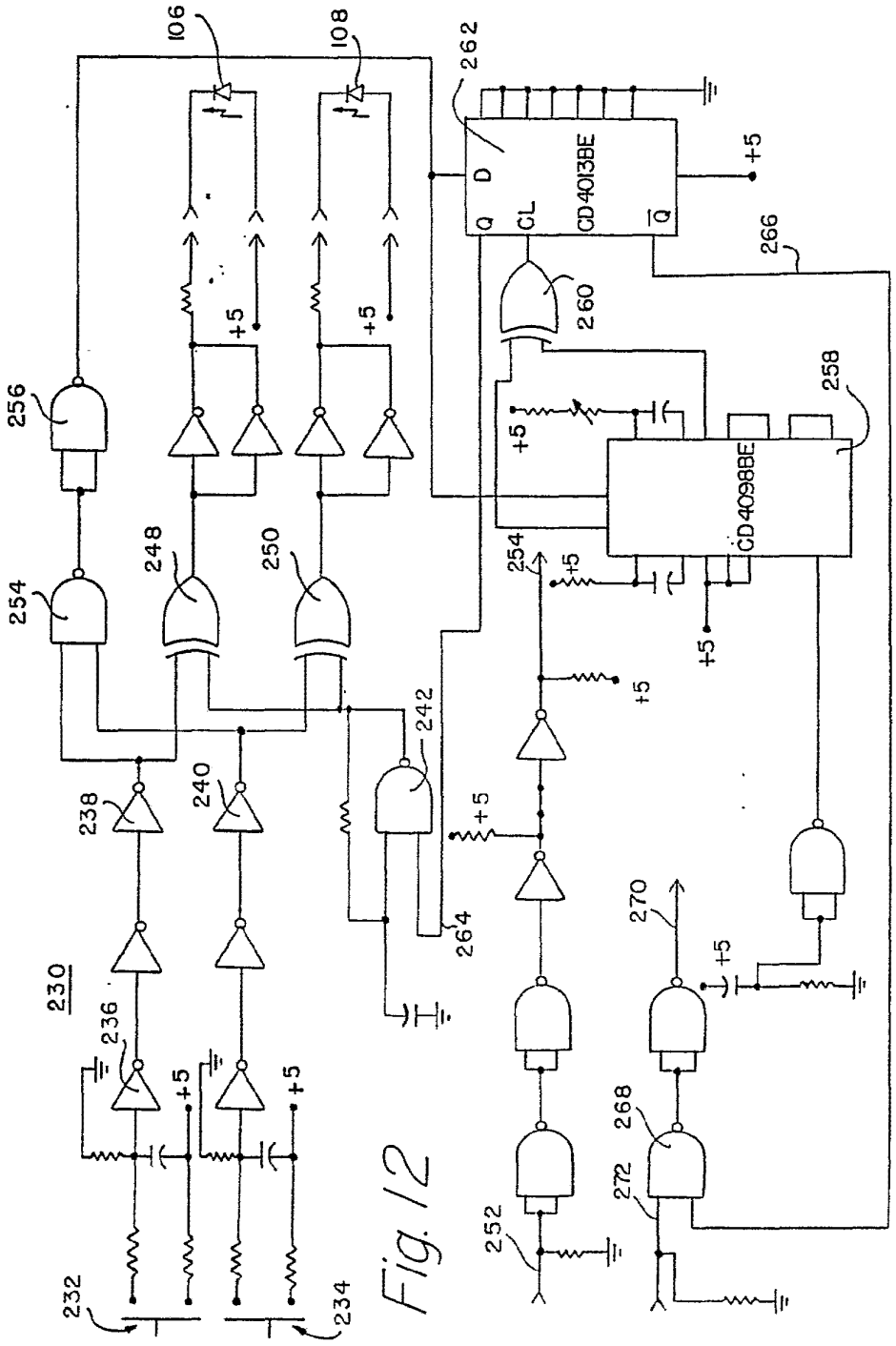
106
108
262
CD4013BE
D
Q
CL
Q
+5
266
260
256
258
CD4098BE
254
248
250
242
238
240
230
236
232
234
264
270
268
272
252

Fig. 12

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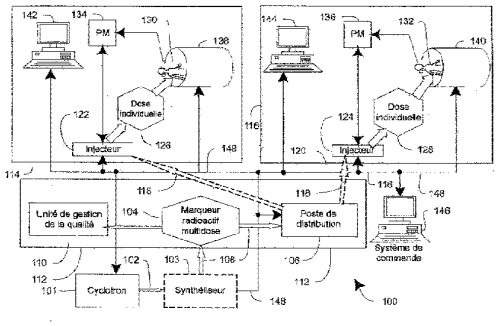
(54) SYSTEMES, PROCEDES ET APPAREILS DE PERFUSION DE PRODUITS RADIOPHARMACEUTIQUES.

(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.



FR 2 867 084 - A1

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.

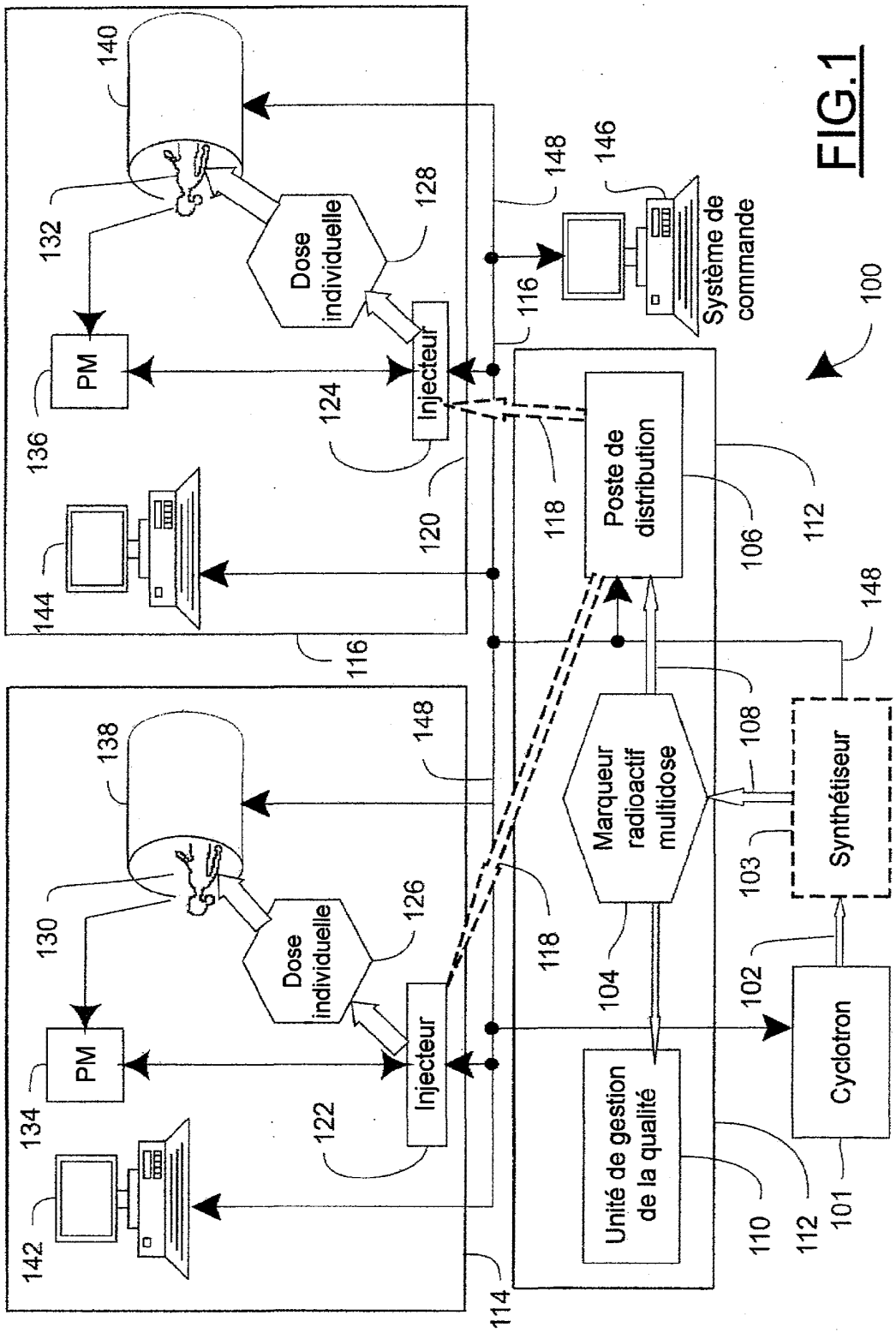

140
132
Dose individuelle
128
148
146
Système de commande
116
100
PM
136
124
Injecteur
120
118
Poste de distribution
106
112
144
116
148
138
Marqueur radioactif multidose
108
Synthétiseur
103
130
Dose individuelle
126
118
104
102
PM
134
122
Injecteur
Cyclotron
Unité de gestion de la qualité
110
112
101
142
114

FIG.1

FIG.2

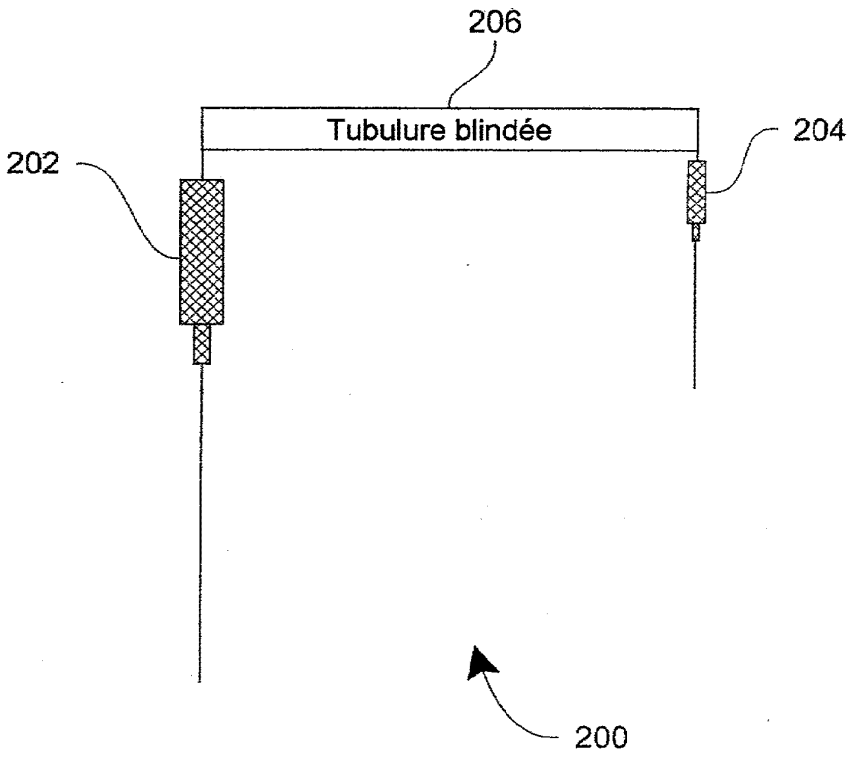
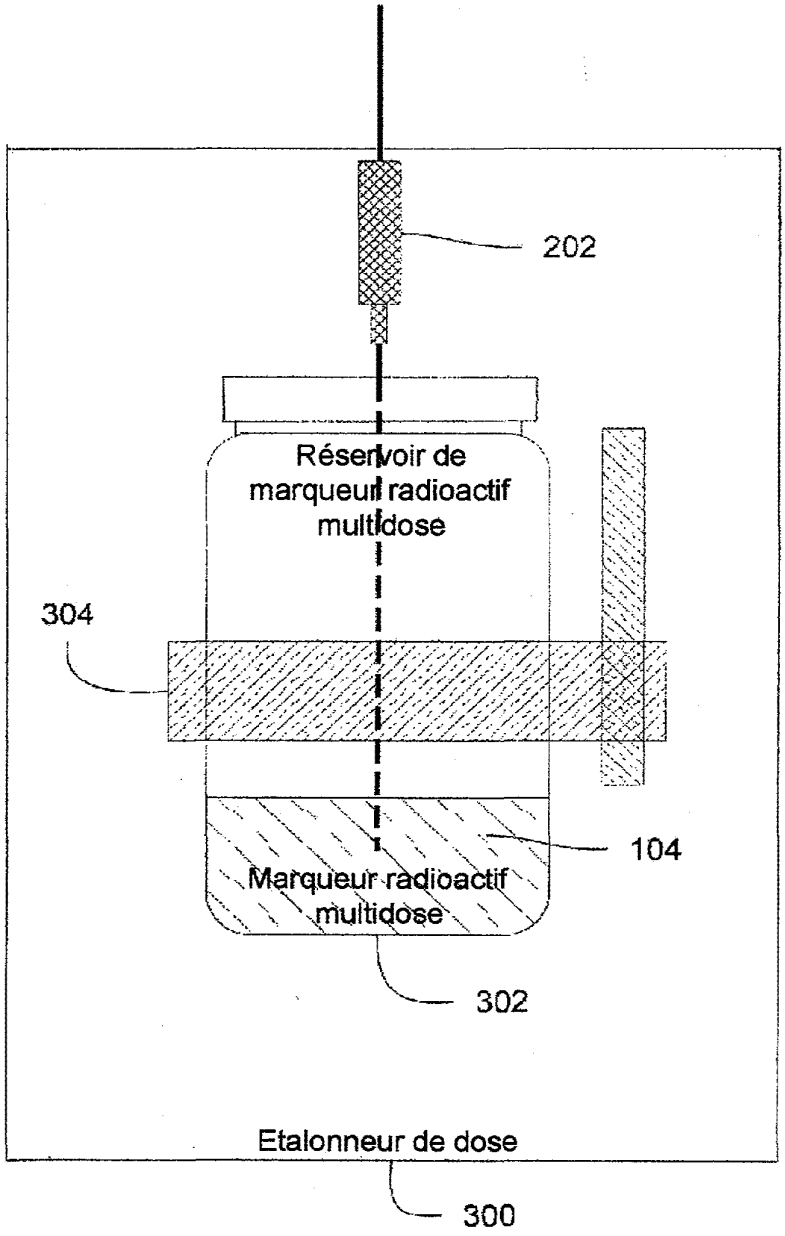


FIG.3


202
Réservoir de marqueur radioactif multidose
304
104
Marqueur radioactif multidose
302
Etalonneur de dose
300

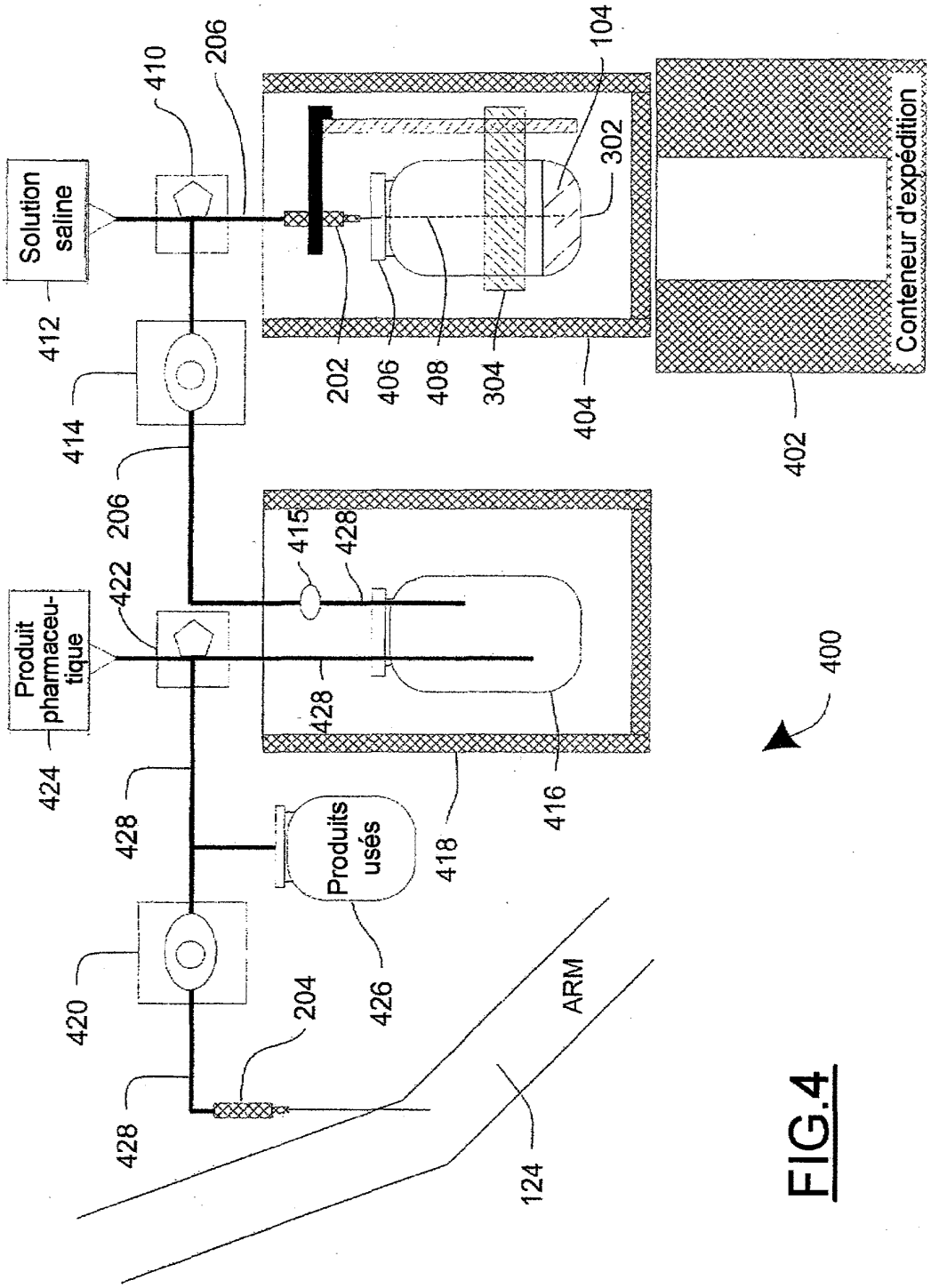

Solution saline
Produit pharmaceutique
Produits usés
Conteneur d'expédition
ARM
400
402
404
410
206
104
302
202
406
408
304
412
414
415
428
422
424
416
418
420
426
204
124

FIG.4

FIG.5

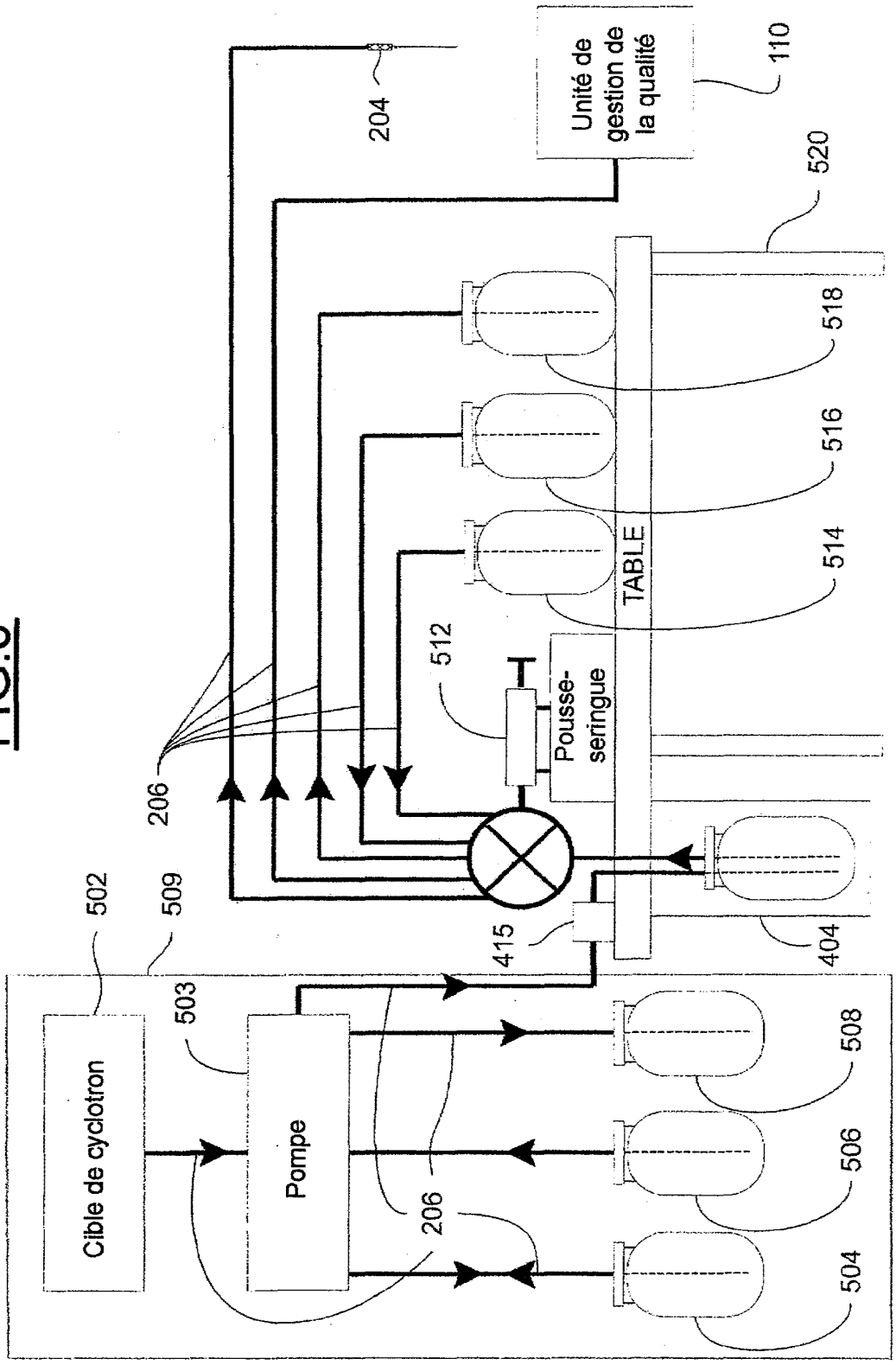

Unité de gestion de la qualité
110
204
520
518
516
514
TABLE
512
Pousse-seringue
206
502
509
503
415
404
Cible de cyclotron
Pompe
508
506
504
206

FIG.6

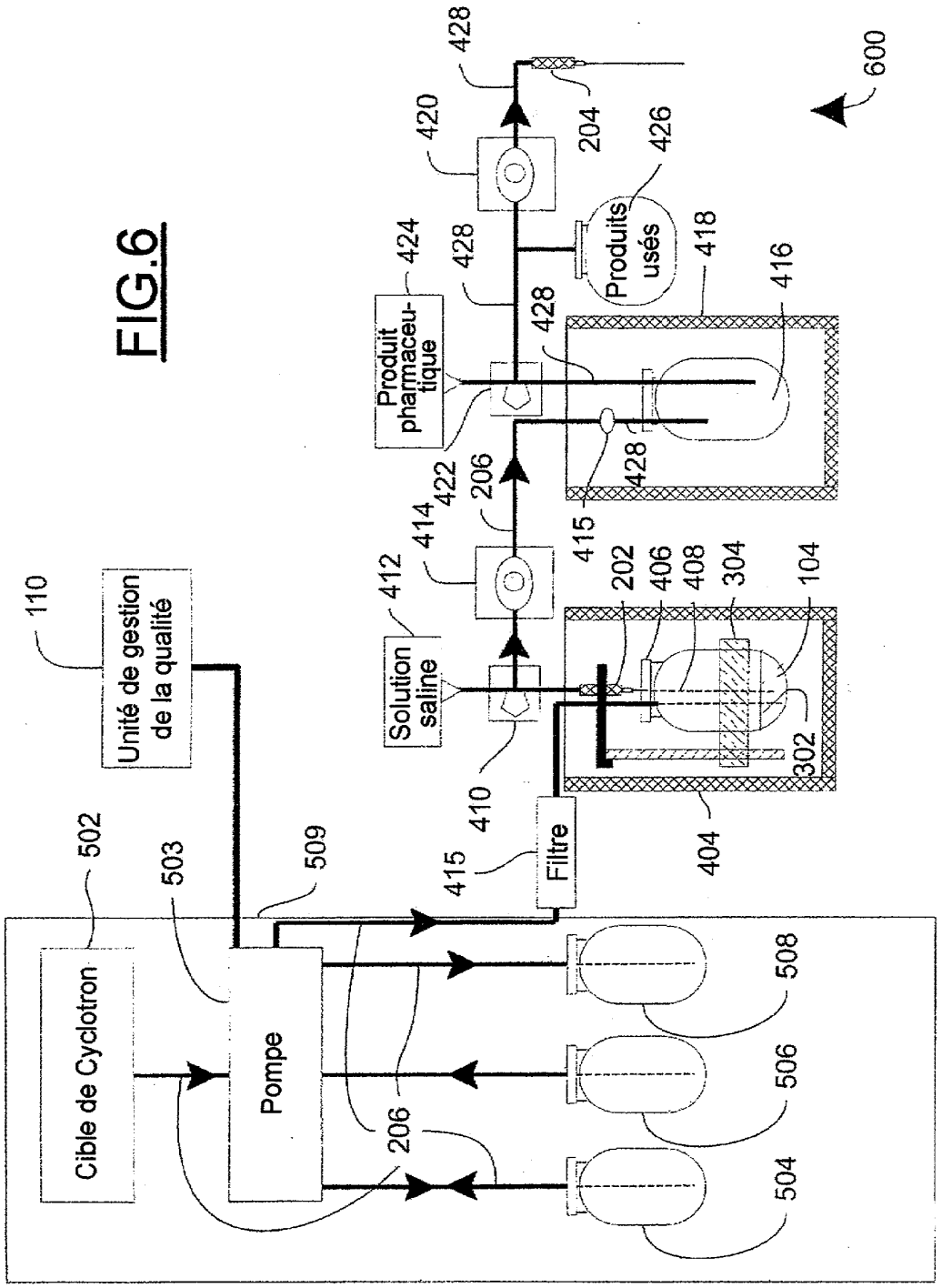

600
110
Unité de gestion de la qualité
502
Cible de Cyclotron
503
Pompe
509
206
504
506
508
Filtre
415
410
404
412
Solution saline
414
422
206
415
202
406
408
304
104
302
424
Produit pharmaceutique
428
420
428
204
426
Produits usés
418
416
428

FIG.7

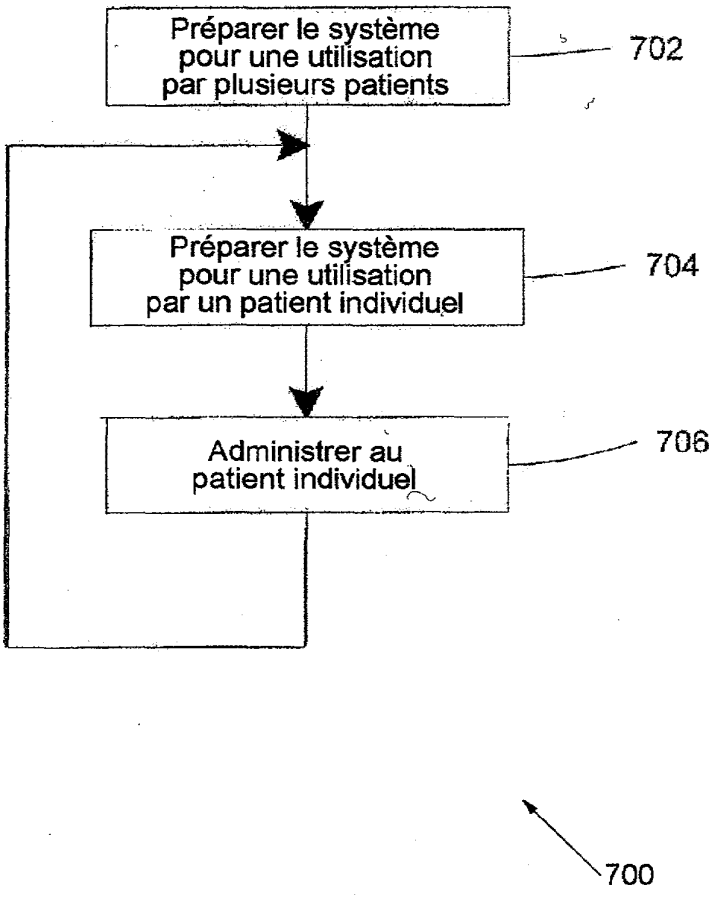

Préparer le système pour une utilisation par plusieurs patients
702
Préparer le système pour une utilisation par un patient individuel
704
Administrer au patient individuel
706
700

FIG.8

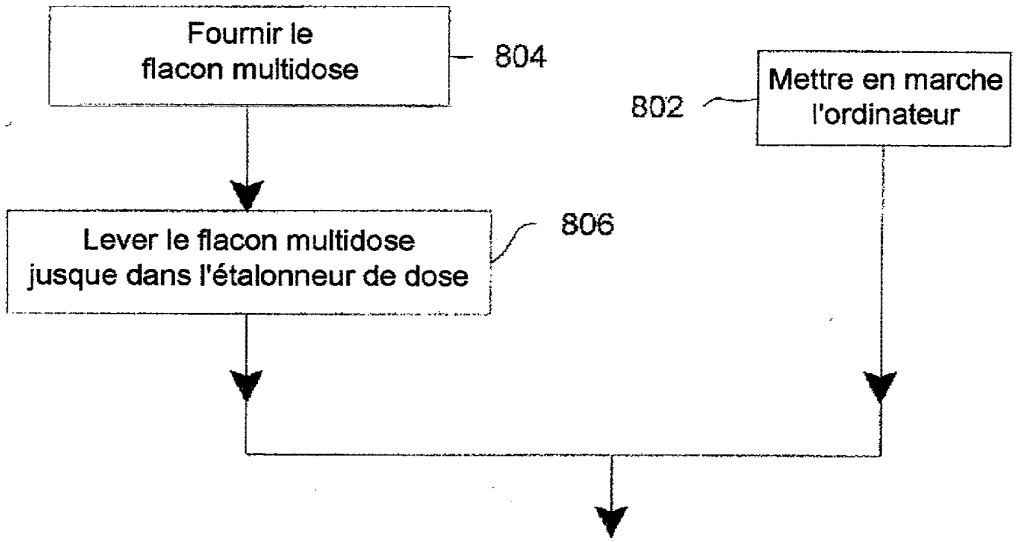

Fournir le flacon multidose
804
Mettre en marche l'ordinateur
802
Lever le flacon multidose jusque dans l'étalonneur de dose
806
800

FIG.9

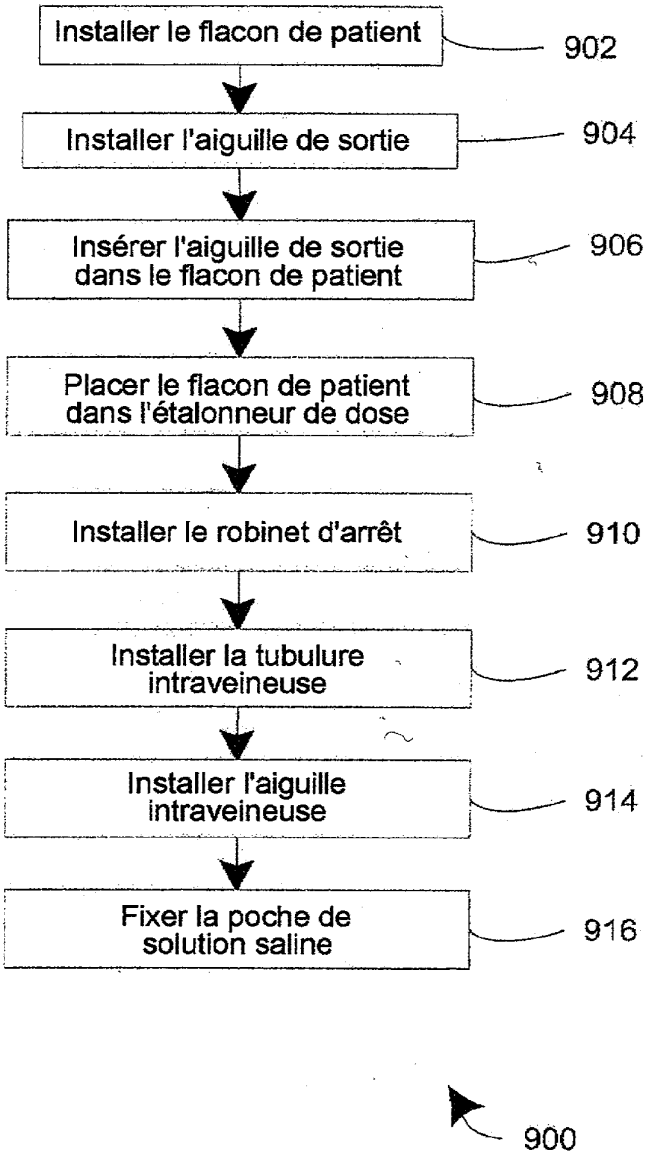

Installer le flacon de patient
902
Installer l'aiguille de sortie
904
Insérer l'aiguille de sortie dans le flacon de patient
906
Placer le flacon de patient dans l'étalonneur de dose
908
Installer le robinet d'arrêt
910
Installer la tubulure intraveineuse
912
Installer l'aiguille intraveineuse
914
Fixer la poche de solution saline
916
900

FIG.10

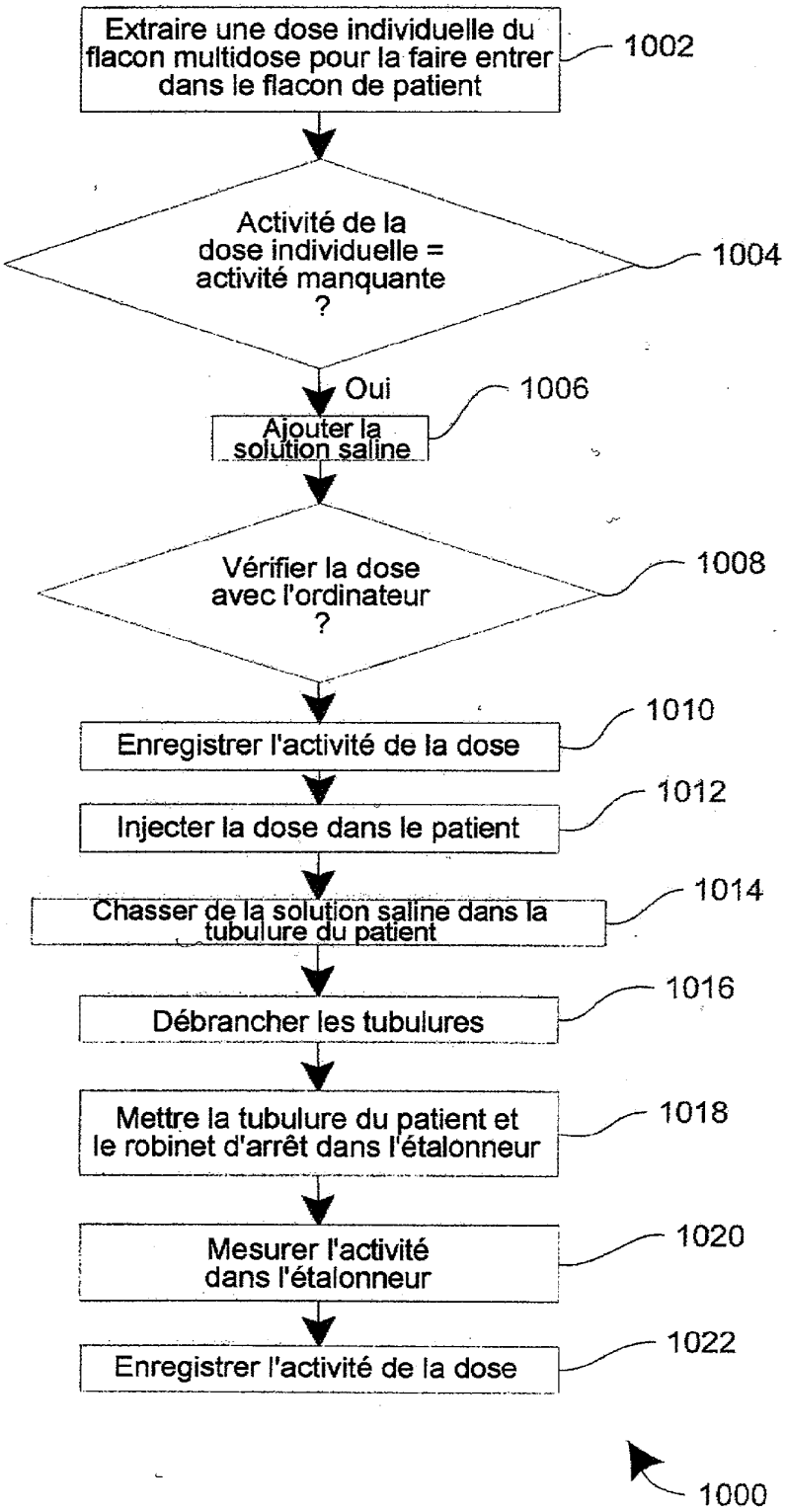
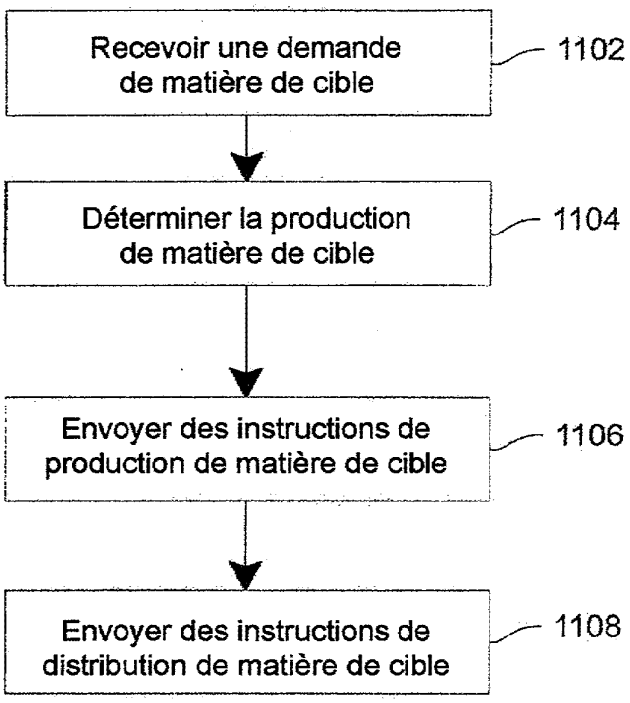

Extraire une dose individuelle du flacon multidose pour la faire entrer dans le flacon de patient
1002
Activité de la dose individuelle = activité manquante ?
1004
Oui
1006
Ajouter la solution saline
Vérifier la dose avec l'ordinateur ?
1008
Enregistrer l'activité de la dose
1010
Injecter la dose dans 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

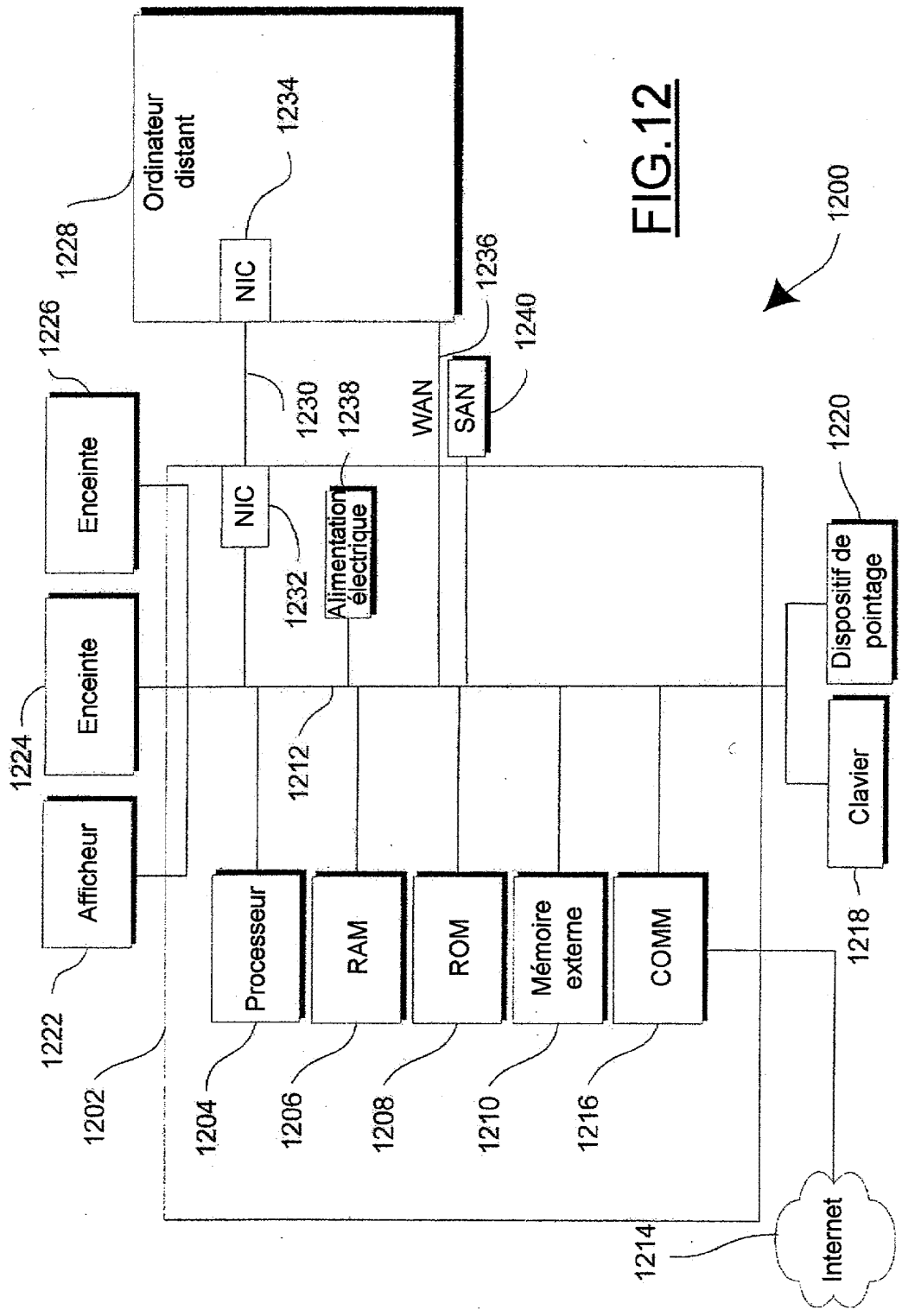

Ordinateur distant
1228
1234
NIC
1236
1240
WAN
SAN
1226
1230
1238
Enceinte
NIC
Alimentation électrique
1232
1220
Dispositif de pointage
1224
Enceinte
1212
Clavier
1218
Afficheur
1222
Processeur
RAM
ROM
Mémoire externe
COMM
1202
1204
1206
1208
1210
1216
1214
Internet
1200

FIG.12

Automatic injection system for radiopharmaceutical products, comprises an injector connected to an extractor that selects a dose of a radiopharmaceutical product

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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

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US2008242915 (A1)

JP2005326398 (A)

DE102005010154 (A1)

Cited documents:

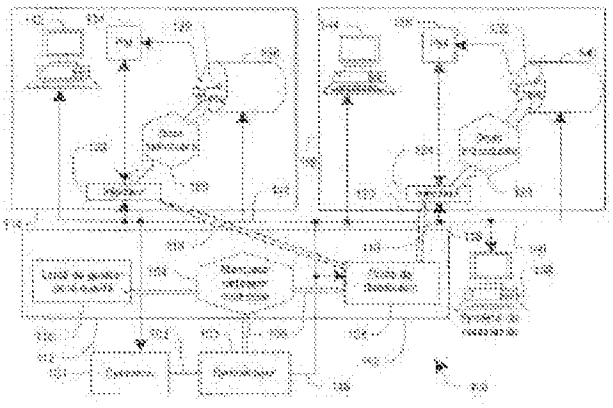
US2003004463 (A1)

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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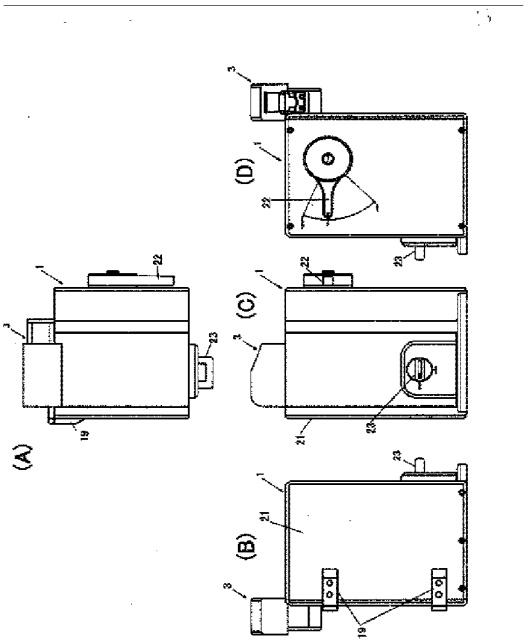
(54)【発明の名称】放射性薬剤吸引装置

(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。

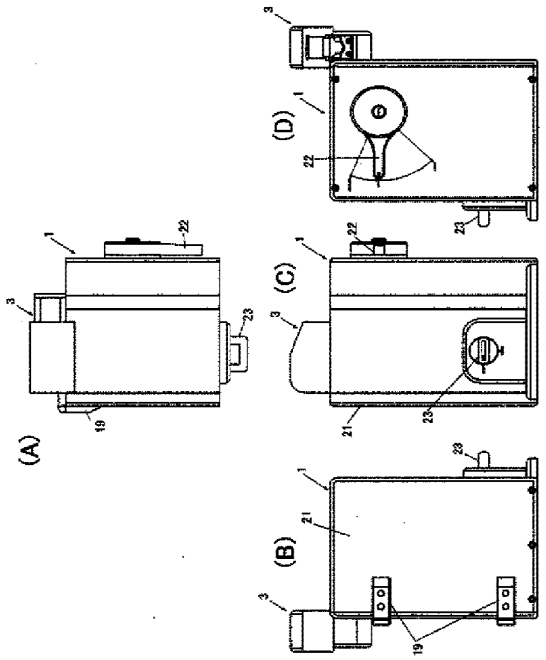
【図10】は図１のシリンジ用遮蔽器にシリンジが収納された状態を示す水平断面図である。

【符号の説明】

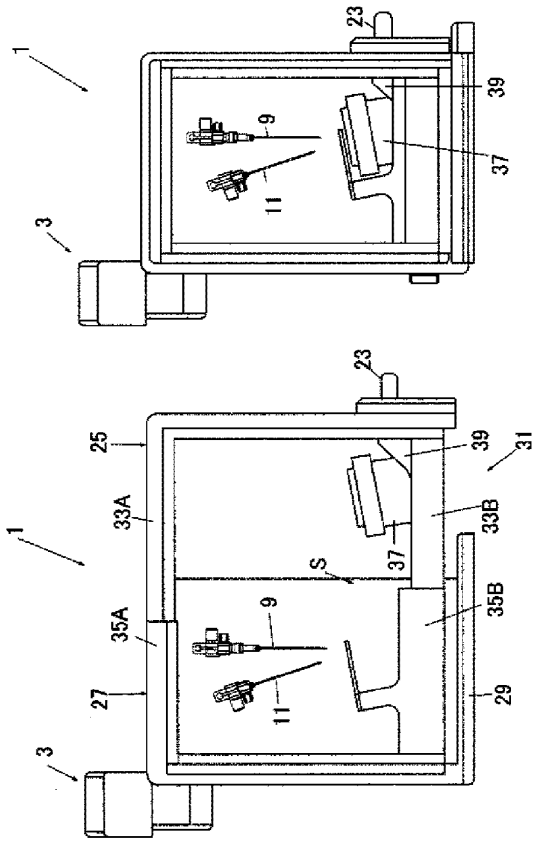
【0072】

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。

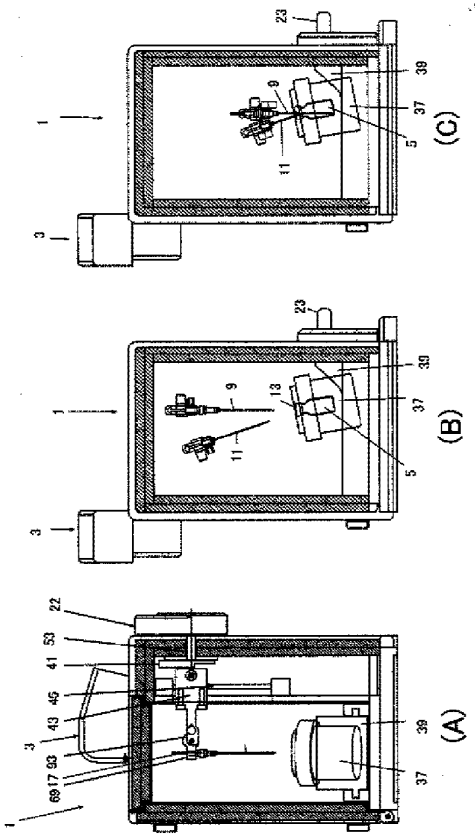
【図1】



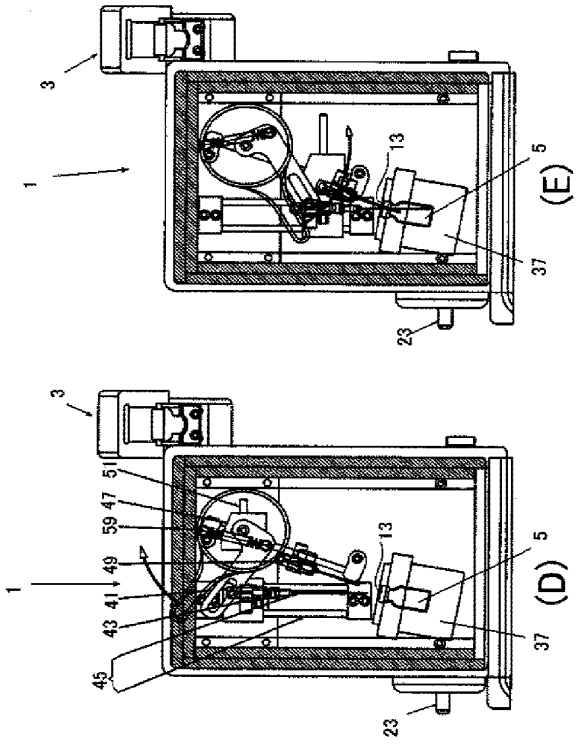
【図2】



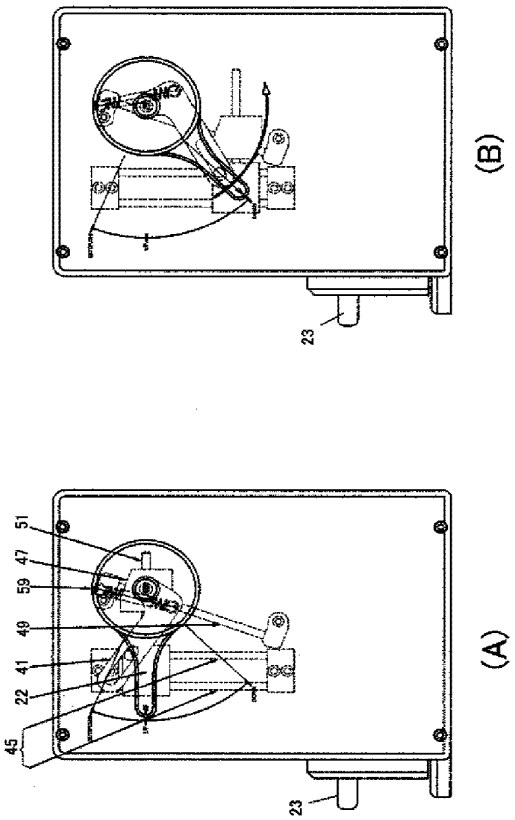
【図3】



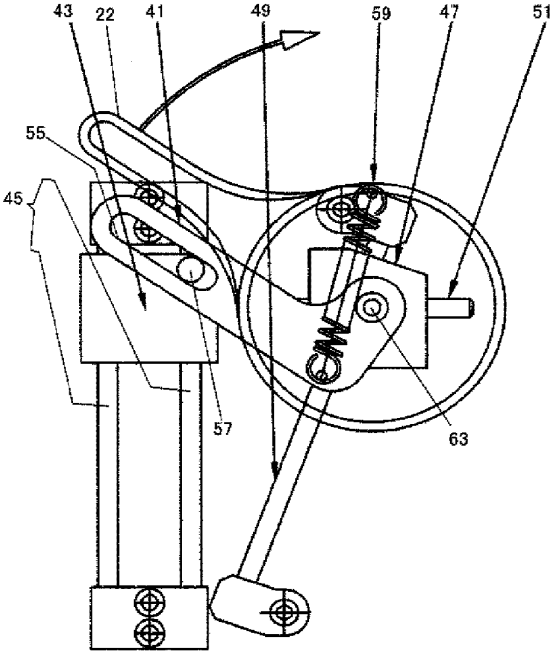
【図4】



【図5】


(B)
23
(A)
51
47
59
49
41
22
45
23

【図6】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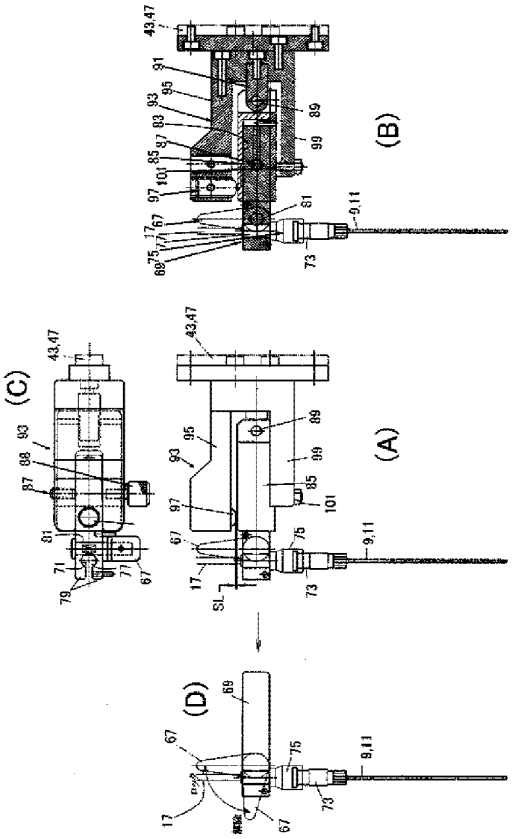
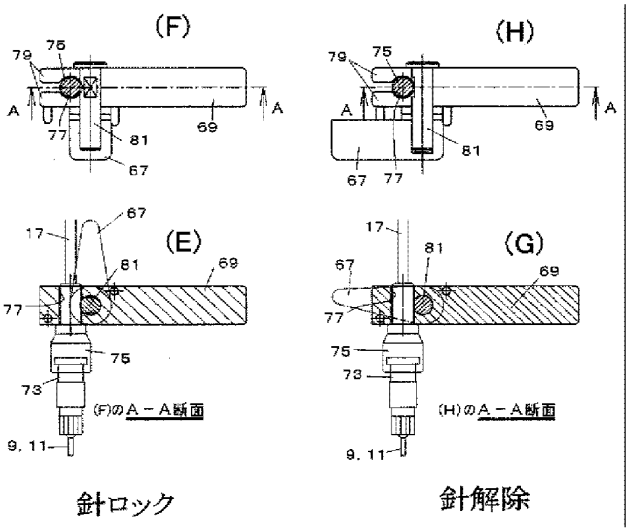
63

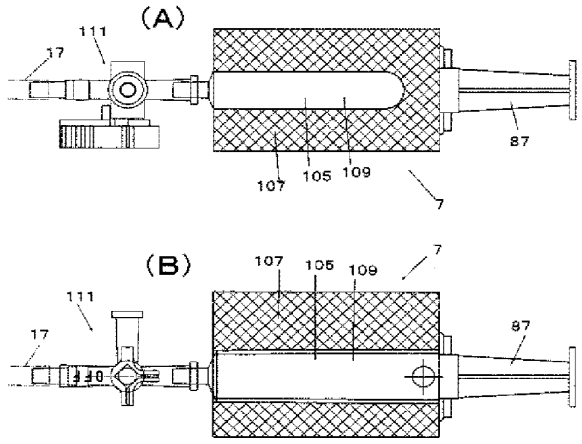
【図7】


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
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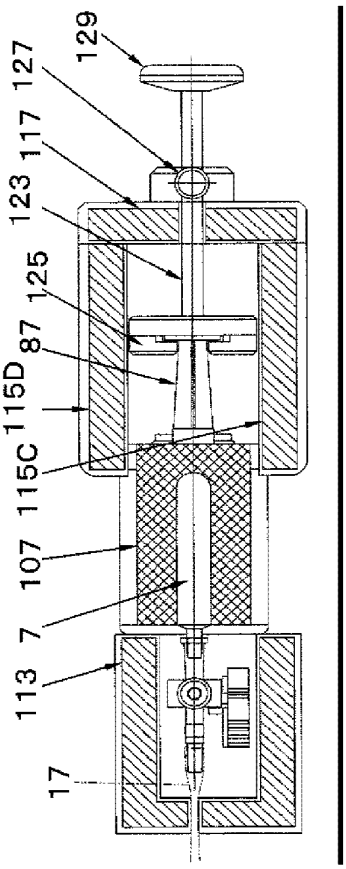
87
107
105
109
7
(B)
107
105
109
7
111
17
87

【図10】


129
127
117
123
125
87
115D
115C
107
7
113
17

Patent Abstracts of Japan

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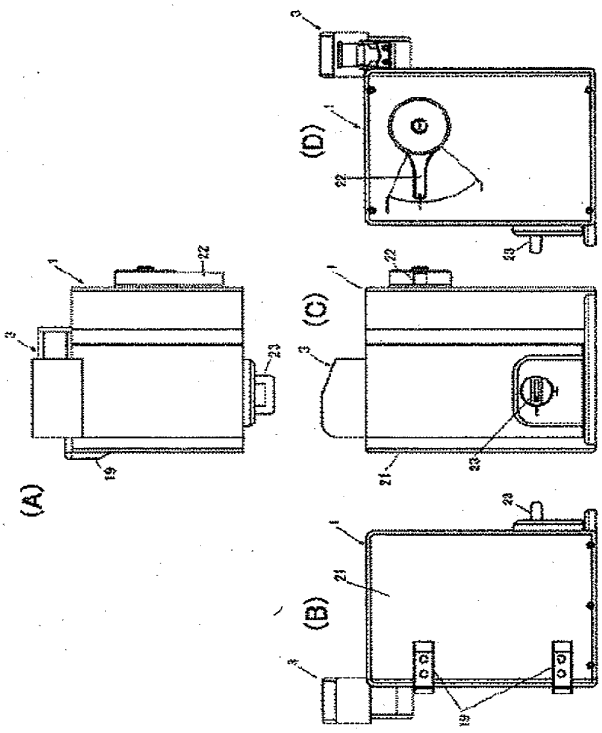
APPLICANT : SD GIKEN:KK;

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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	5/00	３２０		5/00	３２０	
		３３０			３３０	
Ｇ２１Ｇ	4/08		Ｇ２１Ｇ	4/08		

審査請求　未請求　請求項の数４　ＯＬ　（全 5 頁）

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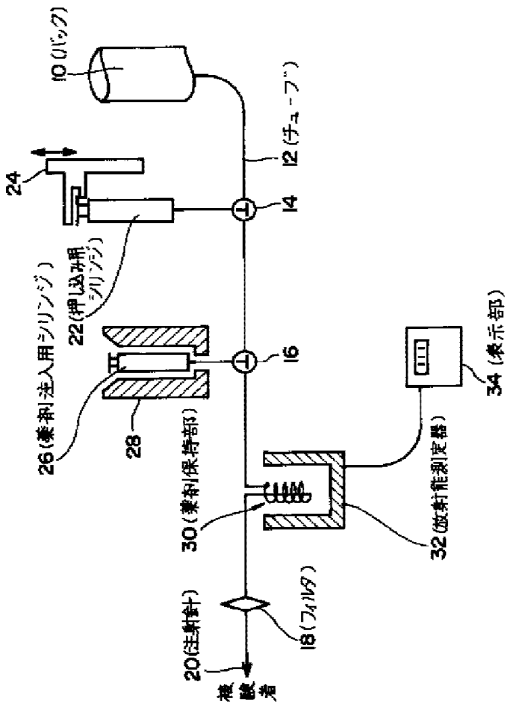
最終頁に続く

(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

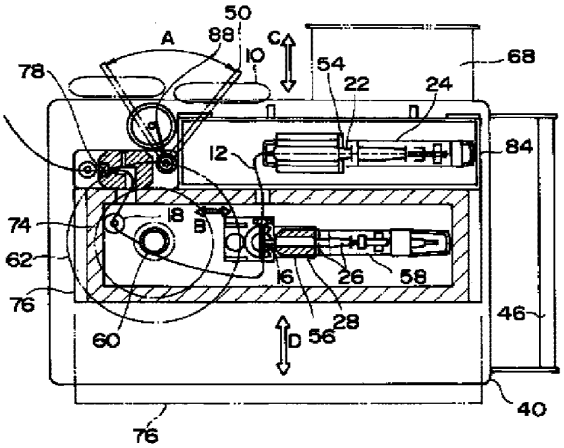
【図４】同じく右側面から見た縦断面図

【図５】同じく要部の背面図

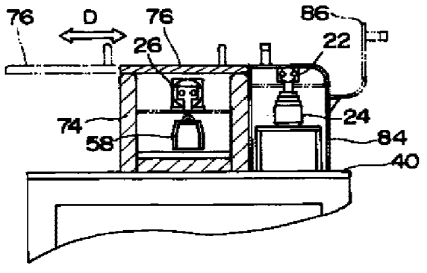
【符号の説明】

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

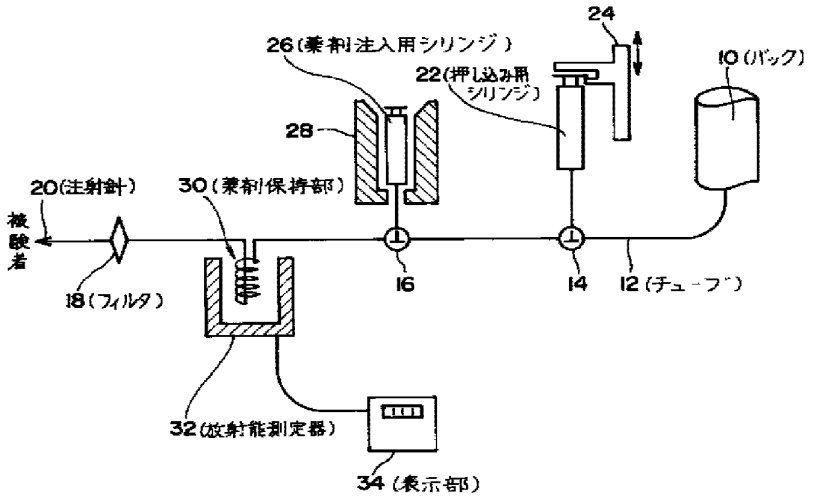
【図３】



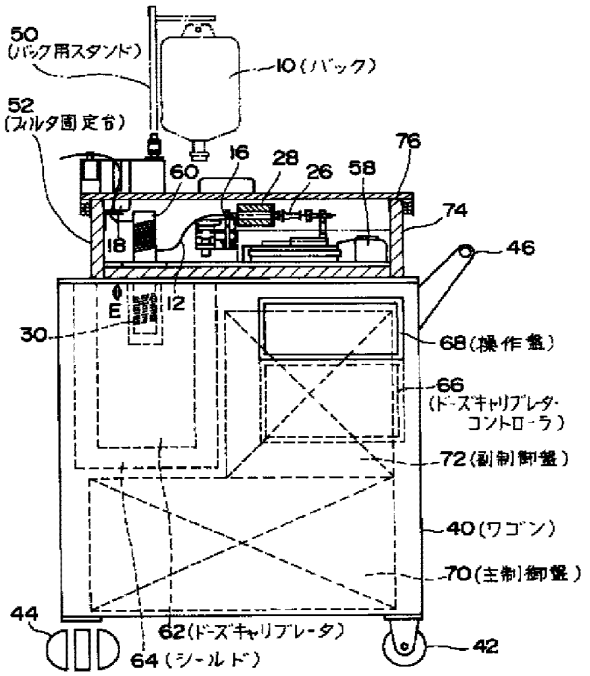
【図４】



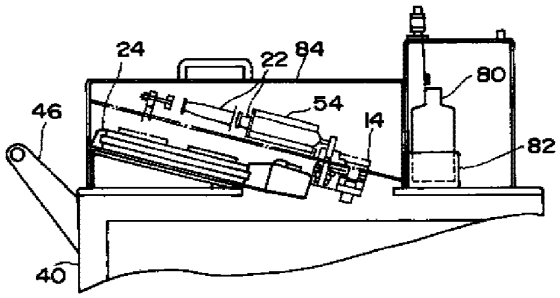
【図1】



【図2】



【図5】



フロントページの続き

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Ｆターム(参考)　4C066 AA07 BB01 CC03 DD12 FF05 HH02 LL06 LL19 QQ43

EUROPEAN PATENT OFFICE

Patent Abstracts of Japan

PUBLICATION NUMBER : 2000350783
PUBLICATION DATE : 19-12-00

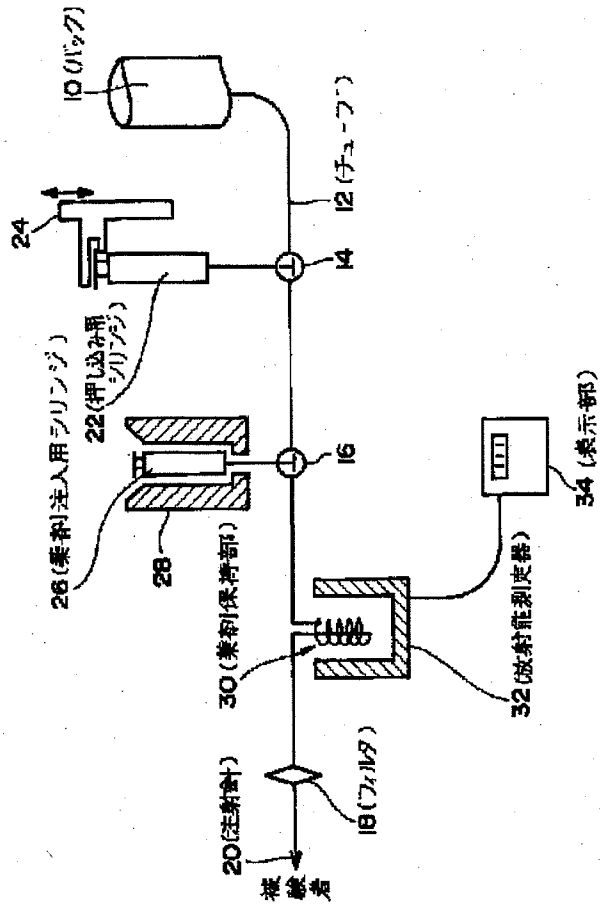
APPLICATION DATE : 14-06-99
APPLICATION NUMBER : 11166230

APPLICANT : SUMITOMO HEAVY IND LTD;

INVENTOR : SUZUKI TAKAFUMI;

INT.CL. : A61M 5/14 A61M 5/00 G21G 4/08

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.

Electronic Acknowledgement Receipt

EFS ID:	6276426
Application Number:	12137363
International Application Number:	
Confirmation Number:	7372
Title of Invention:	INFUSION SYSTEM CONFIGURATIONS
First Named Inventor/Applicant Name:	Charles R. Quirico
Customer Number:	22859
Filer:	Elisabeth Lacy Belden
Filer Authorized By:	
Attorney Docket Number:	56782.1.6
Receipt Date:	16-OCT-2009
Filing Date:	11-JUN-2008
Time Stamp:	14:27:59
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)	4thSIDS_56782-1-6.pdf	861897 49719eb510f032066710d432d8a0a849109788c6	no	5

Warnings:	
Information:	

2	Foreign Reference	WO9956117A1.pdf	1299254 021d516ba323664bf4eaa2984a9680b3f8779f83	no	31
Warnings:					
Information:					
3	Foreign Reference	WO2005002971A1.pdf	786004 74ebc85658451adab8f3d793213966aec617ac54	no	22
Warnings:					
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4	Foreign Reference	WO2006129301A2.pdf	8063321 ca5d9340c1342351071eb4c9a28f631424ab8dac	no	152
Warnings:					
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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
Warnings:					
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7	Foreign Reference	EP0160303A2.pdf	1600444 a1d4f192673b0413e221e8d53cf8298f7e894755	no	42
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8	Foreign Reference	EP0310148A2.pdf	940420 d65761328c609b56b84279ae9a8fbcc9784b741a	no	20
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9	Foreign Reference	FR2867084A1.pdf	2313624 ad8f4d54a0d08f1d0e2b34957241b7027f0e4914	no	46
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10	Foreign Reference	FR2867084Abstract.pdf	166387 5ee64633d0345f3c63dc0aa457047ec59bd40765	no	1
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Information:					

11	Foreign Reference	JP2006325826A.pdf	751423 6499fff7b8d76ffc068e84c28c4819d0a3c8d698	no	18
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12	Foreign Reference	JP2006325826Abstract.pdf	205713 f3bac4c407c20dc79a9f509eed83cf2af3d8ccc2	no	1
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13	Foreign Reference	JP2000350783A.pdf	250118 9299a2273b04952054d73dfdf73ee4373612caa0	no	5
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14	Foreign Reference	JP2000350783Abstract.pdf	205893 7c72b781cd4e5ab680721cefd817693c2310ace9	no	1
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National Stage of an International Application under 35 U.S.C. 371

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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	12137363
Filing Date	2008-06-11
First Named Inventor	Charles R. Quirico
Art Unit	3637
Examiner Name	
Attorney Docket Number	56782.1.6

U.S.PATENTS Remove

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	
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	8	5039863		1991-08-13	Matsuno et al.	

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	First Named Inventor	Charles R. Quirico
	Art Unit	3637
	Examiner Name	
	Attorney Docket Number	56782.1.6

	9	5258906		1993-11-02	Kroll et al.	
	10	5274239		1993-12-28	Lane et al.	
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137363
	Filing Date	2008-06-11
	First Named Inventor	Charles R. Quirico
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	Examiner Name	
	Attorney Docket Number	56782.1.6

	20	6901283	B2	2005-05-31	Evans, III et al.	
	21	7169135	B2	2007-01-30	Duchon et al.	
	22	7256888	B2	2007-08-14	Staehr et al.	
	23	7413123	B2	2008-08-19	Ortenzi	

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	1	20070282263	A1	2007-12-06	Kalafut et al.	
	2	20080071219	A1	2008-03-20	Rhinehart et al.	
	3	20080166292	A1	2008-07-10	Levin et al.	

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	Application Number	12137363
	Filing Date	2008-06-11
	First Named Inventor	Charles R. Quirico
	Art Unit	3637
	Examiner Name	
	Attorney Docket Number	56782.1.6

	1	2006007750	WO	A1	2006-01-26	UNIVERSITÄT ZÜRICH		☐

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137363
	Filing Date	2008-06-11
	First Named Inventor	Charles R. Quirico
	Art Unit	3637
	Examiner Name	
	Attorney Docket Number	56782.1.6

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Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ 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)	2009-07-15
Name/Print	Elisabeth Lacy Belden	Registration Number	50,751

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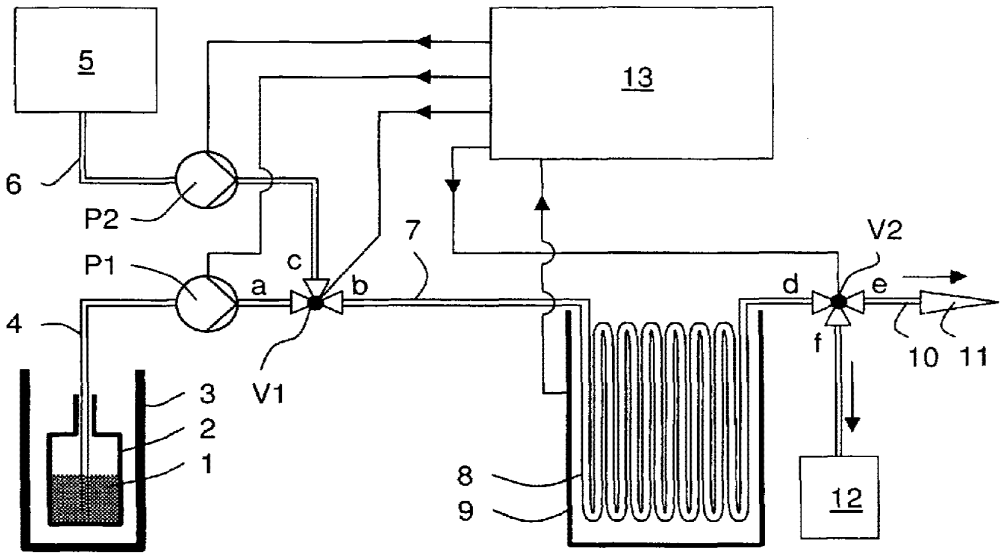
(54) **Title:** METHOD AND DEVICE FOR ACCURATE DISPENSING OF RADIOACTIVITY



(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).

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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).

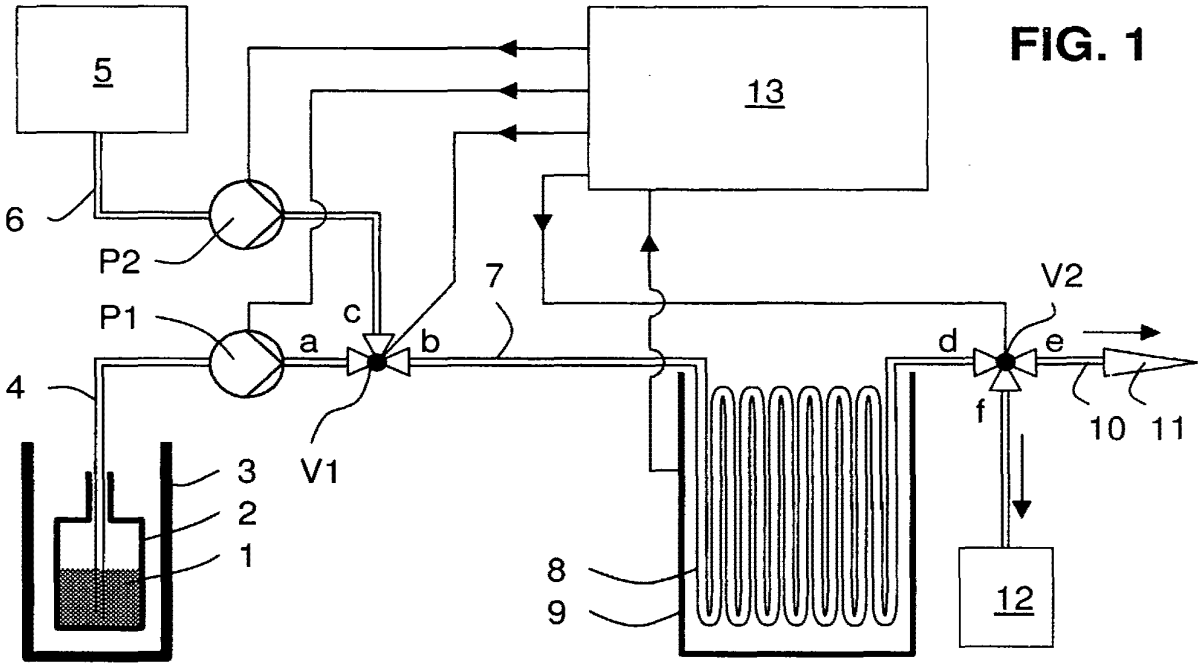

FIG. 1

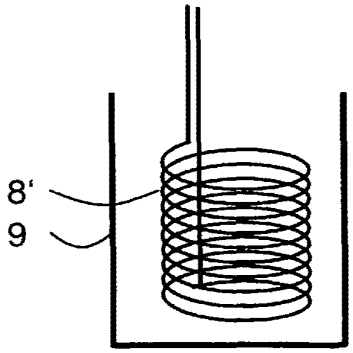

FIG. 2

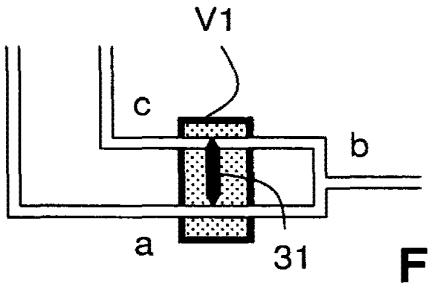

FIG. 3A

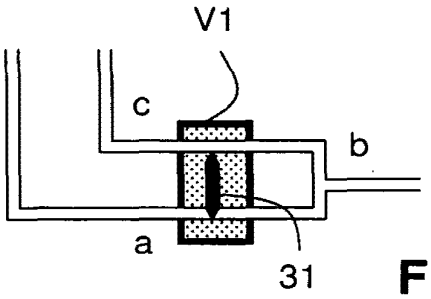

FIG. 3B

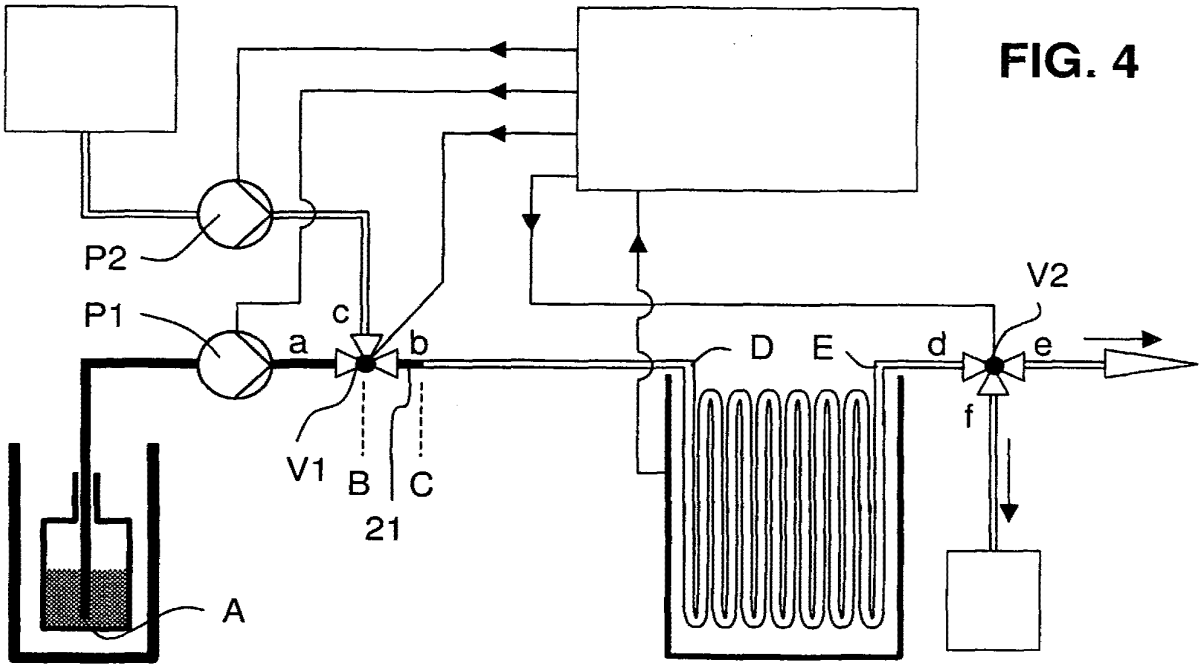

FIG. 4

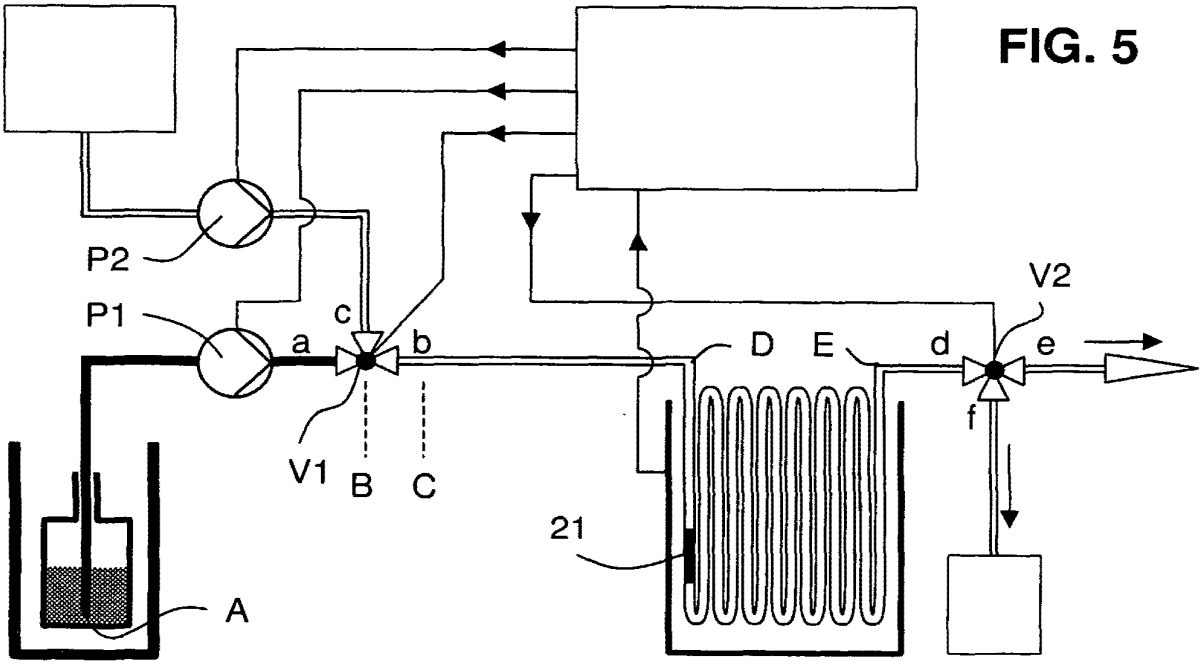

FIG. 5

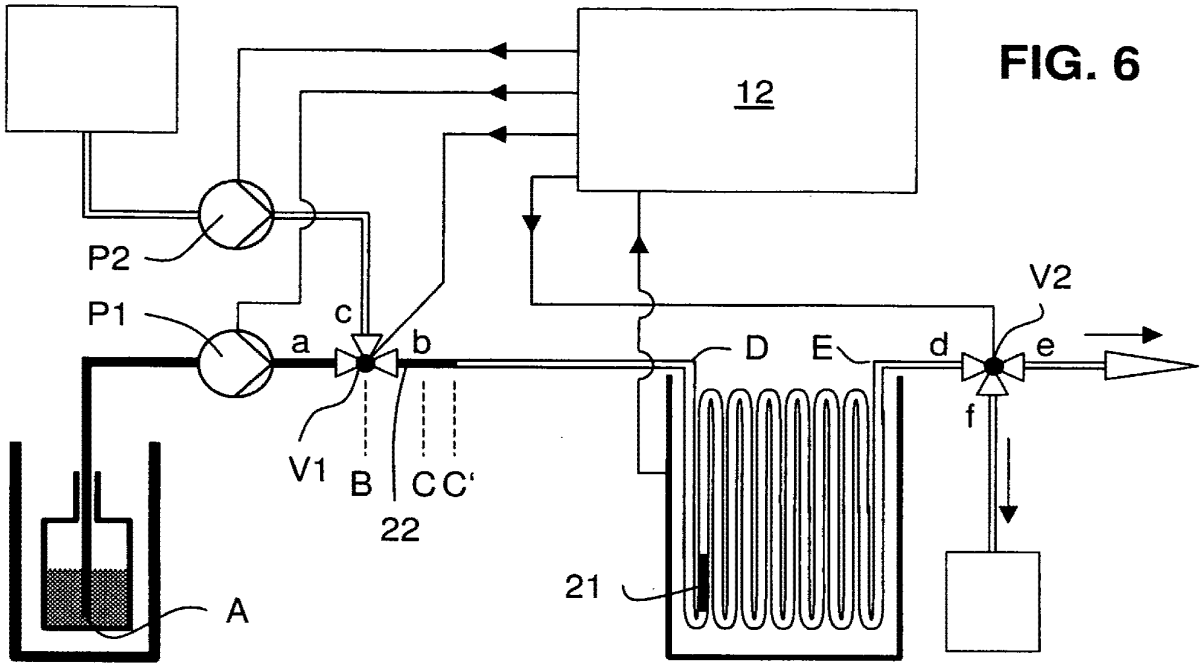
12
P2
P1
a
c
b
V1
B
C
C'
22
A
D
E
d
e
V2
f
21

FIG. 6

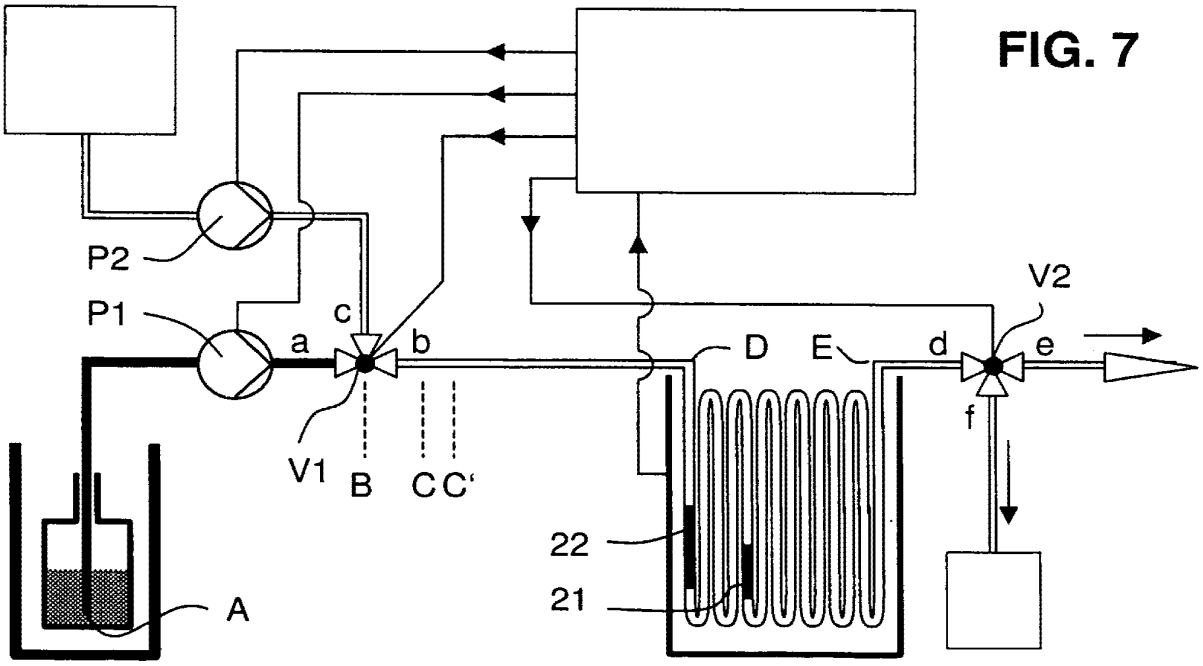
P2
P1
a
c
b
V1
B
C
C'
A
D
E
d
e
V2
f
22
21

FIG. 7

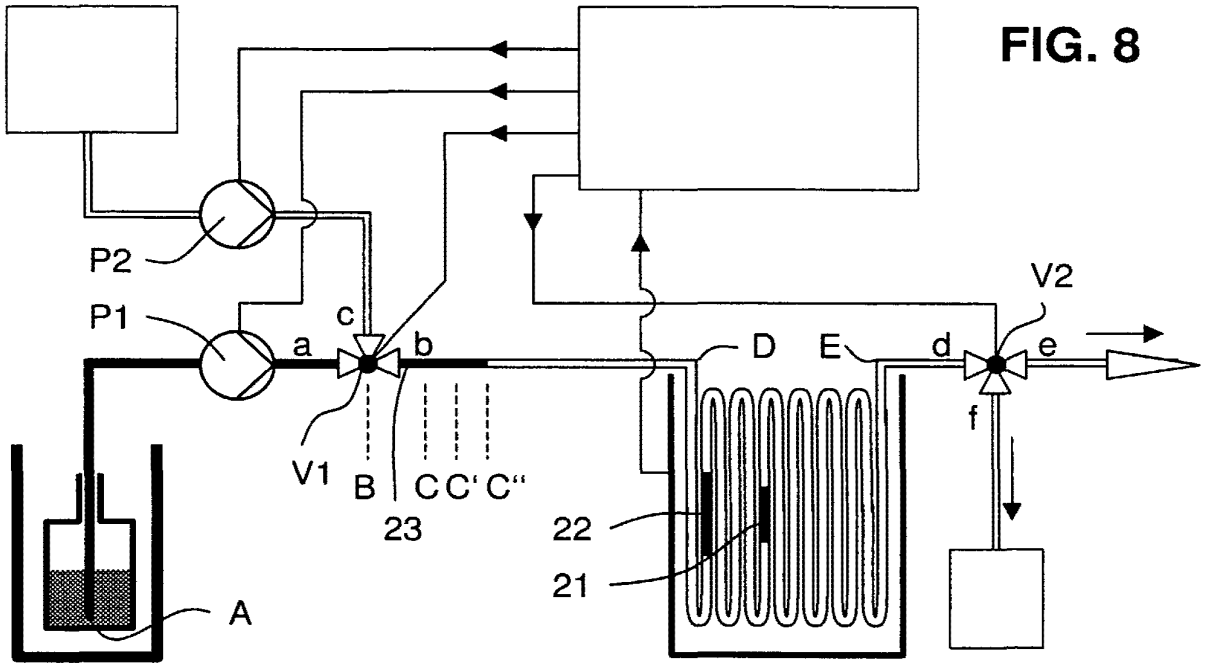

FIG. 8

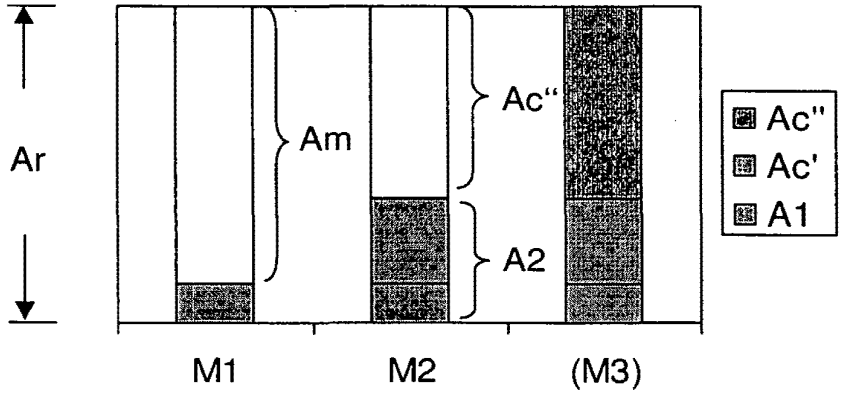

FIG. 10

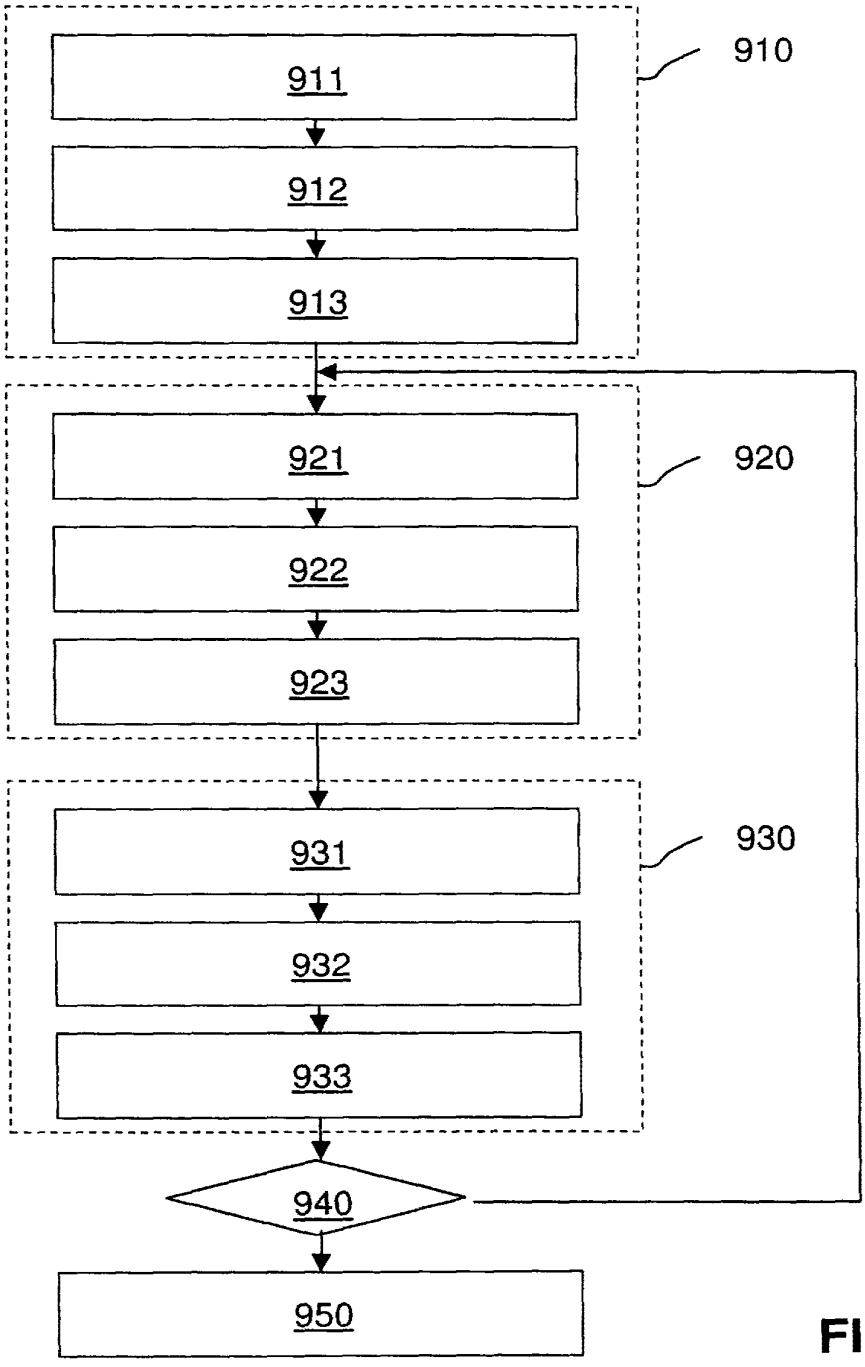

FIG. 9

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.

° 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 document 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
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
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US 2003004463 A1	02-01-2003	US 2004260143 A1	23-12-2004
		US 2003216609 A1	20-11-2003

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(Not for submission under 37 CFR 1.99)

Application Number	12137363
Filing Date	2008-06-11
First Named Inventor	Charles R. Quirico
Art Unit	3763
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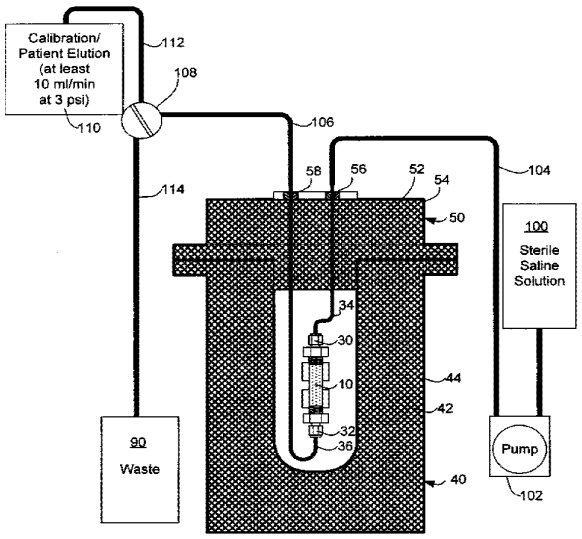
(54) Title: A RUBIDIUM GENERATOR FOR CARDIAC PERFUSION IMAGING AND METHOD OF MAKING AND MAINTAINING SAME



(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.

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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.

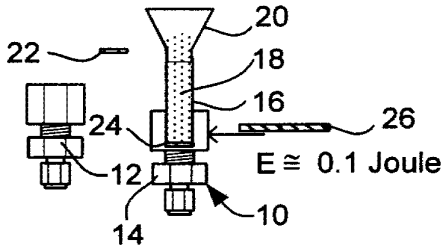
20
22
18
16
24
26
E ≅ 0.1 Joule
12
10
14

FIG. 1

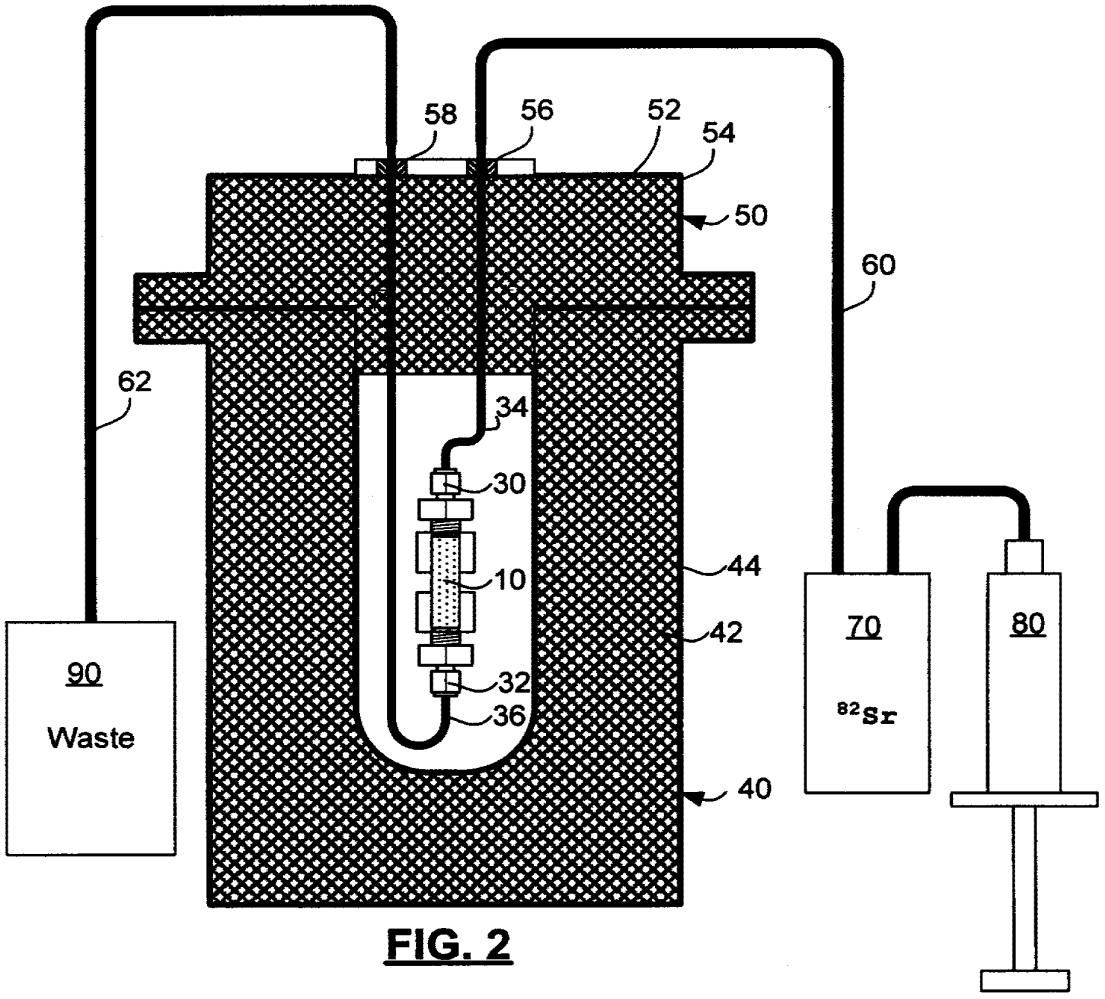
58
56
52
54
50
60
62
34
30
10
44
42
90
Waste
70
82Sr
80
32
36
40

FIG. 2

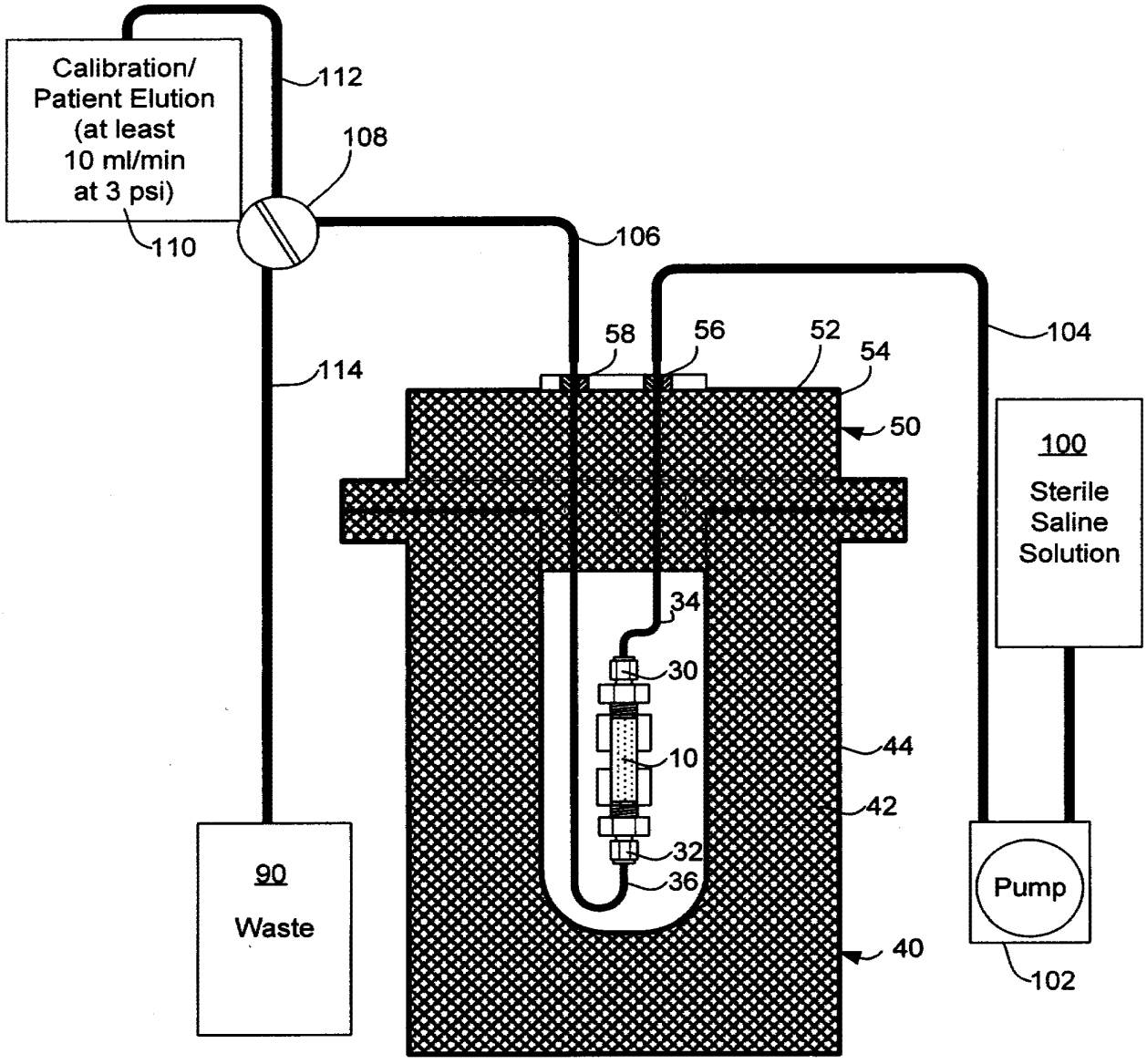
Calibration/
Patient Elution
(at least
10 ml/min
at 3 psi)
110
112
108
106
114
58
56
52
54
104
50
100
Sterile
Saline
Solution
34
30
10
44
42
32
36
90
Waste
Pump
40
102

FIG. 3

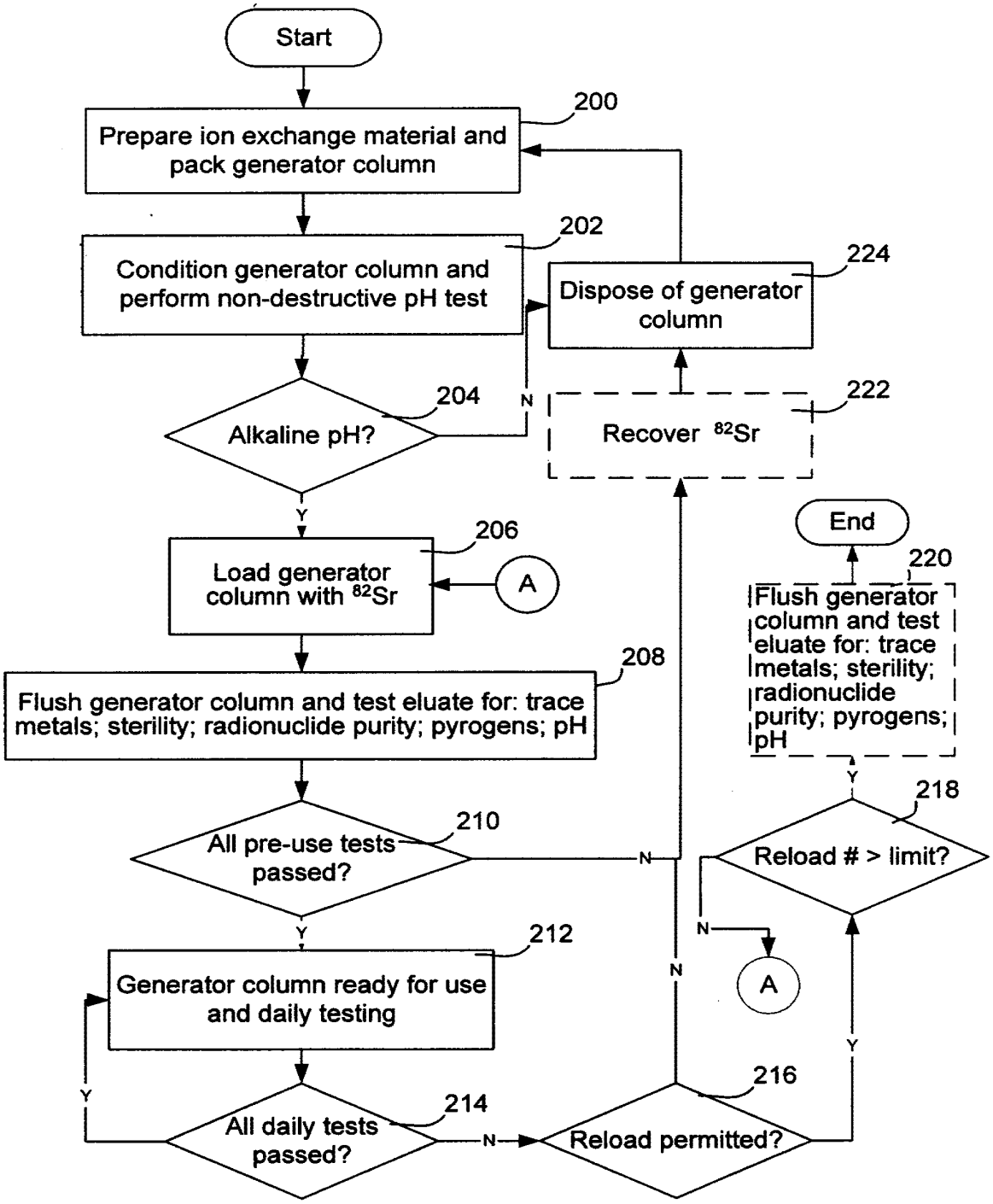
Start
Prepare ion exchange material and pack generator column
200
Condition generator column and perform non-destructive pH test
202
Alkaline pH?
204
N
Y
Dispose of generator column
224
Recover ^{82}Sr
222
Load generator column with ^{82}Sr
206
A
Flush generator column and test eluate for: trace metals; 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

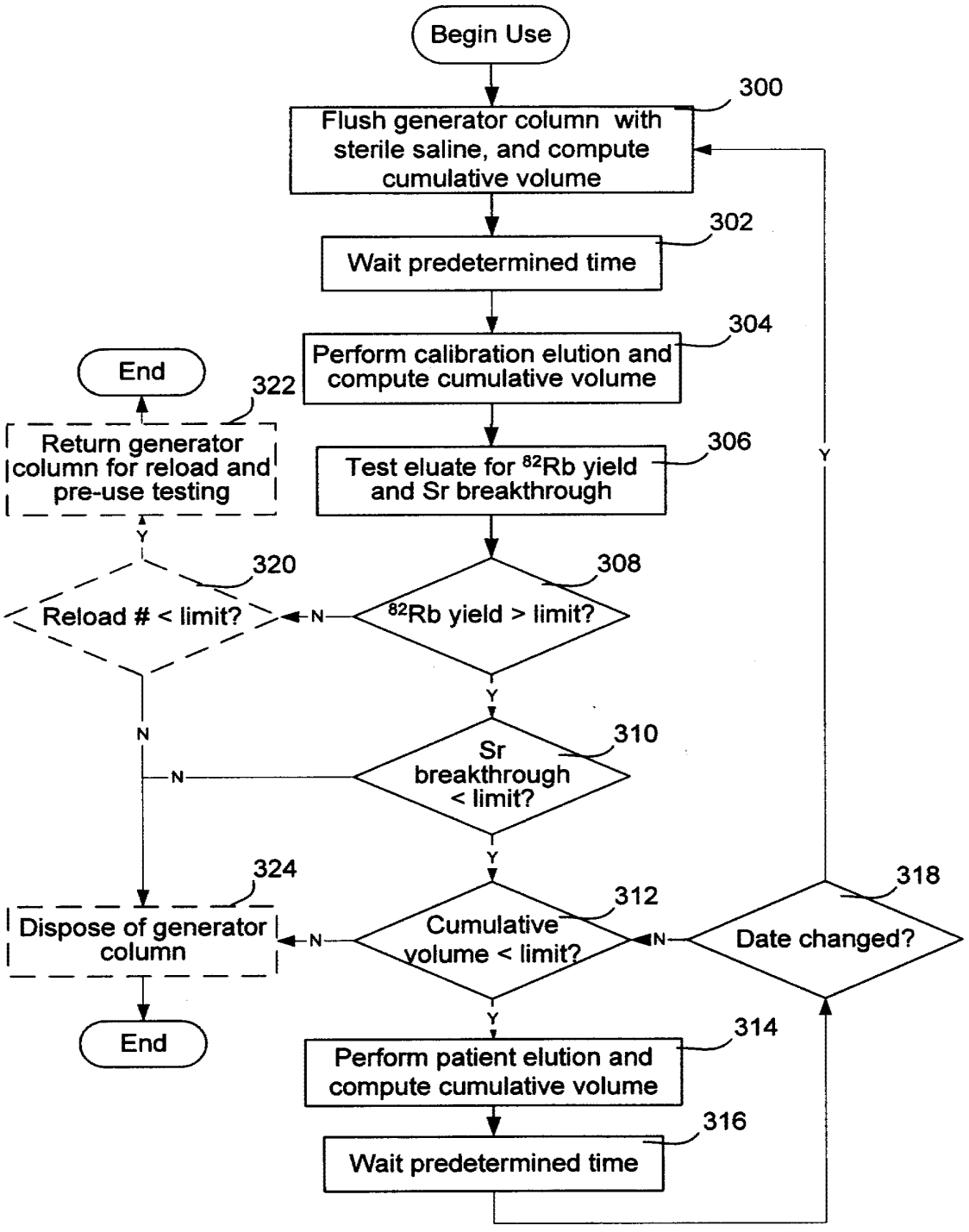
Begin Use
300
Flush generator column with sterile saline, and compute cumulative volume
302
Wait predetermined time
304
Perform calibration elution and compute cumulative volume
306
Test eluate for 82Rb yield and Sr breakthrough
308
82Rb yield > limit?
N
320
Reload # < limit?
Y
322
Return generator column 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 :

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"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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		CA1115551 A1	05-01-1982
		CH637843 A5	31-08-1983
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		FR2422426 A1	09-11-1979
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		NL7808498 A	12-10-1979
		SE7809128 A	11-10-1979
US3935884	03-02-1976	NONE	
US2845136	29-07-1958	NONE	
US3164980	12-01-1965	NONE	

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(30) Priority Data:
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(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:
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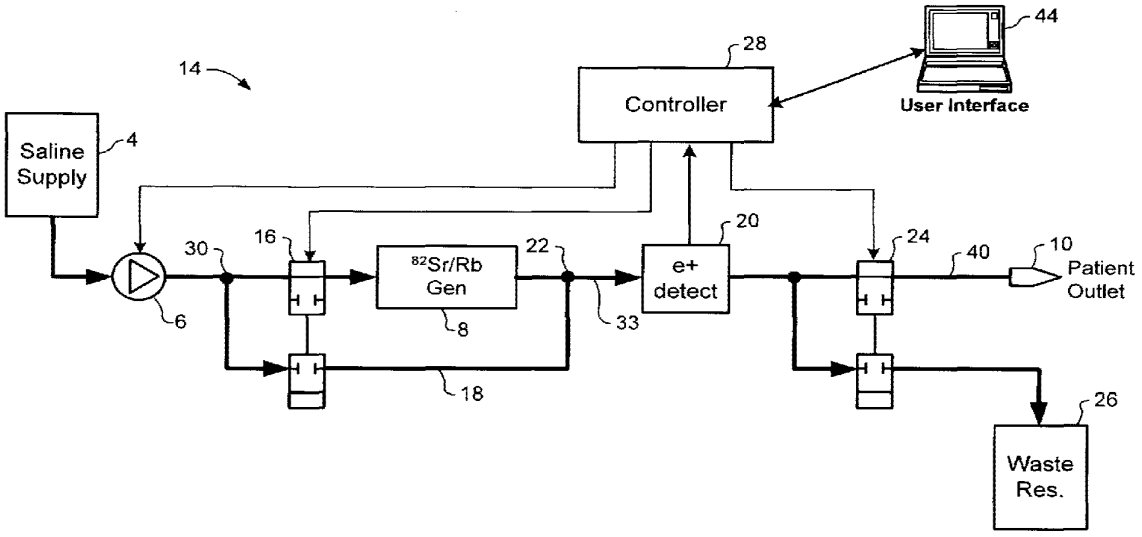
[Continued on next page]

(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.

WO 2007/104133 A1

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.

WE CLAIM:

1. 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, the method comprising steps of:

during each elution run:

obtaining a plurality of successive concentration parameter values at predetermined intervals, each concentration parameter value being indicative of a respective instantaneous activity concentration of the active saline solution;

computing respective error values between each concentration parameter value and a target activity concentration value of the elution run; and

accumulating error data based on a plurality of the computed error values; and

between successive elution runs, adjusting at least one performance parameter of the elution system based on the accumulated error data.

2. A method as claimed in claim 1, wherein the step of adjusting at least one performance parameter of the elution system comprises a step of tuning a performance model of the generator valve.

3. A method as claimed in claim 2, wherein the accumulated error data comprises the computed error values as a function of an estimated flow ratio.

4. A method as claimed in claim 3, wherein the step of tuning a performance model of the generator valve comprises steps of:

calculating a slope of the error data; and

adjusting a response slope parameter of the generator valve model based on the calculated slope of the error data.

5. A method as claimed in claim 2, wherein the error data comprises one or more error values accumulated during a period in which a target activity concentration of an elution exceeds the predicted activity concentration of that elution.

6. A method as claimed in claim 5, wherein the step of tuning a performance model of the generator valve comprises steps of:

calculating a slope of the error data; and

adjusting an upper limit parameter of the generator valve based on the calculated slope of the error data.

7. A method as claimed in claim 6, wherein the step of adjusting the upper limit parameter comprises steps of:

if the calculated slope is zero, reducing the upper limit parameter by a predetermined increment; and

otherwise, calculating an adjusted upper limit parameter value using the calculated slope.

8. A method as claimed in claim 2, wherein the error data comprises a difference between a predicted elution duration required to achieve a desired total activity dose and an actual elution duration.

9. A method as claimed in claim 8, wherein the step of tuning a performance model of the generator valve comprises a step of adjusting a hysteresis factor H based on the difference between the predicted and actual elution durations.

10. A method as claimed in claim 1, further comprising a step of enforcing a predetermined delay between successive elution runs.

11. A method as claimed in claim 1, further comprising steps of:

defining a plurality of operating modes of the elution system; and

during each elution run, automatically transitioning between selected ones of the operating modes, in accordance with user-input parameters of the elution run.

12. A method as claimed in claim 11, wherein the plurality of operating modes comprise:

a "Bypass-to-waste" mode in which the entire saline flow is directed through the bypass line and into a waste reservoir;

a "patient line flush" mode in which the saline flow is directed through the bypass line and out through a patient outlet;

a "waiting for threshold" mode in which the saline flow is directed through the generator, and the active saline solution directed into the waste reservoir; and

an "elution" mode in which the saline flow is proportioned between the generator and the bypass line, and the active saline solution directed out through the patient outlet.

13. A method as claimed in claim 11, wherein the user-input parameters comprise:

at least one of a desired duration of the elution, and a desired saline flow rate; and

at least one of a target activity concentration profile, and a total eluted activity dose.

14. A method as claimed in claim 1, further comprising steps of:

defining a set of one or more predetermined elution runs, each having respective set of predetermined parameters; and

executing the set of predetermined elution runs in accordance with a predetermined schedule.

15. A method as claimed in claim 14, wherein the predetermined schedule defines a daily protocol.

16. A method as claimed in claim 14, wherein the set of one or more predetermined elution runs comprises a

calibration elution for calibrating any one or more of:

a performance of the generator;

a proportionality constant between the concentration parameter value and the instantaneous activity concentration of the active saline solution.

17. A method as claimed in claim 16, wherein the calibrated performance of the generator comprises either one or both of:

^{82}Rb activity concentration vs. eluted volume; and

^{82}Sr breakthrough.

18. A positron detector for detecting instantaneous ^{82}Rb activity concentration of an active saline solution generated by an ^{82}Sr/^{82}Rb elution system, the positron detector comprising:

a scintillation fiber disposed adjacent a feed line for conveying the active saline solution;

a photon counter operatively coupled to the scintillation fiber for detecting photons generated by positron annihilation within the scintillation fiber; and

a radiation shield surrounding the scintillation fiber and at least a portion of the feed line, for shielding at least the scintillation fiber from spurious radiation.

19. A positron detector as claimed in claim 18, wherein a thickness of the radiation shield is on the order of ½ inch.

20. A positron detector as claimed in claim 18, wherein the radiation shield surrounds a length of the feed line corresponding to at least five times an outer diameter or the feed line, in each direction from the scintillation fiber.

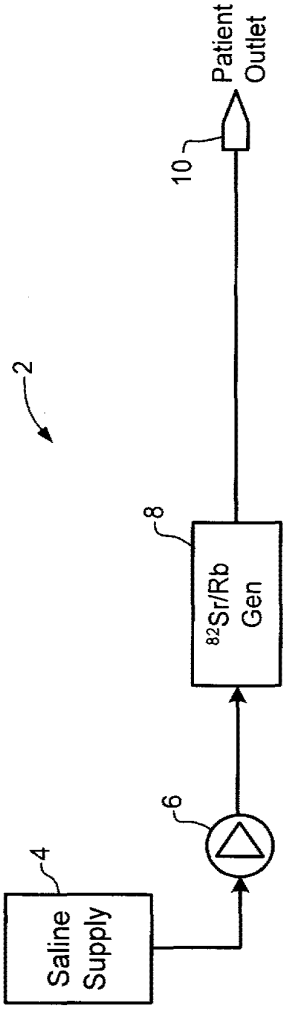


Figure 1a
(Prior Art)

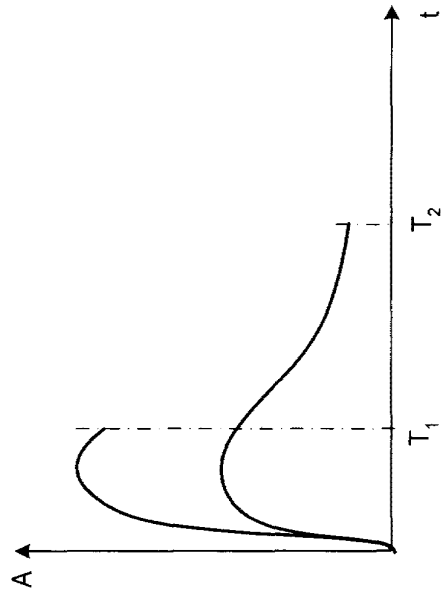


Figure 2b
(Prior Art)

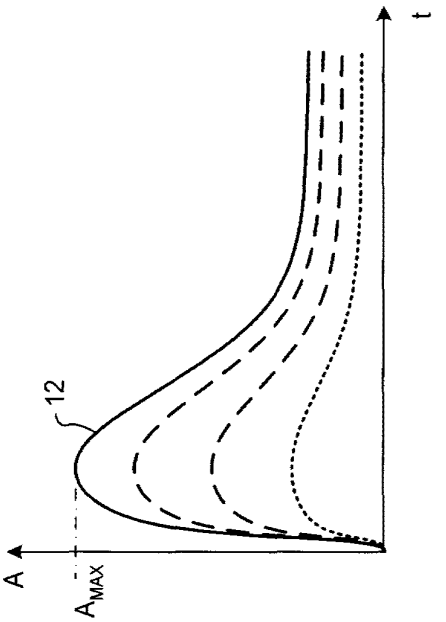


Figure 2a
(Prior Art)

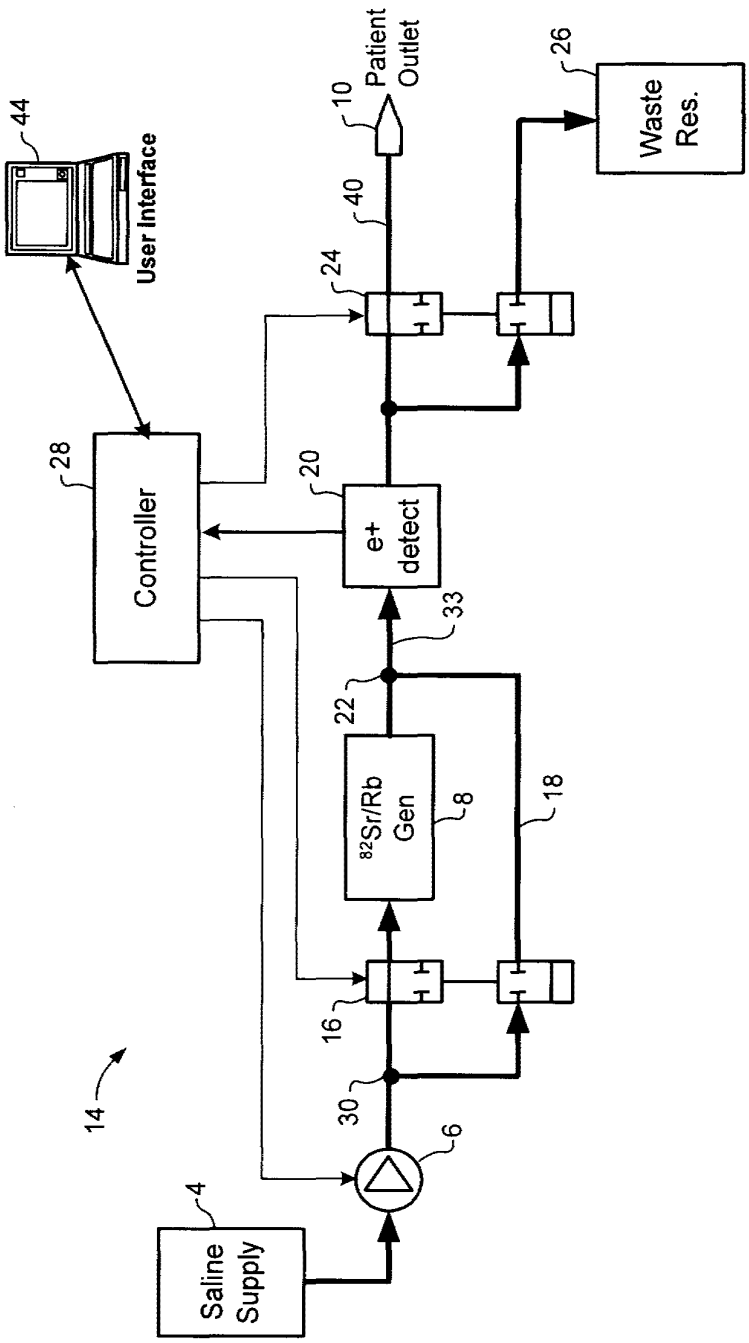

Saline Supply
4
Controller
28
User Interface
44
Patient Outlet
10
Waste Res.
26
e+ detect
20
^{82}Sr/Rb Gen
8
14
16
18
22
24
30
33
40
6

Figure 3

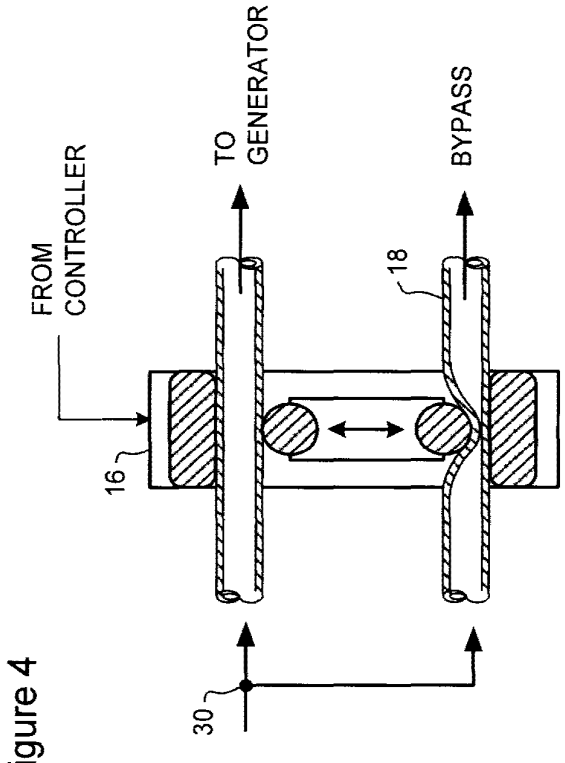


Figure 4

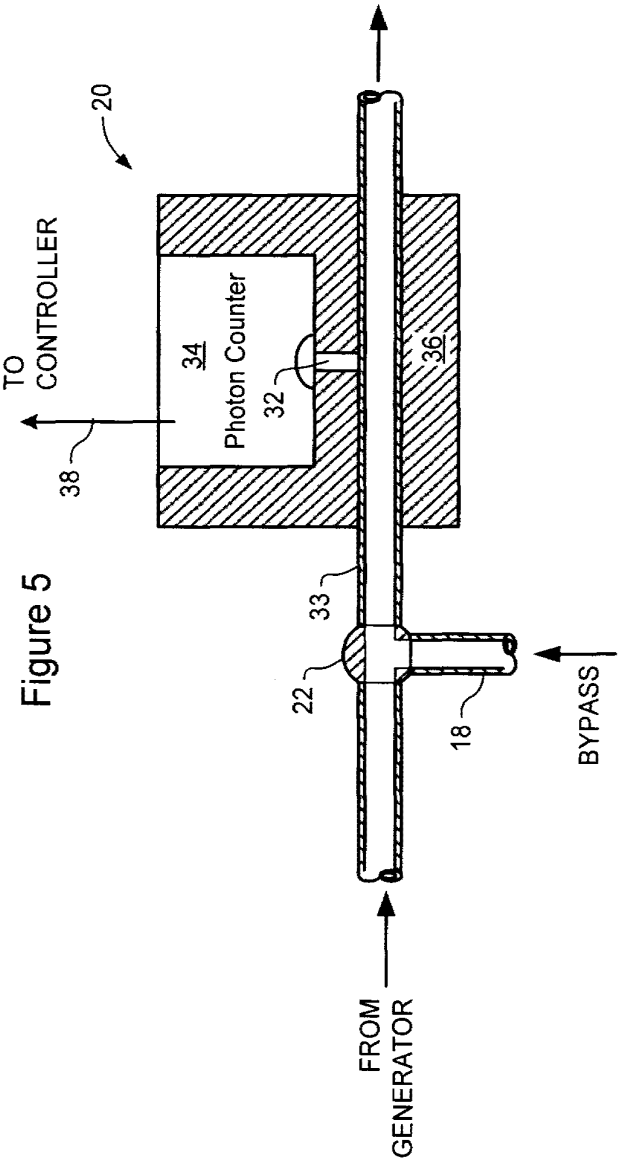


Figure 5

Figure 6a

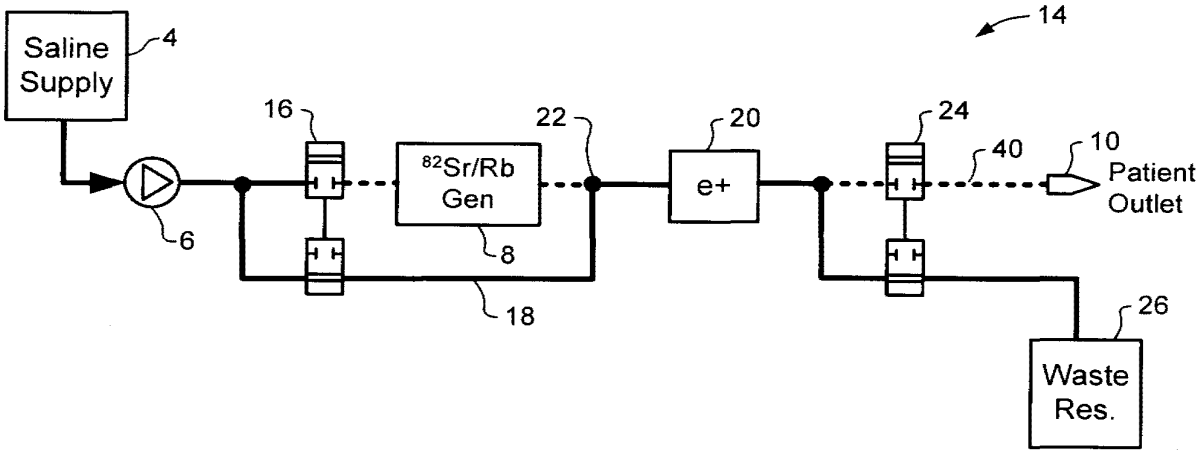


Figure 6b

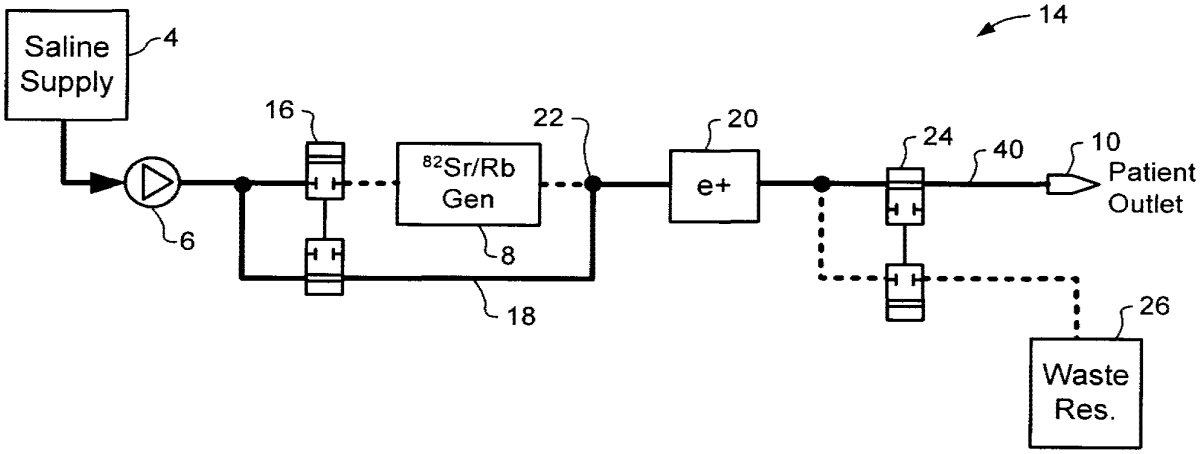


Figure 6c

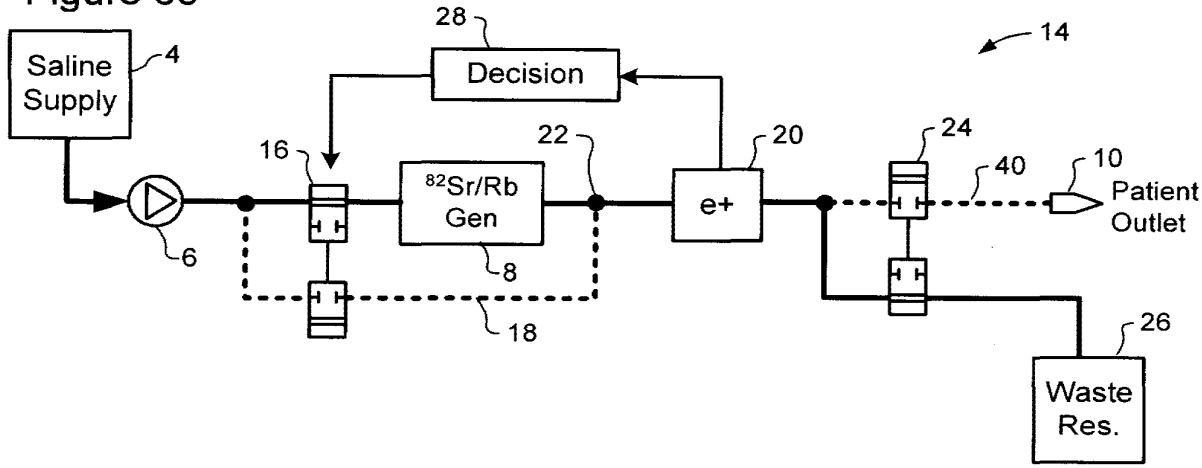


Figure 6d

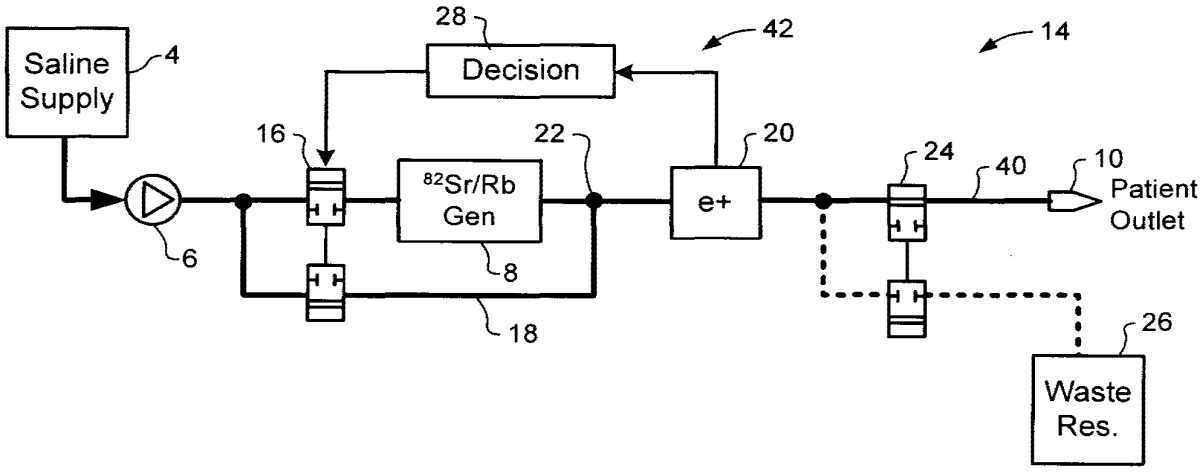

Saline Supply
4
28
Decision
42
14
16
22
20
24
40
10
Patient Outlet
82Sr/Rb Gen
e+
6
8
18
26
Waste Res.

Figure 7a

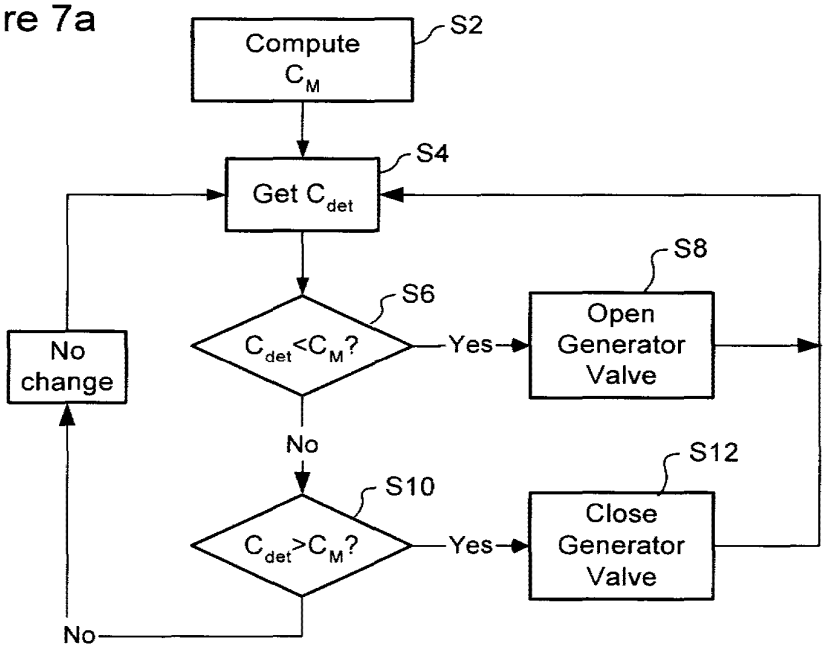


Figure 7b

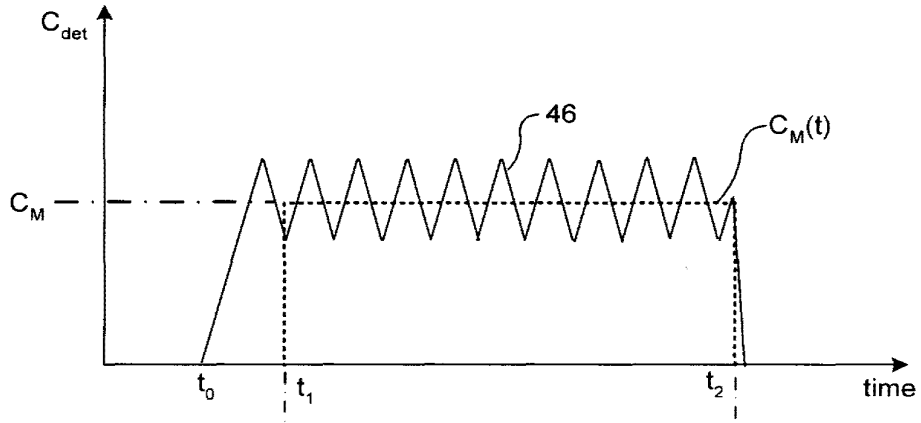


Figure 7c

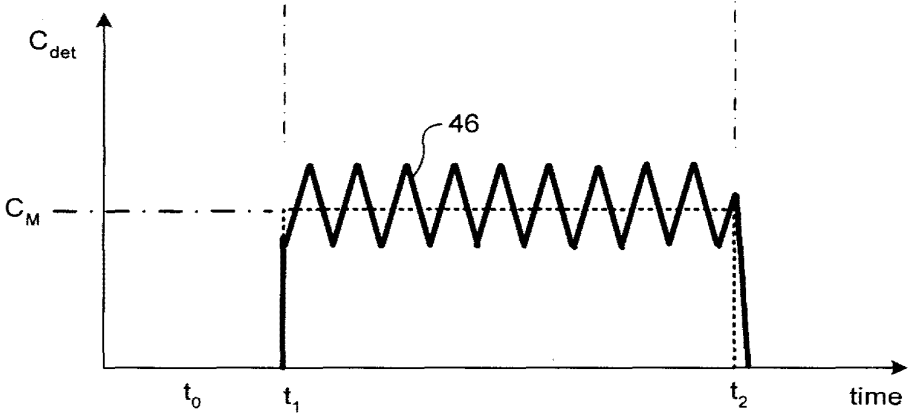


Figure 8a

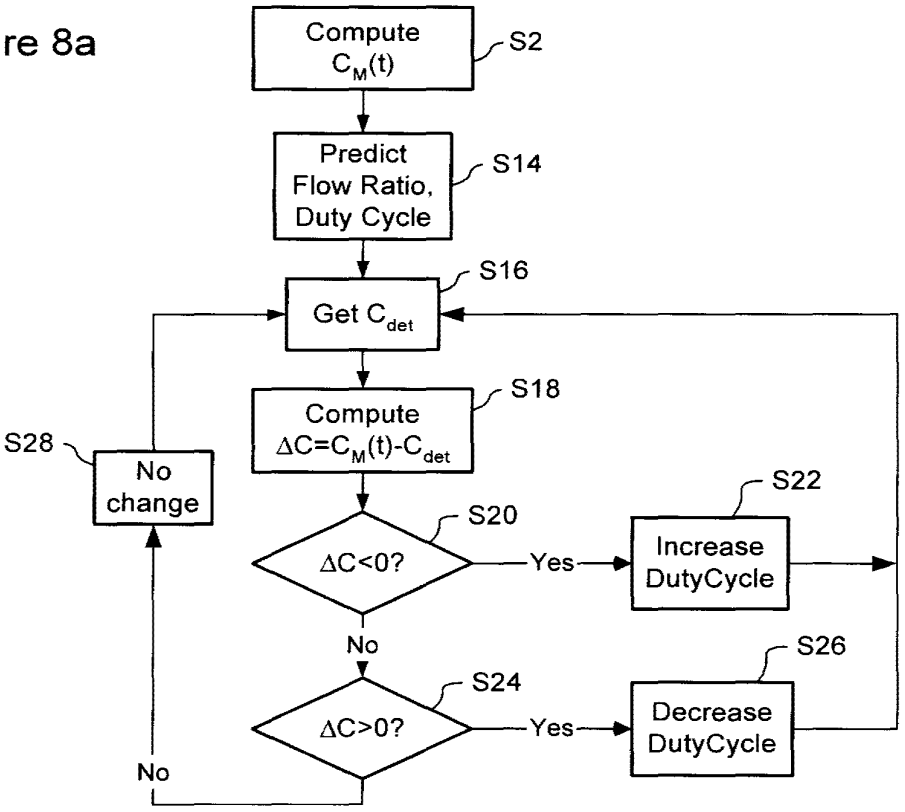


Figure 8b

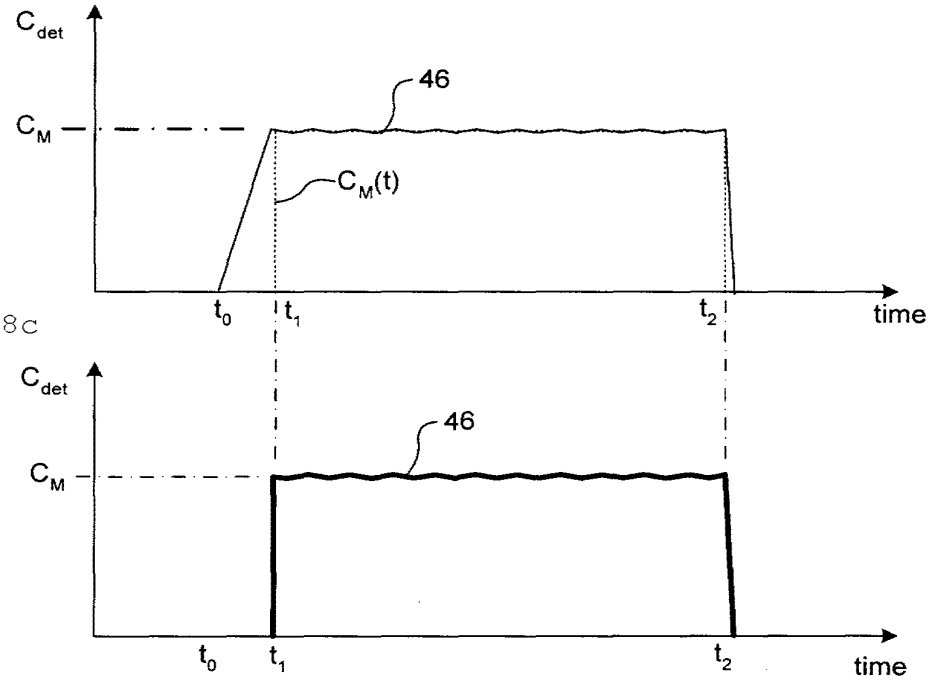


Figure 8c

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2007/000295

A. CLASSIFICATION OF SUBJECT MATTER
IPC: ***A61M 36/06*** (2006.01) , ***A61M 36/08*** (2006.01) , ***G01T 1/164*** (2006.01) , *G01T 1/20* (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(8): A61M All (2006.01) + G01T All (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)
QPat, QWeb, Delphion (Keywords used: positron emission tomography, myocard* perfusion, radiation detector, scintillation fibre, generator, etc.)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JP 2000131443 A (CHIBA, K. et al.) 12 May 2000 (12-05-2000) * Figs 1-6; Abstract; Machine translation *	18-20
A	JP 7231884 A (OKADA, H. et al.) 5 September 1995 (05-09-1995) * Figs. 1-7; Abstract *	18-20
A	US 4975583 A (SPOWART, A.R.) 4 December 1990 (04-12-1990) * Fig. 2; Abstract; Columns 2-3 *	18-20
A	US 6713765 B2 (TESTARDI, L.R.) 30 March 2004 (30-03-2004) * Whole document *	18-20
A	ALVAREZ-DIAZ, Teresa M. et al., Manufacture of strontium-82/rubidium-82 generators and quality control of rubidium-82 chloride for myocardial perfusion imaging in patients using positron emission tomography, Applied Radiation and Isotopes, vol. 50, no. 6, 1999, pp. 1015-1023	1-17

[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)	18 May 2007 (18-05-2007)

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	Valérie Dubé 819- 934-4261

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the 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. [ ] Claim Nos. :
because they relate to subject matter not required to be searched by this Authority, namely :

2. [ ] Claim 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. [ ] Claim Nos. :
because they are dependant claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. 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 :

- Claims 1-17 pertain to a method of controlling an 82Sr/82Rb elution system, the system comprising a generator valve, an 82Sr/82Rb generator and a bypass line and providing an active saline solution, the method comprising: during each elution run, obtaining concentration values, computing error values between the obtained values and a target value, accumulating error data and adjusting a system parameter accordingly.
- Claims 18-20 pertain to a positron detector for detecting 82Rb activity concentration of an active saline solution generated by an 82Sr/82Rb elution system, the detector comprising a scintillation fibre adjacent a feed line, a photon counter and a radiation shield.

The common feature between aforesaid groups of claims is an 82Sr/82Rb elution system generating an active saline solution. However, such a system is already well known in the art and therefore cannot be regarded as constituting a single common inventive feature linking

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [X] As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

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 claim 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 claim Nos. :

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	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	1-17
A	YANO, Y, Essentials of a Rubidium-82 Generator for Nuclear Medicine, International journal of radiation applications and instrumentation. Part A, Applied radiation and isotopes, vol. 38, no. 3, Great Britain, 1987, pp. 205-211	1-17
A	KENSETT, M. J. et al., Experience with a 82Sr/82Rb Generator for Clinical Use, International journal of radiation applications and instrumentation. Part A, Applied radiation and isotopes, vol. 38, no. 3, Great Britain, 1987, pp. 227-231	1-17
A	SAHA, G. et al., Use of the 82Sr/82Rb Generator in Clinical PET Studies, International journal of radiation applications and instrumentation. Part B, Nuclear medicine and biology, vol. 17, no. 8, Great Britain, 1990, pp. 763-768	1-17

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CA2007/000295

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
JP 2000131443 A	12-05-2000	NONE	
JP 7231884 A	05-09-1995	NONE	
US 4975583 A	04-12-1990	AU1299288 A EP0346369 A1 GB8704074 D0 JP2502217 T WO8806297 A1	14-09-1988 20-12-1989 25-03-1987 19-07-1990 25-08-1988
US 6713765 B2	30-03-2004	NONE	

Electronic Acknowledgement Receipt

EFS ID:	5367208
Application Number:	12137363
International Application Number:	
Confirmation Number:	7372
Title of Invention:	INFUSION SYSTEM CONFIGURATIONS
First Named Inventor/Applicant Name:	Charles R. Quirico
Customer Number:	22859
Filer:	Elisabeth Lacy Belden
Filer Authorized By:	
Attorney Docket Number:	56782.1.6
Receipt Date:	20-MAY-2009
Filing Date:	11-JUN-2008
Time Stamp:	13:56:22
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_6_IDS3.pdf	806383 cfc78e8ec3a836d86060c74582ffc8e9c29abdc7	no	4

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Information:	

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2	Foreign Reference	56782_1_WO07071022A1.pdf	994962 47ddcf6b6a69dde75265b82836f3bcb67c12bf04	no	24
Warnings:					
Information:					
3	Foreign Reference	56782_1_WO07104133A1.pdf	1590246 8d23d4809a08099ece4791dcd9a549165275715a	no	42
Warnings:					
Information:					
			Total Files Size (in bytes):	3391591	

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If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

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	12137363
Filing Date	2008-06-11
First Named Inventor	Charles R. Quirico
Art Unit	3763
Examiner Name	
Attorney Docket Number	56782.1.6

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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
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	1	2008140351	WO	A2	2008-11-20			☒

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137363
	Filing Date	2008-06-11
	First Named Inventor	Charles R. Quirico
	Art Unit	3763
	Examiner Name	
	Attorney Docket Number	56782.1.6

	1		☐

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Examiner Signature		Date Considered	

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[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137363
	Filing Date	2008-06-11
	First Named Inventor	Charles R. Quirico
	Art Unit	3763
	Examiner Name	
	Attorney Docket Number	56782.1.6

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ 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)	2009-01-19
Name/Print	Elisabeth Lacy Belden	Registration Number	50,751

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

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2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

AUTOMATED STRONTIUM-RUBIDIUM INFUSION SYSTEM

The invention relates to medical engineering, and particularly to means for automation of a process for producing a diagnostic solution from a radionuclide strontium-rubidium generator and remote carrying out a checked infusion with automatic checking main process characteristics, such as an introduced activity value, presence of air bubbles as well as a solution weight and activity in a waste container.

One of the most perspective directions in the nuclear diagnostics is the positron emission tomography (PET). Such short and ultra-short living isotopes as C-11, O-15, N-13, and F-18 are used in the PET centers. This obliges to have cyclotrons at the place of diagnostic for making such isotopes. It is possible to widen the functionality of the PET diagnostics in use of generator systems having a parent radionuclide lifetime significantly longer that a lifetime of radionuclides made in cyclotrons of the PET centers. Generator systems ^{82}Sr ($t_{1/2}$ = 25.6 days) $\rightarrow$ ^{82}Rb ($t_{1/2}$ = 75 seconds) and ^{68}Ge ($t_{1/2}$ = 271 days) $\rightarrow$ ^{68}Ga ($t_{1/2}$ = 78.3 minutes) are the most promising systems among the PET isotope generators.

Therefore, it is possible to say with respect to generator isotopes that any clinics having PET scanners within a region, a country or a group of countries are to be provided with said isotopes.

Generator systems can find the widest use in so called mobile PET scanners mounted in auto-trailers and called for servicing clinics that have no both own cyclotrons and own PET scanners. Absence of "affixment" of such a mobile PET scanner to an isotope base substantially widens a radius of the territory serviced thereby.

A strontium-rubidium infusion system for producing a diagnostic solution from a radionuclide strontium-rubidium generator and carrying out a checked infusion is known (US 4,562,829, 1986), said system comprising: an eluent tank connected by respective pipes of a transporting system via a first three-way valve to a syringe pump; a strontium-rubidium generator with a first filter and a first pressure sensor at an input; a second three-way valve whose first opening is coupled via a second filter to means for infusing an eluent into a patient and whose second opening is coupled to an eluate surplus storing and collecting means; radioactivity measurement means; and a check and control system. The prior art system is not optimal in a degree of radioactive radiation protection and in a service life of a generator column.

The disclosed invention is directed to elimination of the listed disadvantages. The technical result to be accomplished by using the inventive system consists in enhancement of

effectiveness in carrying out of a diagnostic procedure due to automation of the infusion procedure, reducing undesirable irradiation doses for a patient and maintenance personnel, increasing exploitation lifetimes of a generator column.

The essence of the disclosed invention consists in that an automated strontium-rubidium infusion system comprises: an eluent tank, a strontium-rubidium generator with a filter and a pressure sensor at an input; means for infusing an eluent into a patient, said tank, generator and means being connected by a transporting system to pipes and two three-way valves; radioactivity measuring means; and a check and control unit. At the same time, the eluent tank is connected via first and second openings of the first three-way valve to a syringe pump, a first opening of the second three-way valve is coupled by pipes via a second filter to the means for infusing the eluent into the patient and is coupled by a second opening thereof to a waste receptacle. The system further comprises: third and fourth three-way valves; first and second air bubble detectors coupled to the check and control unit being in communication with a computer, said third three-way valve being connected by first and second openings via pipes to a third opening of the first three-way valve and to an input of the strontium-rubidium generator, respectively, an output of the generator being coupled to a first opening of the fourth three-way valve, wherein the third opening of the third valve and a second opening of the fourth valve are in communication by a pipe, the first air bubble detector is mounted on a pipe between the eluent tank and the first opening of the first valve while the second detector is mounted on a pipe between the third openings of the fourth and second valves.

Further, the radioactivity measurement means include first and second activity sensors. At the same time, the first activity sensor is placed on a pipe between the third openings of the fourth and second valves and is embodied as a beta detector.

A radiation protection of the eluate surplus collecting and storing means may be implemented as a protection box including waste weight check means in the form of a force sensor, while the second activity sensor in the form of a gamma detector may be mounted within an opening of the protective box in order to determine a radioactivity level.

A column of the strontium-rubidium generator has a radiation protection including external main and transportation protective containers, said main protection container being mounted stationary on a shelf of a bogie.

The system is mounted in a closed movable housing. Further, the housing is provided with a shifting tabletop.

The essence of the invention is explained by drawings as follows:

Fig. 1 is a diagram of an infusion system;

Fig. 2 is a general side view of a generator plant;

Fig. 3 is a general top view of the generator plant.

Conditional notation used in drawings is listed below:

1 – Eluent tank

2, 3, 4, 5 – three-way valves

6, 7 – activity sensors

8, 9 – pressure sensors

10 – Syringe pump

11 – strontium-rubidium generator

12 – Check and control unit

13 – Weight sensor

14 – Remote computer

15, 16 – filters

17, 18 – air bubble detectors

19 – Means (needle) for infusing an eluent into a patient

20 – Eluent and eluate waste receptacle

21 – Movable housing

22 – Stand

23 – Protective container of strontium-rubidium generator

24 – Protective container for beta detector

25 – Power supply source

26 – Protective box of waste reservoir

27 – Shifting tabletop

An automated strontium-rubidium infusion system includes means for generating rubidium-82 in a solution which can be infused into a patient, exactly, a rubidium-strontium generator 11 (Fig. 1) of a traditional type in a transporting container. This container is placed in a protective external main container 23 and fulfils a main radiation protection function together with the latter. The assembled system may be mounted in a movable housing 21 (Fig. 2) covered by decorative panels (not shown). There is a stand 22 mounted on a tabletop and having an eluent tank fastened thereon. There are a syringe pump 10 and a computer 14 further mounted here. Components mounted on an upper shelf of the movable housing 21 are as follows:

- the main protective container 23 into which a standard transporting container with the strontium-rubidium generator 11 is placed;

- a protective box 24 with a beta activity detector placed therein and measuring the activity of a solution passed through the strontium-rubidium generator 11;

- a power supply source 25.

A protective box 26 is placed at a lower shelf, said box having an eluent and eluate waste receptacle arranged therein.

A top lid of the container 23 is turned back in Fig. 3, which makes it possible to see a cavity into which the transporting container with the strontium-rubidium generator 11 is placed. In order to make easier the access to the main protective container 23 during recharging a generator system (there are removal of the transporting container with the used column of the strontium-rubidium generator 11 and installation of a transporting container with a fresh column), a tabletop part is made as a shifting tabletop 27 which provides convenience in operation.

Further, the system includes means for infusion, exactly (Fig. 1): a remote-controlled syringe pump 10 whose rod is actuated, for example, by a step motor; means for automated filling the syringe pump with an eluent (a 0.9% NaCl solution); a system for transporting an eluent and an eluate to a patient or an eluent and eluate waste receptacle, said transporting system being provided with multi-way (three-way) valves 2 to 5 (Fig. 1) that ramify the transporting system in accordance with a job making program; antibacterial protection means, exactly, antibacterial filters 15 and 16 at an input and at an output of the transporting system; eluate activity measurement means 6 and 7 for monitoring and dozing in infusion into a patient; pressure measurement means 8 and 9 for measurement a pressure in the transporting system, said means being designed for measuring occlusion as well; an eluent and eluate waste receptacle 20 also capable of measuring a solution activity value and a solution weight in a waste reservoir 13; means 12 for automated check throughout the eluation process and components thereof, implemented by on-board or remote computers 14.

The tank 1 with an eluent (for example, brine) is connected by a plastic fitting to a pipe (for example, an infusion tube that has an outer diameter of 2.5 mm with an inner diameter of 1.5 mm). Lengths of such tubes (pipes) are used further to build the transporting system as a whole for infusion. Other end of the pipe is attached via an air bubble detector 17 that generates a signal to a check and control unit 12 in case of passing an air bubble, and said unit generates a control signal to valves 2, 3, 4, and 5 as a result of which the eluent solution comprising the air bubble is removed into the eluent and eluate waste receptacle 20 and does not passes through the column of the strontium-rubidium generator 11.

The valve 2 switches the infusion system into one of two possible operating modes for: (1) filling the syringe when the syringe pump 10 operates for suction the brine from the eluent tank 1 (via the first and second openings of the valve); or (2) infusing, that is, supplying the brine from the filled syringe of the syringe pump 10 into the infusion system (via the first and third openings of the valve).

Further, the three-way valve 2 is connected by a length of a connecting tube to the first opening of the third three-way valve 4 whose second opening is connected via the first filter 15 to an input of the column of the strontium-rubidium generator 11. The first pressure sensor 8 checks a pressure at the input of the column of the strontium-rubidium generator 11.

The third opening of the valve 4 via a length of a connecting tube is connected to the second opening of the fourth three-way valve 5. This valve (the first opening) also has connections to an output tube of the column of the strontium-rubidium generator 11 and an extension of the infusion system in the third opening.

When the syringe pump operates in the operating "infusion" mode, the pair of three-way valves 4, 5, while operating in synchronism, allows either pumping the brine from the syringe 10 via the column of the strontium-rubidium generator 11 further to the infusion system already in the form of an eluate, that is, a Rb-82-enriched solution, or pumping the brine into the infusion system while by-passing the strontium-rubidium generator 11. Thus operating mode is used when a necessary Rb-82 activity amount has been made and should be delivered to a patient 19 while the infusion system should be filled with the inactive brine at the end of infusion into the patient. When the brine pumping mode is used, practically the entire transporting system, exceptive for a connecting pipe from the strontium-rubidium generator output to the fourth three-way valve, will be filled with the non-radioactive brine and will not be a source of additional undesirable radioactivity for the patient and the maintenance personnel; additionally, a brine volume necessary to after-press the made eluate into the patient will not pass through and deplete the column of the strontium-rubidium generator, because it is known that a potency of the generator depends not only upon a time of using thereof but also upon a volume of the brine passed through the generator.

There are a first radioactivity detector 6 (a beta detector) and a second air bubble detector 18 mounted on a pipe from the third opening of the fourth three-way valve 5 to the third opening of the second three-wave valve 3, said air bubble detector being similar to the first air bubble detector 17.. When an air bubble is detected, the detector 18 generates a signal to the check and control unit that generates a control signal to the second three-way valve 3. As a result, an eluate comprising the air bubble is removed into the eluent and eluate waste

receptacle 20. If an air bubble is not detected, the eluate is directed via the first of said three-way valve 3 and the second filter 16 into the patient, that is, onto a needle 19.

The radioactivity detector 6 operates in real time and measures the Rb-82 activity at a location of the detector 18.

The check for filling said waste receptacle with a liquid is carried out by a force sensor (not shown). To measure a radioactivity present in the eluent and eluate waste receptacle, the second radioactivity sensor 7 (a gamma detector) is used. The radiation protection of the eluate surplus collecting and storing means is implemented as a protection box including a force sensor, while the second activity sensor is mounted within an opening of the protective box.

During infusion into the patient, the second three-way valve 3 is switched for passing the eluent to a pipe connected to the needle 19 via a Millipore filter 16. There is a second pressure sensor 9 mounted in this section which allows measurement of an occlusion pressure when an Rb-82-containing solution in administered into the patient.

The process of operating the strontium-rubidium infusion system takes place under control of a control computer program that registers a status of each of devices included in the infusion system at moments of starting and finishing a step, and also registers actions of said devices under condition of their normal functioning and in case if an emergency situation occurs.

To exclude overfilling the eluent and eluate waste receptacle 20 with a radioactive liquid, a level of said liquid is remotely checked using the force sensor; in doing so, there is monitoring of a total container and liquid weight (volume) and a limit value thereof. Additionally, by fixing a weight of the empty waste collection receptacle, a system for scheduled interrogating the check and control unit receives information that the receptacle is mounted in a container. A maximum waste volume in the receptacle is 250 ml.

The check and control unit 12 is coupled to a remote computer whose display displays a graphical mnemonic diagram of the generator device, said diagram providing observation of parameters to be checked in an automatic mode and parameters for operating control of individual members (the electromagnetic three-way valves 2 to 5 and the pump 10) in a manual mode. The diagram makes it possible to observe a current state of all members (the valves 2 to 5, the air bubble detectors 17, 18) of the disclosed infusion system, and operation of the syringe pump 10. The system also allows reception of information about parameters of a pressure in a line from the pressure sensors 8, 9, and reception of information about an

eluate activity at an output of the generator column 11 and a total activity, a weight of the eluate and eluent waste receptacle 20, an activity in said receptacle from the detectors 6, 7.

The check and control unit 12 of the system is connected to control members of the generator plant, that is, the electromagnetic three-way valves 2, 3, 4, 5 and the pump 10, and also includes members for gathering and processing signals from the sensors 6, 7 (the radioactivity sensors), 8, 9 (the pressure sensors), and 17, 18 (the bubble detectors). The control unit 12 is in communication with a panel personal computer (PPC) or any other remote computer (14) through an Ethernet channel. The control unit receives commands from the PPC or remote computer to execute individual steps of the generator plant operating program and informs said computers about a current state of members controlled thereby and a state of system sensors.

The disclosed system improves the safety of use due to the fact that automation of the infusion process has allowed significant reduction in the radioactive irradiation because the system includes additional members that provide ramification of pipes. As a result, it is possible to after-press the made eluate into the patient by the eluent while by-passing the strontium-rubidium generator. At the same time, the pipe is pumped through by the non-radioactive eluent and there is no additional depletion of the strontium-rubidium generator, which makes the life thereof longer. Further, the risk of presence of air bubbles in the eluent delivered into the patient is excluded because of introducing air bubbles into the system of detectors, while detection of said air bubbles immediately results in direction of the eluent and eluate wastes to the eluent and eluate waste receptacle via branches of the pipe without depletion of the strontium-rubidium generator.

CLAIMS

1. An automated strontium-rubidium infusion system comprising:

an eluent tank;

a strontium-rubidium generator with a filter and a pressure sensor at an input;

means for infusing an eluent into a patient, said tank, generator and means being connected by a transporting system to pipes and two three-way valves;

radioactivity measuring means; and

a check and control unit,

wherein the eluent tank is connected via first and second openings of the first three-way valve to a syringe pump, a first opening of the second three-way valve is coupled by pipes via a second filter to the means for infusing the eluent into the patient and is coupled by a second opening thereof to a waste receptacle,

said system being characterized in that it further comprises:

third and fourth three-way valves;

first and second air bubble detectors coupled to the check and control unit being in communication with a computer,

said third three-way valve being connected by first and second openings via pipes to a third opening of the first three-way valve and to an input of the strontium-rubidium generator, respectively, an output of the generator being coupled to a first opening of the fourth three-way valve,

wherein the third opening of the third valve and a second opening of the fourth valve are in communication by a pipe, the first air bubble detector is mounted on a pipe between the eluent tank and the first opening of the first valve while the second detector is mounted on a pipe between the third openings of the fourth and second valves.

2. The system according to claim 2, characterized in that the radioactivity measurement means include first and second activity sensors.

3. The system according to claim 3, characterized in that the first activity sensor is placed on a pipe between the third openings of the fourth and second valves and is embodied as a beta detector.

4. The system according to claim 2, characterized in that the waste receptacle is implemented as a protection box including waste weight check means in the form of a force

sensor, while the second activity sensor in the form of a gamma detector is mounted within an opening of the protective box.

5. The system according to claim 1, characterized in that the strontium-rubidium generator has a radiation protection including external main and transportation protective containers, said main protection container being mounted stationary on a shelf of a bogie.

6. The system according to claim 1, characterized in that it is mounted in a closed movable housing.

7. The system according to claim 6, characterized in that the housing is provided with a shifting tabletop.

(12) МЕЖДУНАРОДНАЯ ЗАЯВКА, ОПУБЛИКОВАННАЯ В СООТВЕТСТВИИ С ДОГОВОРОМ О ПАТЕНТНОЙ КООПЕРАЦИИ (PCT)

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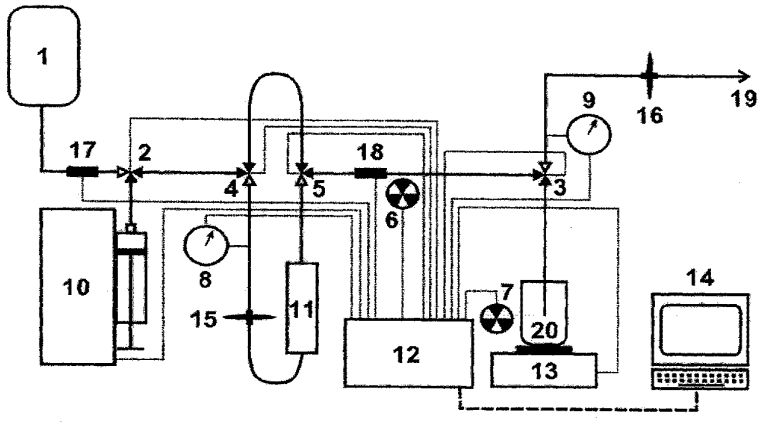
[продолжение на следующей странице]

(54) **Title:** AUTOMATED STRONTIUM-RUBIDIUM INFUSION SYSTEM

(54) **Название изобретения:** АВТОМАТИЗИРОВАННАЯ СТРОНЦИЙ - РУБИДИЕВАЯ ИНФУЗИОННАЯ СИСТЕМА



Фиг. 1

(57) **Abstract:** The invention relates to medical engineering. The inventive automated strontium-rubidium infusion system comprises a container with eluent, a strontium-rubidium generator with a filter and a pressure sensor and an eluate infusion unit, which are connected by means of a transporting system provided with pipes and two three-way valves, radioactivity measuring means and a control and operating unit. An eluent container is connected to a syringe pump via the first valve, the second three-way valve is connected to the eluate infusion unit and a waste receptacle via the second filter. First and second air bubbles detectors are connected to the control and operating unit. The second three-way valve is connected to the first three-way valve and to the input of the strontium-rubidium generator. The generator output is connected to the fourth valve which is connected to the third valve. The first air bubbles detector is placed between the eluent container and the first valve and the second air bubbles detector is placed between the fourth and second valves.

[продолжение на следующей странице]

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Декларация в соответствии с правилом 4.17:
— *об авторстве изобретения (правило 4.17 (iv))*

Опубликована:
— *с отчётом о международном поиске*

(57) Реферат: Изобретение относится к медицинской технике. Автоматизированная стронций - рубидиевая инфузионная система содержит емкость с элюентом, стронций-рубидиевый генератор с фильтром и датчиком давления, средство для инфузии элюата, соединенные системой транспортировки с трубопроводами и двумя трехходовыми клапанами, средства для измерения радиоактивности и блок контроля и управления. Емкость с элюентом через первый клапан соединена со шприцевым насосом, второй трехходовой клапан соединен через второй фильтр со средством для инфузии элюата и со сборником отходов. Первый и второй детекторы воздушных пузырьков подключены к блоку контроля и управления. Второй трехходовой клапан связан с первым трехходовым клапаном и входом стронций-рубидиевого генератора. Выход генератора подключен к четвертому клапану, соединенному с третьим клапаном. Первый детектор воздушных пузырьков установлен между емкостью с элюентом и первым клапаном, а второй детектор - между четвертым и вторым клапанами.

Автоматизированная стронций – рубидиевая инфузионная система

Изобретение относится к медицинской технике, в частности к средствам автоматизации процесса производства диагностического раствора от радионуклидного стронций-рубидиевого генератора и дистанционного проведения контролируемой инфузии, с автоматическим контролем основных характеристик процесса, таких как величина вводимой активности, величина окклюзии, наличие воздушных пузырей, а также вес и активность раствора в контейнере с отходами.

Одним из наиболее перспективных направлений в ядерной диагностике является позитронно-эмиссионная томография (ПЭТ). Для работы в ПЭТ-центрах используют такие коротко и ультра-короткоживущие изотопы как – C-11, O-15, N-13, F-18. Это обязывает иметь на месте проведения диагностики циклотроны для наработки таких изотопов. Возможности ПЭТ-диагностики могут быть существенно расширены при использовании генераторных систем, время жизни материнского радионуклида которых значительно превышает время жизни нарабатываемых на циклотронах ПЭТ-центров радионуклидов. Наиболее перспективными среди изотопных генераторов для ПЭТ стоят генераторные системы ^{82}Sr ($t_{1/2}$=25,6 дней) → ^{82}Rb ($t_{1/2}$=75 сек) и ^{68}Ge ($t_{1/2}$=271 дней) → ^{68}Ga ($t_{1/2}$=68,3 мин).

Поэтому в применении к генераторным изотопам можно говорить о снабжении ими любых клиник, обладающих ПЭТ-сканнерами, в рамках региона, государства или группы государств.

Наибольшее применение генераторные системы могут найти в смонтированных в автотрейлерах так называемых мобильных ПЭТ, вызываемых для обслуживания клиник, не имеющих не только собственных циклотронов, но и собственных ПЭТ-сканнеров. При отсутствии «привязки» такого мобильного ПЭТ-сканнера к изотопной базе существенно расширяется радиус обслуживаемой им территории.

Известна стронций-рубидиевая инфузионая система производства диагностического раствора от радионуклидного стронций-рубидиевого генератора и проведения контролируемой инфузии (US 4562829, 1986), включающая емкость с элюентом, соединенную соответствующими трубопроводами системы транспортировки через первый трехходовой клапан с шприцевым насосом, стронций-рубидиевый генератор с первыми фильтром и датчиком давления на входе, второй трехходовой клапан, первое отверстие которого подключено через второй фильтр к средству для инфузии элюата пациенту, а второе – к средству для сбора и хранения излишков элюата, средства для измерения радиоактивности и система контроля и управления. Известная система не является оптимальной по степени защиты от радиоактивного излучения и по сроку службы генераторной колонки.

Предлагаемое изобретение направлено на устранение перечисленных недостатков. Достигаемый при ее использовании технический результат заключается в повышении эффективности проведения диагностической процедуры за счет автоматизации процедуры инфузии, снижении доз нежелательного радиоактивного облучения пациента и обслуживающего персонала, увеличении сроков эксплуатации генераторной колонки.

Сущность предлагаемого изобретения заключается в том, что автоматизированная стронций – рубидиевая инфузионная система, содержит емкость с элюентом, стронций-рубидиевый генератор с фильтром и датчиком давления на входе, средство для инфузии элюата пациенту, соединенные системой транспортировки с трубопроводами и двумя трехходовыми клапанами, средства для измерения радиоактивности и блок контроля и управления. Причем емкость с элюентом через первое и второе отверстия первого трехходового клапана соединена с шприцевым насосом, первое отверстие второго трехходового клапана подключено трубопроводами через второй фильтр к средству для инфузии элюата пациенту, а второе отверстие – к сборнику отходов. В систему

дополнительно введены третий и четвертый трехходовые клапаны, первый и второй детекторы воздушных пузырьков, подключенные к блоку контроля и управления, связанного с компьютером, при этом третий трехходовой клапан связан первым и вторым отверстиями через трубопроводы с третьим отверстием первого трехходового клапана и входом стронций – рубидиевого генератора, соответственно. Выход генератора подключен к первому отверстию четвертого трехходового клапана, причем третье отверстие третьего клапана и второе отверстие четвертого клапана связаны трубопроводом, первый детектор воздушных пузырьков установлен на трубопроводе между емкостью с элюентом и первым отверстием первого клапана, а второй детектор установлен на трубопроводе между третьими отверстиями четвертого и второго клапанов.

Кроме того, средства для измерения радиоактивности включают первый и второй датчики активности. При этом первый датчик активности размещен на трубопроводе между третьими отверстиями четвертого и второго клапанов и выполнен в виде бета-детектора.

Радиационная защита средства для сбора и хранения излишков элюата может быть выполнена в виде защитного бокса, включающего средство контроля веса отходов в виде датчика усилия, а в отверстии защитного бокса установлен второй датчик активности для определения уровня радиоактивности отходов в виде гамма-детектор.

Колонка стронций – рубидиевого генератора имеет радиационную защиту, включающую, предпочтительно, внешний основной и транспортный защитные контейнеры, при этом основной защитный контейнер стационарно установлен на полке тележки.

Система устанавливается в закрытом перемещаемом корпусе. Кроме того, корпус снабжен сдвигающейся столешницей.

Сущность изобретения поясняется следующими чертежами:

Фиг. 1 – схема инфузионной системы;

фиг. 2 – представлен общий вид генераторной установки сбоку;

фиг. 3 – общий вид генераторной установки сверху.

Ниже перечислены условные обозначения, используемые на черетже:

1 – емкость с элюентом

2, 3, 4, 5 – трехходовые клапаны

6, 7 – датчики активности

8, 9 – датчики давления

10 – шприцевой насос

11 – стронций-рубидиевый генератор

12 – блок контроля и управления

13 – датчик веса

14 – удаленный компьютер

15, 16 – фильтры

17, 18 – детекторы воздушных пузырьков

19 – средство для инфузии элюата пациенту (игла)

20 – сборник отходов элюента и элюата

21 – перемещаемый корпус

22 – штатив

23 – защитный контейнер стронций – рубидиевого генератора

24 – защитный контейнер для бета – детектора

25 – источник питания

26 – защитный бокс емкости для отходов

27 – сдвигающаяся столешница.

Автоматизированная стронций – рубидиевая инфузионная система включает в себя средства для генерации рубидия-82 в растворе, который может быть введен пациенту, а именно стронций-рубидиевый генератор 11 (фиг.1), обычного типа в транспортном контейнере. Этот контейнер помещается в защитный внешний основной контейнер 23 и совместно с последним осуществляет функцию основной радиационной защиты. Система в сборе может устанавливаться в перемещаемом корпусе 21 (фиг.

2), закрытым декоративными панелями (не показано). На столешнице установлен штатив 22 с укрепленном на нем емкостью с элюентом 1. Кроме того, здесь установлен шприцевой насос 10 и компьютер 14. На верхней полке перемещаемого корпуса 21 установлены:

- основной защитный контейнер 23, внутрь которого помещен стандартный транспортный контейнер со стронций-рубидиевым генератором 11;
- защитный бокс 24 с размещенным внутри него детектором бета-активности, измеряющим активность раствора, прошедшего через стронций-рубидиевый генератор;
- источник питания 25.

На нижней полке размещен защитный бокс 26, внутри которого располагается сборник отходов элюента и элюата.

На фиг. 3 верхняя крышка контейнера 23 откинута, что позволяет увидеть полость, внутрь которой помещается транспортный контейнер со стронций-рубидиевым генератором 11. Для того, чтобы облегчить доступ к основному защитному контейнеру 23 во время перезарядки генераторной системы (извлекается транспортный контейнер с отработавшей колонкой стронций-рубидиевого генератора 11 и устанавливается транспортный контейнер со свежей генераторной колонкой) – часть столешницы выполнена в виде сдвигающейся столешницы 27, обеспечивающей удобство при работе.

Кроме того, система включает в себя средства для проведения инфузии, а именно (фиг. 1): шприцевой дистанционно управляемый инфузионный насос 10, шток которого приводится в действие, например, шаговым двигателем; средства для автоматизированного заполнения шприцевого насоса элюентом 1 (0.9 % раствором NaCl); систему транспортировки элюента и элюата до пациента или сборника отходов элюента и элюата, снабженную многоходовыми (трехходовыми) клапанами 2 – 5 (фиг.1), осуществляющими ветвление системы транспортировки в

соответствии с программой проведения работ; антибактериальные средства защиты, а именно антибактериальные фильтры 15 и 16 на входе и выходе системы транспортировки; средства измерения активности элюата для текущего контроля и дозирования при инфузии в пациента 6 и 7; средства измерения давления 8 и 9 в транспортной системе, в том числе и для измерения окклюзии; сборник отходов элюента и элюата 20, в том числе с измерением величины активности и веса раствора в емкости для отходов 13 и осуществления защиты от радиоактивности; средства автоматизированного контроля всего процесса элюации и его составных частей 12, осуществляемого с помощью бортового или удаленного компьютеров 14.

В описываемой системе емкость с элюентом 1 (соляным раствором) соединена пластиковым фитингом с трубопроводом (например, трубочкой для инфузий, которая имеет внешний диаметр 2.5 мм при внутреннем диаметре 1.5 мм). Отрезки таких трубочек (трубопроводы) далее используются для построения всей транспортной системы для инфузии. Другой конец трубопровода подсоединен через детектор воздушных пузырьков 17, который, в случае прохождения воздушного пузырька, вырабатывает сигнал на блок контроля и управления 12, который вырабатывает управляющий сигнал на клапаны 2, 3, 4 и 5, в результате чего, раствор элюента, содержащий воздушный пузырек, удаляется в сборник отходов элюента и элюата 20, не проходя колонку стронций-рубидиевого генератора 11.

Клапан 2 осуществляет перевод инфузионной системы в один из двух возможных режимов работы: (1) заполнение шприца при работе шприцевого насоса 10 на всасывание соляного раствора из емкости с элюентом 1 (через первое и второе отверстия клапана) или (2) инфузию, т.е. подачу соляного раствора из заполненного шприца шприцевого насоса 10 в инфузионную систему (через первое и третье отверстия клапана).

Трехходовой клапан 2 далее соединен отрезком соединительной трубки с первым отверстием третьего трехходового клапана 4, второе отверстие которого соединено через первый фильтр 15 с входом колонки стронций-рубидиевого генератора 11. Контроль давления на входе в колонку стронций-рубидиевого генератора 11 осуществляется первым датчиком давления 8.

Третьим отверстием клапан 4, через отрезок соединительной трубки, подсоединен ко второму отверстию четвертого трехходового клапана 5. Этот клапан также имеет соединения с выходной трубкой колонки стронций-рубидиевого генератора 11 (первое отверстие) и продолжением инфузионной системы на третьем отверстии.

В режиме работы шприцевого насоса «инфузия» пара трехходовых клапанов 4, 5, работая синхронно, позволяет либо прокачивать соляной раствор из шприца 10 через колонку стронций-рубидиевого генератора дальше в инфузионную систему уже в виде элюата, т.е. раствора, обогащенного Rb-82, либо прокачивать соляной раствор в инфузионную систему, минуя стронций-рубидиевый генератор 11. Этот режим работы используется тогда, когда необходимое количество активности Rb-82 наработано и оно должно быть доставлено пациенту 19, а инфузионная система должна быть заполнена неактивным соляным раствором на конец инфузии в пациента. При использовании режима прокачки соляного раствора практически вся инфузионная система, за исключением соединительного трубопровода от выхода из стронций-рубидиевого генератора до четвертого трехходового клапана, будет заполнена нерадиоактивным соляным раствором и не будет являться источником дополнительной нежелательной радиоактивности на пациента и обслуживающий персонал; кроме того, объем соляного раствора, необходимый для додавливания наработанного элюата в пациента не будет проходить через колонку стронций-рубидиевого генератора и истощать ее, т.к. известно, что потенция генератора зависит не только от времени его

эксплуатации, но также и от объема пропущенного через него соляного раствора.

На трубопроводе от третьего отверстия четвертого трехходового клапана 5 до третьего отверстия второго трехходового клапана 3 установлены первый детектор радиоактивности 6 (бета-детектор) и второй детектор воздушных пузырьков 18, аналогичный первому детектору пузырьков 17. При обнаружении воздушного пузырька, детектор 18 вырабатывает сигнал на блок контроля и управления, который вырабатывает управляющий сигнал на клапан второго трехходового клапана 3. В результате, элюат содержащий воздушный пузырек, удаляется в сборник отходов элюента и элюата 20. Если воздушный пузырек не обнаружен, элюат направляется через первое отверстие трехходового клапана 3 и второй фильтр 16 в пациента, т.е. на иглу 19

Детектор радиоактивности 6 работает в режиме реального времени и измеряет активность Rb-82 в месте расположения детектора 18.

Контроль за наполнением сборника для отходов жидкостью осуществляется с помощью датчика усилий (не показан). Для измерения радиоактивности, содержащейся в сборнике для отходов элюента и элюата используется второй датчик радиоактивности 7 (гамма-детектор). Радиационная защита средства для сбора и хранения излишков элюата выполнена в виде защитного бокса, в состав которого включен датчик усилия, а в отверстии защитного бокса установлен второй датчик активности.

При осуществлении инфузии в пациента второй трехходовой клапан 3 переключен на пропускание элюата на трубопровод соединенный с иглой 19 через миллипоровский фильтр 16. На этом отрезке установлен второй датчик давления 9, позволяющий измерять давление окклюзии при введении раствора, содержащего Rb-82, в пациента.

Процесс работы стронций-рубидиевой инфузионной системы происходит под управлением управляющей компьютерной программы, в которой прописывается состояние каждого из устройств, входящих в инфузионную систему, на момент начала и окончания выполнения шага, также прописываются действия этих устройств и условия их функционирования в нормальных условиях и в случае возникновения аварийной ситуации.

Для исключения переполнения в сборнике отходов элюента и элюата 20 радиоактивной жидкости, осуществляется дистанционный контроль за предельным значением ее уровня с помощью датчика усилия, при этом контролируется общий вес тары и жидкости, осуществляется текущий контроль за значением веса (объема) жидкости и за предельным его значением. Кроме того, фиксируя вес пустой тары для сбора отходов, система регламентного опроса блока контроля и управления установки получает информацию о том, что тара установлена в контейнере. Максимальный объём отходов в таре составляет 250 мл.

Блок контроля и управления подключен к удаленному компьютеру, на дисплее которого отображается графическая мнемосхема генераторного устройства, обеспечивающая наблюдение контролируемых параметров в автоматическом режиме и оперативного управления отдельными элементами (электромагнитными трехходовыми клапанами 2 - 5, насосом 10) в ручном режиме. Схема позволяет наблюдать за текущим состоянием всех элементов описываемой системы инфузии (клапанов 2-5, детекторов воздушных пузырьков 17, 18) и за работой шприцевого насоса 10. Также она позволяет получать информацию о параметрах давления в магистралях от датчиков давления 8, 9, активности элюата на выходе из генераторной колонки 11 и суммарной активности, веса емкости сборника отходов элюента и элюата 20, активности в емкости с отходами от детекторов 6,7.

Блок контроля и управления 12 системы связан с управляющими элементами генераторной установки – электромагнитными трехходовыми

клапанами 2, 3, 4, 5 и насосом 10, а также включает элементы для сбора и обработки сигналов с датчиков 6, 7 (датчики радиоактивности), 8, 9 (датчики давления), 17, 18 (детекторы воздушных пузырьков). Блок управления 12 связан с панельным персональным компьютером (PPC) или любым другим удаленным компьютером (14) по каналу Ethernet. Он получает команды от PPC или удаленного компьютера на выполнение отдельных шагов программы работы генераторной установки и информирует их о текущем состоянии управляемых им элементов и состоянии датчиков системы.

Описываемая система повышает безопасность эксплуатации, так как автоматизация процесса инфузии позволила значительно сократить радиоактивное облучение за счет введения в систему дополнительных клапанов, обеспечивающих ветвление трубопроводов. В результате, появилась возможность додавливания наработанного элюата в пациента элюентом, минуя стронций – рубидиевый генератор. При этом трубопровод прокачивается нерадиоактивным элюентом и не происходит дополнительного истощения стронций – рубидиевого генератора, что увеличивает срок его эксплуатации. Кроме того, исключается риск содержания воздушных пузырьков в элюанте, доставляемого пациенту, за счет введения в систему детекторов воздушных пузырьков, при обнаружении которых, элюент сразу направляется к сборнику отходов элюента и элюата через ответвления трубопровода, не истощая стронций – рубидиевый генератор.

Формула изобретения

1. Автоматизированная стронций – рубидиевая инфузионная система, содержащая емкость с элюентом, стронций-рубидиевый генератор с фильтром и датчиком давления на входе, средство для инфузии элюата пациенту, соединенные системой транспортировки с трубопроводами и двумя трехходовыми клапанами, средства для измерения радиоактивности и блок контроля и управления, причем емкость с элюентом через первое и второе отверстия первого трехходового клапана соединена с шприцевым насосом, первое отверстие второго трехходового клапана подключено трубопроводами через второй фильтр к средству для инфузии элюата пациенту, а второе отверстие – к сборнику отходов, отличающаяся тем, что дополнительно введены третий и четвертый трехходовые клапаны, первый и второй детекторы воздушных пузырьков, подключенные к блоку контроля и управления, связанного с компьютером, при этом третий трехходовой клапан связан первым и вторым отверстиями через трубопроводы с третьим отверстием первого трехходового клапана и входом стронций – рубидиевого генератора, соответственно, выход генератора подключен к первому отверстию четвертого трехходового клапана, причем третье отверстие третьего клапана и второе отверстие четвертого клапана связаны трубопроводом, первый детектор воздушных пузырьков установлен на трубопроводе между емкостью с элюентом и первым отверстием первого клапана, а второй детектор установлен на трубопроводе между третьими отверстиями четвертого и второго клапанов.

2. Система по п.1, отличающаяся тем, что средства для измерения радиоактивности включают первый и второй датчики активности.

3. Система по п.2, отличающаяся тем, что первый датчик активности размещен на трубопроводе между третьими отверстиями четвертого и второго клапанов и выполнен в виде бета-детектора.

4. Система по п.1, отличающаяся тем, что радиационная защита сборника отходов выполнена в виде защитного бокса, включающего

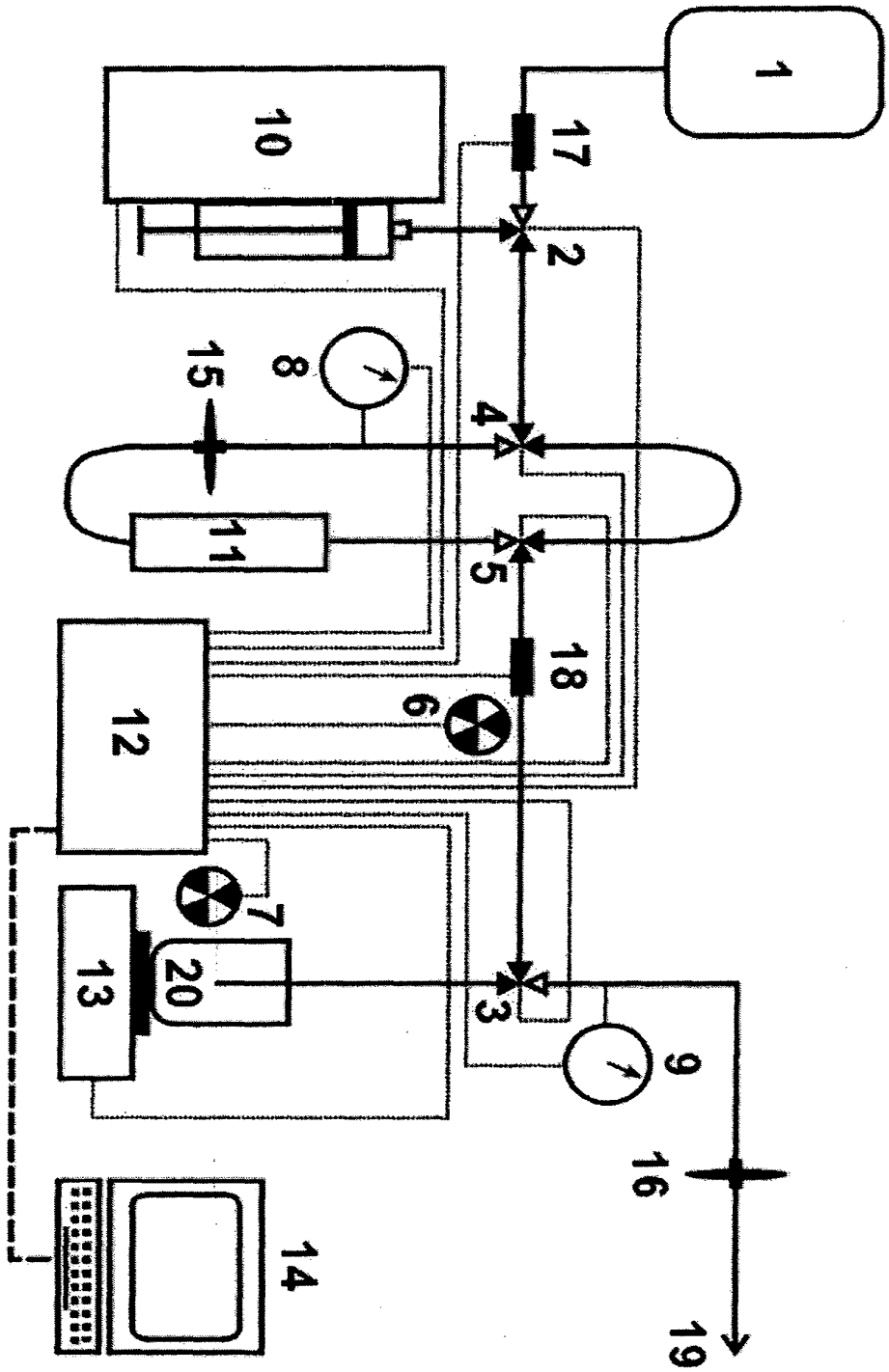
средство контроля веса отходов, выполненного в виде датчика усилия, а в отверстии

защитного бокса установлен второй датчик активности для определения радиоактивности отходов, в виде гамма-детектора.

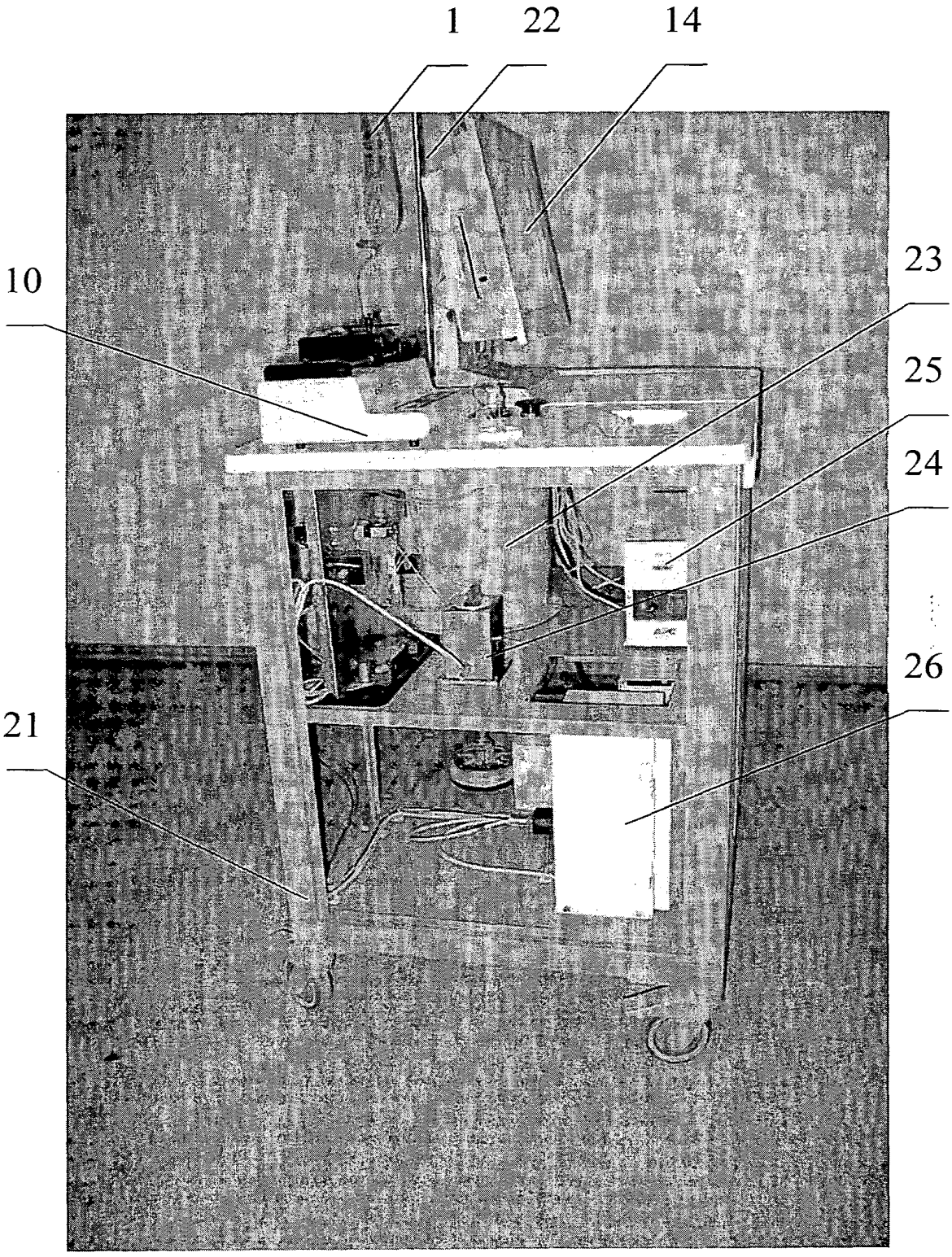
5. Система по п.1, отличающаяся тем, что стронций – рубидиевый генератор имеет радиационную защиту, включающую внешний основной и транспортный защитные контейнеры, при этом основной защитный контейнер стационарно установлен на полке тележки.

6. Система по п.1, отличающаяся тем, что она установлена в закрытом перемещаемом корпусе.

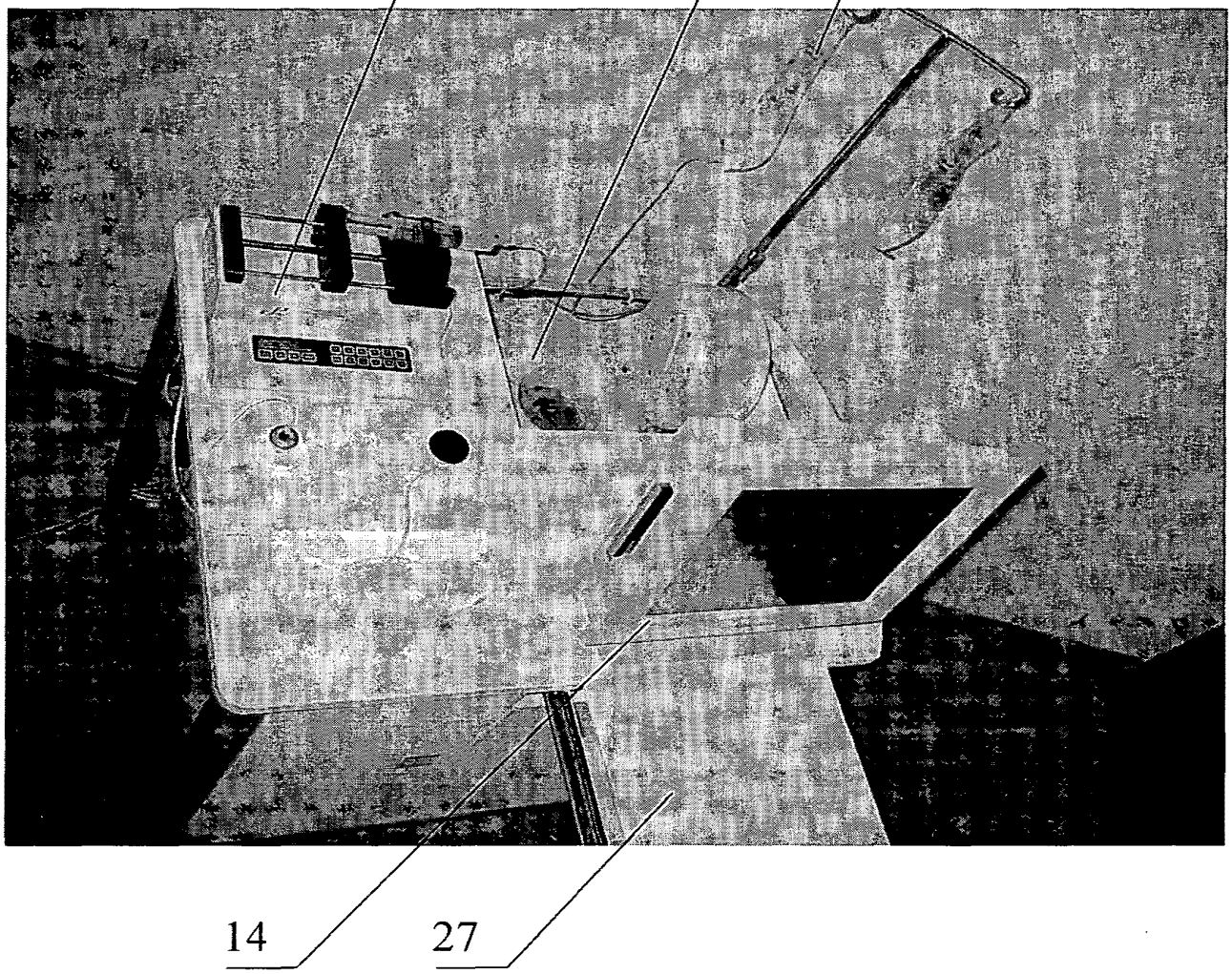
7. Система по п.6, отличающаяся тем, что корпус снабжен сдвигающейся столешницей.



Фиг. 1



Фиг. 2



Фиг. 3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/RU2008/000211

A. CLASSIFICATION OF SUBJECT MATTER

A61M 5/168 (2006.01)
A61M 36/06 (2006.01)
A61B 6/00 (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)
A61M 36/00-36/06, 5/00-5/155, AGIB 6/00-6/10, A61M 5/168

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 practicable, search terms used)
http://www. uspto. gov; http://depatisnet.dpma.de; http://ep.espacenel.com; http://www.fips.ru; http://www.eapatis.com

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4562829 A (E.R. SQUIBB & SONS, INC.), 07.01.1986, the abstract, figure 1	1-7
A	EP 0310148 A (E.R. SQUIBB & SONS, INC), 05.04.1988, the claims, figure	1-7
A	RU 2219959 C2 (FEDERALNOE GOSUDARSTVENNOE UNITARNOE PREDPRIYATIE NAUCHNO-ISSLEDOVATELSKY INSTITUT ELEKTROMEKHANIKI) 27.12.2003, the claims, figure 1	1-7

☐ Further documents are listed in the continuation of Box C. ☐ 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
24 July 2008	04 September 2008
Name and mailing address of the ISA/ RU	Authorized officer
Facsimile No.	Telephone No.

Form PCT/ISA/210 (second sheet) (April 2005)

ОТЧЕТ О МЕЖДУНАРОДНОМ ПОИСКЕ

Международная заявка № PCT/RU 2008/000211

А. КЛАССИФИКАЦИЯ ПРЕДМЕТА ИЗОБРЕТЕНИЯ: ***A61M 5/168*** *(2006.01)*
A61M 36/06 *(2006.01)*
Согласно Международной патентной классификации МПК ***A61B 6/00*** *(2006.01)*

В. ОБЛАСТИ ПОИСКА:

Проверенный минимум документации (система классификации с индексами классификации):

Другая проверенная документация в той мере, в какой она включена в поисковые подборки:

A61M 36/00-36/06, 5/00-5/155, A61B 6/00-6/10, A61M 5/168

Электронная база данных, использовавшаяся при поиске (название базы и, если, возможно, используемые поисковые термины): http://www. uspto. gov; http://depatisnet.dpma.de; http://ep.espacenet.com; http://www.fips.ru; http://www.eapatis.com

С. ДОКУМЕНТЫ, СЧИТАЮЩИЕСЯ РЕЛЕВАНТНЫМИ:

Категория*	Цитируемые документы с указанием, где это возможно, релевантных частей	Относится к пункту №
A	US 4562829 A (E.R. SQUIBB & SONS, INC.) 07.01.1986, реферат, фиг. 1	1-7
A	EP 0310148 A (E.R. SQUIBB & SONS, INC) 05.04.1989, формула, фиг.	1-7
A	RU 2219959 C2 (ФЕДЕРАЛЬНОЕ ГОСУДАРСТВЕННОЕ УНИТАРНОЕ ПРЕДПРИЯТИЕ НАУЧНО-ИССЛЕДОВАТЕЛЬСКИЙ ИНСТИТУТ ЭЛЕКТРОМЕХАНИКИ) 27.12.2003, формула, фиг. 1	1-7

☐ последующие документы указаны в продолжении графы С. ☐ данные о патентах-аналогах указаны в приложении

* Особые категории ссылочных документов:

A документ, определяющий общий уровень техники и не считающийся особо релевантным

E более ранняя заявка или патент, но опубликованная на дату международной подачи или после нее

L документ, подвергающий сомнению притязание (я) на приоритет, или который приводится с целью установления даты публикации другого ссылочного документа, а также в других целях (как указано)

O документ, относящийся к устному раскрытию, использованию, экспонированию и т.д.

P документ, опубликованный до даты международной подачи, но после даты испрашиваемого приоритета

T более поздний документ, опубликованный после даты международной подачи или приоритета, но приведенный для понимания принципа или теории, на которых основывается изобретение

X документ, имеющий наиболее близкое отношение к предмету поиска; заявленное изобретение не обладает новизной или изобретательским уровнем, в сравнении с документом, взятым в отдельности

Y документ, имеющий наиболее близкое отношение к предмету поиска; заявленное изобретение не обладает изобретательским уровнем, когда документ взят в сочетании с одним или несколькими документами той же категории, такая комбинация документов очевидна для специалиста

& документ, являющийся патентом-аналогом

Дата действительного завершения международного поиска: 24 июля 2008 (24.07.2008)	Дата отправки настоящего отчета о международном поиске: 04 сентября 2008 (04.09.2008)
Наименование и адрес ISA/RU ФГУ ФИПС, РФ,123995, Москва, Г-59, ГСП-5, Бережковская наб., 30,1 Факс:(499) 243-3337	Уполномоченное лицо: Л. Черепанова Телефон № (499) 240-25-91

Форма PCT/ISA/210 (второй лист)(июль 2008)

Electronic Acknowledgement Receipt

EFS ID:	4634335
Application Number:	12137363
International Application Number:	
Confirmation Number:	7372
Title of Invention:	INFUSION SYSTEM CONFIGURATIONS
First Named Inventor/Applicant Name:	Charles R. Quirico
Customer Number:	22859
Filer:	Elisabeth Lacy Belden
Filer Authorized By:	
Attorney Docket Number:	56782.1.6
Receipt Date:	20-JAN-2009
Filing Date:	11-JUN-2008
Time Stamp:	11:40:02
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_6_IDS2.pdf	756410 59c7e603eee5830eb3c4d9a1608e3c7225787f33	no	4

Warnings:	
Information:	

A U.S. Patent Number Citation or a U.S. Publication Number Citation is required in the Information Disclosure Statement (IDS) form for autoloading of data into USPTO systems. You may remove the form to add the required data in order to correct the Informational Message if you are citing U.S. References. If you chose not to include U.S. References, the image of the form will be processed and be made available within the Image File Wrapper (IFW) system. However, no data will be extracted from this form. Any additional data such as Foreign Patent Documents or Non Patent Literature will be manually reviewed and keyed into USPTO systems.

2	Foreign Reference	56782_1_WO08140351A1.pdf	2108847 898d2e8296aea121d5dbb5ba800d0676d167dda4	no	28

Warnings:

Information:

Total Files Size (in bytes):	2865257

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
12/137,363	06/11/2008	Charles R. Quirico	56782.1.6

CONFIRMATION NO. 7372

POA ACCEPTANCE LETTER

22859
INTELLECTUAL PROPERTY GROUP
FREDRIKSON & BYRON, P.A.
200 SOUTH SIXTH STREET
SUITE 4000
MINNEAPOLIS, MN 55402

OC000000033936556

Date Mailed: 01/08/2009

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 01/05/2009.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

/sabuna/

Office of Data Management, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

POWER OF ATTORNEY TO PROSECUTE APPLICATIONS BEFORE THE USPTO

I hereby revoke all previous powers of attorney given in the application identified in the attached statement under 37 CFR 3.73(b).

I hereby appoint:

☒ Practitioners associated with the Customer Number: 22859

as attorney(s) or agent(s) to represent the undersigned before the United States Patent and Trademark Office (USPTO) in connection with any and all patent applications assigned only to the undersigned according to the USPTO assignment records or assignment documents attached to this form in accordance with 37 CFR 3.73(b).

The practitioners associated with customer number 022859 (Fredrikson & Byron, P.A.) are hereby granted authorization to sign the attached statement under 37 CFR §3.73(b) that evidences ownership by **Bracco Diagnostics, Inc.**

Please change the correspondence address for the application identified in the attached statement under 37 CFR 3.73(b) to:

☒ The address associated with the Customer Number: 22859

OR

☐ Firm or Individual Name			
Address			
City		State	Zip
Country			
Telephone		Email	

Assignee Name and Address:

Bracco Diagnostics, Inc.
107 College Road East
Princeton, NJ 08540

A copy of this form, together with a statement under 37 CFR 3.73(b) (Form PTO/SB/96 or equivalent) is required to be filed in each application in which this form is used. The statement under 37 CFR 3.73(b) may be completed by one of the practitioners appointed in this form if the appointed practitioner is authorized to act on behalf of the assignee, and must identify the application in which this Power of Attorney is to be filed.

SIGNATURE of Assignee of Record

The individual whose signature and title is supplied below is authorized to act on behalf of the assignee

Signature			
Name	Michael R. von Ohlen	Date 5/9/08	
Title	Corporate Counsel	Telephone 609-514-2303	

Electronic Acknowledgement Receipt

EFS ID:	4550636
Application Number:	12137363
International Application Number:	
Confirmation Number:	7372
Title of Invention:	INFUSION SYSTEM CONFIGURATIONS
First Named Inventor/Applicant Name:	Charles R. Quirico
Customer Number:	22859
Filer:	Elisabeth Lacy Belden
Filer Authorized By:	
Attorney Docket Number:	56782.1.6
Receipt Date:	05-JAN-2009
Filing Date:	11-JUN-2008
Time Stamp:	13:04:01
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	Assignee showing of ownership per 37 CFR 3.73(b).	56782_1_6_Statement.pdf	202404 c72075bb4453c5674dacc53787ad76f0a2f485af	no	2

Warnings:	
Information:	

2	Power of Attorney	56782_PowerofAttorney.pdf	58043 283a0d970401b4122cc59ee7ac526c528e684bf5	no	1

Warnings:	
Information:	
Total Files Size (in bytes):	260447

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/96 (12-08)
Approved for use through 01/31/2009. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

STATEMENT UNDER 37 CFR 3.73(b)

Applicant/Patent Owner: Charles R. Quirico et al.

Application No./Patent No.: 12/137,363 Filed/Issue Date: June 11, 2008

Entitled: INFUSION SYSTEM CONFIGURATIONS

Bracco Diagnostics, Inc. , a corporation
(Name of Assignee) (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that it is:

1. ☑ the assignee of the entire right, title, and interest; or
2. ☐ an assignee of less than the entire right, title and interest
(The extent (by percentage) of its ownership interest is _____ %)

in the patent application/patent identified above by virtue of either:

A. ☑ An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel 022011, Frame 0380, or for which a copy therefore is attached.

OR

B. ☐ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: _____ To: _____
The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame _____, or for which a copy thereof is attached.

2. From: _____ To: _____
The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame _____, or for which a copy thereof is attached.

3. From: _____ To: _____
The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame _____, or for which a copy thereof is attached.

☐ Additional documents in the chain of title are listed on a supplemental sheet.

☑ As required by 37 CFR 3.73(b)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (*i.e.*, a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

/Elisabeth Lacy Belden/ January 5, 2009
Signature Date

Elisabeth Lacy Belden 612-492-7000
Printed or Typed Name Telephone Number

Patent Agent
Title

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

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United States Patent and Trademark Office
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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
12/137,363	06/11/2008	3763	2170	56782.1.6	36	4

CONFIRMATION NO. 7372

UPDATED FILING RECEIPT

22859
INTELLECTUAL PROPERTY GROUP
FREDRIKSON & BYRON, P.A.
200 SOUTH SIXTH STREET
SUITE 4000
MINNEAPOLIS, MN 55402

Date Mailed: 12/08/2008

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

Applicant(s)

Charles R. Quirico, Warren, NJ;
Ernest Balestracci, Iselin, NJ;
Daniel Darst, Zimmerman, MN;
Eric J. Krause, Big Lake, MN;
Vishal N. Lokhande, Mountain View, CA;
Jacob S. Childs, Minneapolis, MN;

Assignment For Published Patent Application

BRACCO DIAGNOSTICS, INC., Princeton, NJ

Power of Attorney: None

Domestic Priority data as claimed by applicant

Foreign Applications

Permission to Access - A proper **Authorization to Permit Access to Application by Participating Offices** (PTO/SB/39 or its equivalent) has been received by the USPTO.

If Required, Foreign Filing License Granted: 06/23/2008

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 12/137,363**

Projected Publication Date: 12/17/2009

Non-Publication Request: No

Early Publication Request: No

Title

INFUSION SYSTEM CONFIGURATIONS

Preliminary Class

604

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

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Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

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Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

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22859
Customer Number

Patent
Case No.: 56782.1.6

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Charles R. Quirico		
Application No.:	12/137,363	Group Art Unit:	3763
Filed:	June 11, 2008	Examiner:	
Title:	INFUSION SYSTEM CONFIGURATIONS		

Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO NOTICE TO FILE MISSING PARTS
OF A NON-PROVISIONAL APPLICATION

In response to the Notice to File Missing Parts of Application - Filing Date Granted mailed June 24, 2008, submitted herewith is an executed Declaration and Replacement Sheets (23 sheets). Submitted herewith in the amount of $130 is the surcharge fee. The Commissioner is hereby authorized to grant any extensions of time, including those that may be due under 37 C.F.R. §1.136, and to charge any fees that may be required, including those under 37 C.F.R. §§ 1.16 and 1.17, during the entire pendency of this application to Deposit Account No. 06-1910.

Entry of this document should complete all of the filing formalities and fully satisfy all requirements of the Notice to File Missing Parts. Accordingly, examination and allowance of this application in due course are respectfully solicited.

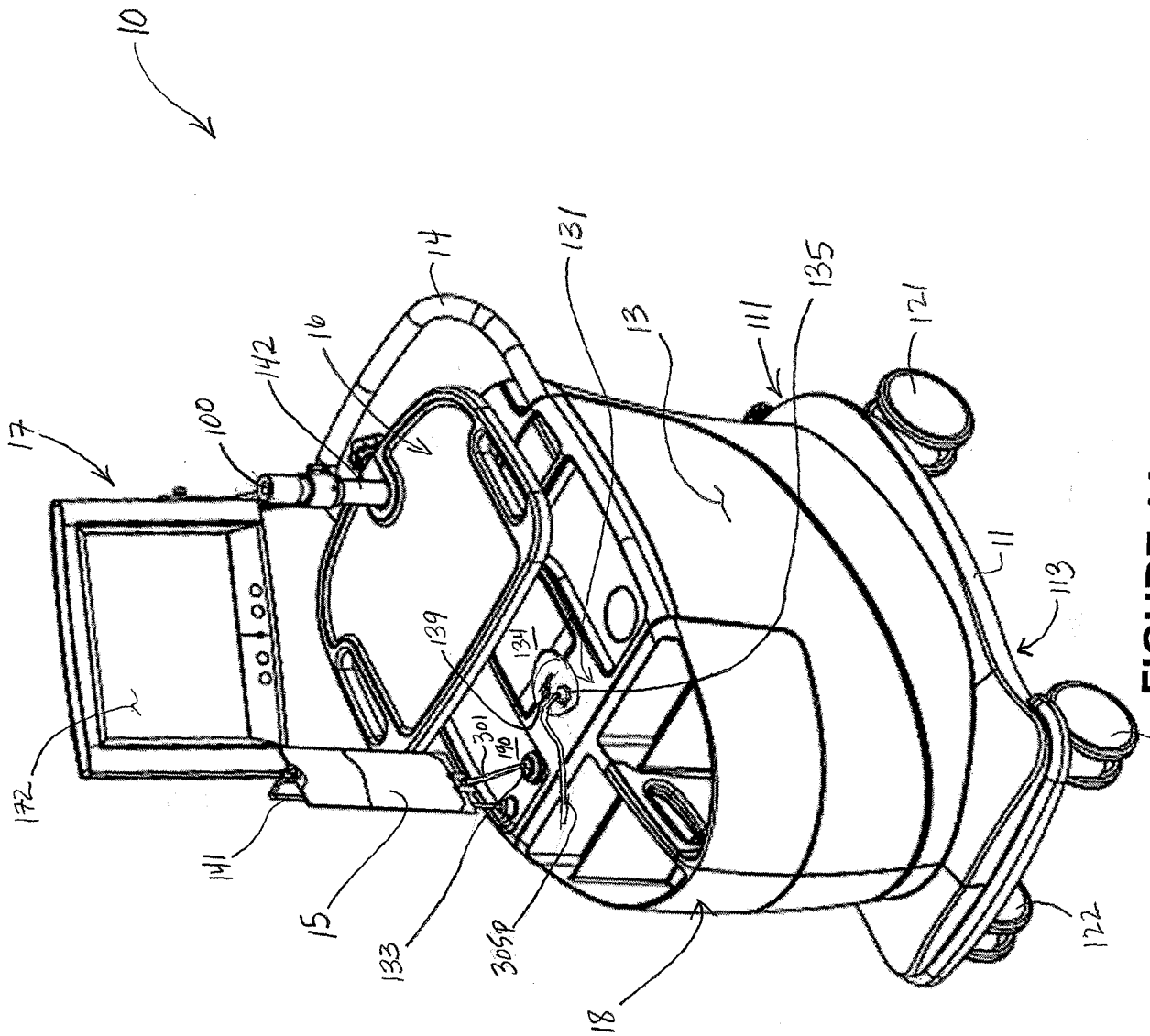
The Commissioner is hereby authorized to charge any underpayment or credit any overpayment to Deposit Account No. 06-1910.

Respectfully submitted,

November 24, 2008
Date

/Elisabeth Lacy Belden/
Elisabeth Lacy Belden
Registration No. 50,751

Fredrikson & Byron, P.A.
200 South Sixth Street, Suite 4000
Minneapolis, MN 55402-1425 USA
Telephone: (612) 492-7000
Facsimile: (612) 492-7077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17
100
142
16
14
131
13
111
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121
11
113
122
172
141
15
133
3059
18
139
134
301
190

FIGURE 1A

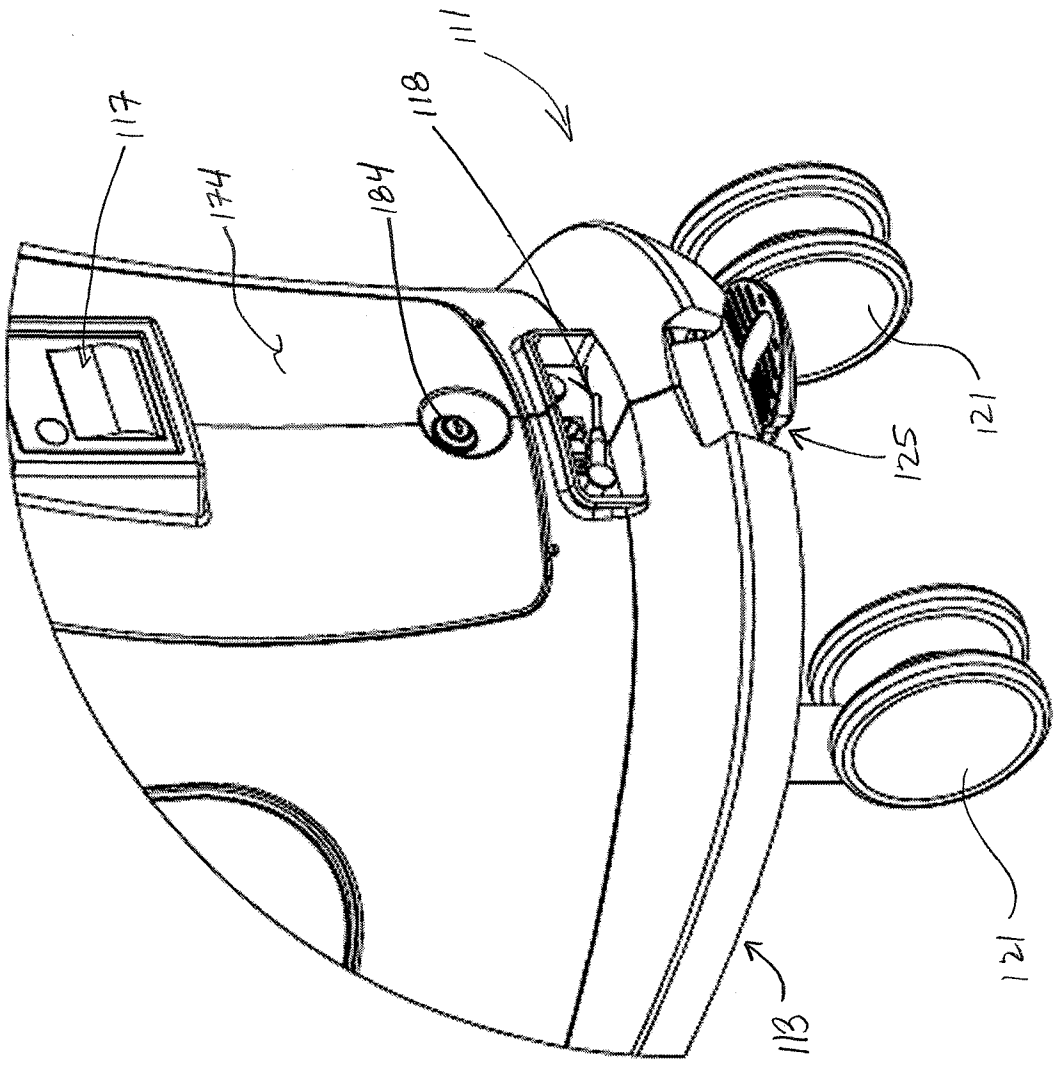
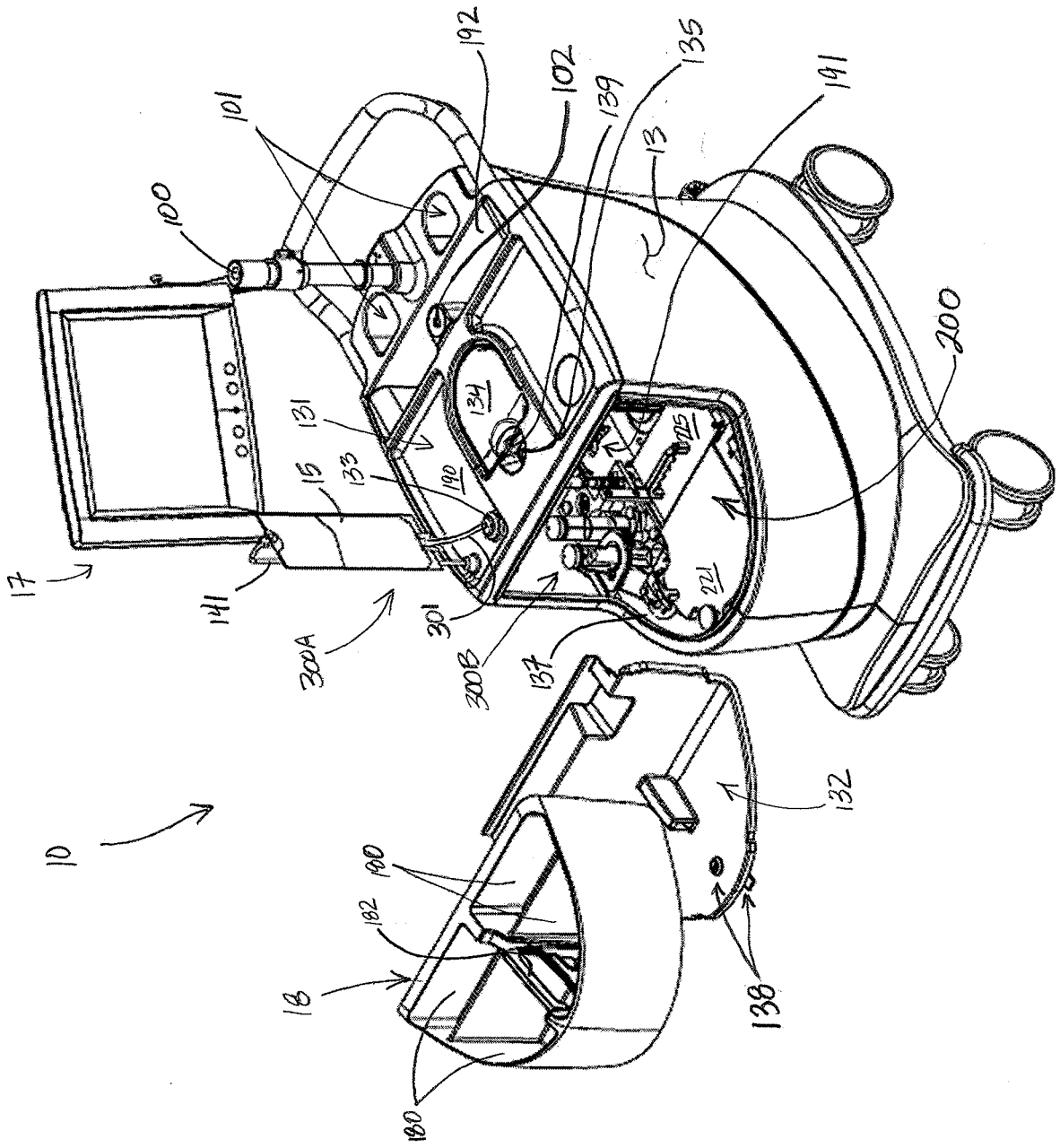


FIGURE 1B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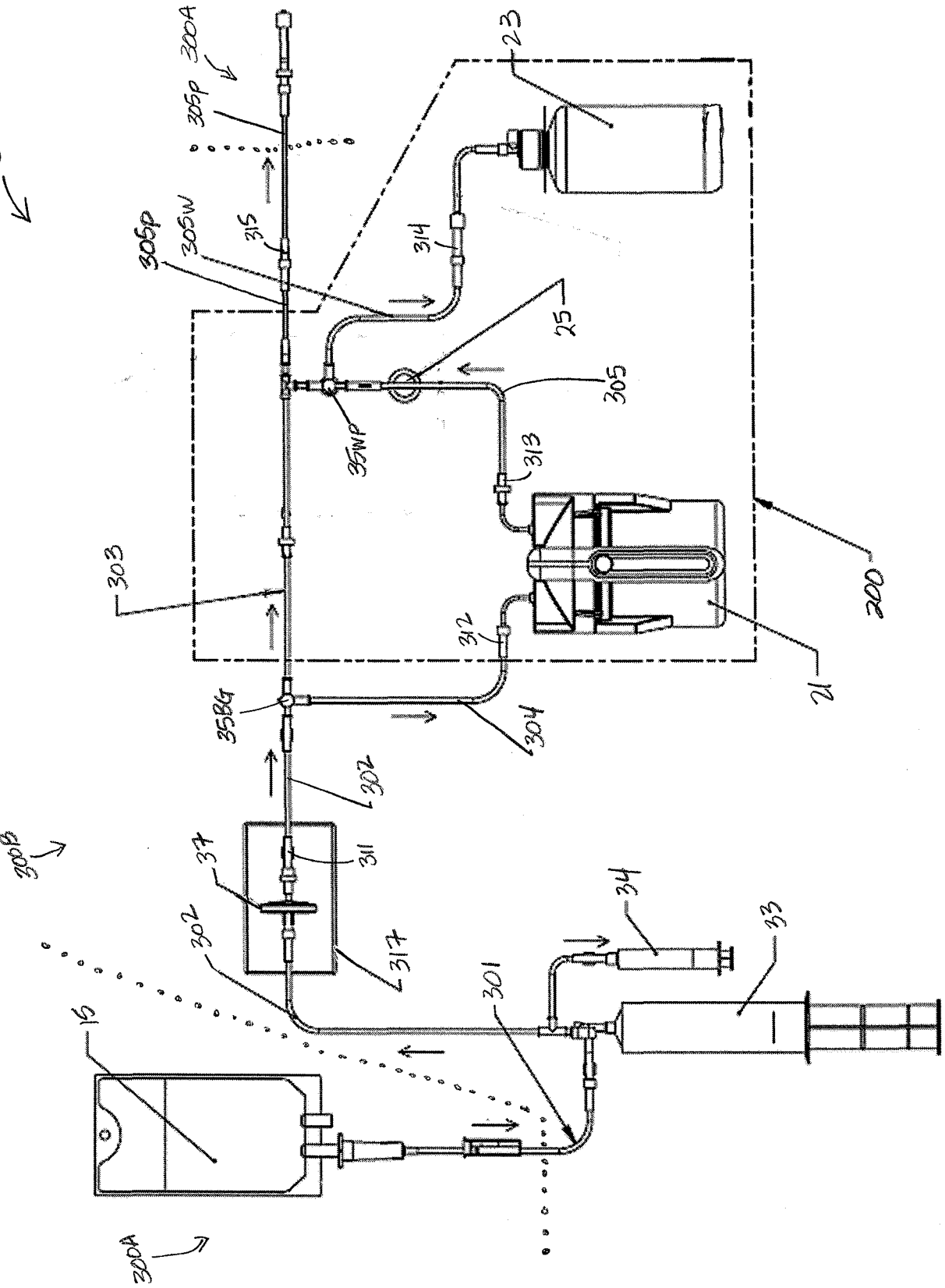
17
100
101
102
131
133
134
135
137
138
139
141
180
182
190
191
192
200
300A
300B
301
132
18
13
15

FIGURE 1C


300
300A
300B
305P
305SW
305WP
305BG
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21
23
25
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34
37

FIGURE 1D

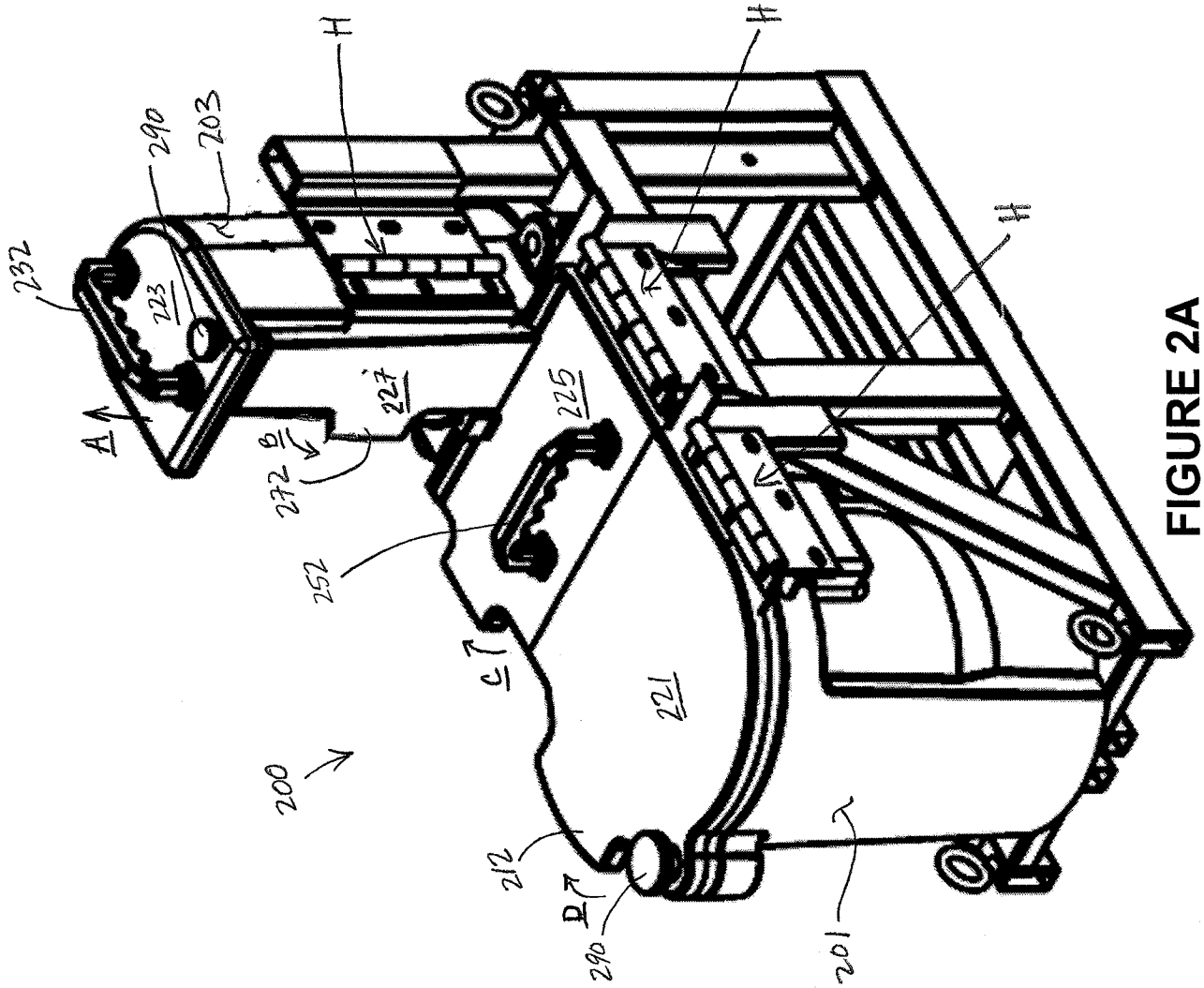


FIGURE 2A

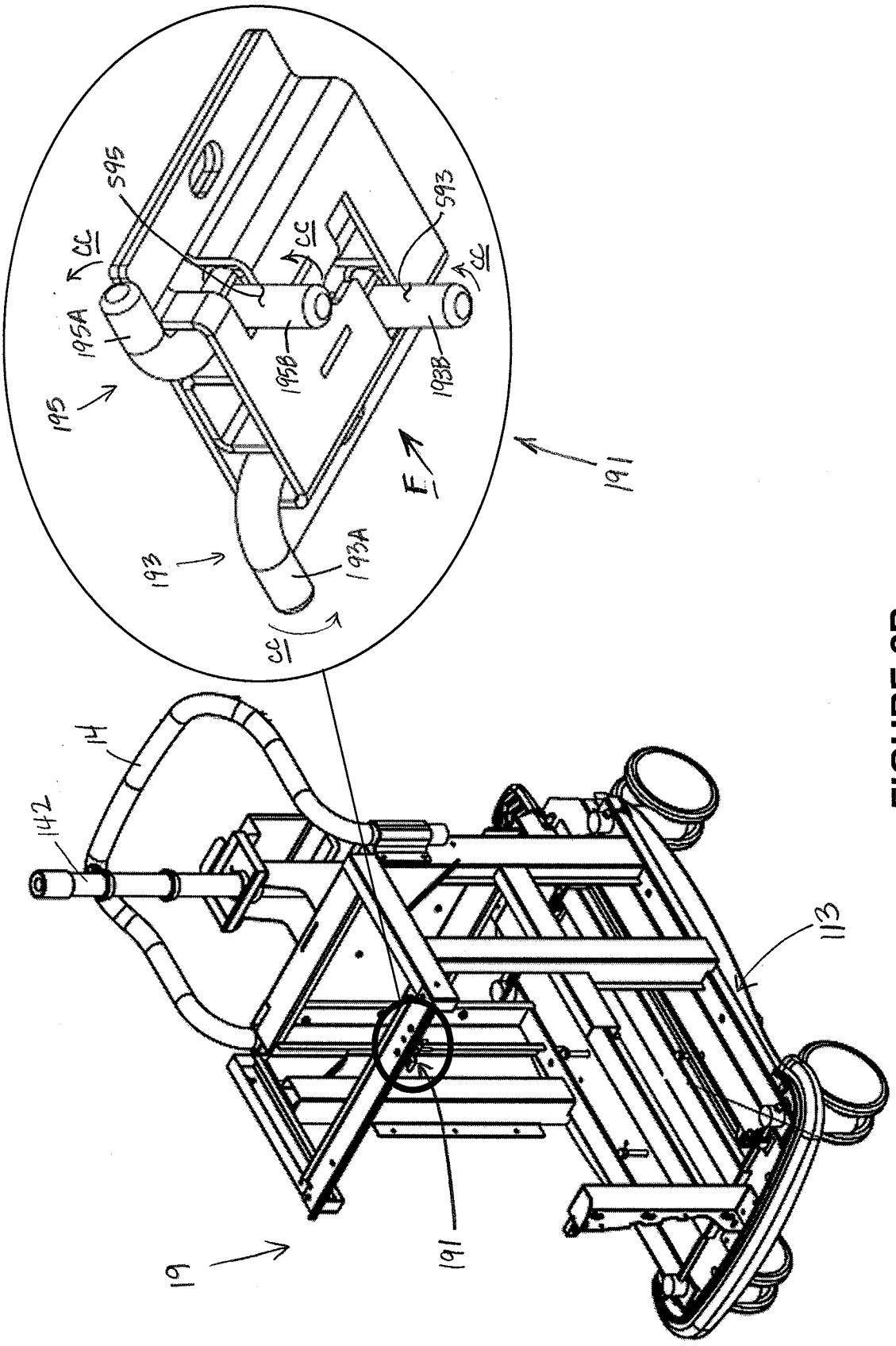
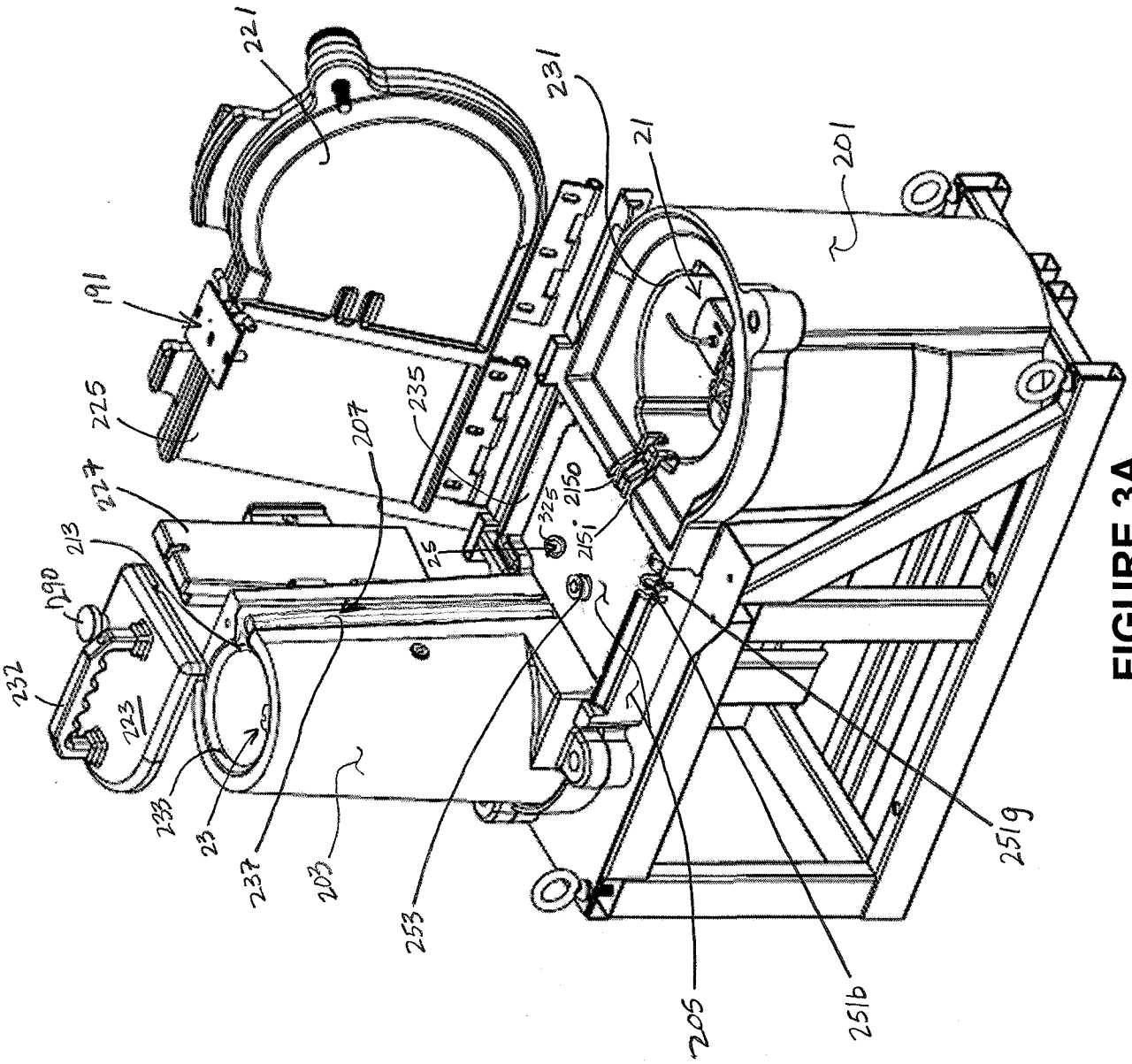


FIGURE 2B


221
231
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201
191
225
207
235
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190
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223
233
23
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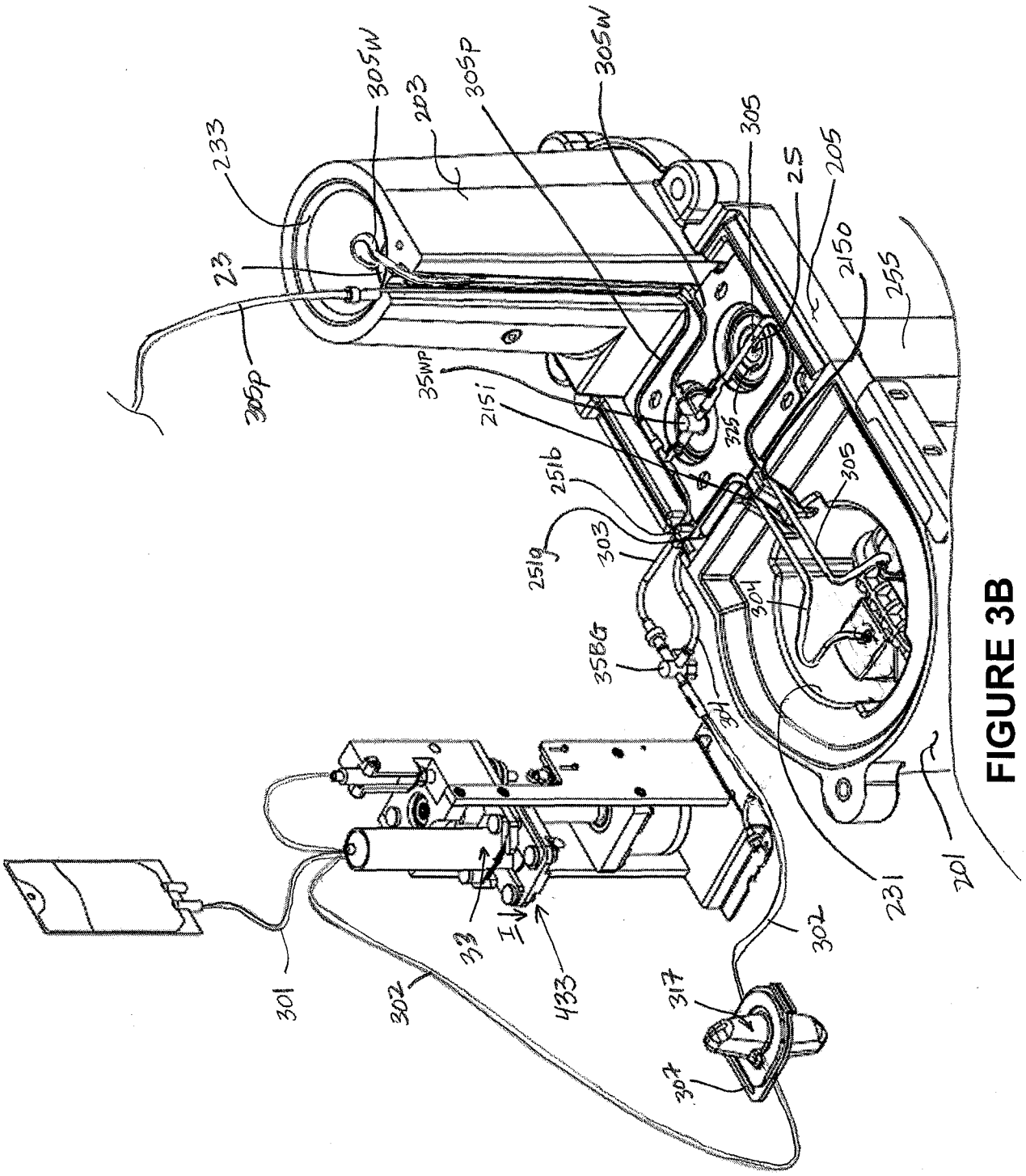
203
253
325
215i
2150
25
2519
2516
206

FIGURE 3A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203
305P
305W
233
305
25
205
23
2150
255
305P
35WP
2151
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35BG
231
201
301
302
33
I
433
317
307
302

FIGURE 3B

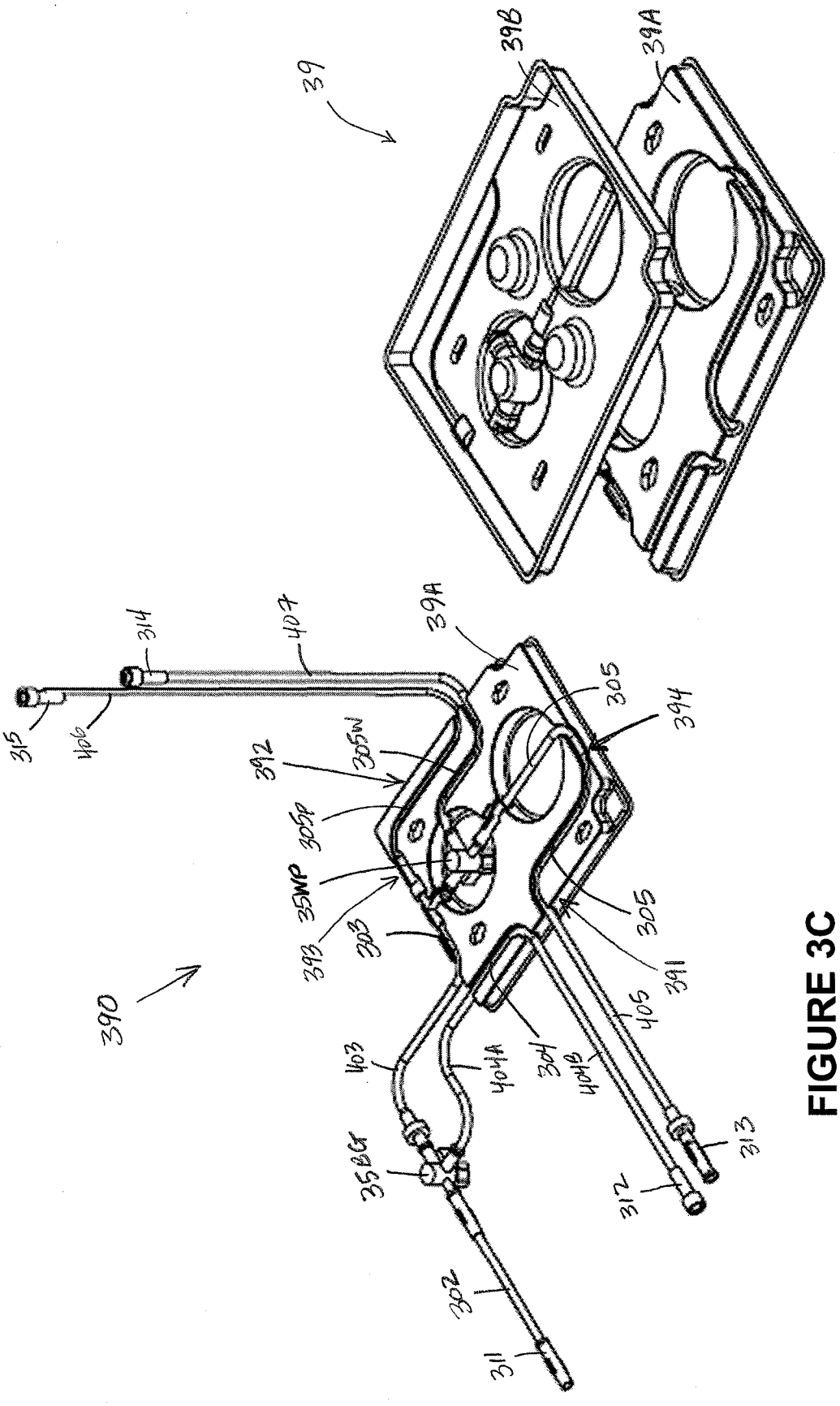
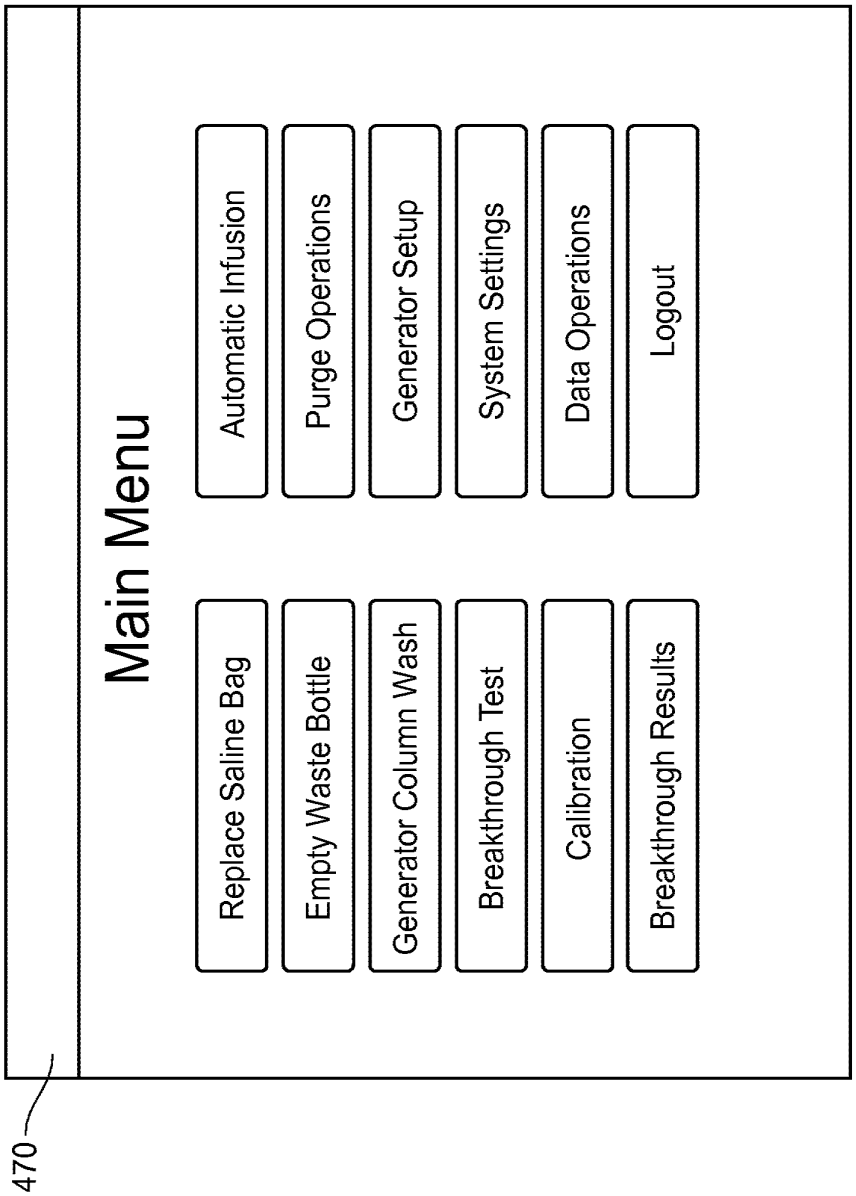


FIGURE 3D

FIGURE 3C

Fig. 4


Main Menu
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
470

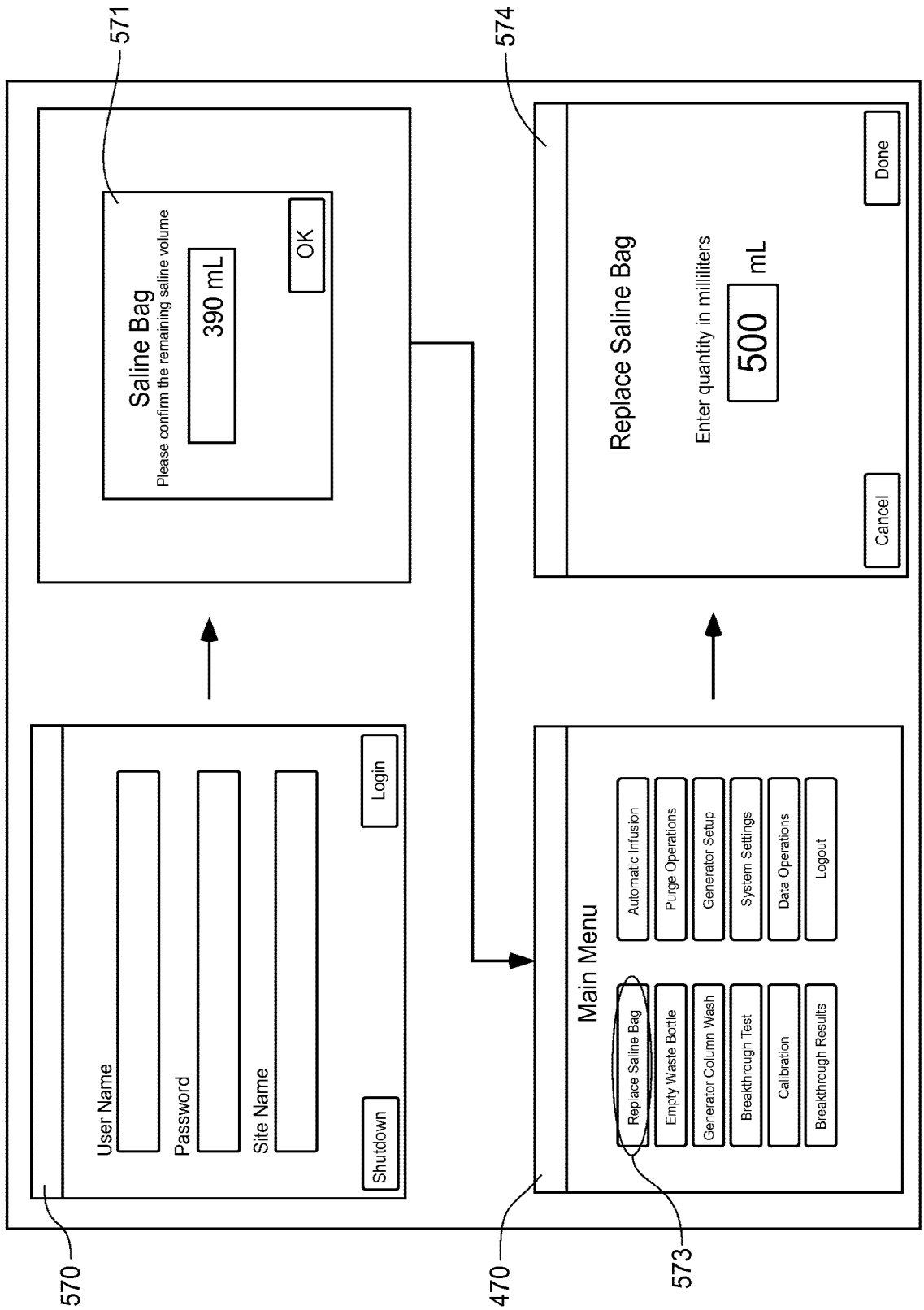

571
574
Saline Bag
Please confirm the remaining saline volume
390 mL
OK
Replace Saline Bag
Enter quantity in milliliters
500
mL
Done
Cancel
User Name
Password
Site Name
Login
Shutdown
Main Menu
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
570
470
573

Fig. 5A

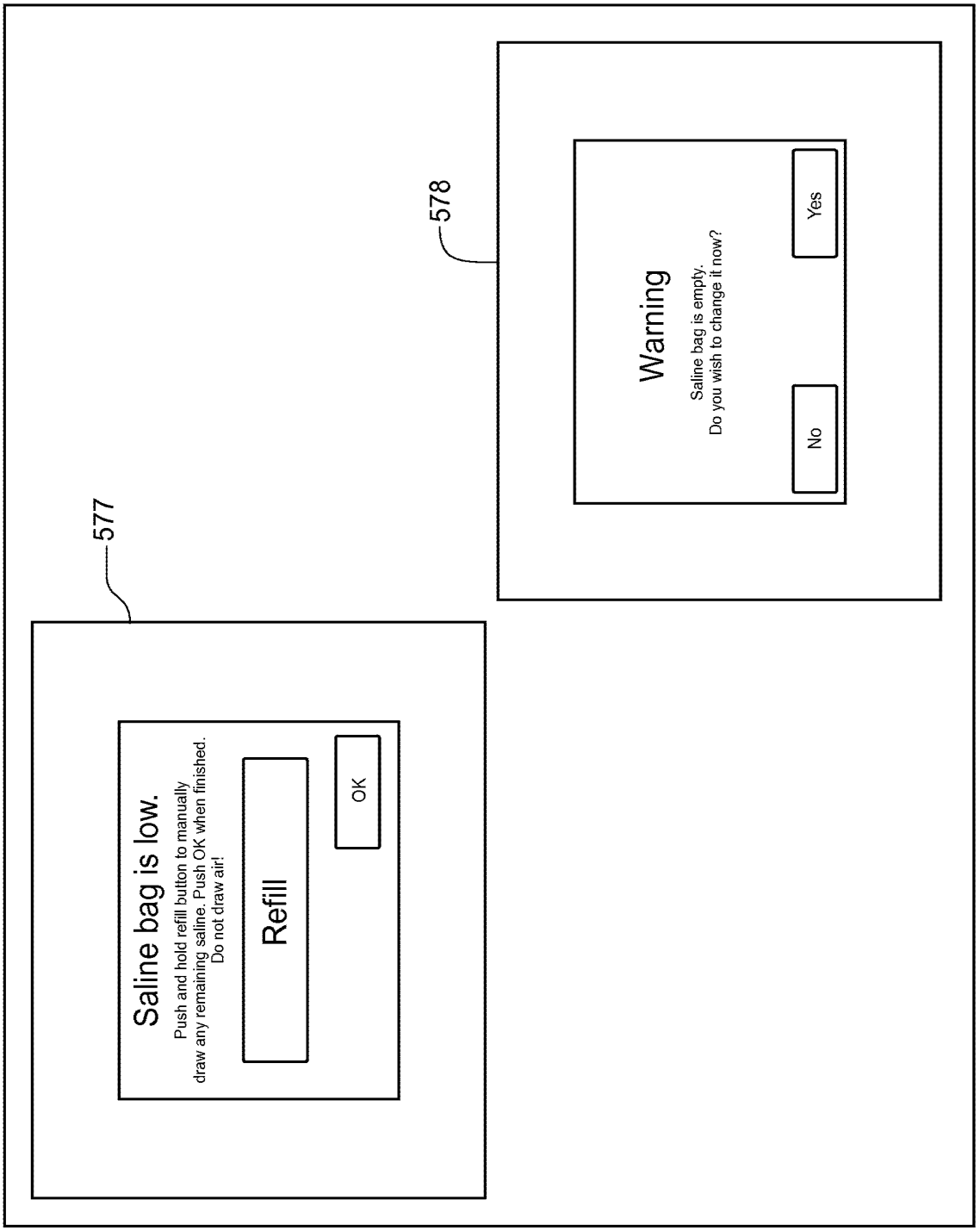

577
Saline bag is low.
Push and hold refill button to manually draw any remaining saline. Push OK when finished.
Do not draw air!
Refill
OK
578
Warning
Saline bag is empty.
Do you wish to change it now?
No
Yes

Fig. 5B

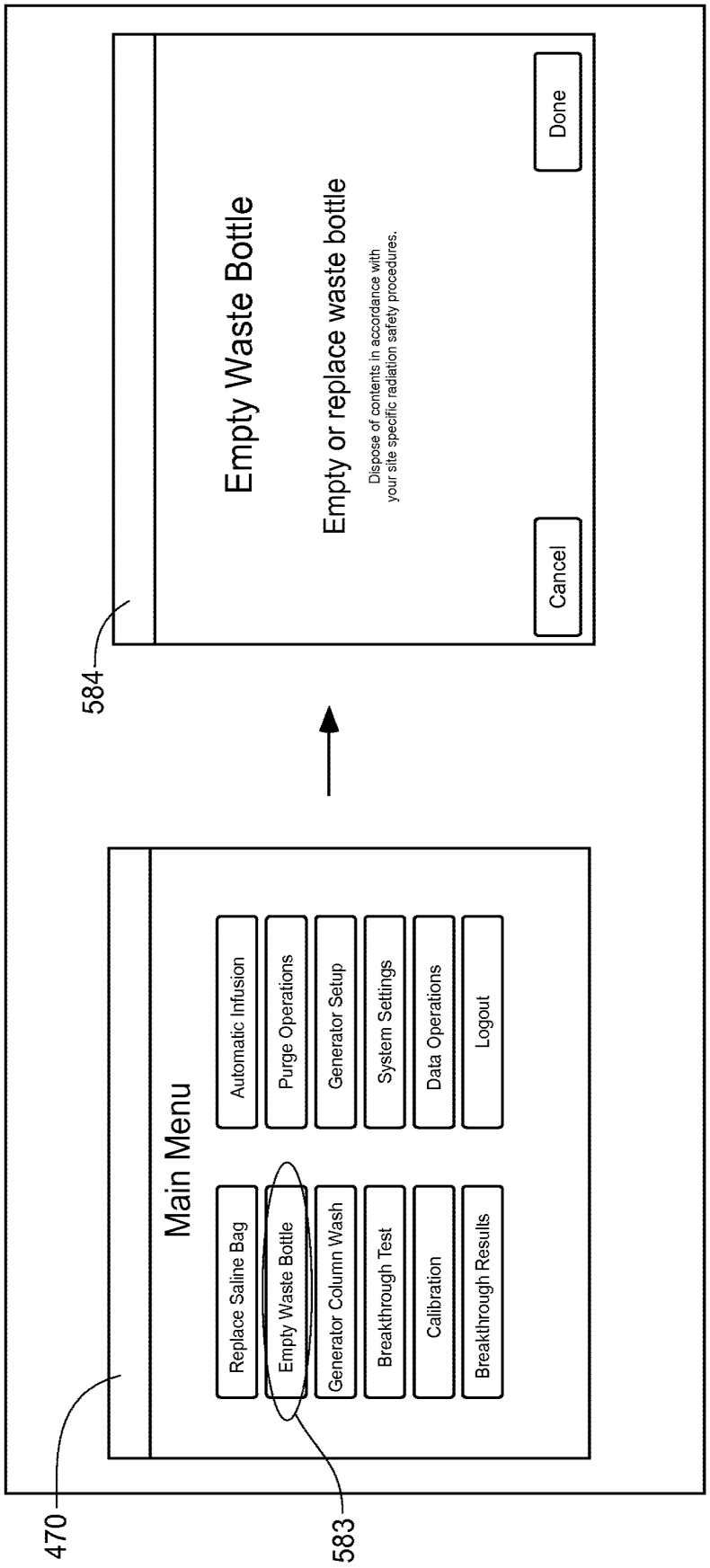

Main Menu
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
Empty Waste Bottle
Empty or replace waste bottle
Dispose of contents in accordance with your site specific radiation safety procedures.
Cancel
Done
470
583
584

Fig. 5C

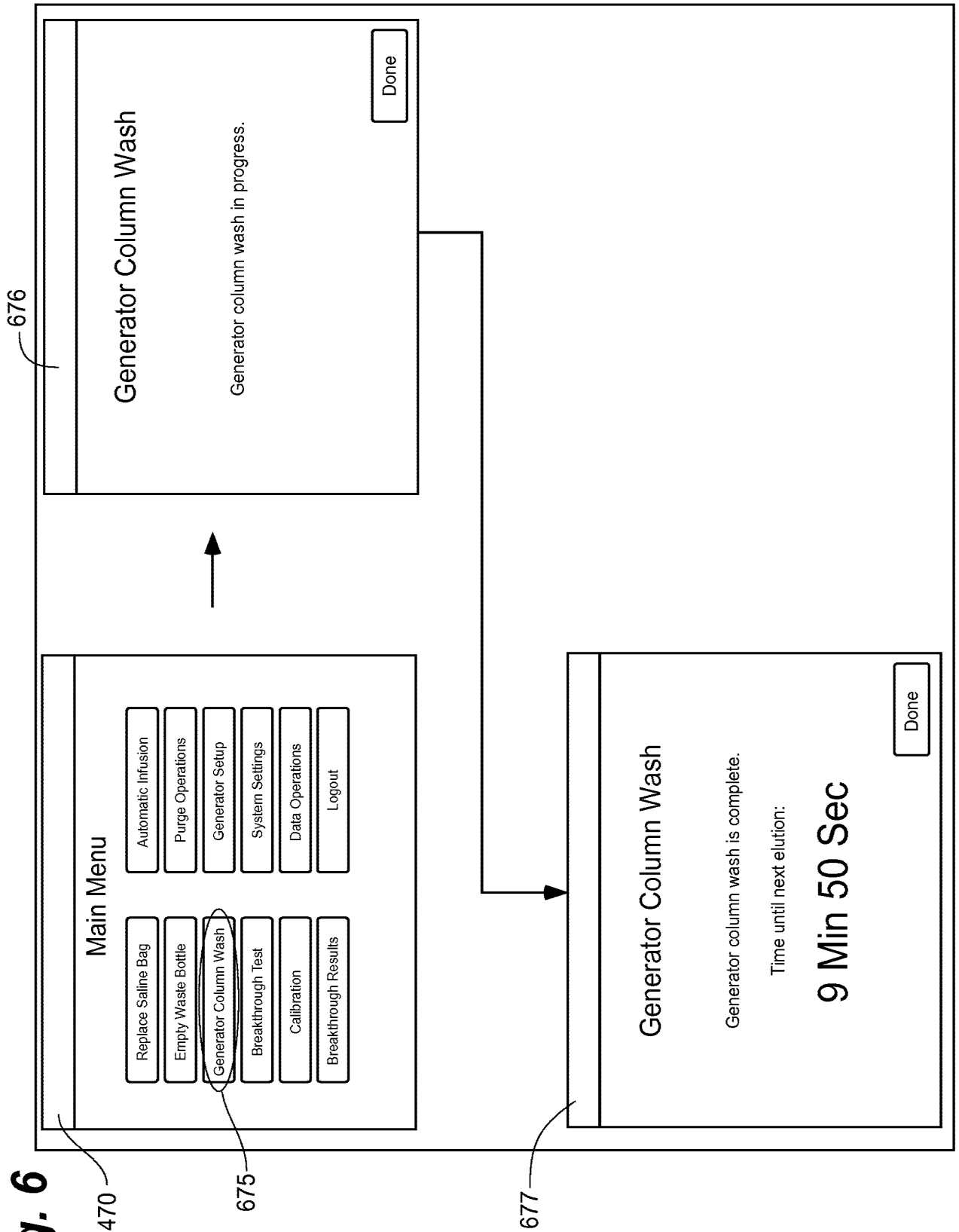

Main Menu
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
Generator Column Wash
Generator column wash in progress.
Done
Generator Column Wash
Generator column wash is complete.
Time until next elution:
9 Min 50 Sec
Done
470
675
676
677

Fig. 6

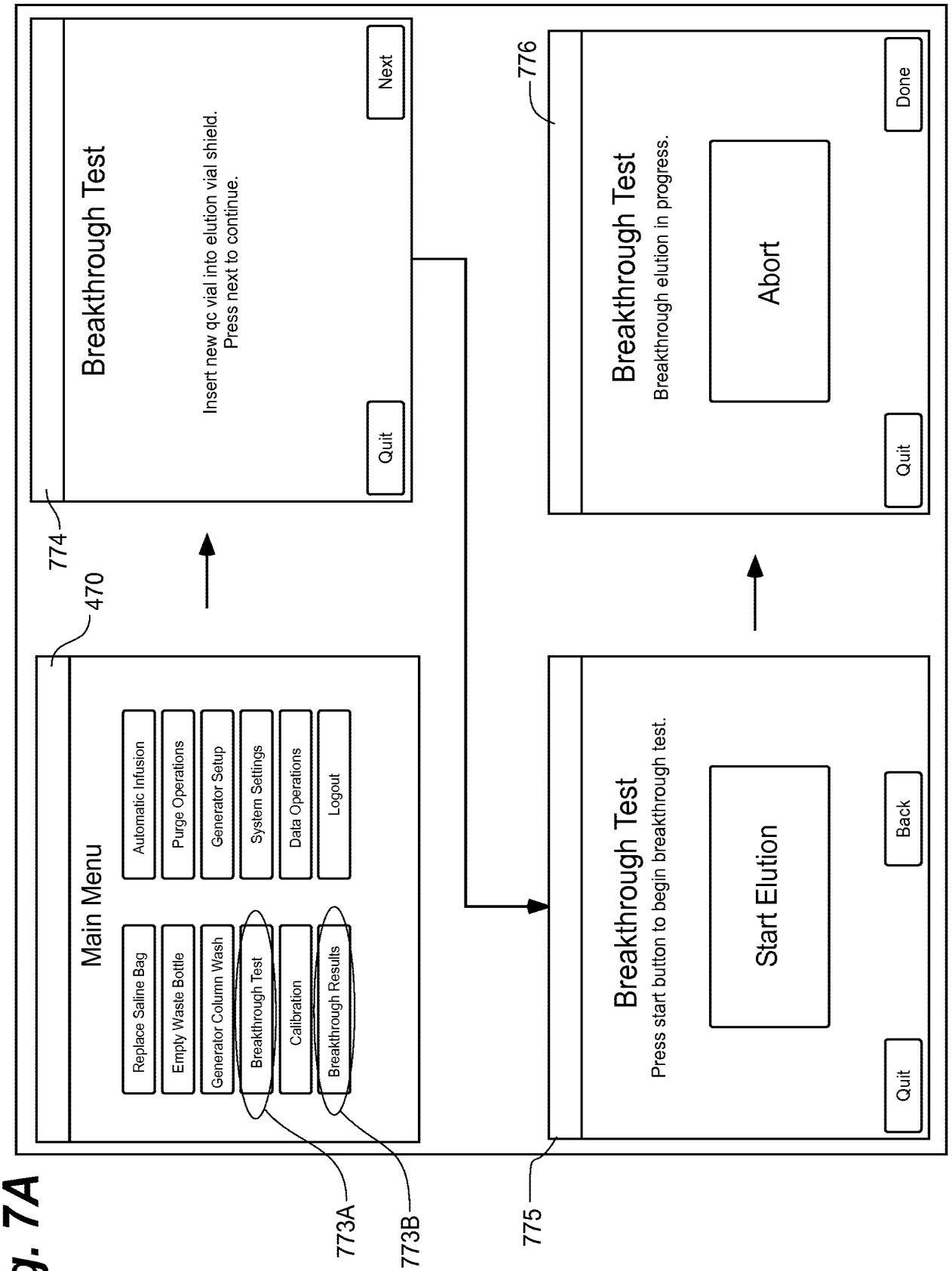

Main Menu
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
470
Breakthrough Test
Insert new qc vial into elution vial shield.
Press next to continue.
Next
Quit
774
Breakthrough Test
Press start button to begin breakthrough test.
Start Elution
Back
Quit
775
Breakthrough Test
Breakthrough elution in progress.
Abort
Done
Quit
776
773A
773B

Fig. 7A

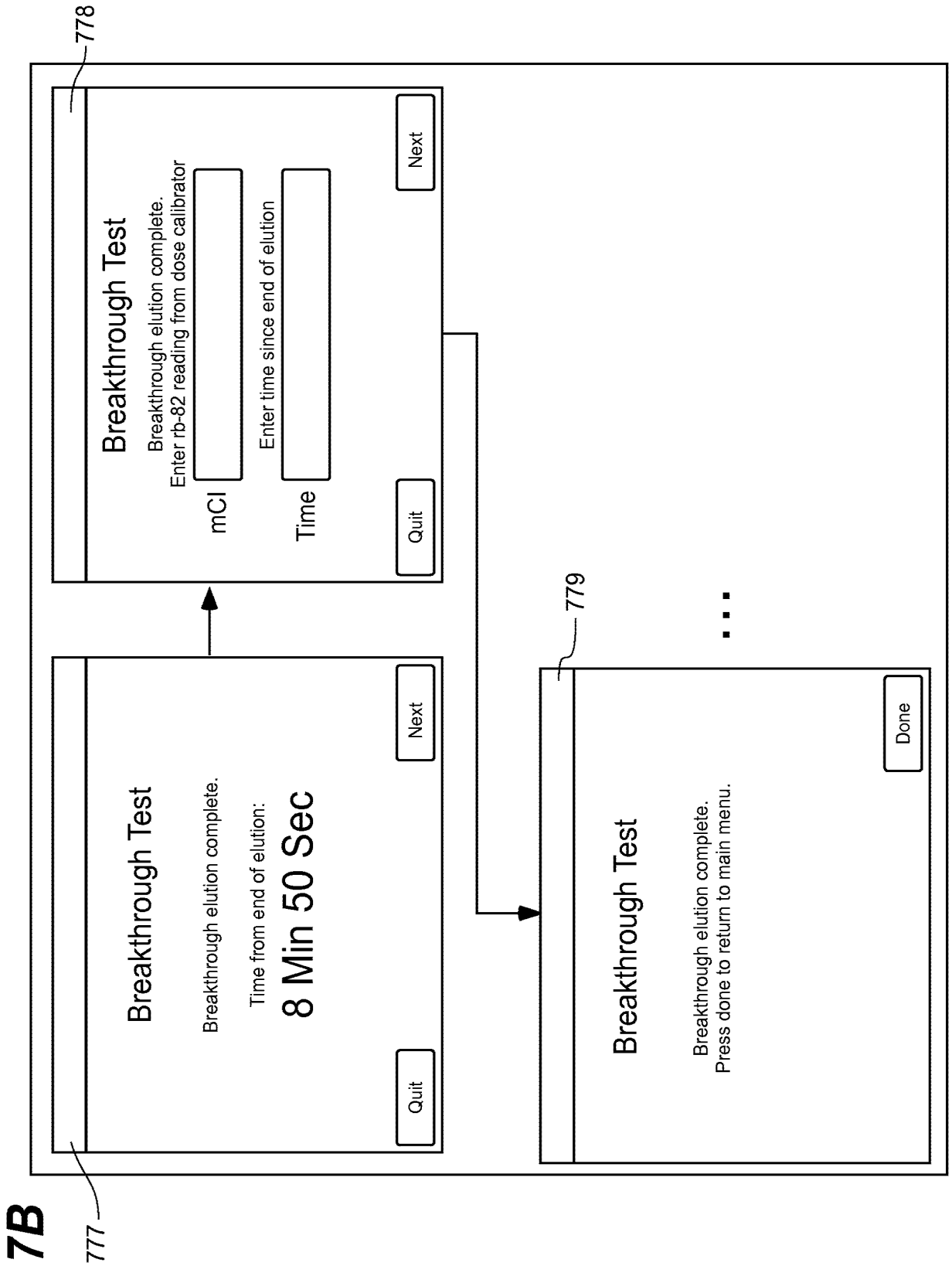

778
Breakthrough Test
Breakthrough elution complete.
Enter rb-82 reading from dose calibrator
mCI
Enter time since end of elution
Time
Next
Quit
777
Breakthrough Test
Breakthrough elution complete.
Time from end of elution:
8 Min 50 Sec
Next
Quit
779
Breakthrough Test
Breakthrough elution complete.
Press done to return to main menu.
Done

Fig. 7B

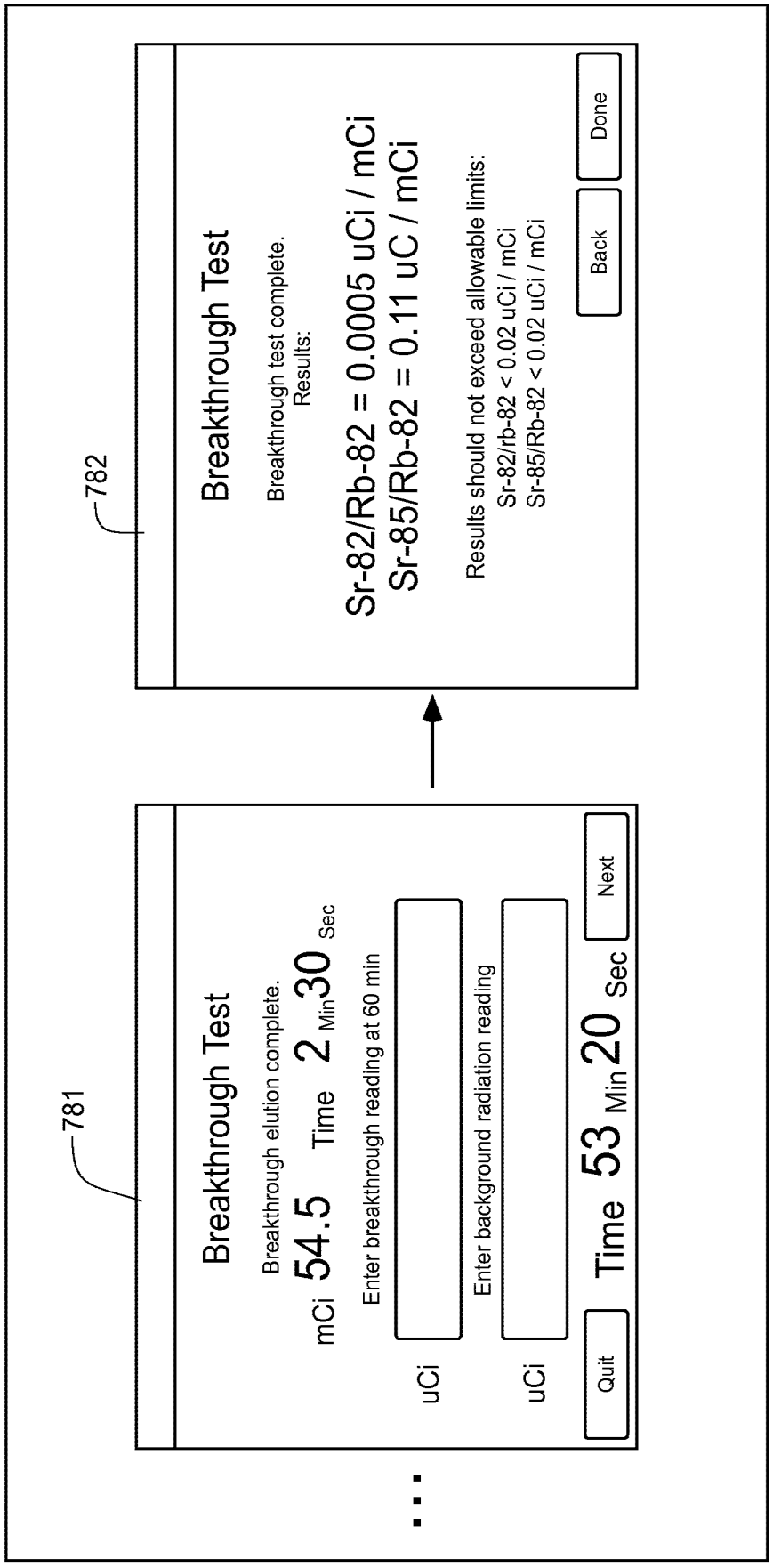

781
Breakthrough Test
Breakthrough elution complete.
mCi 54.5 Time 2 Min 30 Sec
Enter breakthrough reading at 60 min
uCi
Enter background radiation reading
uCi
Quit
Time 53 Min 20 Sec
Next
782
Breakthrough Test
Breakthrough test complete.
Results:
Sr-82/Rb-82 = 0.0005 uCi / mCi
Sr-85/Rb-82 = 0.11 uC / mCi
Results should not exceed allowable limits:
Sr-82/rb-82 < 0.02 uCi / mCi
Sr-85/Rb-82 < 0.02 uCi / mCi
Back
Done

Fig. 7C

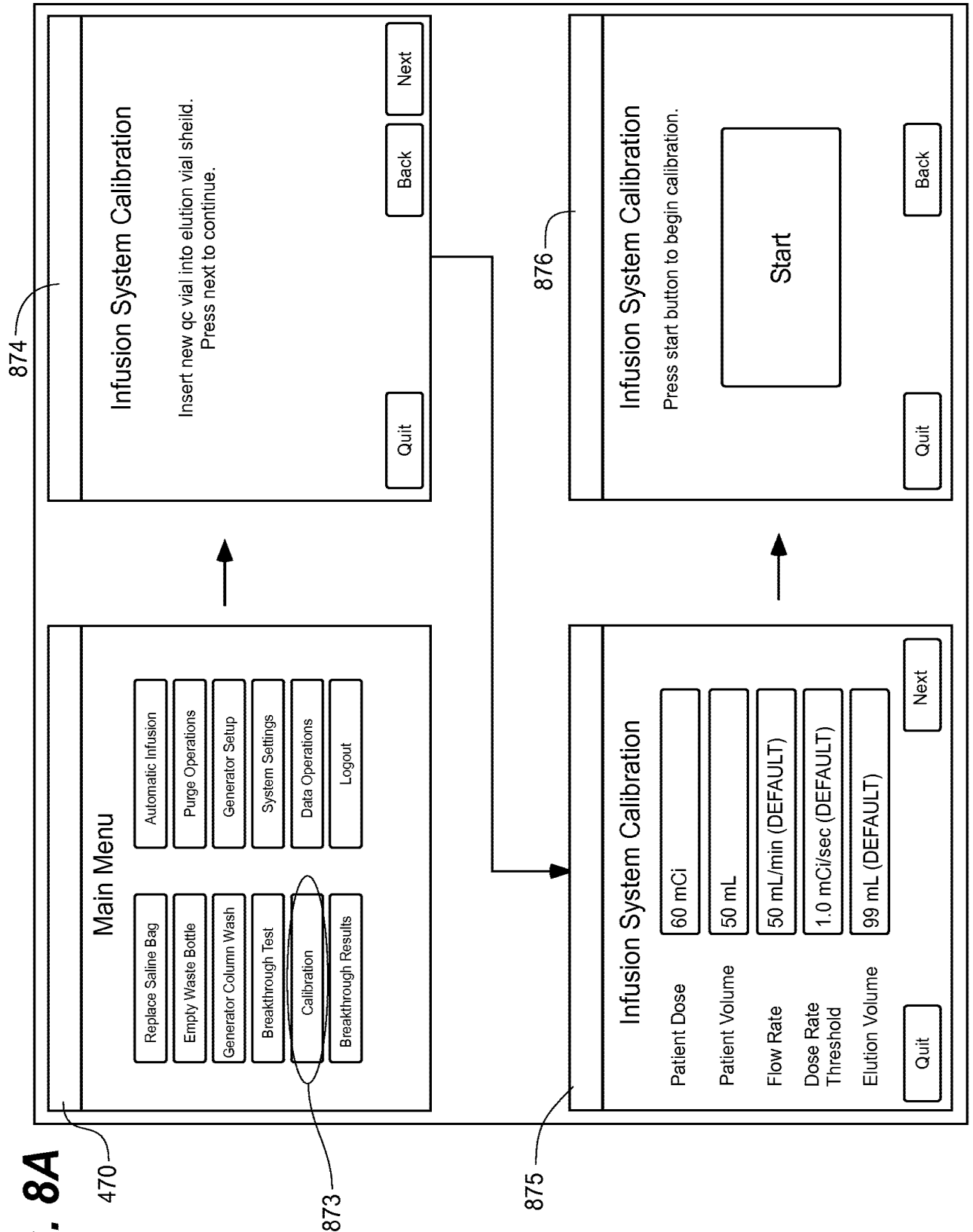

Main Menu
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
Infusion System Calibration
Insert new qc vial into elution vial sheild.
Press next to continue.
Quit
Back
Next
Infusion System Calibration
Press start button to begin calibration.
Start
Quit
Back
Infusion System Calibration
Patient Dose
60 mCi
Patient Volume
50 mL
Flow Rate
50 mL/min (DEFAULT)
Dose Rate Threshold
1.0 mCi/sec (DEFAULT)
Elution Volume
99 mL (DEFAULT)
Quit
Next
470
873
874
875
876

Fig. 8A

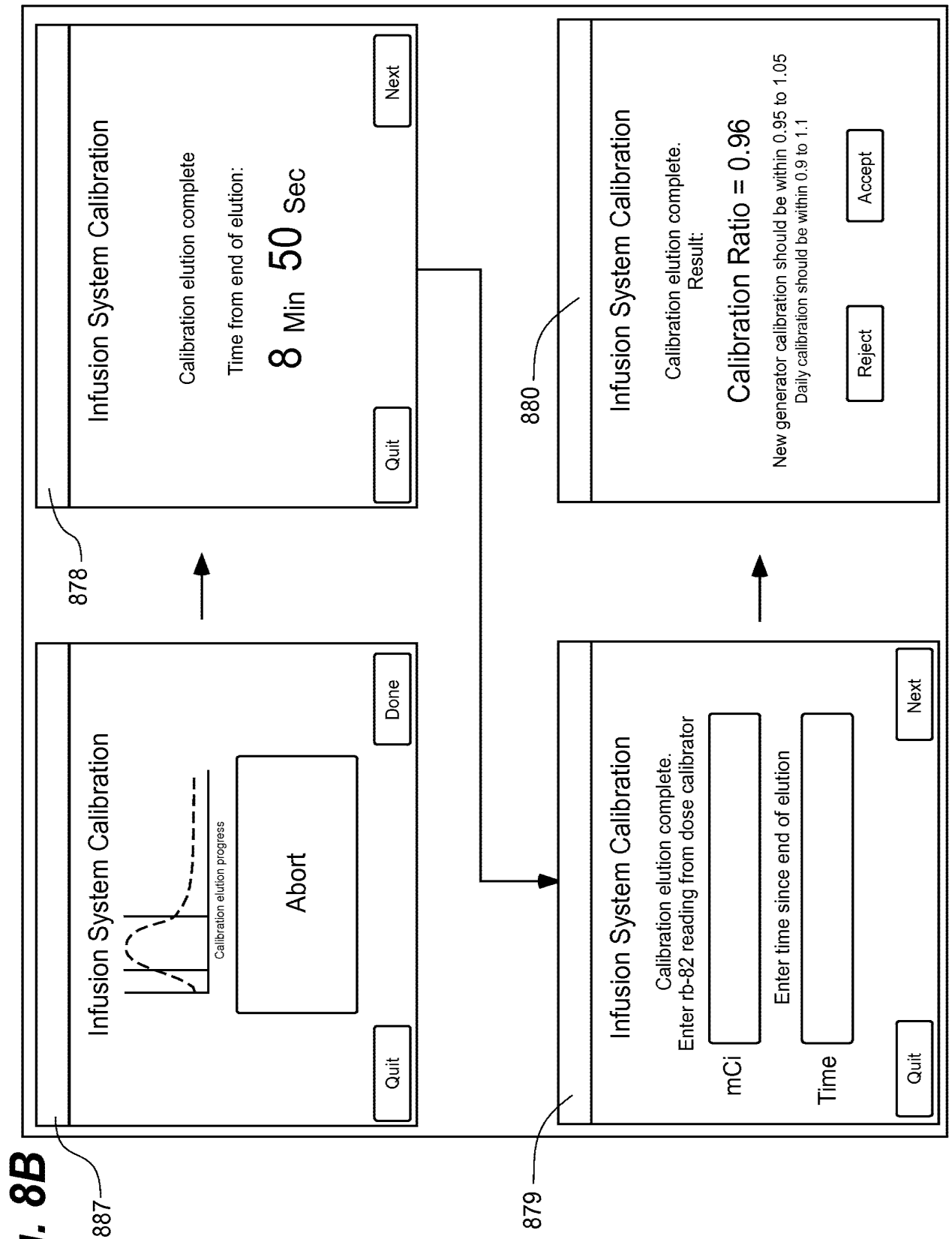

Infusion System Calibration
Calibration elution progress
Abort
Done
Quit
887
Infusion System Calibration
Calibration elution complete
Time from end of elution:
8 Min 50 Sec
Next
Quit
878
Infusion System Calibration
Calibration elution complete.
Enter rb-82 reading from dose calibrator
mCi
Enter time since end of elution
Time
Next
Quit
879
Infusion System Calibration
Calibration elution complete.
Result:
Calibration Ratio = 0.96
New generator calibration should be within 0.95 to 1.05
Daily calibration should be within 0.9 to 1.1
Reject
Accept
880

Fig. 8B

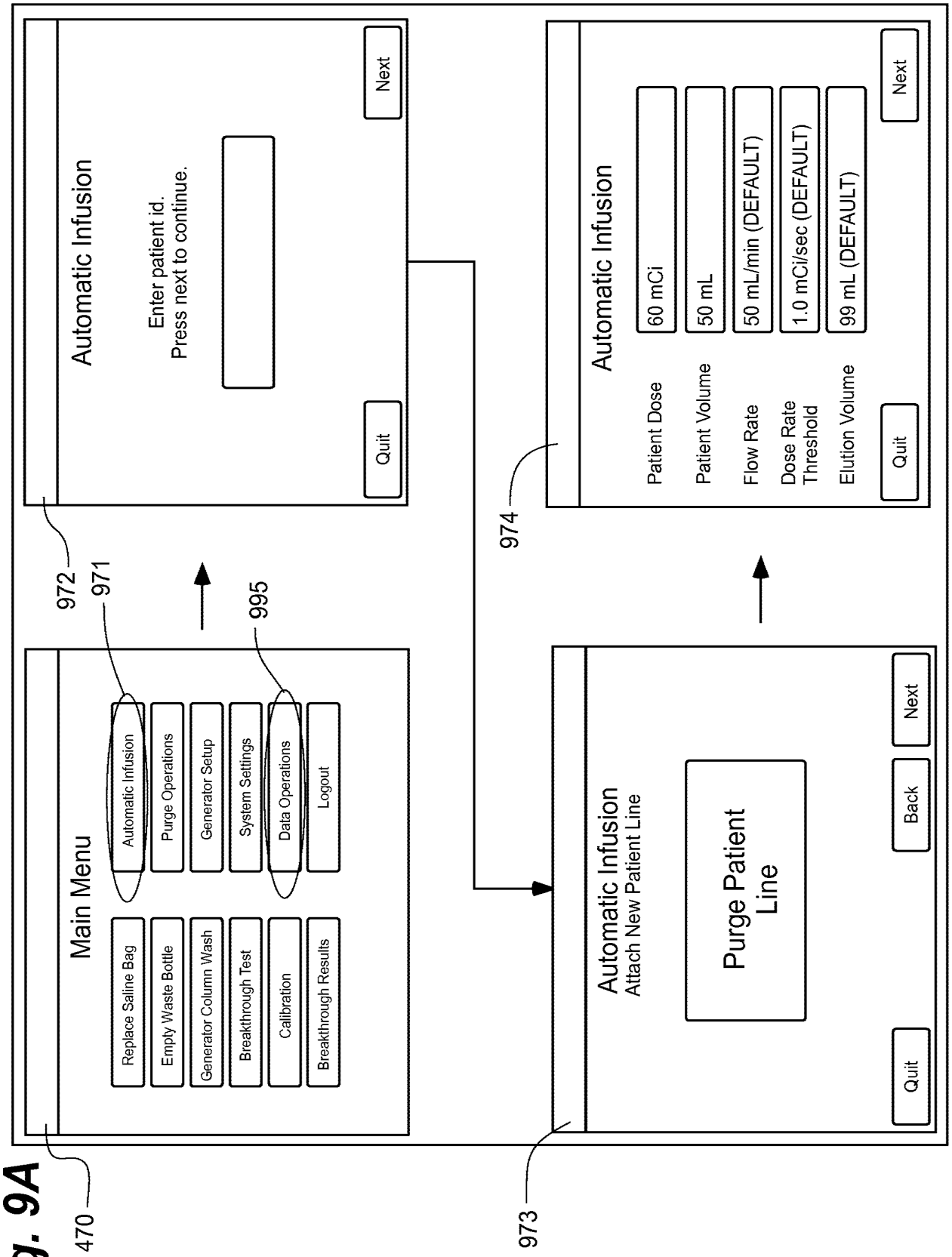

Main Menu
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
Automatic Infusion
Enter patient id.
Press next to continue.
Quit
Next
Automatic Infusion
Attach New Patient Line
Purge Patient Line
Quit
Back
Next
Automatic Infusion
Patient Dose
60 mCi
Patient Volume
50 mL
Flow Rate
50 mL/min (DEFAULT)
Dose Rate Threshold
1.0 mCi/sec (DEFAULT)
Elution Volume
99 mL (DEFAULT)
Quit
Next
470
971
972
973
974
995

Fig. 9A

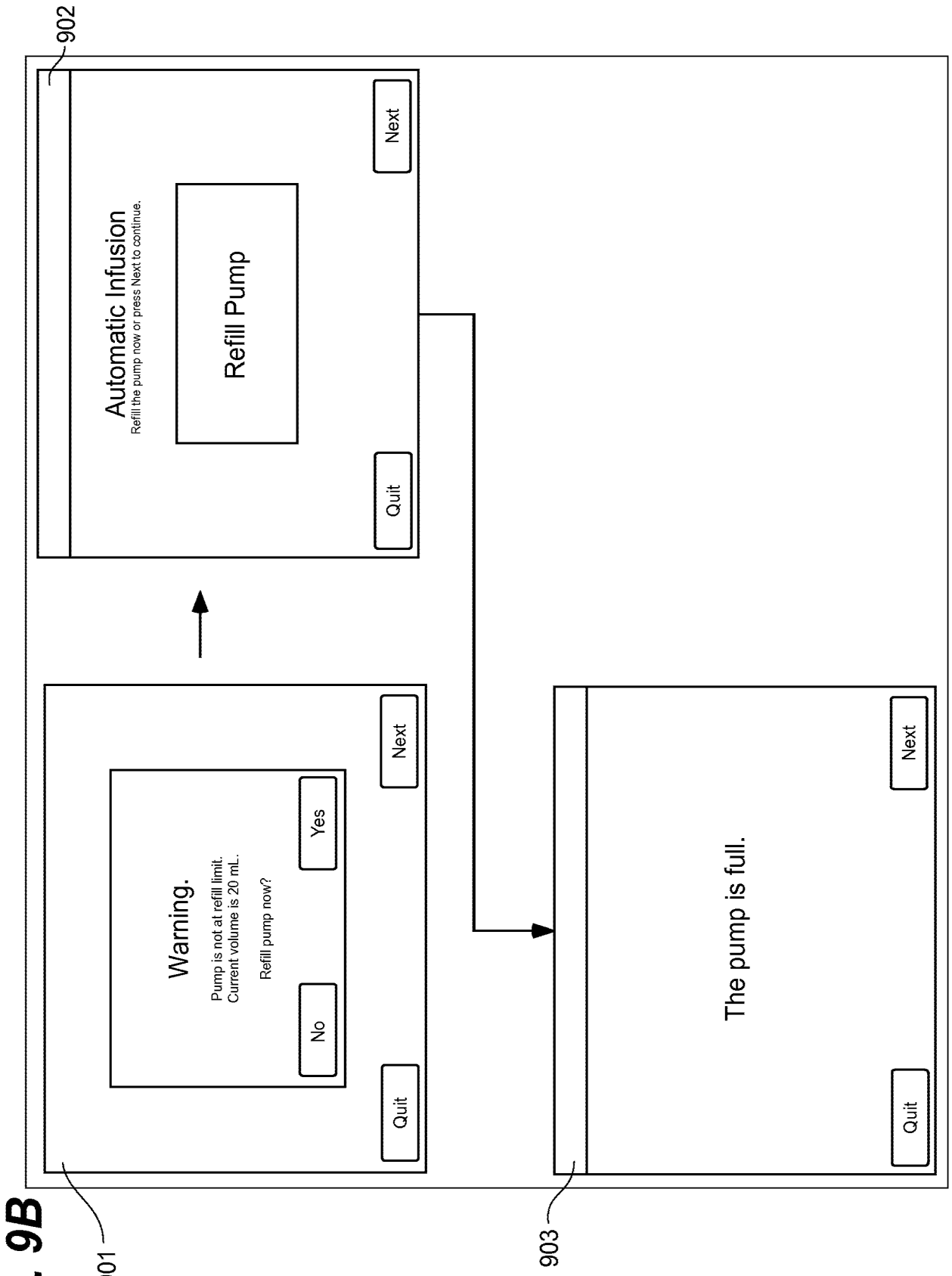

902
Automatic Infusion
Refill the pump now or press Next to continue.
Refill Pump
Next
Quit
Warning.
Pump is not at refill limit.
Current volume is 20 mL.
Refill pump now?
Yes
No
Next
Quit
The pump is full.
Next
Quit
901
903

Fig. 9B

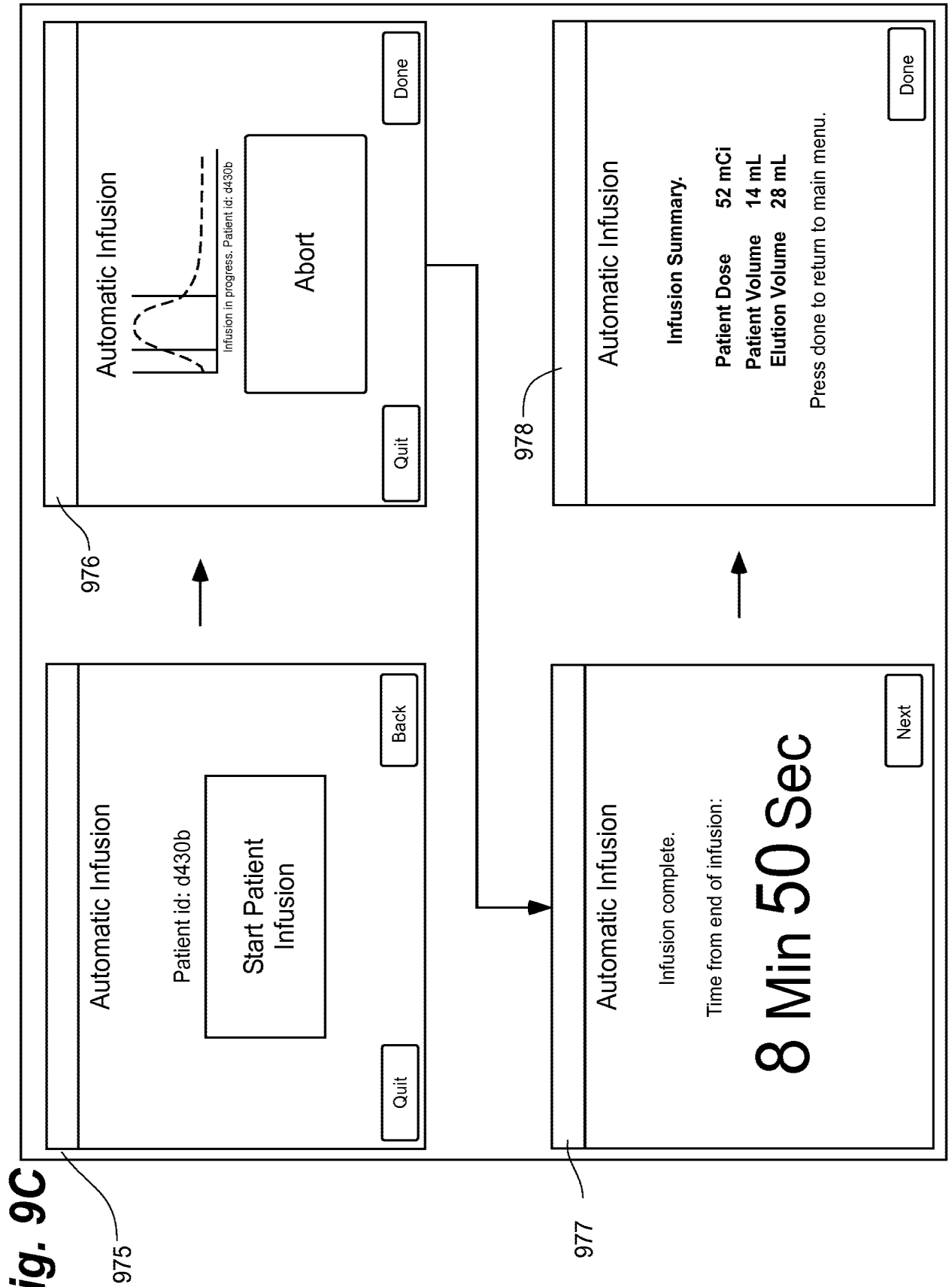

Automatic Infusion
Patient id: d430b
Start Patient Infusion
Back
Quit
975
Automatic Infusion
Infusion in progress. Patient id: d430b
Abort
Done
Quit
976
Automatic Infusion
Infusion complete.
Time from end of infusion:
8 Min 50 Sec
Next
977
Automatic Infusion
Infusion Summary.
Patient Dose 52 mCi
Patient Volume 14 mL
Elution Volume 28 mL
Press done to return to main menu.
Done
978

Fig. 9C

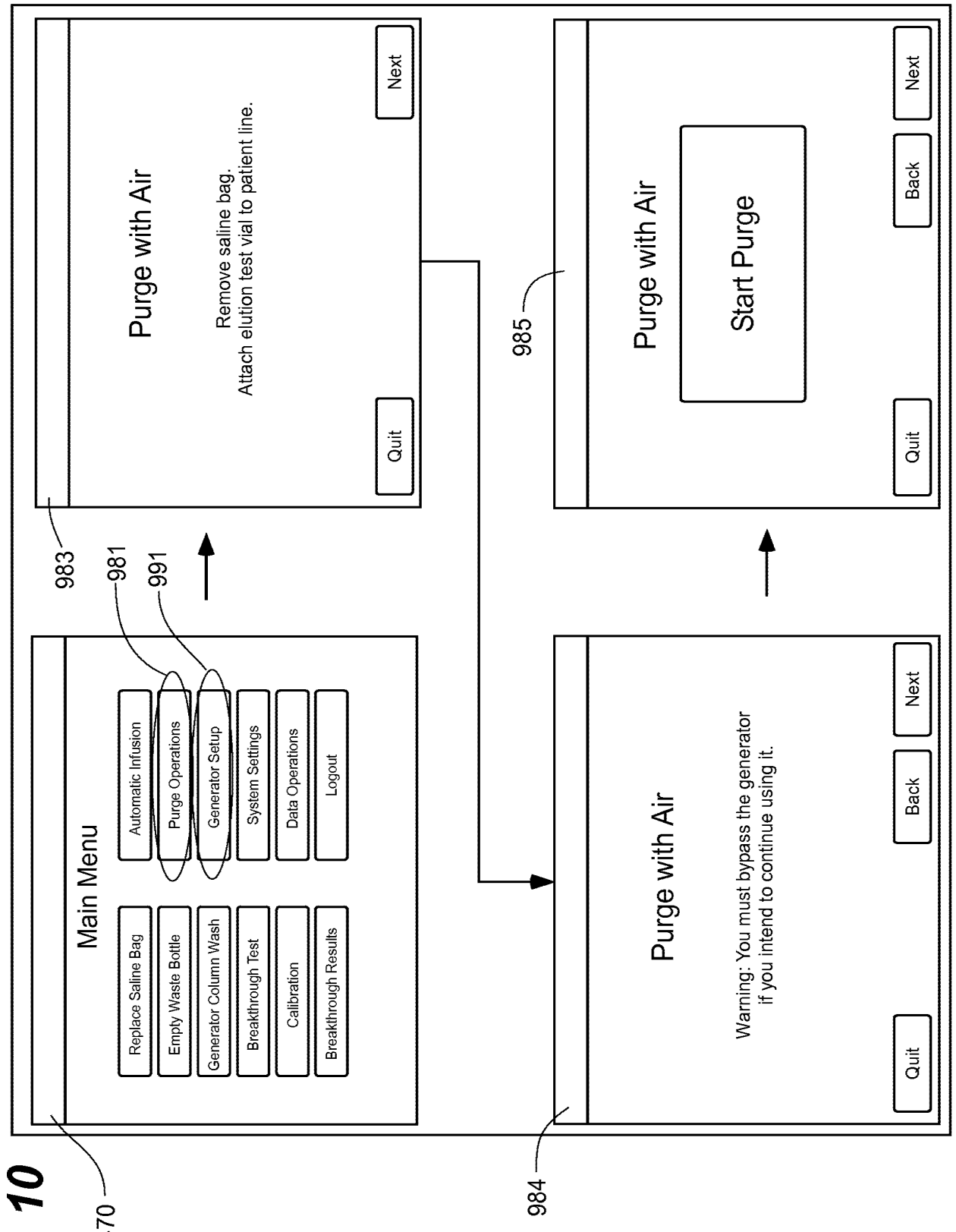

Main Menu
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
Purge with Air
Remove saline bag.
Attach elution test vial to patient line.
Quit
Next
Purge with Air
Start Purge
Quit
Back
Next
Purge with Air
Warning: You must bypass the generator
if you intend to continue using it.
Quit
Back
Next
470
981
983
984
985
991

Fig. 10

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Attorney Docket Number	56782.1.6
First Named Inventor	Charles R. Quirico
COMPLETE IF KNOWN	
Application Number	12/137,363
Filing Date	June 11, 2008
Art Unit	3763
Examiner Name	

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(Title of the Invention)

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NAME OF SOLE OR FIRST INVENTOR:	☐ A petition has been filed for this unsigned inventor
Given Name (first and middle [if any])	Family Name or Surname
Charles R.	Quirico

Inventor's Signature	Date
Charles Quirico	11/18/08

Residence: City	State	Country	Citizenship
Warren	NJ	US	US

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19 Robin Road			
City	State	Zip	Country
Warren	NJ	07059	US

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Given Name (first and middle (if any))	Family Name or Surname
Ernest	Balestracci

X Inventor's Signature: Ernest Balestracci — X Date: 11-18-08

Residence: City	State	Country	Citizenship
Iselin	NJ	US	US

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Iselin	NJ	08830	US

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Daniel	Darst

Inventor's Signature — Date

Residence: City	State	Country	Citizenship
Zimmerman	MN	US	US

Mailing Address: 25540 96th Street NW

City	State	Zip	Country
Zimmerman	MN	55398	US

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Given Name (first and middle (if any))	Family Name or Surname
Eric J.	Krause

Inventor's Signature — Date

Residence: City	State	Country	Citizenship
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Mailing Address: 3360 Lake Ridge Drive

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Vishal N.	Lokhande
Inventor's Signature	Date

Residence: City	State	Country	Citizenship
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100 N. Whisman Road, Apt. #1412

Mailing Address

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Mountain View	CA	94043	US

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Jacob S.	Childs
Inventor's Signature	Date

Residence: City	State	Country	Citizenship
Minneapolis	MN	US	US

30 W. 22nd Street, Apt. 202

Mailing Address

City	State	Zip	Country
Minneapolis	MN	55404	US

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Given Name (first and middle [if any]) Charles R.	Family Name or Surname Quirico
Inventor's Signature	Date

Residence: City Warren	State NJ	Country US	Citizenship US
Mailing Address 19 Robin Road			
City Warren	State NJ	Zip 07059	Country US

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Inventor's Signature _____ Date _____

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Mailing Address

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Daniel	Darst

Inventor's Signature _____ Date 11/04/08

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Inventor's Signature			Date
Iselin Residence: City	NJ State	US Country	US Citizenship
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PTO/SB/02A (07-07)
Approved for use through 08/30/2010, OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

DECLARATION

ADDITIONAL INVENTOR(S)
Supplemental Sheet

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name (first and middle (if any))	Family Name or Surname
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Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

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Inventor's Signature — Date

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Minneapolis	MN	55404	US

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name (first and middle (if any))	Family Name or Surname

Inventor's Signature — Date

Residence: City	State	Country	Citizenship

Mailing Address

City	State	Zip	Country

PTO/SB/22 (10-08)
Approved for use through 11/30/2008. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARMENT OF COMMERCE

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a) **FY 2009** ***(Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).)***	Docket Number (Optional) 56782.1.6
Application Number 12/137,363	Filed June 11, 2008
For INFUSION SYSTEM CONFIGURATIONS	
Art Unit 3763	Examiner

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

		Fee	Small Entity Fee	
☐	One month (37 CFR 1.17(a)(1))	$130	$65	$
☐	Two months (37 CFR 1.17(a)(2))	$490	$245	$
☑	Three months (37 CFR 1.17(a)(3))	$1110	$555	$ 1110
☐	Four months (37 CFR 1.17(a)(4))	$1730	$865	$
☐	Five months (37 CFR 1.17(a)(5))	$2350	$1175	$

☐ Applicant claims small entity status. See 37 CFR 1.27.

☐ A check in the amount of the fee is enclosed.

☑ Payment by credit card. Form PTO-2038 is attached.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☑ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 061910.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71.
Statement under 37 CFR 3.73(b) is enclosed (Form PTO/SB/96).

☑ attorney or agent of record. Registration Number 50,751

☐ attorney or agent under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

/Elisabeth Lacy Belden/ — Signature

2008-11-24 — Date

Elisabeth Lacy Belden — Typed or printed name

612-492-7000 — Telephone Number

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below.

☐ Total of _____ forms are submitted.

This collection of information is required by 37 CFR 1.136(a). The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 6 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal

Application Number:	12137363
Filing Date:	11-Jun-2008
Title of Invention:	INFUSION SYSTEM CONFIGURATIONS
First Named Inventor/Applicant Name:	Charles Quirico
Filer:	Elisabeth Lacy Belden
Attorney Docket Number:	56782.1.6

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Late filing fee for oath or declaration	1051	1	130	130
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension - 3 months with $0 paid	1253	1	1110	1110
Miscellaneous:				
			Total in USD ($)	**1240**

Electronic Acknowledgement Receipt

EFS ID:	4346003
Application Number:	12137363
International Application Number:	
Confirmation Number:	7372
Title of Invention:	INFUSION SYSTEM CONFIGURATIONS
First Named Inventor/Applicant Name:	Charles Quirico
Customer Number:	22859
Filer:	Elisabeth Lacy Belden
Filer Authorized By:	
Attorney Docket Number:	56782.1.6
Receipt Date:	24-NOV-2008
Filing Date:	11-JUN-2008
Time Stamp:	17:35:07
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$1240
RAM confirmation Number	4981
Deposit Account	
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Applicant Response to Pre-Exam Formalities Notice	56782_1_6_ResponseToMP.pdf	69779 06336f59b486c91c87740f46dedb1686b0080fc8	no	1
Warnings:					
Information:					
2	Drawings-only black and white line drawings	56782_1_5_6_7_8_ReplacementDrawings.pdf	3359510 ae834f3ef728a795bd8e3c6fc52bbf8aba052235	no	23
Warnings:					
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3	Oath or Declaration filed	56782_1_6_Declaration.pdf	949999 30394e5afcaef79fffb166cfdf3da86f93e3dfcb	no	15
Warnings:					
Information:					
4	Extension of Time	56782_1_6_Extension_3Mo.pdf	350791 f1db640a79d33990ed325a101ea368015d67946e	no	2
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5	Fee Worksheet (PTO-06)	fee-info.pdf	32227 4514d90a7a2bb9edaf647f4d73a2d2a55680dcbc	no	2
Warnings:					
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		Total Files Size (in bytes):	4762306		

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<u>New Applications Under 35 U.S.C. 111</u>
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

<u>National Stage of an International Application under 35 U.S.C. 371</u>
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

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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	12137363
Filing Date	2008-06-11
First Named Inventor	Charles R. Quirico
Art Unit	
Examiner Name	
Attorney Docket Number	56782.1.6

U.S.PATENTS Remove

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	3710118		1973-01-09	Holgate et al.	
	2	4562829		1986-01-07	Bergner	
	3	4585009		1986-04-29	Barker et al.	
	4	4585941		1986-04-29	Bergner	
	5	6870175	B2	2005-03-22	Dell et al.	
	6	7204797	B2	2007-04-17	Reilly et al.	

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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137363
	Filing Date	2008-06-11
	First Named Inventor	Charles R. Quirico
	Art Unit	
	Examiner Name	
	Attorney Docket Number	56782.1.6

	1	20050278066	A1	2005-12-15	Graves et al.	

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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] ¡	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	0102121	EP	A1	1984-03-07	DeJong, Rudolf et all		☐
	2	2007016170	WO	A1	2007-02-08	Fago		☐
	3	2007030249	WO	A2	2007-03-15	Gibson		☐
	4	2007149108	WO	A2	2007-12-27	Pollard		☐

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NON-PATENT LITERATURE DOCUMENTS Remove

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]
	1	BRACCO Brochure, "Rubidium 82 Infusion System, Easy to Operate...Automated...Complete", (C)Bracco Diagnostics, Inc., 0605-002NA, June 2001. (2 pages)	☐
	2	BRACCO, "Cardio-Gen82(R) Infusion System User's Guide", pages 1-42	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137363
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	First Named Inventor	Charles R. Quirico
	Art Unit	
	Examiner Name	
	Attorney Docket Number	56782.1.6

	3	IMAGING TECHNOLOGY NEWS, web exclusive: "FDG-PET Injector Thrusts New Life into Molecular Imaging", April 2008, 2 pages.	☐

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Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137363
	Filing Date	2008-06-11
	First Named Inventor	Charles R. Quirico
	Art Unit	
	Examiner Name	
	Attorney Docket Number	56782.1.6

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ 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)	2008-11-12
Name/Print	Elisabeth Lacy Belden	Registration Number	50,751

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

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4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

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6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

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(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: 0 102 121
A1

(12) # EUROPEAN PATENT APPLICATION

(21) Application number: 83201201.7

(51) Int. Cl.³: G 21 G 1/04

(22) Date of filing: 18.08.83

(30) Priority: 26.08.82 NL 8203349

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(84) Designated Contracting States:
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(74) Representative: Swsters, Pieter D., Drs. et al,
Octrooibureau ZOAN B.V. Apollolaan 151
NL-1077 AR Amsterdam(NL)

(54) **Shielding device for a reservoir comprising a radioactive material.**

(57) The invention relates to a shielding device for a reservoir comprising a radioactive material and having an inlet and an outlet aperture, in particular a column for a radio-isotope generator, comprising a lead cover for the reservoir in which a closable access for the reservoir is recessed. The shielding device furthermore is provided with means which the device can be moved forward.

EP 0 102 121 A1

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Shielding device for a reservoir comprising a radioactive material.

The invention relates to a shielding device for a reservoir comprising a radioactive material and having an inlet and an outlet aperture, in particular a column for a radio-isotope generator, comprising a lead cover for the reservoir in which a closeable access for the reservoir is recessed.

A radioisotope generator is to be understood to mean herein a device for generating a radioactive isotopes comprising liquid. Such a liquid is prepared by eluting a column in which a parent isotope is present which produces a daughter isotope by decay. In this elution only the daughter isotope is eluted from the column by means of a suitable eluent.

Radioactive isotopes having a half-life up to a few days are frequently used in medicine for diagnostic purposes. One radioactive isotope frequently used for diagnostic examinations is technetium-99m. However, for certain applications, for example, for cardiological examinations, the comparatively long half-life of technetium-99m, namely 6 hours, is a disadvantage. As a result of this the radioactive material remains circulating in the body for a long period of time, so that an immediate repetition of a certain diagnostic examination with the same isotope is not possible.
However, very short-living radioactive isotopes having a half-life up to a few minutes, for example gold-195m, rubidium-82 and krypton-81m, are suitable for such above-mentioned examinations. Krypton-81m is used for lung function examinations, while rubidium-82 and gold-195m have proved suitable for blood circulation studies. An interesting application of gold-195m was described recently in Netherlands non-prepublished Patent Application 8201591 in the name of Applicants.

Gold-195m is an isotope having a half-life of 30.6 sec. and emits gamma rays of 261 keV which, due to the energy and intensity, are suitable to enable a good observation with apparatus usual for this purpose, for example, a gamma camera.

It is known from Netherlands Patent Application 8002235 in the name of Applicants to generate gold-195m from the radioactive parent isotope mercury-195m in a satisfactory manner. This process is preferably carried out in a so-called radio-isotope generator, in this case a Hg/Au generator, from which the user can withdraw a quantity of radioactive isotope-containing liquid at any desired instant. Such an instantaneous production is of great practical importance due to the rapid decay of the comparatively short-living isotope.

An improved method of preparing gold-195m is described in Netherlands non-prepublished Patent Application 8202407 also in the name of Applicants.

In view of the high radiation intensity, extensive safety measures have to be taken to shield the parent isotope present in the generator. Therefore the generator comprises a lead screening jacket which provides a sufficient safety upon storage and transport. The screening jacket surrounding the generator is generally considered to be an insufficient safety against radioactive radiation for hospital or laboratory personnel who are regularly in the direct proximity of the generator. It is therefore necessary to surround the generator with an extra lead shielding device.

Such a device should not only provide a good shielding from radioactive radiation, but, in connection with the necessity of a regular replacement, should also be readily accessible for the reservoir with radioactive material, in particular the generator column.

Therefore, various shielding devices are known from literature substantially all of which are destined for a column for generating technetium-99m, a radioactive isotope having a comparatively long half-life, and all of which are fixedly arranged.

When a very short-living radioactive isotope is used for diagnostic purposes, the time between the preparation of the isotope and the administration to a patient

should be minimized. In the case of the above-mentioned gold-195m isotope having a half-life of approximately 30 seconds, it is very much desired, if not necessary, to administer said isotope directly from the generator to the patient. In a clinic in which radioactive isotopes for diagnostic purposes are used, the apparatus necessary for detection, for example, a gamma camera with special collimator and a computer, is usually fixedly arranged. For a radiodiagnostic examination the patient is then brought (wheeled) to the detection apparatus.

It is therefore obvious to give the very short-living material to be used for the examination, in particular a generator for producing a very short-living isotope, a fixed place close to the detection apparatus. It is feasible that high requirements as regards the shielding from radioactive radiation have to be imposed upon such a device beside the patient to be examined ("bed-side arrangement"). In fact, not only the hospital personnel familiar with handling radioactive material will have to be present near the radiation source for a longer period of time, but also other personnel accompanying the patient will have to be shielded from unnecessary radioactive radiation. Moreover it is of utmost importance for the examination that the source of radiation should be shielded carefully from the gamma camera which is very disturbance--sensitive to background radiation.

A fixed arrangement as suggested above which would satisfy these requirements, however, has important practical disadvantages, namely:

(1) it is not possible to move the device around the patient's bed. This is a disadvantage because in examinations with very short-living radioactive isotopes, the organ, for example, the heart, has to be inspected usually in various directions by means of the gamma camera, so as to gain optimum insight in the function of the organ. A fixed bed-side arrangement of the radioactive material to be administered considerably

restricts the possibilities of moving the bed with the patient with respect to the gamma camera. This disadvantage is the larger since, for reasons which will be stated hereinafter, the connection between the source of the radioactive material and the patient should be as short as possible.

(2) Assembling of the device must take place for the greater part under aseptic conditions because the radioactive material must be introduced into the patient's body directly and cannot be previously subjected to a separate sterilization.
Because the device with radioactive material, in particular the radio isotope generator, will be used for a longer period of time, such an assembling should be carried out under so-called laminar flow conditions, and therefore requires provisions which are particularly difficult to realize in an examination room.

(3) Another important disadvantage relates to the working with radioactive material upon assembling the device. As a matter of fact, the shielding from radioactive radiation is not yet optimum during the assembly, so that such an assembly, in which large quantities of not yet optimally shielded activity are handled, should therefore take place in a so-called hot-lab of a nuclear medical department of a clinic and not in an examination room for patients where in addition disturbance-sensitive detection apparatus is arranged.

It is the object of the present invention to provide a shielding device for a reservoir comprising radioactive material, in particular a column for a radioisotope generator, which does not exhibit the above-mentioned disadvantages.

For that purpose, the shielding device according to the invention is provided with means with which the device can be moved forward. The complete device comprising radioactive material can now be assembled in suitable rooms intended for this purpose and can then be wheeled to

the examination room beside the patient's bed. Because the shielding device can be freely shifted, the device can be moved at will around the patient during the examination. Such a movable shielding device for a column for a radioisotope generator is moreover more flexible because the device can be used, if desired, for any generator, for example, a rubidium-krypton-81m, a strontium-rubidium 82 or a mercury-gold 195m generator.

It is of course necessary that the shielding device should also satisfy all conventional safety requirements in addition to the above-mentioned radiological safety requirements. This involves, for example, that the device should be sufficiently stable and be protected as well as possible from calamities, for example, a fire; in the latter case, of course, it should be prevented that the radioactive radiation can pass the shielding device and enter the examination room.

Preferably the device in addition comprises provisions for the safe handling of radioactive material, such as a receptacle for waste fluid, a work-top, etc. These provisions enable the user to carry out various manipulations with radioactive materials at different places without risky manually displacing these materials, because, as a matter of fact, the device can be moved forward.

On its lower side the shielding device preferably comprises at least three, preferably five, casters to be able to easily turn and manoeuvre the heavy device in the restricted space around a patient. As a result of the lead cover, a shielding device according to the invention approaches a weight of approximately 360 kg.

Furthermore it is desired to provide the device with a grip at a height which is suitable for hand-movement. For this purpose, a grip consisting of a circumferential tubular or rod-shaped member connected to the outside of the lead cover has proved particularly suitable. When such a grip having no projections is used, it is

avoided that components of the device or connections can be drawn along or loose during movement of the shielding device.

When using the device it is often necessary to temporarily store radioactive waste material. For example, when a gold-195m generator is used, the generator column must first be rinsed several times with eluent before an eluate is obtained having a composition which is sufficiently constant for administration to a patient. It is therefore advantageous that the device moreover comprises a separate lead-shielded space for a receptacle for radio-active waste material.

Because the radioactive liquid has to be introduced directly into the patient's body, the means for doing this are preferably connected on or to the shielding-device.

In a suitable embodiment the shielding device according to the invention comprises a base in which the means to move the device are present, a central part of reduced outside diameter in which the lead cover for the reservoir containing radioactive material is present, and a top part which comprises: the lead closure for the access in the cover, the grip, the access to the shielded space for the waste reservoir and the means to introduce a radioactive liquid into a patient's body.

As a result of the large diameter of grip and base as compared with that of the reservoir shielded by means of a lead cover, the distance between the radiation source and the operating personnel is increased, for example, by a factor of approximately 2. As a result of this the radiation received is still further reduced, for example, by a factor of approximately 4 as compared with the radiation at the outer surface of the shielded reservoir.

Lead is vulnerable because is is a soft metal. Moreover, it has a low melting-point, 327°C, so that in the case of a fire, it will melt and drip away, thus allo-

wing radioactive radiation to be released from the cover. Therefore, the lead cover for the reservoir consists preferably and in agreement with the requirements which are imposed upon the storage of radioactive material in various countries, of a lead vessel which is open at its top and which is enclosed between sheet material of iron or steel, protected on the outside against corrosion, or of stainless steel, while the open top end accessible for the reservoir can be closed by a lead lid provided with the same sheet material on the outside, an aperture for a connection between the reservoir and the means for introducing a radioactive liquid into a patient's body being present in the lid or between the vessel and the lid. The sheet material which can withstand high temperatures ensures sufficient safety for the ambience in the case of a calamity, for example, a fire, so that the lead shielding remains contained and no undesired radioactive radiation can get out of the shielding system.

It cannot always be avoided that a little radioactive liquid is spilled when installing or using the source of the radioactive material. Then it is difficult to thoroughly clean the vessel which forms part of the heavy shielding device. Therefore, a stainless steel vessel is preferably present between the substantially lead vessel and the reservoir, which stainless steel vessel comprises on its open top a radially outwardly projecting flange to which the lid can be sealingly connected.

The shielding device in accordance with the invention serves in particular for shielding a radio isotope generator. The provisions necessary upon eluting a generator column are preferably connected on or to the above-mentioned top part of the device, namely a reservoir for the eluent for the generator column which communicates with the column; means for pumping or injecting the eluent out of the eluent reservoir into the column; means for bringing the resulting eluate out of the column into a patient's body; means for adding a rinsing of formulating

liquid to the eluate; and a tube which is connected on one side to the means for adding the rinsing or formulating liquid and which on its other side has a member which can be connected to an auxiliary means to admit liquids to the blood vessels or body cavities of a patient.

In order to be able to handle all operating members easily, rapidly and safely, a connection and operating block or tray is connected to the top part, in which block are accommodated injection means for the eluent and the eluate, valves to prevent undesired directions of flow of liquids, cocks to enable or block the passage of liquids, and connection provisions for the means provided in the block both mutually and to the tubes which are connected to the reservoirs, the column and the auxiliary means to be used for the administration to a patient. Preferably the operating block or tray is attached on top of the lid of the lead vessel and the lid is provided with a bore to let pass connecting tubes from the generator to the auxiliary means for injection and from the auxiliary means to the waste fluid receptacle thereby shielding the environment as far as possible from radiation emanating from these tubes when radioactive liquid passes through them. The above embodiment has the advantage that an optimum safety can be reached inspite of the excess pressure at which generally the radioactive liquid is administered to a patient. Moreover, the path which the eluate has to cover, hence the distance between the generator and the patient, can be kept as short as possible. This latter is of importance in particular because, when very short-living radio-isotopes are used, high requirements are generally imposed upon the volume to be administered to the patient and in which the radioactive material is present. As described in the above-mentioned Netherlands Patent Application 8201591, repeated administrations within a short period of time are necessary for various applications. In order to enable such examinations, the volume in which the reactivity is

present must be as small as possible.

The invention will now be described in greater detail with reference to an embodiment which is shown in the accompanying drawings.

Figure 1 is a side-view of a shielding device according to the invention; figure 2 shows the same shielding device from top. Figure 1 is for the greater part a longitudinal sectional view of the shielding device taken on the line I-I of fig. 2, viewed in the direction of the arrows. Figure 3 is a longitudinal sectional view of a part of the device taken on the line III-III of fig. 2.

The operation of the device will be described in detail with reference to figure 4. Figure 4 shows an exploded view of a part of the device.

The base 21 of the screening device shown in Figure 1 comprises a base plate 23 which is hooded with a stove-enamelled sheet iron cap 22 below which five casters 24 are connected so as to be rotatable.

The central part 25 is mounted on said base plate and comprises a lead vessel 26 which is enclosed between stove-enamelled sheet iron 27. A second vessel 29 which is manufactured from stainless steel and comprises a radially outwardly projecting flange 28 is provided in the vessel. The generator 31 is placed in vessel 29. Between the bottoms of the vessels 27 and 29 a space 30 remains in which heating elements, for example a heating plate, can be accommodated. As described in the above-mentioned Netherlands Patent Application 8202407 it may be useful when certain radio isotope generators are used, for example, a gold-195m generator, to heat the generator column during the elution. If desired, a bore may be recessed in vessel 26 for leading through a supply for the heating means.

As shown in figures 1 and 2 a grip 33 in the form of a circumferential tube which is connected to the vessel by means of three spoke-shaped elements 34 is provided around the top part of the device. The vessel 26 can be closed on its top side by means of a lead lid 36 mounted

in stove-enamelled sheet iron 35 and connected to the vessel so as to be pivotable at 37. For compensation of the weight of the lid, a spring mechanism 38 is provided. The lid can be clamped sealingly on the vessel (flange 28) by means of a clamping lock 39 provided with a handle. A bore 32 is present in lid 36 for leading through two connection tubes, the outlets of which are framed in a suitable mount 45, comprising a steel tube encased in lead, erected on the lid of the lead vessel and forming a base for an operating block or tray. Between the circumferential grip and the upper edge of the lead vessel, a circumferential stainless steel top 40 having upright edges is present on which auxiliary means necessary for using the device can be placed.

A small lead vessel 41, also mounted in stove--enamelled sheet iron, for a receptacle 12a for waste material is present in an aperture of the top 40, which vessel is connected to the large vessel 27 and can be closed by means of a lead lid 43 provided with a grip 44.

On top of mount 45 is connected an operating block or tray 46 in or on which two syringes can be accomodated, as well as other auxiliary means needed during operation of the device.

Figure 3 shows a waste overflow bottle 12b placed on top 40. The inlet of the overflow bottle is connected to the outlet tube 11b of receptacle 12a.

As shown in Figure 1, two reservoirs 1 and 2 for eluent and rinsing or formulating liquid, respectively, are clamped in a stand 16 mounted on the edge of vessel 27.

As shown in Figure 4, two syringes 5 and 9 provided on their front sides with connection means in the form of Luer cones are connected to three-way cocks, the former directly to a three-way cock 4a and the latter to a three--way cock 4b via two valves 8a and 8b.

The use of the device shown will be explained with reference to figure 4. All connections between the various components, for the greater part tube connections

and Luer connections, are produced under laminar flow conditions.

During operation of the device the tube connections are provided between eluent reservoir 1 and an outlet of three-way cock 4a, the inlet aperture of the generator column 13 and the other outlet of three-way cock 4a, the reservoir with rinsing or formulating liquid 2 and valve 8a, the drain aperture of the generator column 15 and valve 8b, the receptacle for waste fluid 12a and an outlet of three-way cock 4b and the auxiliary means to be used for administration to a patient and the other outlet of three-way cock 4b.

When the device is used, first three-way cock 4b is opened to communicate the eluate duct 7 through cock 10b and valve 8b with the waste fluid receptacle 12a. Overflow bottle 12b is connected to receptacle 12a through a tube 11b and serves as an extra safety. By means of three-way cock 4a, syringe 5 is communicated with eluent reservoir 1, after which the syringe is filled with 2 ml of eluent. Eluent reservoir 1 and rinsing agent reservoir 2, clamped in stand 16, are provided with dropping chambers 3a and 3b. After opening the cock 10a, syringe 9 is filled with a saline solution from reservoir 2 (through valve 8a); the tube is then closed by clamping by means of clamb 17. After having turned three-way cock 4a, the contents of syringe 5 are injected through tube 6 into the generator column 14 at 13; after-rinsing is carried out with 2 ml of saline solution from syringe 9. All the wash liquid (eluate) rinsed through the column and leaving the generator column at 15, as well as the rinsing liquid is collected through tubes 7 and 11a in the waste receptacle 12a.

After having repeated this operation several times, the generator is ready for connection to a patient. For that purpose, a sterile tube, connected to three-way cock 4b, is filled with a saline solution from syringe 9 after opening said valve, and is then connected to an

auxiliary means to administer the radioactive liquid to a patient, for example, a needle or a catheter. After having placed the patient in a suitable position below a gamma camera, the generator is eluted with 2 ml of eluent by means of syringe 5, the eluate being injected directly into the patient. All remaining radioactivity is then removed from the device by rinsing with 10 ml of saline solution from reservoir 2 by means of syringe 9.

The examination may be repeated any desirable number of times.

CLAIMS:

1. A shielding device for a reservoir comprising a radioactive material and having an inlet and an outlet aperture, in particular a column for a radio-isotope generator, comprising a lead cover for the reservoir in which a closable access for the reservoir is recessed, characterized in that the shielding device is provided with means with which the device can be moved forward.

2. A device as claimed in Claim 1, characterized in that the device comprises in addition provisions for the safe handling of radioactive material.

3. A device as claimed in Claim 1 or 2, characterized in that the device comprises on its lower side at least three, preferably five, casters.

4. A device as claimed in any of the preceding Claims, characterized in that the device comprises a grip, preferably consisting of a circumferential tubular or rod-shaped member connected to the outside of the lead cover.

5. A device as claimed in any of the preceding Claims, characterized in that the device comprises in addition a separate lead-shielded space for a reservoir for radioactive waste material.

6. A device as claimed in any of the preceding Claims, characterized in that the device is provided with means for introducing a radioactive liquid into a patient's body, while the environment is shielded as far as possible from radiation emanating from these means when radioactive liquid passes through them.

7. A device as claimed in Claim 6, characterized in that the device comprises a base in which the means to move the device are present, a central part of reduced outside diameter in which the lead cover for the reservoir containing the radioactive material is present, and a top part which comprises: the lead closure for the access in the cover, the grip, the access to the shielded space for the waste reservoir and the means to introduce a radioactive liquid into a patient's body.

8. A device as claimed in Claim 7, characterized in that the lead cover for the reservoir consists of a lead vessel which is open at its top and which is enclosed between sheet material of iron or steel treated externally against corrosion, or of stainless steel, while the open top end accessible for the reservoir can be closed by means of a lead lid provided on its outside with the same sheet material, an aperture for a connection between the reservoir and the means for introducing a radioactive liquid into a patient's body being present in the lid or between the vessel and the lid.

9. A device as claimed in Claim 8, characterized in that a vessel of stainless steel which at its open top side comprises a radially outwardly projecting flange to which the lid can be sealingly connected, is present between the substantially lead vessel and the reservoir.

10. A shielding device as claimed in any of the Claims 7-9 for a radio-isotope generator, characterized in that there are additionally connected on or to the top part: a reservoir for an eluent for the generator column which communicates with the column; means for pumping or injecting the eluent out of the eluent reservoir into the column; means to bring the resulting eluate out of the column into a patient's body; means to add a rinsing or formulating liquid to the eluate; and a tube which is connected on one side to the means for adding the rinsing or formulating liquid and which comprises on the other side a member which can be connected to an auxiliary means to admit liquid to blood vessels or body cavities of a patient.

11. A device as claimed in Claim 10, characterized in that a connection and operating block or tray is connected to the top part, in which block are accomodated injection means for the eluent and the eluate, valves to prevent undesired directions of flow of liquids, cocks to enable or block the passage of liquids, and connection means for the means accomodated in the block both mutually

and to the tubes which are connected to the reservoirs, the column and the auxiliary means to be used for administering to a patient.

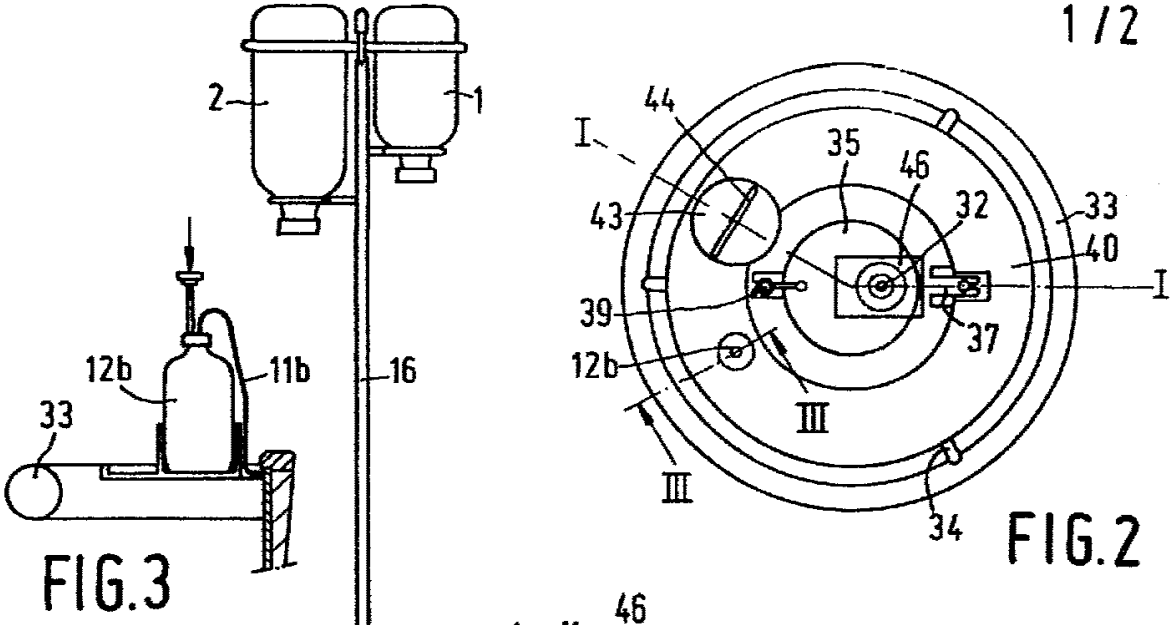

FIG.3

FIG.2

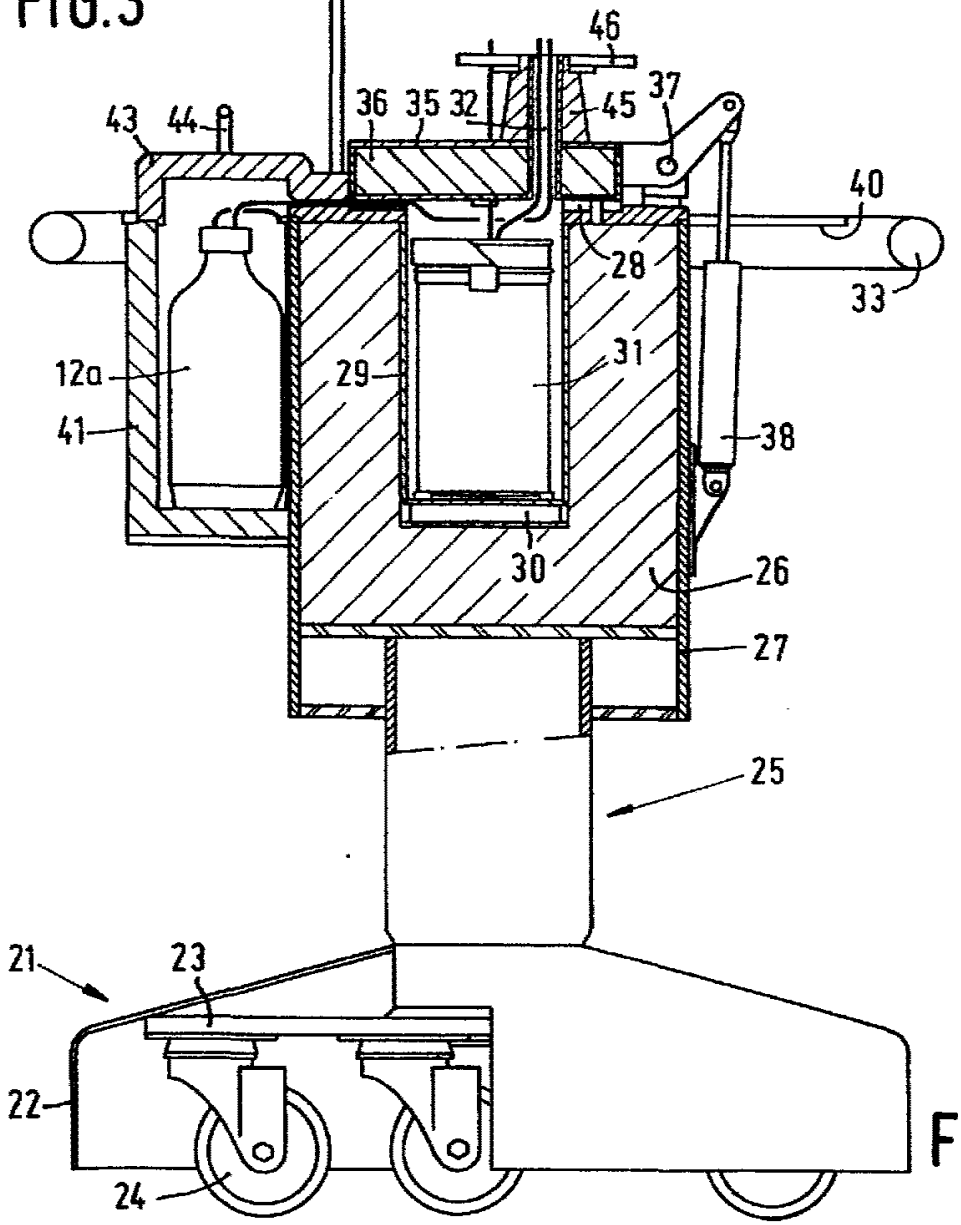

FIG.1

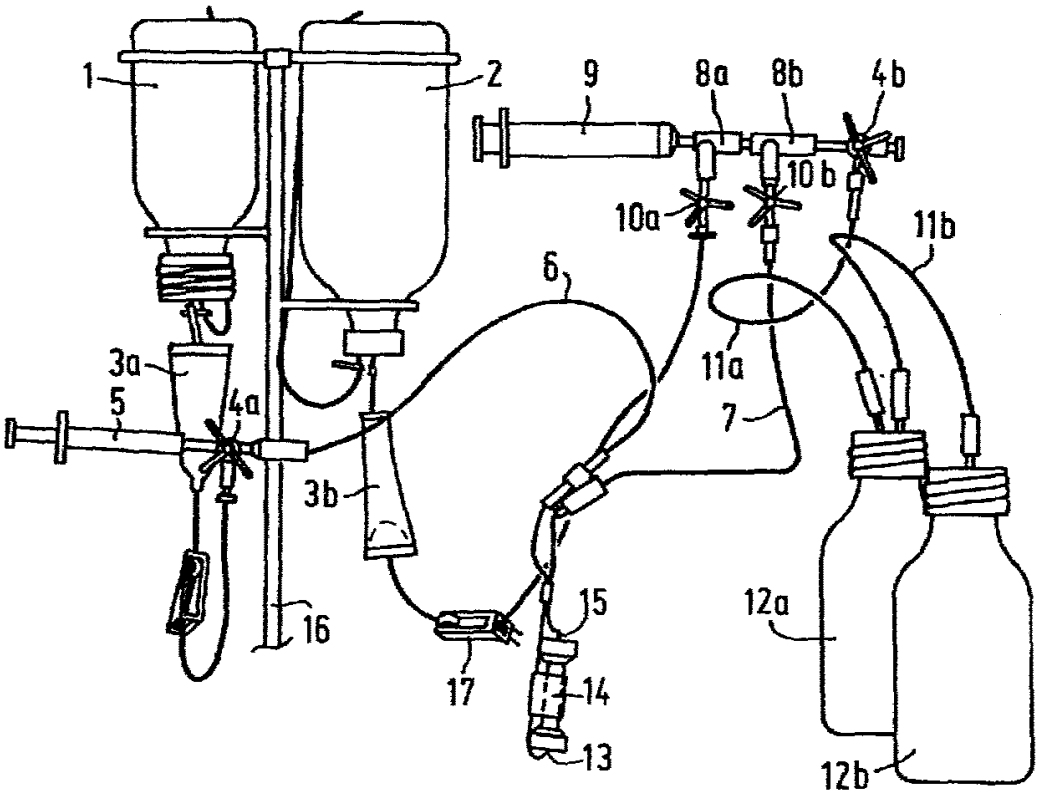

FIG. 4

European Patent Office

EUROPEAN SEARCH REPORT

0102121

Application number

EP 83 20 1201

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl. ³)
A	GB-A-1 234 020 (C.E.A.) * Claim 1; figure 1; page 2, lines 83-90; page 3, lines 68-76 *	1,2,7	G 21 G 1/04
A	GB-A-2 033 288 (BYK MALLINCKRODT) * Claim 1; figure 1; page 3, lines 29-40 *	1,2	
A	US-A-3 710 118 (R.L. HOLGATE) * Claims 1,2 *	1,10	

TECHNICAL FIELDS SEARCHED (Int. Cl. ³)

G 21 G
G 21 F

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	17-11-1983	NICOLAS H.J.F.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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A : technological background
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T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
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& : member of the same patent family, corresponding document

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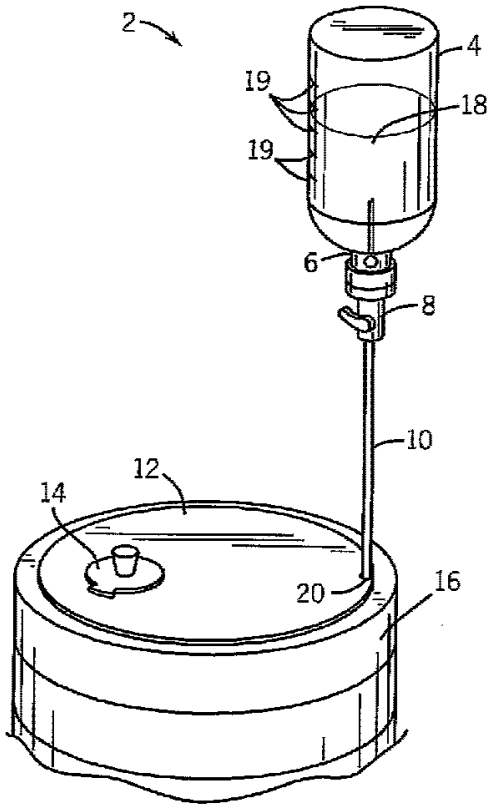
(54) Title: SYSTEM AND METHOD OF IDENTIFYING ELUANT AMOUNTS SUPPLIED TO A RADIOISOTOPE GENERATOR



(57) Abstract: The invention, is directed to a system including a shielded container (16) , a radioisotope generator disposed within the shielded container, and an elution supply mechanism. The elution supply mechanism may include an eluant supply container (4) at least partially external to the shielded container (16) , a conduit (10) extending between an inlet (20) of the radioisotope generator and an outlet (6, 8) of the eluant supply container, and an eluant visualization portal.

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SYSTEM AND METHOD OF IDENTIFYING ELUANT AMOUNTS SUPPLIED TO A RADIOISOTOPE GENERATOR

FIELD OF THE INVENTION

[0001] The invention relates generally to the field of nuclear medicine. Specifically, the invention relates to a system and method of identifying an amount or flow of eluant in an elution system configured to enable extraction of a radioactive material from a radioisotope generator for use in the practice of nuclear medicine.

BACKGROUND

[0002] This section is intended to introduce the reader to various aspects of art that may be related to various aspects of the present invention, which are described and/or claimed below. This discussion is believed to be helpful in providing the reader with background information to facilitate a better understanding of the various aspects of the present invention. Accordingly, it should be understood that these statements are to be read in this light, and not as admissions of prior art.

[0003] Nuclear medicine is a branch of health science that utilizes radioactive material for diagnostic and therapeutic purposes by injecting a patient with a small dose of the radioactive material, which concentrates in certain organs or biological regions of the patient. Radioactive materials typically used for nuclear medicine include Technetium-99m, Indium-113m, and Strontium-87m among others. Some radioactive materials naturally concentrate toward a particular tissue; for example, iodine concentrates toward the thyroid. However, radioactive materials are often combined with a tagging or organ-seeking agent, which targets the radioactive material for the desired organ or biologic region of the patient. These radioactive materials alone or in combination with a tagging agent are typically defined as radiopharmaceuticals in the field of nuclear medicine. At relatively lower doses of the radiopharmaceutical, a radiation imaging system (e.g., a gamma camera) can provide an image of the organ or biological region that collects the radiopharmaceutical. Irregularities in the image are often indicative of a pathologic condition, such as cancer. Higher doses of the radiopharmaceutical may be used to deliver a therapeutic dose of radiation directly to the pathologic tissue, such as cancer cells.

[0004] A variety of elution systems are used to generate radiopharmaceuticals. Unfortunately, radioactive shielding containers of these systems tend to block visualization of the state and progress of the elution process. For example, the amount of available eluant

and/or the amount of extracted eluate are generally unknown without opening one or more of the radioactive shielding containers. Rather, the pharmacist typically has to wait an estimated amount of time to ensure the process is complete, which results in wasted time or premature termination of the process. If a specific amount of eluate is desired, then the time estimation may tend to result in too much or too little of the eluate.

SUMMARY

[0005] The present invention, in certain embodiments, is directed to identifying or monitoring a volume, mass, weight, displacement or flow of a supply element (e.g., eluant) and/or an output eluate associated with eluting a radioisotope from a generator product in the field of nuclear medicine. Specifically, in some embodiments, visual access may be provided into an eluant supply container to facilitate performance of elution procedures. For example, a visual portal into an eluant supply container during an elution can provide data for measuring and calculating metrics relating to completion of full or partial elutions and data relating to when a generator is available for milking. Other embodiments may measure an amount or flow of eluant and/or eluate, such that a user can directly view the measurement (e.g., scale or flow meter) or indirectly view the measurement on a remote display screen or computer.

[0006] Certain aspects commensurate in scope with the originally claimed invention are set forth below. It should be understood that these aspects are presented merely to provide the reader with a brief summary of certain forms the invention might take and that these aspects are not intended to limit the scope of the invention. Indeed, the invention may encompass a variety of aspects that may not be set forth below.

[0007] In accordance with a first aspect of the present invention, there is provided a system having a shielded container, a radioisotope generator disposed within the shielded container, and an elution supply mechanism. The elution supply mechanism has an eluant supply container at least partially (and in some cases, completely) external to the shielded container, a conduit extending between an inlet of the radioisotope generator and an outlet of the eluant supply container, and an eluant visualization portal.

[0008] In accordance with a second aspect of the present invention, there is provided a system that includes a radiation shielded container having a receptacle and a cover disposed over an opening in the receptacle, a radioisotope generator disposed within the receptacle below the cover, and an eluant supply mechanism. The eluant supply mechanism includes an eluant supply container and a conduit coupled with the eluant supply container and the

radioisotope generator. The conduit is disposed at least partially within the shielded container, and an eluant measurement device is coupled to the eluant supply mechanism.

[0009] A third aspect of the present invention is directed to a method of using a radioisotope elution system. With regard to this third aspect, a radioisotope generator that is disposed inside a radiation shielded container receives an amount of eluant. The amount of eluant received by the radioisotope generator is visually indicated outside the radiation shielded container. In addition, radioactive material is eluted from the radioisotope generator.

[0010] In accordance with a fourth aspect of the present invention, there is provided a system including an eluant supply mechanism and a radiation shielded lid having an aperture defined therein. The eluant supply mechanism includes an eluant supply container, a conduit coupled to the eluant supply container and at least partially disposed in the aperture, and an eluant measurement feature.

[0011] Various refinements exist of the features noted above in relation to the various aspects of the present invention. Further features may also be incorporated in these various aspects as well. These refinements and additional features may exist individually or in any combination. Again, the brief summary presented above is intended only to familiarize the reader with certain aspects and contexts of the present invention without limitation to the claimed subject matter.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] These and other features, aspects, and advantages of the present invention will become better understood when the following detailed description is read with reference to the accompanying drawings in which like characters represent like parts throughout the drawings, wherein:

[0013] FIG. 1 is a perspective view of an exemplary embodiment of a generator product including a visually accessible eluant supply bottle, a vented spike, a stop cock, tubing, a shielded lid, a shielded lid plug, and a shielded container;

[0014] FIG. 2 is a partial cross-sectional side view of an exemplary embodiment of the generator product, wherein the tubing may pass through an aperture defined along an edge of the lid and into the shielded container;

[0015] FIG. 3 is a top view of an exemplary embodiment of a portion of the generator product, wherein the lid may be mounted over an opening in the shielded container;

[0016] FIG. 4 is a cross-sectional side view of an exemplary embodiment of the generator product, wherein the tubing may be coupled to the generator via an inlet needle and the lid plug may be replaced by an elution assembly;

[0017] FIG. 5 is a partial perspective view of an exemplary embodiment of the generator product, wherein a syringe pump may be incorporated in the place of the eluant supply bottle;

[0018] FIG. 6 is a partial perspective view of an exemplary embodiment of the generator product, wherein a drip chamber may be incorporated in the tubing;

[0019] FIG. 7 is a partial perspective view of an exemplary embodiment of the generator product that may include the drip chamber, an electronic drop counter, a display, and a computer, wherein the electronic drop counter may be utilized to count the drops passing through the drip chamber;

[0020] FIG. 8 is a partial perspective view of an exemplary embodiment of the generator product, wherein the eluant supply may be utilized with a splitter or manifold to supply a plurality of generators, each disposed within a shielded container;

[0021] FIG. 9 is a partial perspective view of an exemplary embodiment of the generator product, wherein the eluant supply bottle may be at least partially shielded and may include a visualization window that facilitates viewing and measurement of eluant levels in the bottle, and wherein the drip chamber and drop counter may be disposed within the shielded container; and

[0022] FIG. 10 is a partial perspective view of an exemplary embodiment of the generator product, wherein the eluant supply bottle, the drip chamber, and the drop counter may be disposed within the shielded container, and wherein the display may be positioned external to the shielded container along with a portion of a level gauge coupled to the eluant supply bottle.

DETAILED DESCRIPTION OF SPECIFIC EMBODIMENTS

[0023] One or more exemplary embodiments of the present invention are described below. In an effort to provide a concise description of these embodiments, some features of an actual implementation may not be described in the specification. It should be appreciated that in the development of any such actual implementation, as in any engineering or design project, numerous implementation-specific decisions may be made to achieve the developers' specific goals, such as compliance with system-related and business-related constraints, which may vary from one implementation to another. Such a development effort would be a routine

undertaking of design, fabrication, and manufacture for those of ordinary skill having the benefit of this disclosure.

[0024] The embodiments discussed in detail below relate to a system and method for facilitating efficient extraction of radioactive material (e.g., a radioisotope) from a radioisotope generator during a radioisotope elution process. Indeed, embodiments of the present invention facilitate efficient use of time and resources by providing direct or indirect visual access to an eluant supply and/or an eluate output during a radioisotope elution process. In other words, techniques are disclosed for identifying or tracking a volume, mass, weight, displacement, and/or flow of a supply eluant and/or an output eluate associated with eluting a radioisotope from a radioisotope generator via direct visualization or non-visual measurements that can be visualized remotely. As discussed below, these techniques may include a scale to monitor changes in weight of a supply eluant and/or an output eluate. Additionally or alternatively, these techniques may include a flow meter or displacement gauge, graduated volume marks on the supply and/or output container, and so forth.

[0025] FIG. 1 shows an exemplary embodiment of a generator product 2 that includes a visually accessible eluant supply container (here, a bottle) 4, a vented spike 6, a stop cock 8, tubing 10, a radioactivity shielded lid 12, a radioactivity shielded lid plug 14, and a radioactivity shielded container 16 (e.g., an auxiliary shield). In some embodiments, the lid plug 14 may be replaced by an elution assembly. It should be noted that the term "generator product" herein interchangeably refers to both a radioisotope elution system and/or a radioisotope generator assembly. A radioisotope generator assembly may include a radioisotope generator, a radioactivity shielded container, an eluant supply container, a radioactivity shielded lid, and a lid plug. A radioisotope elution system may include the radioisotope generator assembly, wherein the lid plug is replaced with an elution assembly that includes an eluate output container and an elution shield surrounding the eluate output container.

[0026] As illustrated in FIG. 1, the eluant supply container 4 may be entirely or at least partially transparent (or translucent) and external to the shielded container 16, thereby providing a visualization portal into the bottle 4. In some embodiments, the supply bottle 4 may be partially external and/or partially internal to the shielded container 16. The supply bottle 4 can be fully or partially composed of glass, hard plastic, soft plastic, and other appropriate material(s) that allow visual access. As such, a user can visualize eluant 18 disposed within the bottle 4. Because the eluant 18 is visible, a user can observe how much of it has been used during an elution process and/or how much of it remains after an elution process. For example, in the illustrated embodiment, a user can visually monitor the level of eluant in the bottle 4 with respect to index marks 19, which correspond to predefined metrics

(e.g., volume). This facilitates determination of when an elution process is complete. Further, if a partial elution (e.g., an elution to partially fill a standard sized eluate output container) is desired, visual access to the eluant supply may facilitate accurate performance of the partial elution. The eluant supply container 4 may be coupled to a generator disposed within the shielded container 16 via the tubing 10. Incidentally, "coupled" or the like herein generally refers to two or more components that are either directly or indirectly connected to one another. In this particular example, the coupling of the eluant supply container 4 and the generator may be characterized as a fluid coupling of those components. Incidentally, "fluidly coupling" or the like refers to a coupling of first and second components so that molecules of a substance(s) (such as a liquid or gas) may be substantially confined within and capable of flowing between the first and second components.

[0027] The tubing 10 can be a rigid or flexible conduit (e.g., flexible tubing or a needle) capable of enabling flow of the eluant 18 from the eluant supply container 4 to the generator. In some embodiments, the tubing 10 is transparent and/or translucent, which further facilitates observation of the eluant flow from the eluant supply 18 to the generator. The tubing 10 may be coupled to the eluant supply container 4 in any appropriate manner, such as via a stopcock 8 and a vented spike 6. In the illustrated embodiment, the eluant supply container 4 may be made of a generally rigid material that does not collapse as the eluant 18 is evacuated. Accordingly, the vented spike 6 may allow filtered air to enter into the bottle 4 to reduce the likelihood of a vacuum (e.g., a state of negative pressure) inside the bottle 4 when the eluant 18 flows out. In other embodiments, the eluant supply container 4 may be made of flexible material that collapses as it is evacuated with or without aid by the vented spike 6. The stopcock 8 may enable a user to regulate flow of the eluant 18 from the bottle 4 through the tubing 10 and into the generator. For example, the stopcock 8 may include a valve that opens and closes by means of a tapered plug, enabling a user to control flow of eluant 18 between the bottle 4 and the generator.

[0028] The tubing 10 may pass into the shielded container 16 through the lid 12 via an aperture 20 in the lid 12. In some embodiments, the aperture 20 may be formed in a central portion of the lid 12 and may include a nipple or other connection mechanism. However, in the illustrated embodiment, the aperture 20 is disposed along the circumference of the lid 12 such that a gap is formed between the edge of the lid 12 and the shielded container 16. The aperture 20 is illustrated in FIG. 2, which is a partial cross-sectional view of the generator product 2, wherein the tubing 10 passes through the aperture 20 disposed along the edge of the lid 10 and into the shielded container 16. Specifically, FIG. 2 illustrates the tubing 10 passing between the lid 10 and a top section of the shielded container 16 through the aperture 20 and coupling with a generator 22 via a coupling mechanism 24 (e.g., a needle, a nipple,

threaded fastener, flange, and/or the like). In some embodiments, the coupling mechanism 24 may include a check valve that reduces the likelihood of backflow of eluant and/or eluate from the generator 22 to the tubing 10 (and possible even the eluant supply container 4). In some embodiments, the tubing 10 may include a check valve disposed therein to reduce the likelihood of backflow from downstream tubing to upstream tubing and/or to the eluant supply container 4. It should be noted that in some embodiments, the tubing 10 may pass through an opening in the side of the shielded container 16. For example, in some embodiments, the tubing 10 may pass through an opening formed between sectional rings 26 that are stacked to form the shielded container 16.

[0029] FIG. 3 is a top view of a portion of the generator product 2, wherein the lid 12 is mounted over an opening in the shielded container 16. Specifically, FIG. 3 illustrates the aperture 20 disposed along an edge of the lid 12 and forming a gap between the lid 12 and the shielded container 16. As noted above, in some embodiments, the aperture 20 may be located in a generally central location on the lid 12 or in a side portion of the shielded container 16. In some embodiments, the aperture 20 and the tubing 10 may correspond in size so that the tubing 10 is tightly secured when engaged with the aperture 20. In other embodiments, the aperture 20 may be larger than the tubing 10, allowing maneuverability of the tubing 10 while it is engaged in the aperture 20. In still other embodiments, the tubing 10 includes one or more seals or the like that operate to secure the tubing 10 in the aperture 20 and prevent flow (e.g., air flow) in and out of the shielded container 16 through the aperture 20.

[0030] FIG. 4 is a cross-sectional side view of the generator product 2, wherein the tubing 10 is shown coupled to the generator 22 via a hollow inlet needle 28 and the lid plug 14 has been be replaced by an elution assembly 28. The illustrated elution assembly 28 includes an elution shield 32 at least generally disposed about an eluate collection bottle 34. The elution shield 32 is designed to shield users from radioactive elements that are received by elution into the bottle 34. The eluate collection bottle 34 may be coupled to the generator 22 via a hollow outlet needle 36. During a wet elution process (e.g., an elution process wherein the generator generally remains charged), the eluate collection bottle 34 may be coupled to the generator 22 to enable eluate residing in the generator 22 to circulate through the generator 22 and into the evacuated collection bottle 34. The generator 22 is a shielded container that holds a parent radioisotope, such as Molybdenum-99 absorbed to alumina beads or another suitable exchange medium. The daughter radioisotope (e.g., Technetium-99M) is held chemically less tightly than the parent, thereby enabling flowing eluant to flush the desired radioisotope from the radioisotope generator 22 into the collection bottle 34 as eluate.

[0031] The eluate collection bottle 34 may have a standard or predefined volume, which may begin in an evacuated condition. A pressure drop into the evacuated eluate collection bottle 34 may facilitate eluate residing in the generator 22 to begin filling the bottle 34. Correspondingly, eluant 18 from the eluant supply container 4 may begin flowing into the generator 22 to replace the eluate passing to the collection bottle 34. Indeed, once the eluate collection bottle 34 is connected to the generator 22, a user can observe that eluant levels in the eluant supply container 4 go down in an amount generally corresponding to the amount of eluate received in the eluate collection bottle 34. For example, a user can observe the volume of eluant 18 leaving the eluant supply container 4 by comparing the eluant level in the supply bottle 4 over time with the index marks 19. This visualization may tend to facilitate determining when the elution process is complete (e.g., the eluate collection bottle 34 is full), and/or may facilitate performance of partial elutions, in which the eluate collection bottle 34 is partially filled with eluate. It should be noted that in some embodiments, the eluate collection bottle 34 may not begin in an evacuated condition. For example, in some embodiments, other system conditions (e.g., generated pressure and/or gravity) may cause flow into the eluate collection bottle 34.

[0032] FIG. 5 illustrates an alternative embodiment of the generator product 2, wherein a graduated syringe pump 40 may be incorporated in the place of the eluant supply container 4. The syringe pump 40 is adapted to inject the eluant 18 into the generator 22 via the tubing 10. Because the syringe pump 40 generates pressure, an evacuated eluate collection bottle 34 may or may not be used in this embodiment. For example, a collection bottle 34 with a vent for expelling air may be used to collect the eluate. While the syringe pump 40 may drive the elution, the graduations or volumetric marks 19 may enable a user to measure and/or observe the amount of eluant injected into the generator 22. In other embodiments, other electrical and/or mechanical pumps and measurement systems may be used to supply and measure amounts of eluant supplied to the generator 22. For example, the system may include an electrical/mechanical scale, flow meter, and so forth. Moreover, the measurements may be visualized by a user directly or indirectly via a remote monitoring system, e.g., a computer. It should be noted that FIG. 5 also illustrates that the aperture 20 may be disposed in a generally central portion of the lid 12. Additionally, as shown in FIG. 5, the tubing 10 may be coupled to a nipple 42 that passes through the lid 12 and couples to the generator 22 within the shielded container 16.

[0033] FIG. 6 shows an exemplary embodiment of the generator product 2, wherein a drip chamber 44 is incorporated in the tubing 10 to facilitate tracking or identification of an amount of eluant flowing into the generator 22. The drip chamber 44 may facilitate measurement of the eluant passing between the eluant supply container 4 and the generator 22 in a variety of

ways. For example, an observer can manually calculate the amount of transferred eluant by counting the drops that pass through the drip chamber 44. For instance, thirty drops of the eluant may correspond to one milliliter of eluant. As another example, in the embodiment illustrated in FIG. 7, an electronic drop counter 46 may be utilized to count the drops passing through the drip chamber 44 by, for example, detecting motion in the drip chamber 44. In one embodiment, the drop counter 46 may include an infra-red light emitting diode (LED) 48 and a photo detector 50. The LED 48 and photo detector 50 are aligned such that the photo detector 50 receives a light beam from the LED 48. When a drop passes through the drop counter 46, it breaks the light beam and the drop counter 46 outputs and/or stores data corresponding to the break. This facilitates measurement of the number of drops and the provision of metrics relating to the amount of eluant being passed from the eluant supply container 4 through the drip chamber 44 and into the generator 22. Metrics can be calculated from the data retrieved by the drop counter 46 manually, in the drop counter 46 itself, or in other devices capable of receiving data and performing calculations.

[0034] As illustrated in FIG. 7, the drop counter 46 may be communicatively coupled to a display 52 for display of metrics relating to the elution process. The drop counter 46 may be coupled to an electronic device and/or computer 54 (e.g., a laptop computer) to store data, facilitate communication with other devices, and/or perform calculations relating to the elution process. It should be noted that in some embodiment, the display 52 may be incorporated into the computer 54. In other words, rather than having a separate display 52, a computer screen 56 of the computer 54 may be utilized for displaying data associated with the elution process. For example, a volume associated with the number of counted drops (e.g., thirty drops corresponds to one milliliter) can be calculated and displayed on the computer screen 56. A time associated with each counted drop can be displayed on the computer screen 56. The volume and/or time associated with each elution process may be tracked and displayed to enable a user (or the computer 54) to estimate when the generator will be ready for another elution process. For example, a value corresponding to an expected radioactivity level of an elution at a certain time can be calculated and displayed on the computer screen 56. By further example, a user (or the computer) can determine an actual radioactivity level of an eluate at a given time. The radioactivity level information can be programmed into the computer 54 if that information is not already in the computer, for example, which can incorporate other data (e.g., time data from the drop counter 46) to determine an expected radioactivity level at a specified future time. In some embodiments, a certain time when an elution should be performed, based on data from the drop counter 46 and/or predefined data (e.g., a calculated expected radioactivity level), can be calculated and displayed on the computer screen 56.

[0035] FIG. 8 shows another exemplary embodiment of the generator product 2, wherein the eluant supply container (here, a bag) 4 may be utilized with a manifold or splitter 60 to supply a plurality of generators 22, each disposed within a shielded container 16. As illustrated, this generator product 2 may have a variety of different measurement and visualization features that may complement or supplement one another. The single bulk supply of eluant (e.g., eluant supply container 4) may increase the likelihood that the individual generators 22 have sufficient eluant during individual or simultaneous operation. In addition, the total eluate output from all of the generators may be tracked or visualized by comparing the eluant level inside the bag 4 against the index marks 19.

[0036] Still referring to FIG. 8, the computer 54 may be coupled to each of a plurality of drop counters 46 and/or displays 52 that provide data relating to elution processes in each of the generators 22, thus enabling collection and provision of data relating to generator usage individually and/or collectively. For example, based on time stamped usage data and related calculations, the computer 54 may indicate that a particular generator 22 in a set of generators should be milked before the others based on a greater likelihood that it may produce an eluate with an appropriate and/or desired radioactivity level. Further, having a single source of eluant may facilitate rapid replacement of the eluant source (e.g., eluant supply container or bag 4) for multiple generators 22. It should be noted that in the embodiment illustrated in FIG. 8, the eluant supply container or bag 4 may be a transparent or translucent rigid container or a collapsible plastic bag with or without a vent to facilitate flow. Thus, the level of eluant may be directly visualized in the container or bag 4. In some embodiments, the container or bag 4 may be mounted on or hung from a scale 57 to measure weight changes in the container or bag 4 and, thus, track the amount of eluant flowing into the generators. For example, an initial weight of the container or bag 4 may be weighed as a reference, followed by a manual or electronic tracking of reduced weight of the container or bag 4. Alternatively, a separate scale 57 may be attached independently to each of a plurality of eluate supply containers for the generators 22.

[0037] FIG. 9 shows an exemplary embodiment of the generator product 2, wherein the eluant supply container 4 may be at least partially shielded and may include a visualization window 66 that facilitates viewing and measurement of eluant levels in the bottle 4. The window 66 may operate as a visualization portal, which may include index marks 19 that can operate as a measurement feature corresponding to volume or another metric. Further, the illustrated embodiment may include the drip chamber 44 and drop counter 46 disposed within the shielded container 16. Again, the drop counter 46 may be communicatively coupled to the display 52, which may be disposed on the outside of the shielded container 16 to facilitate visual access or identification of the eluant level. Indeed, because the display 52 provides

virtual visual access to the eluant supply, the eluant supply container 4 can be disposed within the shielded container, as illustrated by FIG. 10. It should be noted that in FIG. 10 additional access to the eluant level in the eluant supply container 4 may be provided by a level gauge 68 at least partially external to the shielded container. The level gauge 68 can be electronic (e.g., sensor, switches, and electronic display) or manual (e.g., sight glass, circular sight port, or float).

[0038] While the invention may be susceptible to various modifications and alternative forms, specific embodiments have been shown by way of example in the drawings and have been described in detail herein. However, it should be understood that the invention is not intended to be limited to the particular forms disclosed. Rather, the invention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention as defined by the following appended claims.

CLAIMS:

1. A system, comprising:

a radioactivity shielded container;

a radioisotope generator disposed within the radioactivity shielded container; and

an elution supply mechanism comprising:

an eluant supply container at least partially external to the radioactivity shielded container;

a conduit extending between an inlet of the radioisotope generator and an outlet of the eluant supply container; and

an eluant visualization portal.

2. The system of claim 1, wherein the elution supply mechanism comprises a drip chamber.

3. The system of claim 2, wherein the eluant visualization portal comprises a transparent or translucent portion of the drip chamber.

4. The system of claim 2, comprising a drop counter coupled to the drip chamber.

5. The system of claim 4, comprising an electronic measurement device communicatively coupled to the drop counter.

6. The system of claim 4, wherein the electronic measurement device comprises a computer.

7. The system of claim 1, wherein the radioactivity shielded container comprises a radioactivity shielded lid including an aperture having the conduit extending therethrough.

8. The system of claim 7, wherein the aperture is disposed along an edge of the radioactivity shielded lid.

9. The system of claim 1, wherein the radioactivity shielded container comprises a radioactivity shielded lid having a hollow nipple coupled to the conduit.

10. The system of claim 1, wherein the eluant visualization portal comprises a transparent or translucent portion of the eluant supply container having demarcations corresponding to levels of eluant in the eluant supply container.

11. The system of claim 1, wherein the outlet of the elution supply container comprises a conduit splitter coupled to the conduit and at least one other conduit that leads to a different radioisotope generator.

12. The system of claim 1, wherein the elution supply mechanism comprises a pump.

13. The system of claim 12, wherein the pump comprises an eluant measurement system.

14. A system, comprising:

a radiation shielded container comprising a receptacle and a cover disposed over an opening in the receptacle;

a radioisotope generator disposed within the receptacle; and

an eluant supply mechanism comprising:

an eluant supply container;

a conduit coupled with the eluant supply container and the radioisotope generator, the conduit disposed at least partially within the shielded container; and

an eluant measurement device coupled to the eluant supply mechanism.

15. The system of claim 14, wherein the cover includes an aperture having the conduit extending therethrough.

16. The system of claim 14, wherein the conduit comprises a length of flexible tubing.

17. The system of claim 14, wherein the conduit comprises a hollow needle.

18. The system of claim 14, wherein the eluant measurement device comprises an eluant level gauge coupled with the eluant supply container.

19. The system of claim 14, wherein the eluant measurement device comprises a drip chamber.

20. The system of claim 19, wherein the eluant measurement device comprises a drop counter coupled to the drip chamber.

21. The system of claim 14, wherein the eluant measurement device is at least partially disposed inside the radiation shielded container.

22. The system of claim 21, wherein the eluant measurement device comprises a drop counter disposed within the radiation shielded container.

23. The system of claim 14, comprising an electronic display disposed at least partially external to the radiation shielded container and coupled to the eluant measurement device.

24. The system of claim 14, wherein the eluant measurement device comprises a scale.

25. A method of operating a radioisotope elution system, comprising:

receiving an amount of eluant into a radioisotope generator disposed inside a radiation shielded container;

visually indicating an amount of the eluant received by the radioisotope generator, wherein the visually indicating occurs at a location outside the radiation shielded container; and

eluting radioactive material from the radioisotope generator.

26. The method of claim 25, comprising calculating a metric based on the amount of eluant received into the radioisotope generator.

27. The method of claim 26, comprising calculating a suggested time for performing a future elution based on the metric.

28. The method of claim 25, comprising creating a time stamp when the amount of eluant is received.

29. The method of claim 25, comprising measuring the amount of eluant received from within the radiation shielded container.

30. The method of claim 29, wherein measuring comprises counting drops of the eluant.

31. The method of claim 25, wherein visually indicating comprises electronically displaying a metric of the amount of eluant received.

32. The method of claim 25, wherein visually indicating comprises providing a visual line of sight to the eluant.

33. The method of claim 25, wherein measuring comprises weighing the eluant with a scale.

34. A system, comprising:

a radiation shielded lid comprising an aperture; and

an eluant supply mechanism comprising:

an eluant supply container;

a conduit coupled to the eluant supply container and at least partially disposed in the aperture; and

an eluant measurement feature.

35. The system of claim 34, wherein the eluant measurement feature comprises a drip chamber and an electronic drop counter coupled to the drip chamber.

36. The system of claim 34, wherein the eluant measurement feature comprises an eluant visualization portal.

37. The system of claim 34, wherein the eluant measurement feature comprise a scale.

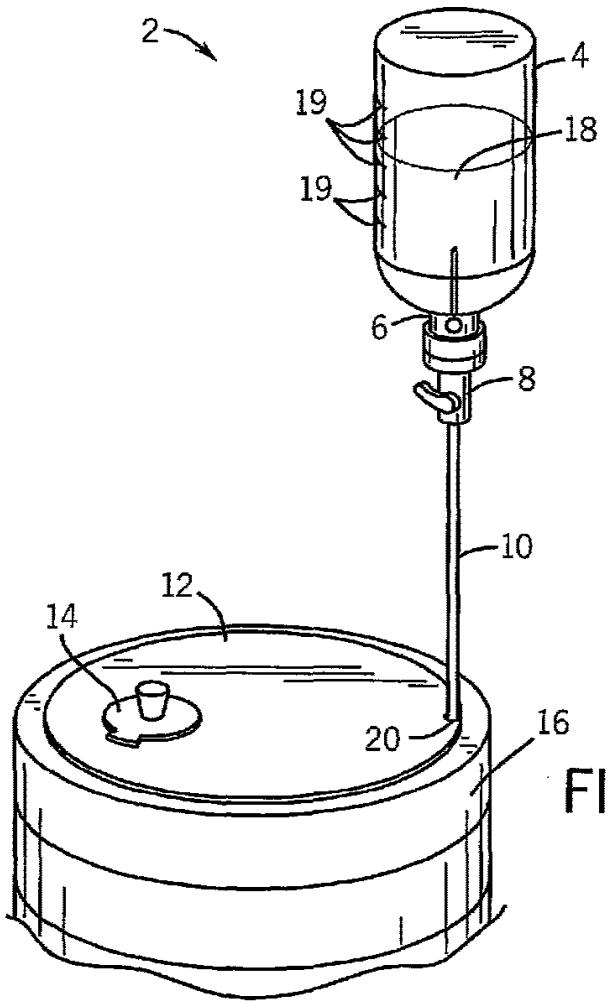


FIG. 1

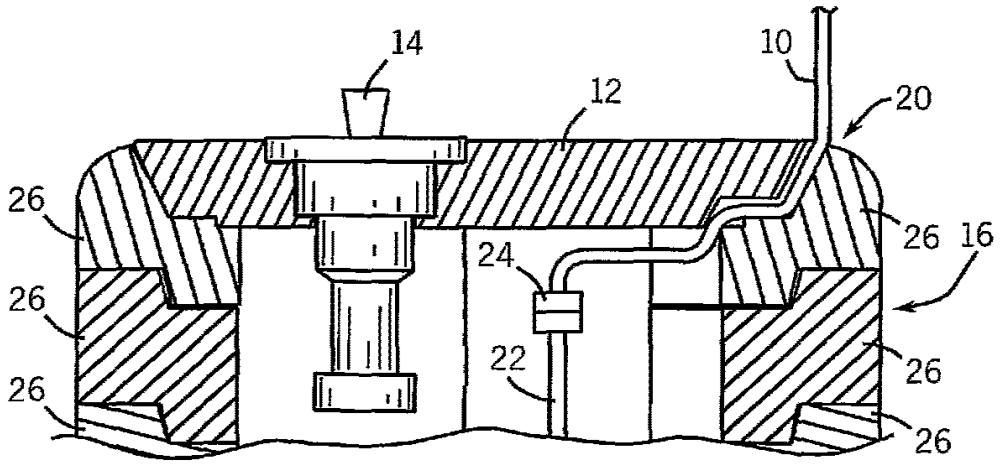


FIG. 2

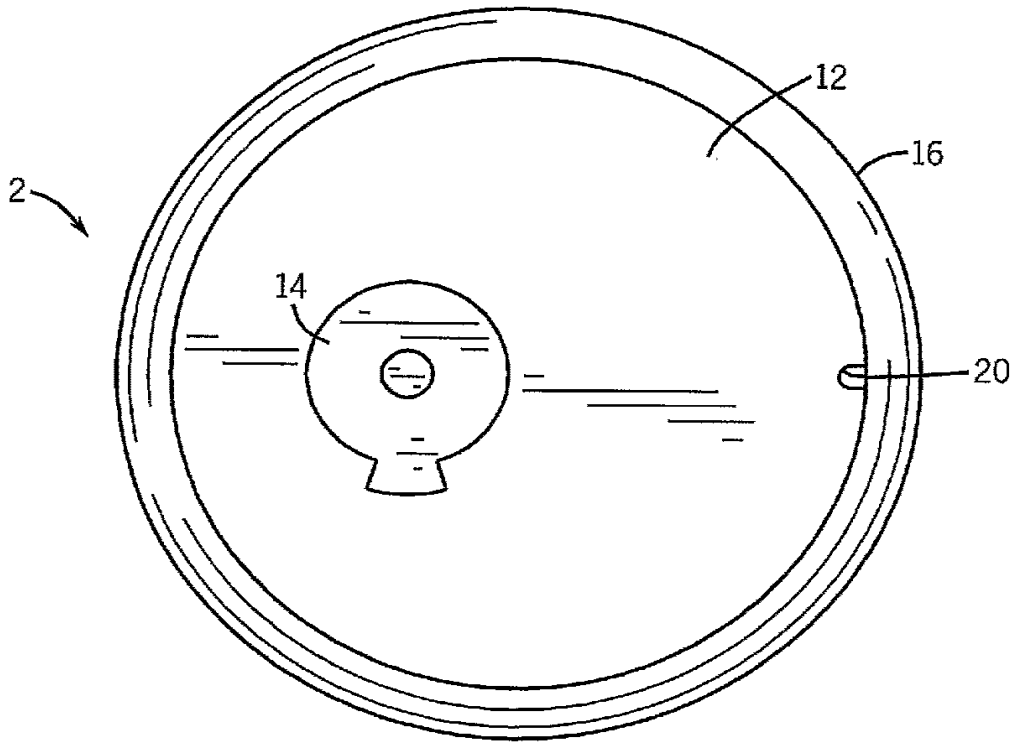


FIG. 3

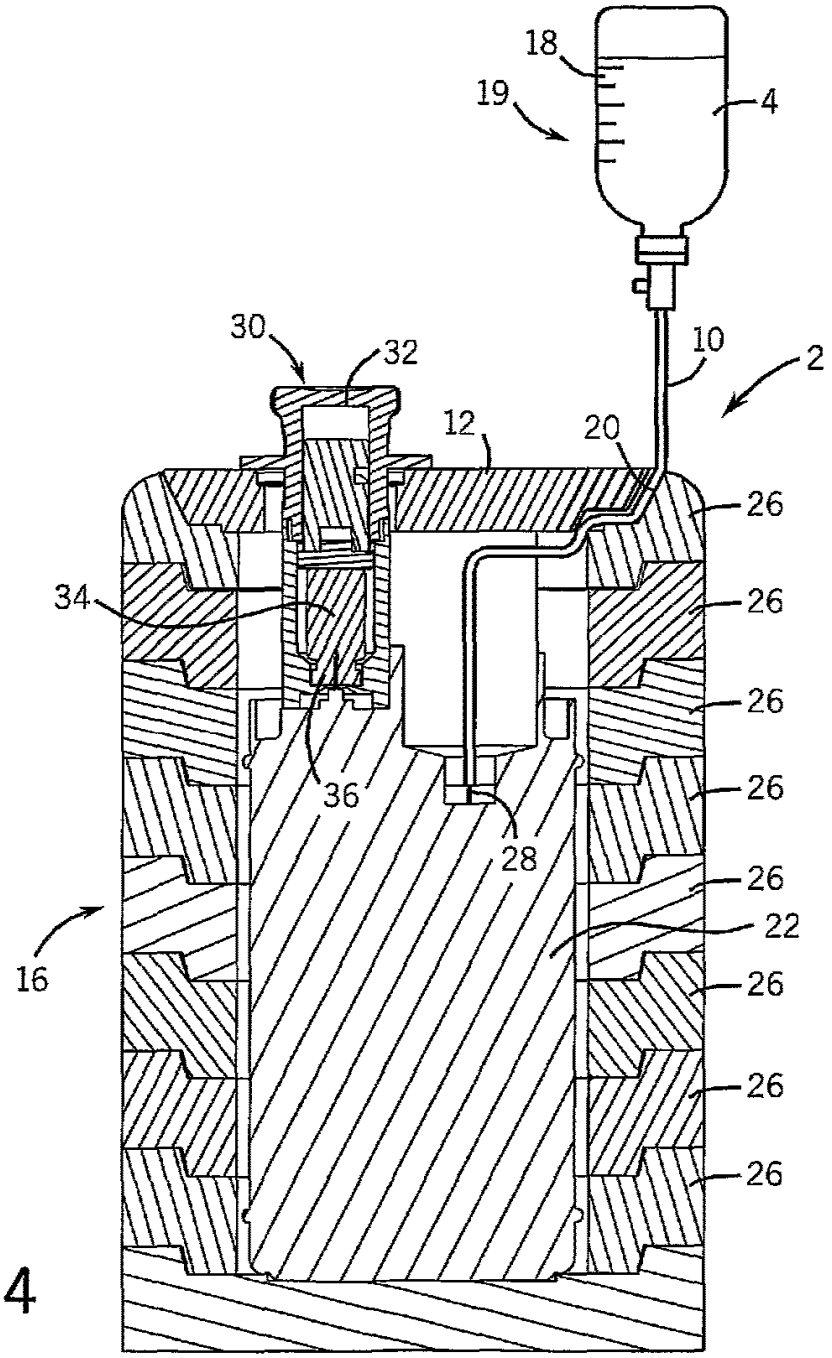
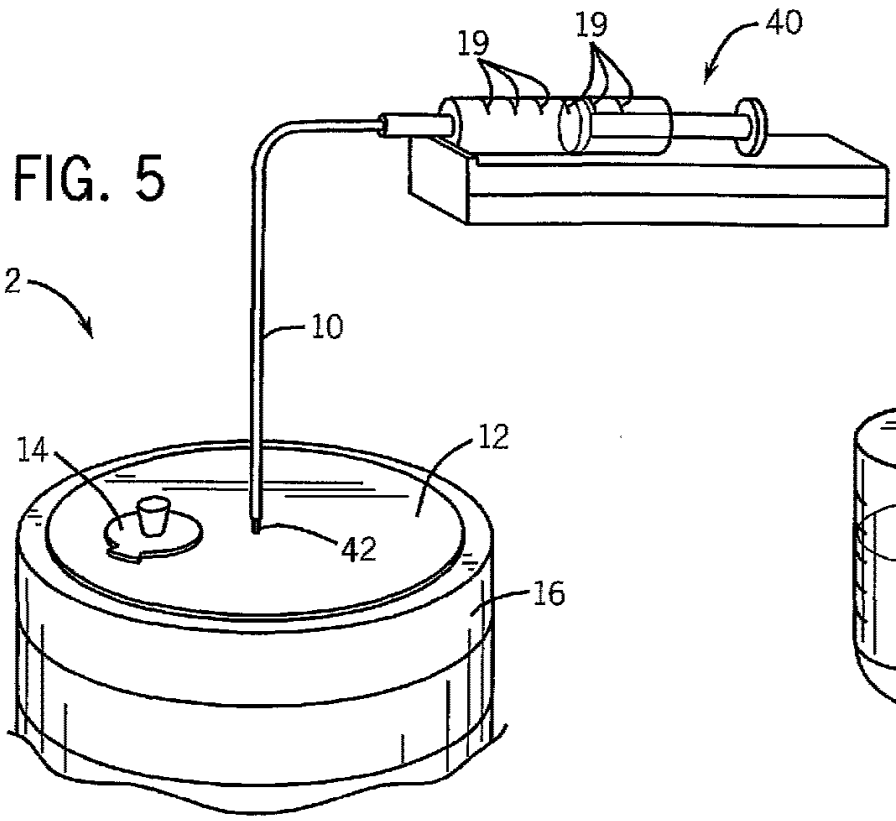


FIG. 4

FIG. 5



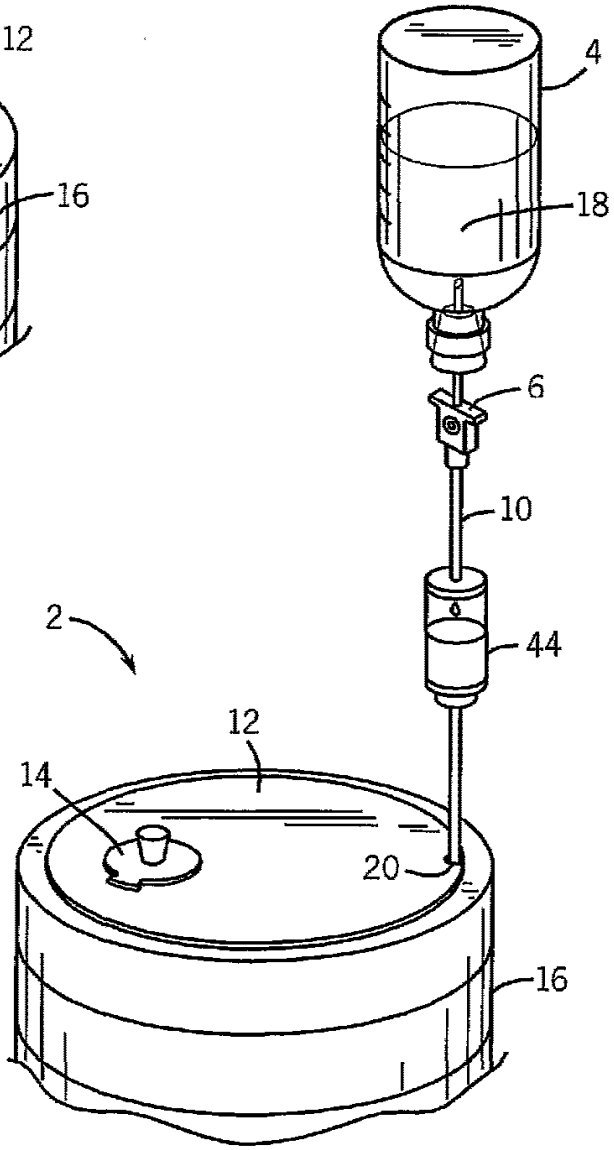


FIG. 6

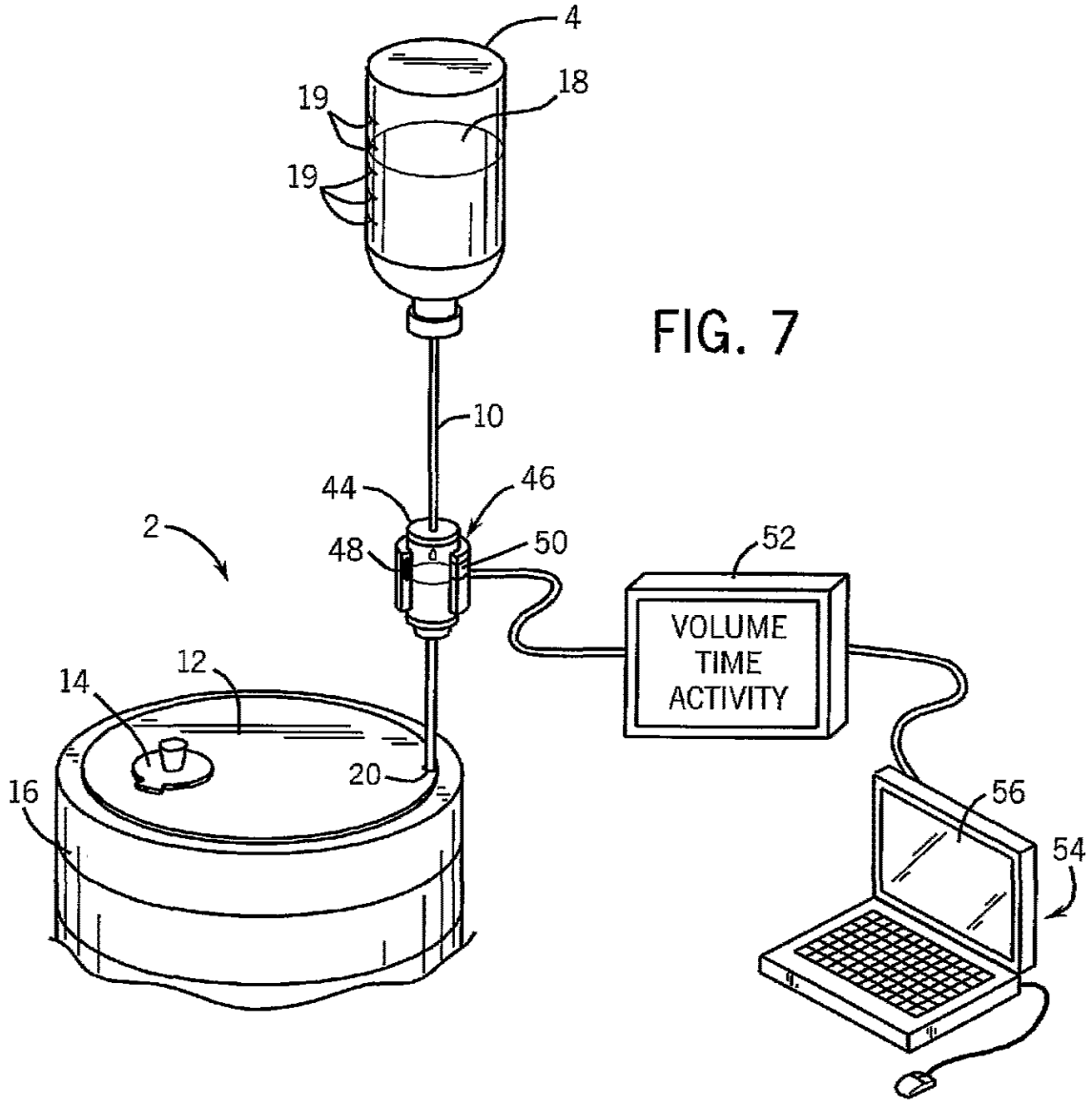

4
19
18
19
10
44
46
2
48
50
52
VOLUME
TIME
ACTIVITY
14
12
16
20
56
54

FIG. 7

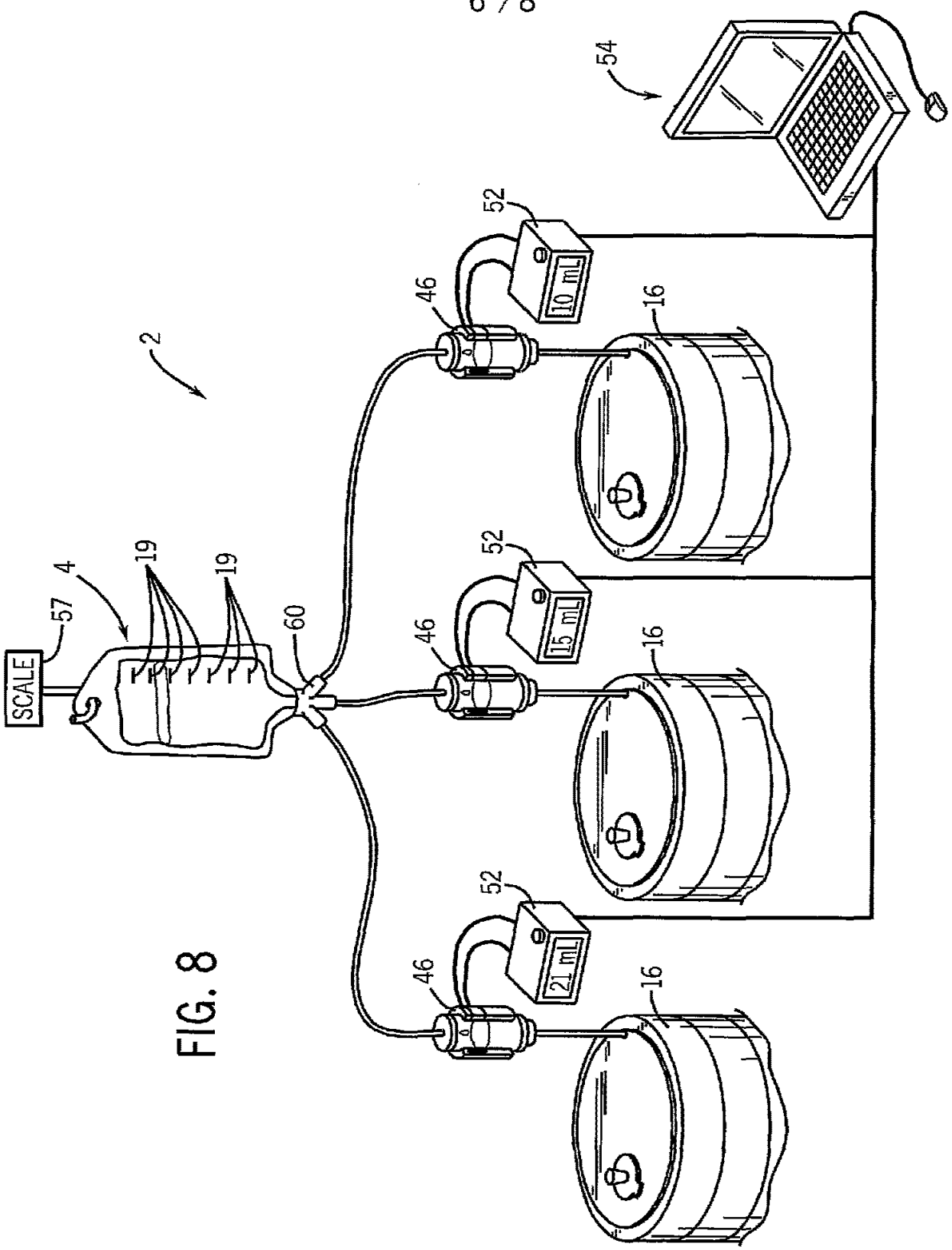


FIG. 8

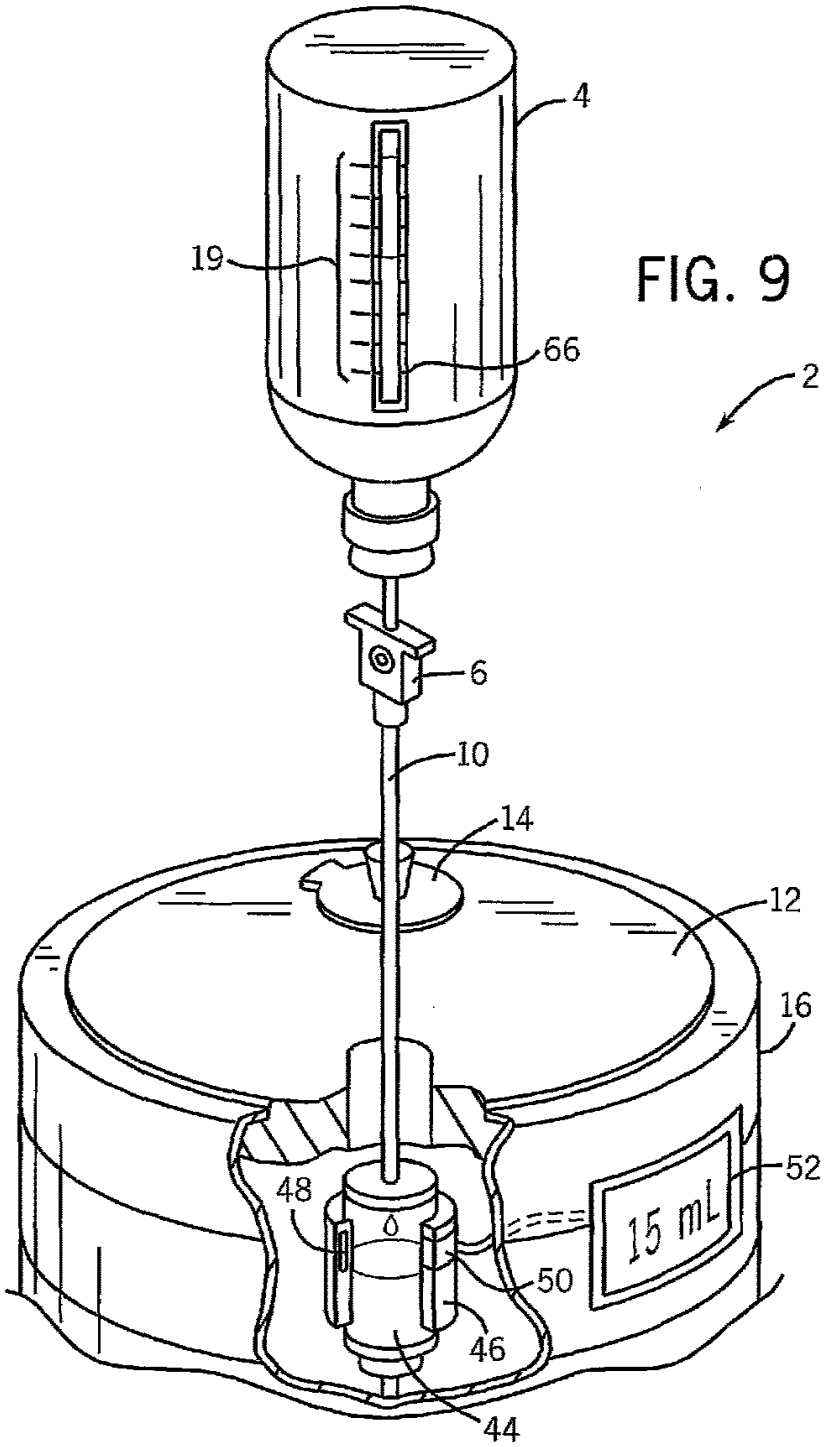


FIG. 9

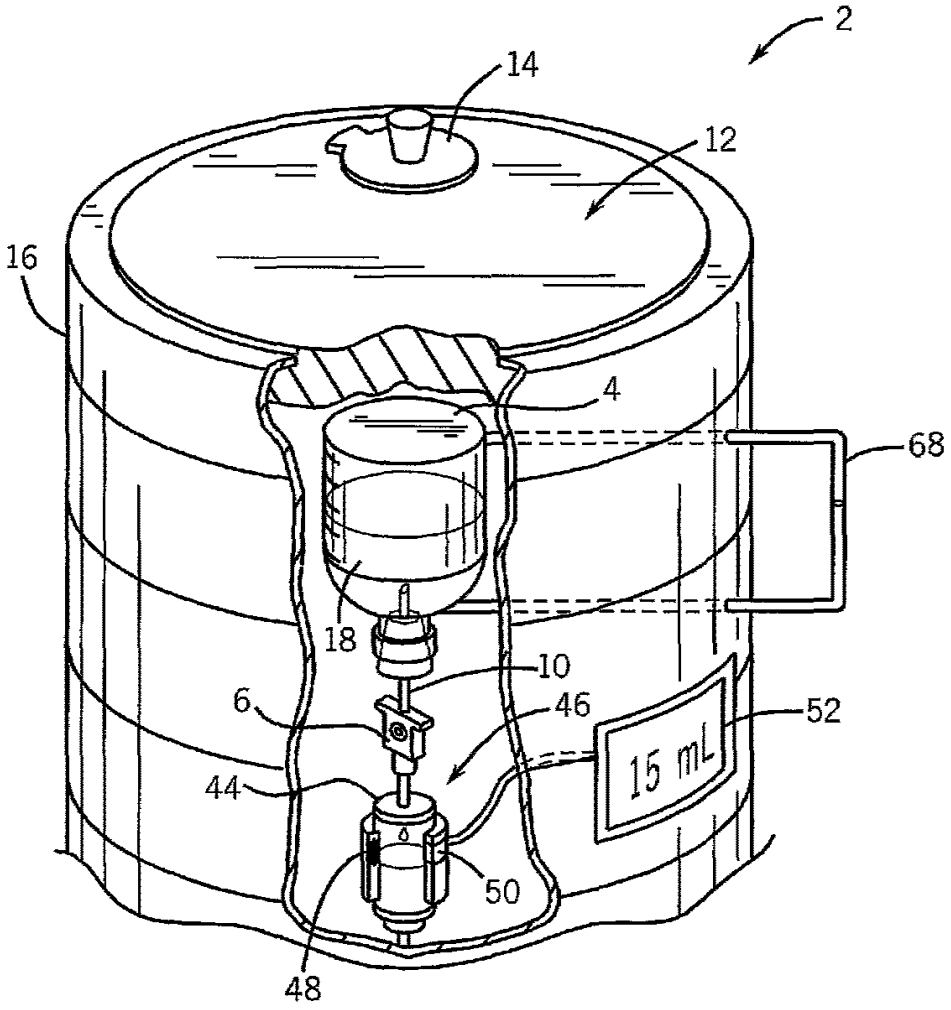


FIG. 10

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/029055

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61N5/00 G21F5/015 G21G4/08

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)
A61N G21F G21G

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 102 121 A (BYK MALLINCKRODT CIL BV [NL]) 7 March 1984 (1984-03-07)	1-3, 7-10, 14-19, 24,25, 32,34, 36,37
Y	page 11, line 13 - line 32; figures 1,4	20,23, 31,35
Y	US 4 321 461 A (WALTER JR DAVID E ET AL) 23 March 1982 (1982-03-23) abstract; claims 1-14; figures 1,3	20,23, 31,35
X	US 3 774 036 A (GERHART J) 20 November 1973 (1973-11-20)	1,12,13, 25,32
Y	abstract; column 4, line 47 - line 49; claims 1,12; figures 1,4	1-3,7, 10,14-19

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[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 document 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
24 November 2006	05/12/2006

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Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/029055

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 03/069632 A2 (SIGMA TAU IND FARMACEUTI [IT]; PAGANELLI GIOVANNI [IT]; CHINOL MARCO [) 21 August 2003 (2003-08-21) page 3, line 13 - line 33; claims 1,7; figures 1-5	1-3,7, 10,14-19
A	EP 0 005 606 A (SHUKLA VISHNU SHANKER) 28 November 1979 (1979-11-28)	

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2006/029055

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. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

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:

see additional sheet

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-20, 23-26, 28, 31-32, 34-37

A splitter in the conduit coupled to at least one other radioisotope generator.

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2. claims: 1-10, 12-26, 28-32, 34-37

A measurement device within the shielded container.

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3. claims: 1-10, 12-20, 23-28, 31-32, 34-37

Calculation of a future elution time based on a metric.

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4. claims: 1-10, 12-20, 23-26, 28, 31-37

Weiging the eluant with a scale.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2006/029055

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
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(54) Title: RADIOISOTOPE GENERATION SYSTEM HAVING PARTIAL ELUTION CAPABILITY

(57) Abstract: In a radioisotope generation system and method for dispensing a radioactive eluate, a radioisotope generator is operable to dispense the eluate. During dispensing, a monitoring system may monitor the dispensed amount of eluate and may generate a signal indicative of the amount of eluate dispensed. In particular embodiments, the monitoring system may generate a signal corresponding to the dispensing of a desired amount of eluate. The monitoring system may particularly monitor the level of fluid in a cavity or container into which the eluate is dispensed, the weight of the eluate dispensed, an elapsed time during which the eluate is dispensed, and/or other characteristic of the dispensed eluate, each of which may be corresponded to the amount of dispensed eluate. The system may be equipped with an interruption system that interrupts the dispensing of the eluate in response to the signal generated by the monitoring system.

RADIOISOTOPE GENERATION SYSTEM HAVING PARTIAL ELUTION CAPABILITY

FIELD OF THE INVENTION

The present invention relates generally to radioisotope generation systems, and more particularly to radioisotope generation systems that facilitate dispensing of a desired amount of eluate from a radioisotope generator.

BACKGROUND

Radioisotope generators are used to obtain a solution comprising a daughter radioisotope (e.g., technetium-99) from a parent radioisotope (e.g., molybdenum-99) which produces the daughter radioisotope by radioactive decay. One common radioisotope generator includes a column containing the parent radioisotope adsorbed on a carrier medium (e.g., alumina). The carrier medium has a relatively higher adsorptive capacity for the parent radioisotope and a relatively lower adsorptive capacity for the daughter radioisotope. As the parent radioisotope decays, a quantity of the desired daughter radioisotope is produced in the column. The column can be washed by passing a suitable eluant (e.g., a sterile saline solution) through the column such that the resulting eluate contains the daughter radioisotope (e.g., in the form of a dissolved salt), which makes the eluate useful in nuclear medicine. For example, the eluate may be adapted for intravenous administration for any of a variety of diagnostic and/or therapeutic procedures.

To obtain a quantity of the eluate from the generator, a container (e.g., a vial) may be connected to an outlet of the column at a tapping point of the generator to receive the eluate containing the daughter radioisotope. The container may be an evacuated container, in which case the partial vacuum in the container is used to draw eluant through the column from an eluant reservoir in fluid communication with an inlet to the column, thereby eluting the daughter radioisotope from the column. Using vacuum pressure in the container to draw eluate out of the generator avoids the need to pressurize the radioactive materials, as would be the result if the fluids were pumped through the column, thereby reducing the risk of accidental release of radioactive materials.

Another advantage of using vacuum pressure in the container to draw eluate out of the generator column is the elimination of the need for moving parts to cause the fluid flow. This may make the system more resistant to mechanical failure and may also render operation of the system relatively simple and clean. Because the eluate may be dispensed directly from the outlet of the generator column to the container, there is no need to clean an intermediate chamber/reservoir of the type used in some prior art systems (e.g., U.S. Patent No. 4,625,118). Unnecessary cleaning is not only undesirable from the standpoint of the cost (in materials and time) of the cleaning itself, but in some circumstances trace residues of cleaning chemicals can also have a negative impact of the yield from the system, as noted in

U.S. Patent No. 5,580,541. Thus, the simplicity of using vacuum pressure in an evacuated container to draw eluate from the generator directly into the container is desirable for a variety of reasons.

The same generator column may be used to fill a number of containers with eluate before the radioisotopes in the column are spent. The amount of eluate needed at any time may vary depending on the number of prescriptions that need to be filled by the radiopharmacy and/or the remaining concentration of radioisotopes in the generator column. One way to vary the amount of eluate drawn from the column is to vary the volume of the containers. For example, different sized containers having volumes ranging from about 5 mL to about 30 mL are common. In particular, standard elution vials having volumes of 5 mL, 10 mL, or 20 mL are currently available in the industry and may be used to facilitate dispensing of the corresponding amount of eluate from the generator column.

Unfortunately, the use of multiple different types of containers has significant disadvantages. For example, a radiopharmacy may use different labels, rubber stoppers, flanged metal caps, lead shields, and/or spacers to handle different sized containers, requiring the radiopharmacy to keep supplies of these items in stock for each type of container. Likewise, packaging for transport of the filled containers to healthcare facilities must also account for the different dimensions of the containers.

Another way to vary the amount of eluate dispensed to a container is to interrupt the elution process before the container is completely filled. For example, U.S. Pat. No. 4,387,303 discloses a system that permits an elution process to be interrupted before the container is completely filled. In particular, the radiopharmacist estimates when to interrupt the dispensing process based on a desire to only partially fill the container to a certain amount. The process is interrupted simply by manually removing the container from the generator tap. By interrupting the elution process at the right time, the container could be partially filled to obtain any desired amount of eluate equal to or less than the capacity of the vial. Another advantage of interrupting the elution process before a container is filled to capacity is that it is easier to draw the eluate from the container when it is not completely filled.

Unfortunately, it is not easy to identify the level of the eluate in a partially filled container. For instance, the container may be housed in a radiation shield that prevents visual inspection of the level of eluate in the container. Educated guesswork and/or trial and error are generally used to interrupt the elution based on an estimate of how much eluate is in the container. However, use of this method can easily lead to overfilling or underfilling of a container, both of which may result in undesirable inefficiencies. Even if it is possible for a person to visually monitor the level of eluate in the container (e.g., through a leaded glass window in the radiation shield), a person would have to dedicate some of his or her attention to monitoring the elution process to stop it at the right time. This would detract from the person's ability to do other things. Further, if the person were distracted, it would be easy to fill the container more than intended.

Thus, some may say there is a need for a radioisotope generation system that facilitates dispensing of a desired amount of eluate from a radioisotope generator.

SUMMARY

One aspect of the invention is directed to a radioisotope generation system for dispensing a radioactive eluate (i.e., an eluate including a radioisotope) into a container for holding such an eluate. A radioisotope generator of the system is operable to dispense the eluate into the container. While the eluate is being dispensed by the generator into the container, a monitoring system monitors the amount of eluate dispensed into the container and generates a signal indicative of the amount of eluate dispensed into the container.

Another aspect of the invention is directed to a radioisotope generation system having a radioisotope generator that is operable to dispense radioactive eluate. An elution shield of the system has an internal cavity for receiving the eluate dispensed from the generator and is constructed at least in part of a radiation-absorbing material. A monitoring system monitors the dispensing of eluate by the generator to the cavity of the shield and is operable to generate a signal in response to the dispensing of a desired amount of eluate into the cavity and/or the elapsing of a predetermined elapsed time during which eluate is dispensed into the cavity.

Still another aspect of the invention is directed to a radioisotope generation system that includes a radioisotope generator for dispensing radioactive eluate. This system also includes a dispensed eluate sensor that may be used to sense an amount of eluate that has been dispensed from the generator, and a signaling device that is communicatively connected with the sensor. Incidentally, "communicatively connected" or the like herein refers to a relationship of first and second components characterized in that at least an electrical signal can be conveyed at least from one of the components to the other.

Yet another aspect of the invention is directed to a method for dispensing a radioactive eluate. In this method, eluate is dispensed from a radioisotope generator into a container while the container and the generator are in fluid communication. Incidentally, "fluid communication" or the like herein refers to a relationship between at least first and second components of a system; this relationship being such that a substance(s) (e.g., a liquid and/or gas) may flow through the system at least from one of the components to the other. In any event, in this method, the dispensing of the eluate into the container is monitored (e.g., using one or more appropriate sensors). Further, a signal (e.g., visible and/or audible) indicative of an amount of eluate dispensed is provided.

Still yet another aspect of the invention is directed to a method of providing a radioactive eluate. In this method, eluate is dispensed from a radioisotope generator into a cavity of an elution shield. An amount of eluate in the cavity is monitored during at least a portion of the eluate being dispensed. A signal (e.g., visible and/or audible) is automatically generated in response to detecting a desired amount of eluate in the cavity and/or a passing of a predetermined elapsed time during which the eluate is dispensed.

In yet another aspect, the present invention is directed to a method of providing a radioactive eluate. In this method, eluate is dispensed from a radioisotope generator into a container while the container and the generator are in fluid communication. An amount of the eluate that is dispensed into

the container is determined, and a signal (e.g., visible and/or audible) is electronically triggered as a result of the amount of eluate that is determined (e.g., a threshold amount).

In still yet another aspect of the invention, an amount of radioactive eluate eluted from a radioisotope generation system in an elution procedure is determined. In addition, an electrical condition of the system is changed based on the amount of eluate that is determined to be eluted. By way of example, a change in electrical condition may refer to a closing and/or opening of an electrical circuit of the system. As another example, a change in electrical condition may refer to an alteration of an electrical signal between first and second components of the system. As still another example, a change in electrical condition may refer to a change in capacitance between first and second electrical conductors of the system.

Various refinements exist of the features noted in relation to the above-mentioned aspects of the present invention. Further features may also be incorporated in the above-mentioned aspects of the present invention as well. These refinements and additional features may exist individually or in any combination. For instance, various features discussed below in relation to any of the illustrated embodiments of the present invention may be incorporated into any of the aspects of the present invention.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a schematic diagram of a radioisotope generation system according to one embodiment of the present invention;

Fig. 2 is an enlarged view of a portion of the system of Fig. 1 illustrating a monitoring system thereof;

Fig. 3 is a schematic diagram of a radioisotope generation system similar to the system of Fig. 1 but further having an automatic interruption system.

Fig. 4 is an enlarged schematic diagram of an alternative embodiment of the monitoring system of Figs. 1 and 3;

Fig. 5 is an enlarged schematic diagram of a monitoring system according to another alternative embodiment;

Fig. 6 is an enlarged schematic diagram of a monitoring system of still another alternative embodiment;

Fig. 7 is a schematic diagram of an alternative embodiment of a radiation generation system of the present invention; and

Fig. 8 is a schematic diagram of one embodiment of a selector useful with the radiation generation system of Figs. 1, 3 and 7.

Corresponding reference characters indicate corresponding parts throughout the drawings.

DETAILED DESCRITPTION OF ILLUSTRATED EMBODIMENTS

Referring now to the drawings, an in particular to Fig. 1, a radioisotope generation system of the present invention is generally designated 101. The system comprises a radioisotope generator having a column 103 containing a carrier, having a parent radioisotope (e.g., Molybdenum - 99) that decays into a daughter radioisotope (e.g., Technetium - 99m), adsorbed thereon. The generator column 103 may be enclosed in a conventional radiation-shield 105 as shown in the embodiment of Fig. 1. The generator column 103 has an inlet 107, which may be connected to an eluant reservoir 111 by a suitable inlet conduit 113. The column 103 also has an outlet 117 that may be connected to a tapping point 119 by a suitable outlet conduit 121.

The eluant reservoir 111 contains eluant (e.g., saline solution or other fluid capable of eluting the daughter radioisotope from the generator column), with the reservoir sized to contain enough eluant for multiple elutions. However, the eluant reservoir may alternatively be sized to contain no more eluant than is sufficient for a single elution without departing from the scope of the invention. The eluant reservoir may be a flexible (e.g., collapsible) bag or a substantially rigid container without departing from the scope of the invention. Where the container is rigid, a pressure relief system (e.g., a filtered vent to atmosphere) may be used so that withdrawal of eluant from the eluant reservoir does not create a vacuum in the eluant reservoir. The eluant reservoir 111 may be suitably mounted on the system 101 above the level of the generator column 103 as shown in Fig. 1.

The tapping point 119 may be constructed to allow a container 125 to be mounted thereon for fluid communication between the container and the generator column 103 via the outlet conduit 121. For example, in one embodiment (illustrated in Fig. 1) a hollow needle 127 capable of piercing a septum on the container 125 may be attached to the end of the outlet conduit 121 to serve as the tapping point. The system 101 may be configured so the tapping point 119 is above the level of the generator column 103 as in the illustrated embodiment. The system 101 may be configured so that the tapping point 119 is also at about the same level as the eluant reservoir 111.

The radioisotope generation system 101 may further comprise an elution shield 131 constructed to have an internal cavity 133 for receiving the eluate from the generator column 103 via the output conduit 121 and tapping point 119. In particular embodiments, the elution shield 131 may be constructed to house the container 125 within the internal cavity 133 thereof with the container connected to the generator at the tapping point as illustrated in Fig. 1. For example, the elution shield 131 shown in the drawings is constructed to have a cavity 133 sized and shaped to hold the container 125 and an opening 139 through which the needle 127 may be inserted to provide fluid communication between the container and the generator column 103 while the container is in the cavity. Other configurations of the radioisotope generation system are also contemplated to be within the scope of the invention, as long as the system is operable to dispense eluate to the cavity of the elution shield, and in particular embodiments to a container disposed in the cavity.

Fluid flow through the system 101 may be suitably controlled by one or more valves. For example, the system 101 may include at least one pinch valve 141, which is operable to selectively block the flow of eluate through the outlet conduit 121 to the container 125 (broadly, the internal cavity 133 of the elution shield 131). The pinch valve 141 may in part define an interruption system of the type described in U.S. Patent No. 4,387,303, which is hereby incorporated by reference to the extent it is consistent, for allowing the flow of eluate to from the generator column 103 to the container 125 to be interrupted before the container is filled to its maximum volume. The term "maximum volume" as used in reference to the container 125 refers to that volume to which an evacuated container would be filled if the elution process were allowed to proceed until the pressure in the container increased enough to stop the inflow of fluids.

The elution shield 131 may comprise one or more radiation-absorbing materials (e.g., lead, tungsten, depleted uranium, etc.) to protect workers from radiation emitted by the eluate after it is received in the container 125. Those skilled in the art will know how to construct an elution shield having a sufficient amount of radiation-absorbing material in view of the type and amount of radiation expected to provide a desired level of protection against radiation exposure. The elution shield 131 may be substantially opaque, as indicated in the drawings, which inhibits manual monitoring of the amount of eluate in the container 125. However, the present invention is not limited to generation systems having opaque elution shields. Accordingly, an elution shield having a viewing window (e.g., leaded glass window) that allows viewing of the contents of the elution shield is contemplated to be within the scope of the invention.

The generation system 101 also comprises a monitoring system 151 capable of automatically monitoring the dispensing of eluate from the generator column 103 to the container 125, e.g., to monitor the amount of eluate dispensed into the container (broadly, into the cavity 133). The monitoring system 151 may generally be any system operable to automatically determine (e.g., sense, measure, meter, calculate, or otherwise gauge) the amount of eluate in the container 125 as eluate is dispensed from the generator column 103 into the container. For example, a radioisotope generation system may include a dispensed eluate sensor capable of determining the amount of eluate eluted from a generator communicatively connected to a signaling device. The dispensed eluate sensor may be a component of the elution shield 131, associated with other components of a radioisotope generation system or even be characterized as a component of the system in and of itself. It is contemplated that the monitoring system 151 may be operable to monitor the dispensing of eluate on a substantially continuous basis or on an intermittent basis.

Referring to Fig. 2, one embodiment of a suitable monitoring system comprises a liquid level sensor 161 capable of detecting the level of the eluate in the container 125. For example, an infrared LED 163 and corresponding infrared detector 165 (e.g., photo diode) may be mounted inside the cavity 133 of the elution shield 131 in spaced relation to one another. The LED 163 (upon operation of the monitoring system) emits light (e.g., infrared light) which reflects off the upper surface 167 of the

liquid back to the detector 165. Data from the detector 165 is transmitted (e.g., by hardwiring or wireless transmission) to a suitable processor 171 having circuitry and/or software enabling it to determine the path length of the reflected light based on the data, and thereby to determine the fluid level of the eluate in the container 125 as a function of the path length of the reflected light. The teachings disclosed in U.S. Patent No. 5,291,031, which is hereby incorporated by reference to the extent it is consistent, may be used to construct a suitable processor capable of measuring the path length of the reflected light. It is contemplated that the container may be configured (e.g., contoured) to alter the path of light from the LED 163 to the upper surface 167 of the liquid and/or from the upper surface of the liquid to the infrared detector 165 to facilitate operation of level sensor 161. For example, the container may focus the light in a manner analogous to a lens. It is also contemplated that one or more lenses that are distinct from the container may be used to focus the light. Further, the use of the level sensor 161 without any lenses and/or with a container that is not configured to modify the path of light in any particular way is within the scope of the invention.

The fluid level in the container 125 corresponds to the amount of eluate in the container. Accordingly, the processor 171 (Fig. 1) is also capable of determining the corresponding amount of eluate in the container 125 based at least in part on the determined fluid level in the container. In particular embodiments, the processor 171 may further compare the determined amount of eluate in the container 125 to a desired amount of eluate to be dispensed into the container.

The monitoring system 151 is further operable to generate a signal once it determines that a desired amount of eluate has been received by (e.g., dispensed into) the container 125 (broadly, the internal cavity 133 of the elution shield 131). In one embodiment, the signal may be perceptible exterior of the elution shield 131, and in particular it may be perceptible to humans (such as radiopharmacists or other operators of the generation system). For example, the signal may be a light (broadly, a visual signal) or noise (broadly, an audible signal) perceptible to workers to alert them that it is time to interrupt the elution process. The monitoring system 151 illustrated in Figs. 1 and 2, for instance, comprises a piezoelectric speaker 175 (broadly, a signaling device) activated by the processor 171 once the processor determines that the desired amount of eluate has been dispensed into the container 125 to make an audible noise perceptible to a worker in the vicinity. The signaling device may be a component of the elution shield 131, as indicated for example by connection of the piezoelectric speaker 175 to the elution shield in Fig. 2. In some embodiments, the processor 117 may function as a signaling device and may be operable to change an electrical condition of the system (e.g., open and/or close a circuit of the system, change a voltage applied to one or more components of the system, etc.) in a manner that is in and of itself imperceptible to unaided humans, although such a change in an electrical condition of the system by the processor may ultimately produce a tangible result (e.g., activation of an interruption system as described below) that may be perceptible to humans, if any are in a position to observe the result.

The generation system 101 may also comprise a selector in communication with the processor 171 and operable to allow a user to pre-select (e.g. prior to operation of the radioisotope generator to dispense eluate into the container) the desired amount of eluate to be dispensed into the container 125. Virtually any device capable of providing user input to the processor 171 can be used as the selector. For example, the selector may comprise a hall effect sensor dial 181 as illustrated in Fig. 8, a set of buttons, a potentiometer, a touch screen display, a computer terminal, or the like. The selector may be operable to allow the user to pre-select the desired amount of eluate from a set of predetermined desired amounts. For example, in the illustrated embodiment of Fig. 8, the hall effect sensor dial has indicia 183 that indicates the desired amount of eluate to be dispensed and a set of magnetic elements 185 and hall effect sensors 187 positioned to determine which of the indicia is aligned with a fixed marking 189 (e.g., a selection arrow). In other embodiments, the selector may instead be operable to allow the user to select any desired amount of eluate within a range of permissible amounts. For example, the selector may allow the user to select a set amount of eluate, or the selector may allow the user to select a certain fill percentage (e.g., 25%, 50%, etc.) of the container.

It is understood that the system 101 may also permit the user to opt to fill the container 125 to its maximum volume, such as by including on the selector a setting for disabling the monitoring system 151 or selecting a desired amount of eluate about equal to the maximum volume of the container. It may be more desirable to stop the dispensing just before the container 125 is filled to its maximum volume (e.g., to facilitate piercing the septum of the container to draw eluate into a syringe) rather than disable the monitoring system 151.

According to one embodiment of a method of the present invention for dispensing a desired amount of eluate to the container 125 (broadly, the cavity 133 of the elution shield 131), a user uses the selector to pre-select a desired amount of eluate to be dispensed from the generator column 103 into the container. An evacuated container 125 may be loaded into the elution shield 131 and connected to the generator column 103 by insertion of the needle 127 through a septum of the container. The pinch valve 141 may be opened (if it was initially closed) such that the vacuum pressure in the container 125 induces the eluant to flow from the eluant reservoir 111, through the inlet conduit 113 and into generator column 103 while eluate comprising the desired daughter radioisotope flows out of the generator column, through the outlet conduit 121, and into the cavity 133, and in the illustrated embodiment into the container. The vacuum pressure in the evacuated container 125 may induce the flow without pressurizing either the eluant or eluate above atmospheric pressure.

The monitoring system 151 monitors the dispensing of eluate into the container 125. For example, for the embodiment illustrated in Figs. 1 and 2, the infrared LED 163 may emit light that is detected by the detector 165 after reflecting off of the upper surface 167 of the eluate in the container 125. The processor 171 determines the amount of eluate in the container 125 based on the fluid level data it receives from the detector 165. When the processor 171 determines that the amount of eluate in the container 125 is in a range from about equal to through greater than the pre-selected desired amount

of eluate, the processor activates the piezoelectric speaker 175 (e.g., by changing a voltage applied to one or more electrodes of the piezoelectric speaker) to produce an audible signal. The processor 117 may activate the piezoelectric speaker when it determines a threshold amount of eluate has been eluted from the generator 103. In one embodiment, the processor 117 activates the piezoelectric speaker just before the amount of eluate in the container reaches the desired amount of eluate to account for the expected delay between activation of the speaker 175 and manual interruption of the elution process.

A person in the vicinity of the radioisotope generation system 101 (e.g., a radiopharmacist or other worker) may perceive the signal (e.g., see in the case of a visual signal and/or hear in the case of an audible signal) from the monitoring system 151 and thereby be alerted to the fact that the desired quantity of eluate has been dispensed into the container 125. The person may then interrupt the flow of eluate into the container 125 (e.g., by manually closing the pinch valve 141 and/or by disconnecting the container 125 from the outlet conduit 121). After the radioisotope generation process is complete, the user may use the selector to change the desired amount of eluate to a different amount and repeat the process to obtain a different amount of eluate in another container.

With reference now to Fig. 3, in another embodiment of a radioisotope generation system 201 of the present invention the system may further comprise an interruption system operable to automatically (as opposed to manually) interrupt the dispensing of eluate into the container 125 in response to an electronic signal generated by the monitoring system 151 once the determined amount of eluate in the container is approximately equal to the desired amount of eluate. For example, the processor 117 may alter an electrical condition of the system (e.g., open and/or close a circuit of the system, change a voltage applied to a component of the system, etc.) to activate the interruption system. It is understood that the electronic signal generated by the monitoring system 151 to activate the interruption system may be instead of, or in addition to, a signal that is perceptible exterior of the elution shield 131 (e.g., an audible or visible signal).

The interruption system may comprise a valve actuator 209 operable to close the pinch valve 141 in response to the signal from the monitoring system 151. Other suitable interruption systems may comprise an actuator (not shown) operable to disconnect the container 125 from the generator column 103 by withdrawing the needle 127 from the container in response to the signal from the monitoring system 151, such as by movement of the container, movement of the needle, or both. Construction and operation of the generation system 201 of Fig. 3 is otherwise substantially the same as the construction and operation of the system 101 of Fig. 1.

It is understood that suitable monitoring systems other than that illustrated in Figs. 1-3 and described previously may be used without departing from the scope of this invention. For example, Fig. 4 illustrates a portion 351 of one alternative embodiment of a suitable monitoring system comprising an ultrasonic liquid level sensor 361 having an ultrasonic transmitter and receiver (e.g., a resonator 363 that transits ultrasound in an active mode and receives ultrasound in a passive mode) mounted in the cavity 133 of the elution shield 131. Operation of the liquid level sensor 361 shown in

Fig. 4 involves emitting ultrasonic energy (e.g., a burst or chirp) from the transmitter 363 and detecting the echo of the ultrasonic energy reflecting off the fluid level surface 167 of the eluate. Data from the ultrasonic detector 363 may be transmitted (by wire or wirelessly) to the processor 171 whereby the processor determines the level of the eluate based on the data relating to the echo. The processor 171 may determine the amount of eluate in the container 125 (broadly, the cavity 133 of the elution shield 131) based at least in part on the determined fluid level of the eluate.

Another embodiment of a suitable monitoring system 451 is illustrated in part in Fig. 5. Such a monitoring system 451 comprises an inductive liquid level sensor 461. The inductive sensor comprises a conductive coil 463 turning about at least a part of the cavity 133 of the elution shield 131, and in the illustrated embodiment about the outer surface of the container 125 within the cavity. The inductance of the coil 463 may vary depending on the fluid level of eluate in the container 125. Operation of the monitoring system 451 of Fig. 5 may include measuring the inductance of the coil 463 and using the processor 171 to determine the level of eluate in the container 125 based on the inductance of the coil. Similarly, a capacitive sensor (not shown) comprising a pair of parallel conductors in opposing relation to one another may be positioned in the cavity so that the capacitance of the conductors varies depending of the level or eluate in the container 125, in which case the monitoring may include measuring the capacitance of the conductors and using the processor 171 to determine the level of eluate as a function thereof. As in previous embodiments, the fluid level of eluate corresponds to the amount of eluate in the container 125 (broadly, the cavity 133).

Fig. 6 illustrates part of yet another embodiment of a suitable monitoring system 551 in which the monitoring system comprises one or more pressure sensors 563 operable to determine the weight of the eluate in the container 125 (broadly, the cavity 133). For example, a pressure sensor 563 may be positioned in the cavity 133 of the elution shield 131 with the weight of the container 125 bearing down against the sensor. Data from the pressure sensor 563 may be sent to the processor 171, which correlates the pressure exerted on the pressure sensor to the weight of eluate in the container 125. The weight of the eluate corresponds to the amount of eluate in the container 125. A system incorporating the monitoring system 551 of Fig. 6 may otherwise operate substantially the same as the systems 101, 201 shown in Figs. 1-3.

Fig. 7 illustrates another embodiment of a radioisotope generation system 601 of the present invention similar to the systems of Figs. 1 and 3. The monitoring system of this embodiment, however, comprises a timer 691 operable to monitor an elapsed time during which eluate is dispensed from the generator column 103 into the container 125 (broadly, the cavity 133 of the elution shield 131). In particular, the elapsed time may be monitored relative to the time at which dispensing of eluate into the container 125 is initiated. The timer 691 can be used to gauge the amount of eluate dispensed into the container 125 based on previously calibrated data regarding the amount of time required for eluate to accumulate in the container under similar operating conditions. In this case, the monitoring system 651 may be operable to generate a signal in response to a predetermined elapsed time corresponding to a

desired amount of eluate to be dispensed into the container 125. The selector may be operable to pre-select the predetermined elapsed time during which eluate is to be dispensed into the container 125.

In one embodiment the timer 691 may comprise a timer initiation system 693 adapted to start the timer automatically upon connection of the container 125 (and/or the elution shield 131) to the outlet conduit 121. For example, one or more sensors 695 (e.g., a hall effect sensor, optical sensor, RFID sensor, proximity sensor, or the like) may generate a signal upon connection of the container 125 to the outlet conduit 121. The timer 691 may be operable to begin monitoring the elapsed time in response to the signal indicating that the container 125 has been connected to the outlet conduit 121. Alternatively, the timer 691 may be started manually by a person when he or she connects the container 125 to the outlet conduit 121 without departing from the scope of the invention.

It is understood that the configuration of the radioisotope generation system can be different from the configurations discussed above and shown in the drawings without departing from the scope of the invention. Although the systems described and shown above involve dispensing of eluate into a container housed within an elution shield, it is understood that the elution system can dispense eluate directly into the cavity of the shield, or that the container may be unshielded, without departing from the scope of the invention.

Although a pinch valve is used to facilitate interruption of the elution in the illustrated embodiments, other types of valves could be used instead without departing from the scope of the invention. Likewise, the invention is operable without any valving as disconnection of the vacuum pressure source (e.g., the partially filled container) may be sufficient to interrupt the elution process in and of itself.

While in each of the illustrated embodiments the monitoring system generates a signal upon determining that the amount of eluate dispensed into the container is approximately equal to a desired amount of eluate, it is contemplated that the monitoring system may instead, or may additionally, generate a continuous or intermittent signal prior to the desired amount of eluate being dispensed into the container, e.g., indicative of the determined amount of eluate in the container (broadly, the cavity). For example, in one embodiment the signal may comprise visual or audible signals that indicate various incremental amounts of eluate dispensed into the container. Examples of such signals include, without limitation, lights, digital displays, alphanumeric displays or other suitable visual indicators of the amount of eluate dispensed into the container. Other examples include audible signals that may or may not increase in intensity as the amount of eluate in the container increases.

When introducing elements of the present invention or the preferred embodiments thereof, the articles "a", "an", "the", and "said" are intended to mean that there are one or more of the elements. The terms "comprising", "including", and "having" are intended to be inclusive and mean that there may be additional elements other than the listed elements. Moreover, the use of "top" and "bottom" and variations of these terms is made for convenience, but does not require any particular orientation of the components.

As various changes could be made in the above products and methods without departing from the scope of the invention, it is intended that all matter contained in the above description and shown in the accompanying drawings shall be interpreted as illustrative and not in a limiting sense.

CLAIMS:

What is claimed is

1. A radioisotope generation system comprising:

a radioisotope generator operable to dispense radioactive eluate into a container; and

a monitoring system operable while the radiation generator system dispenses eluate into the container to monitor the amount of eluate dispensed into the container and to generate a signal indicative of the amount of eluate dispensed into the container.

2. A radioisotope generation system as in claim 1 wherein the monitoring system is operable to generate a signal when a desired amount of eluate has been dispensed into the container.

3. A radioisotope generation system as in claim 2 further comprising a selector for selectively setting the desired amount of eluate to be dispensed into the container.

4. A radioisotope generation system as in claim 2 wherein the generation system is operable to automatically interrupt dispensing of the eluate into the container in response to the signal.

5. A radioisotope generation system as in claim 1 wherein the signal is perceptible exterior of the container.

6. A radioisotope generation system as in claim 5 wherein the signal is at least one of visually and audibly perceptible exterior of the container.

7. A radioisotope generation system as in claim 1 wherein the signal is perceptible by a human.

8. A radioisotope generation system as in claim 1 wherein the monitoring system comprises a level sensor operable to sense a level of eluate in the container, the level corresponding to the amount of eluate in the container.

9. A radioisotope generation system as in claim 8 wherein the level sensor is selected from the group consisting of optical sensors, infrared sensors, ultrasonic sensors, inductive sensors, and capacitive sensors.

10. A radioisotope generation system as in claim 1 wherein the monitoring system comprises a timer operable to monitor an elapsed time during which eluate is dispensed into the container, the elapsed time being relative to a time at which the dispensing of eluate into the container is initiated, the elapsed time corresponding to the amount of eluate in the container.

11. A radioisotope generation system as in claim 10 wherein the monitoring system is operable to generate a signal following dispensing of eluate into the container for a predetermined elapsed time wherein the predetermined elapsed time corresponds to a desired amount of eluate to be dispensed into the container.

12. A radioisotope generation system as in claim 11 wherein the predetermined elapsed time is selectively adjustable at least prior to the dispensing of eluate into the container being initiated.

13. A radioisotope generation system as in claim 10 further comprising a timer initiation system operable to automatically start the timer when dispensing of eluate into the container is initiated.

14. A radioisotope generation system as in claim 13 wherein the timer initiation system comprises a sensor selected from the group consisting of hall effect sensors, optical sensors, and RFID tags.

15. A radioisotope generation system as in claim 1 wherein the monitoring system comprises a sensor operable to determine the weight of eluate in the container, the weight corresponding to the amount of eluate in the container.

16. A method for dispensing radioactive eluate, the method comprising:

dispensing eluate from a radioisotope generator into a container while the container and the generator are in fluid communication;

monitoring the dispensing; and

providing a signal indicative of an amount of the eluate dispensed into the container.

17. A method as in claim 16 wherein the providing comprises providing a signal when the amount of eluate in the container is approximately equal to a desired amount of eluate, the method further comprising interrupting the dispensing of eluate into the container in response to the signal.

18. A method as in claim 17 wherein the interrupting comprises automatically interrupting the dispensing of eluate into the container in response to the signal.

19. A method as in claim 17 wherein the interrupting comprises manually interrupting the dispensing of eluate into the container in response to the signal.

20. A method as in claim 17 further comprising selectively adjusting the desired amount of eluate to be dispensed into the container, the selectively adjusting being conducted prior to the operating of the radioisotope generator.

21. A method as in claim 16 wherein the monitoring comprises monitoring an elapsed time, starting from initiation of the dispensing, during which eluate is dispensed into the container, the elapsed time corresponding to the amount of eluate dispensed into the container.

22. A method as in claim 16 wherein the monitoring comprises sensing a level of eluate in the container, the level corresponding to an amount of eluate dispensed into the container.

23. A method as in claim 16 wherein the monitoring comprises sensing a weight of the eluate in the container, the weight corresponding to an amount of eluate dispensed into the container.

24. A method as in claim 16 further comprising generating an electrical signal based on the monitoring.

25. A method as in claim 24 wherein the providing results from the electrical signal generated.

26. A radioisotope generation system comprising:

a radioisotope generator operable to dispense eluate;

an elution shield having an internal cavity for receiving eluate dispensed from the generator, the elution shield being constructed at least in part of a radiation-absorbing material; and

a monitoring system for monitoring the dispensing of eluate by the generator to the cavity of the shield, the monitoring system being operable to generate a signal in response to at least one of receipt of a desired amount of eluate in the cavity and elapse of a predetermined time period during which eluate is dispensed into the cavity.

27. A radioisotope generation system as in claim 26 further comprising a container disposed in the cavity for receiving the eluate therein, the container being adapted to hold a maximum volume of eluate, the monitoring system being capable of generating the signal in response to receipt of a desired amount of eluate in the container, the desired amount of eluate being less than the maximum volume of the container.

28. A radioisotope generation system as in claim 26 further comprising a container disposed in the cavity for receiving the eluate therein, the container being adapted to hold a maximum volume of eluate, the monitoring system being capable of generating the signal in response to a predetermined

elapsed time during which eluate is dispensed into the container, the predetermined elapsed time corresponding to a desired amount of eluate to be dispensed into the container.

29. A radioisotope generation system as in claim 26 wherein the generation system is operable to automatically interrupt dispensing of the eluate into the cavity in response to the signal.

30. A radioisotope generation system as in claim 26 wherein the signal is perceptible exterior of the elution shield.

31. A radioisotope generation system as in claim 30 wherein the signal is at least one of visually and audibly perceptible exterior of the elution shield.

32. A radioisotope generation system as in claim 26 wherein the signal is perceptible by a human.

33. A radioisotope generation system as in claim 26 wherein the monitoring system comprises a level sensor operable to sense the level of eluate in the cavity, the level corresponding to the amount of eluate in the cavity.

34. A radioisotope generation system as in claim 26 wherein the monitoring system comprises a timer operable to monitor an elapsed time during which eluate is dispensed into the cavity, the elapsed time being relative to a time at which the dispensing of eluate into the cavity is initiated, the elapsed time corresponding to the amount of eluate in the cavity, the monitoring system being operable to generate a signal following dispensing of eluate into the cavity for a predetermined elapsed time wherein the predetermined elapsed time corresponds to the desired amount of eluate in the cavity.

35. A radioisotope generation system as in claim 34 further comprising a timer initiation system operable to automatically start the timer when dispensing of eluate into the cavity is initiated.

36. A radioisotope generation system as in claim 34 wherein the predetermined elapsed time is selectively adjustable at least prior to the dispensing of eluate into the cavity being initiated.

37. A radioisotope generation system as in claim 26 wherein the monitoring system comprises a sensor operable to determine the weight of eluate in the cavity, the weight corresponding to the amount of eluate in the cavity.

38. A method of producing radioactive eluate, the method comprising:

dispensing eluate from a radioisotope generator into a cavity of an elution shield;

monitoring an amount of eluate in the cavity during at least a portion of the dispensing; and

automatically generating a signal in response to detecting at least one of a desired amount of eluate in the cavity and a passing of a predetermined elapsed time during the dispensing.

39. A method as in claim 38 wherein the dispensing comprises dispensing eluate into a container disposed in the cavity of the elution shield, the container being adapted to hold a maximum volume of eluate, wherein the automatically generating occurs in response to receipt of a desired amount of eluate in the container, the desired amount being less than the maximum volume.

40. A method as in claim 38 wherein the dispensing comprises dispensing eluate into a container disposed in the cavity of the elution shield, the container being adapted to hold a maximum volume of eluate, wherein the automatically generating occurs in response to the passing of a predetermined elapsed time during which eluate is dispensed into the container, the predetermined elapsed time corresponding to an amount of eluate in the container less than the maximum volume.

41. A method as in claim 38 further comprising manually interrupting the dispensing in response to the signal.

42. A method as in claim 38 further comprising automatically interrupting the dispensing in response to the signal.

43. A method as in claim 38, wherein the monitoring comprises sensing a level of dispensed eluate in the cavity, the level corresponding to the amount of eluate in the cavity.

44. A method as in claim 38, wherein the monitoring comprises sensing a weight of the eluate in the cavity, the weight corresponding to the amount of eluate in the cavity.

45. A method as in claim 38 further comprising selectively varying at least one of the desired amount of eluate in the cavity and the predetermined elapsed time during which eluate is dispensed into the cavity, wherein the selectively varying occurs prior to the dispensing.

46. A radioisotope generation system comprising:

a radioisotope generator for dispensing radioactive eluate; and

a dispensed eluate sensor capable of determining an amount of eluate eluted from the generator; and

a signaling device communicatively connected with the sensor.

47. A system as in claim 46 wherein the sensor comprises at least one of an optical sensor, an infrared sensor, an ultrasonic sensor, an inductive sensor, and a capacitive sensor.

48. A system as in claim 46 wherein the signaling device is capable of providing at least one of an audio signal and a visual signal.

49. A system as in claim 46 further comprising an elution shield having an internal cavity for receiving eluate dispensed from the generator, wherein the elution shield is constructed at least in part of a radiation-shielding material, and wherein at least one of the dispensed eluate sensor and the signaling device is a component of the elution shield.

50. A system as in claim 49 wherein the dispensed eluate sensor and the signaling device are components of the elution shield.

51. A method of dispensing a radioactive eluate comprising:

determining an amount of radioactive eluate eluted from a radioisotope generator of a radioisotope generation system in an elution procedure; and

changing an electrical condition of the system based on the determining.

52. A method as in claim 51, wherein the changing comprises closing an electrical circuit of the system.

53. A method as in claim 51, wherein the changing comprises opening an electrical circuit of the system.

54. A method as in claim 51, wherein the changing occurs as a result of determining a threshold amount of the eluate.

55. A method as in claim 51, further comprising providing at least one of an audible signal and a visual signal as a result of the changing.

56. A method as in claim 51, wherein the changing comprises altering an electrical signal between first and second components of the system.

57. A method as in claim 51, wherein the changing comprises changing a voltage applied to a component of the system.

FIG. 1

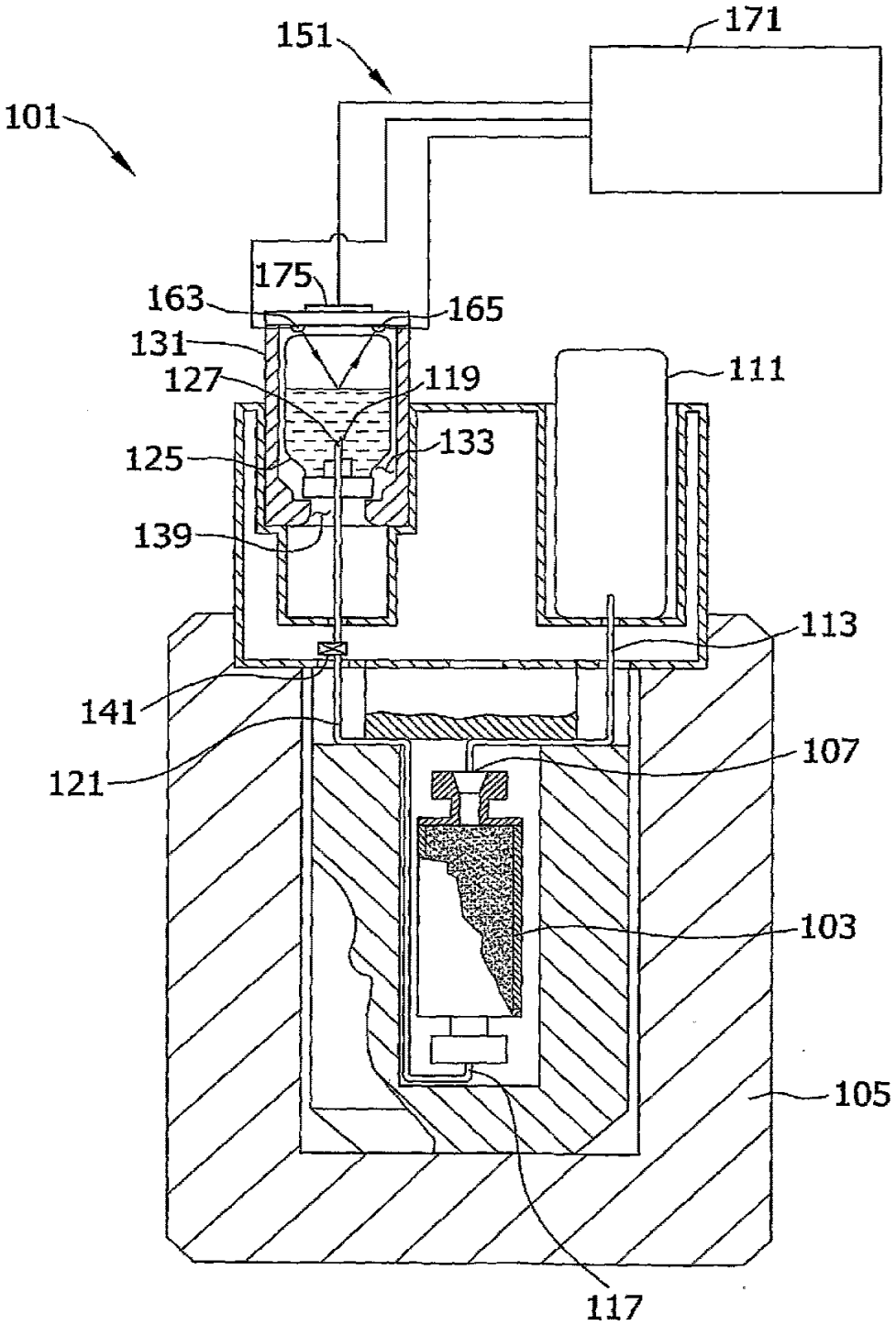
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FIG. 2

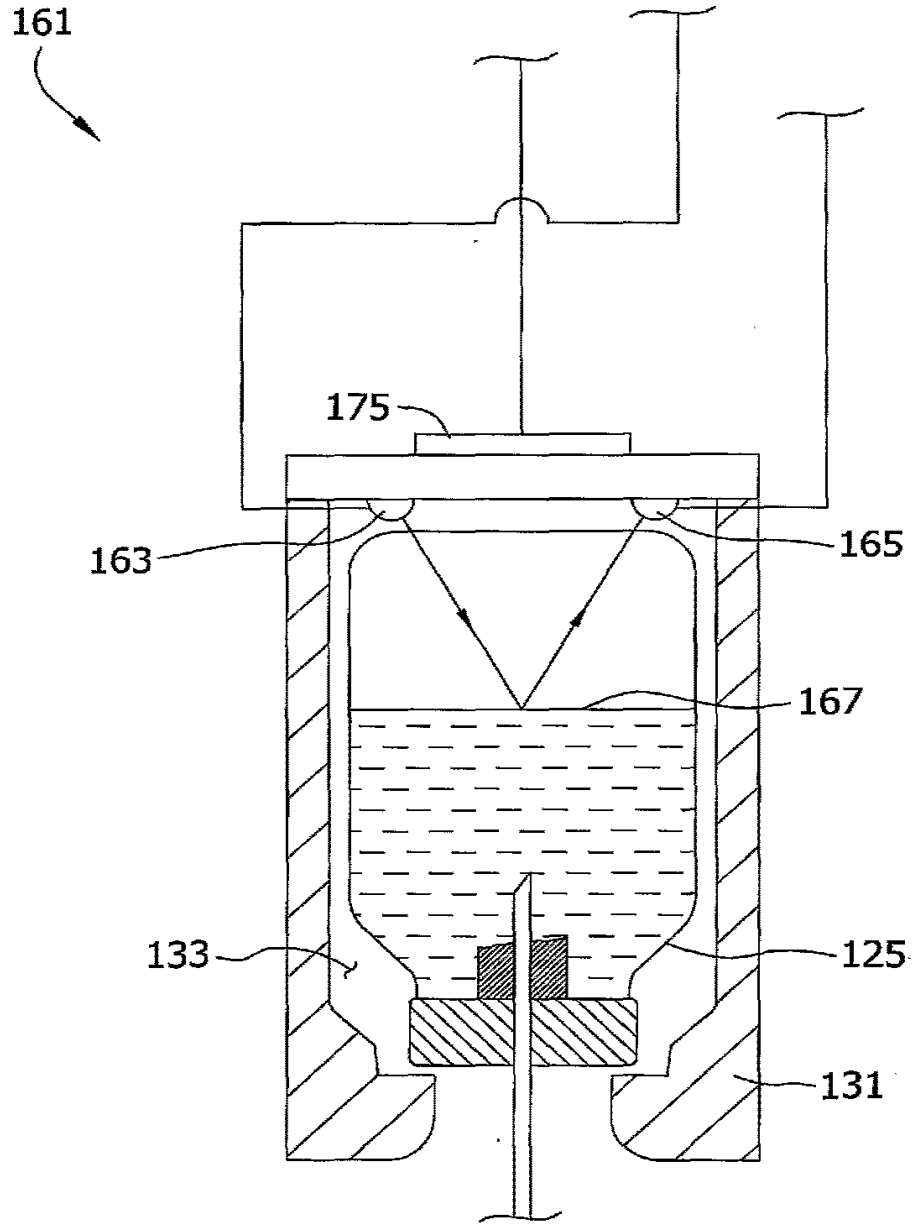

FIG. 3

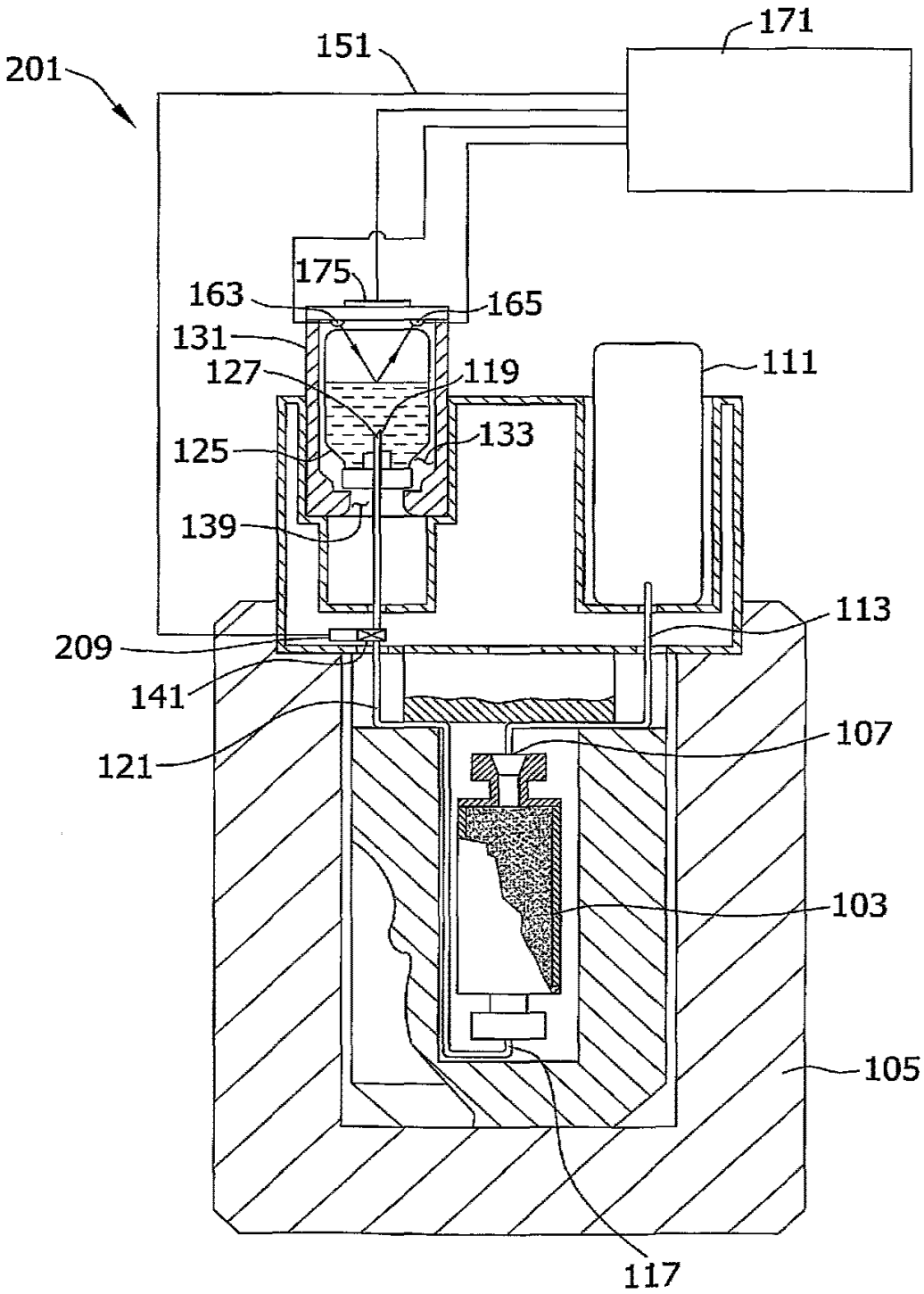
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FIG. 4

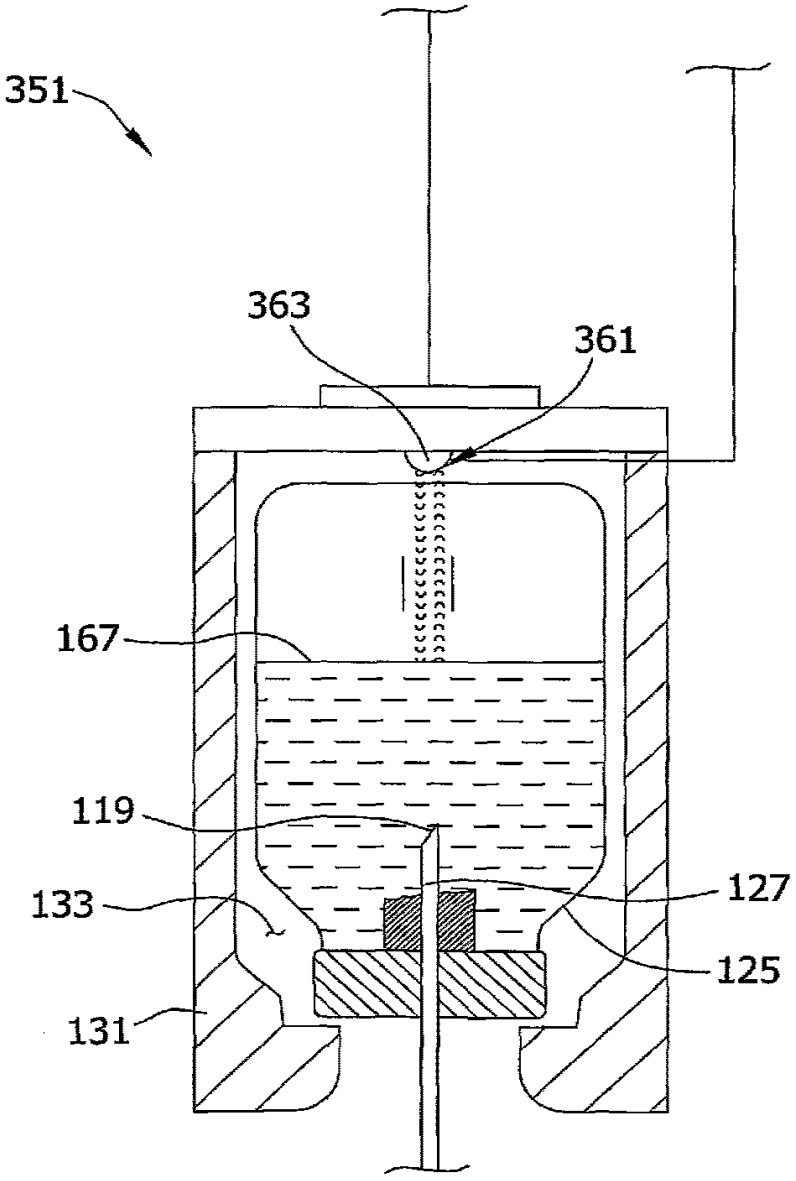

FIG. 5

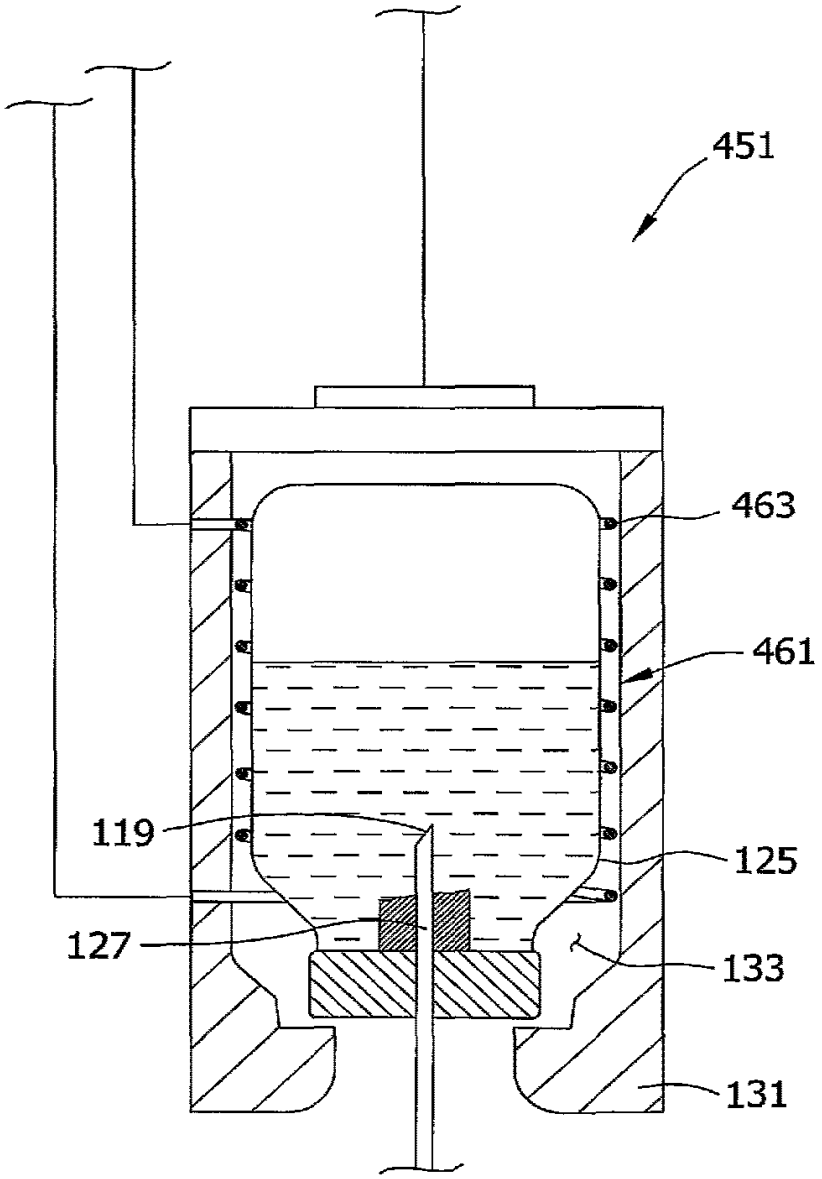

FIG. 6

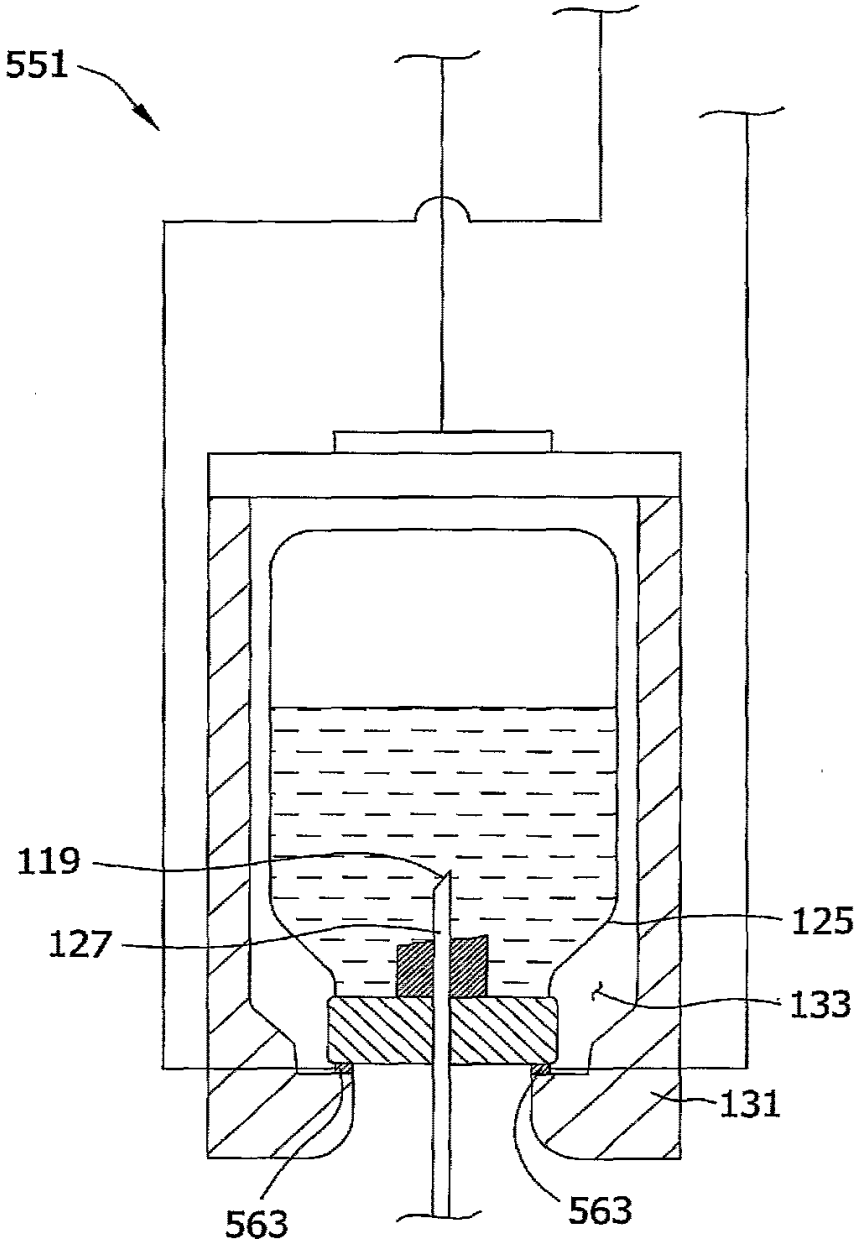

FIG. 7

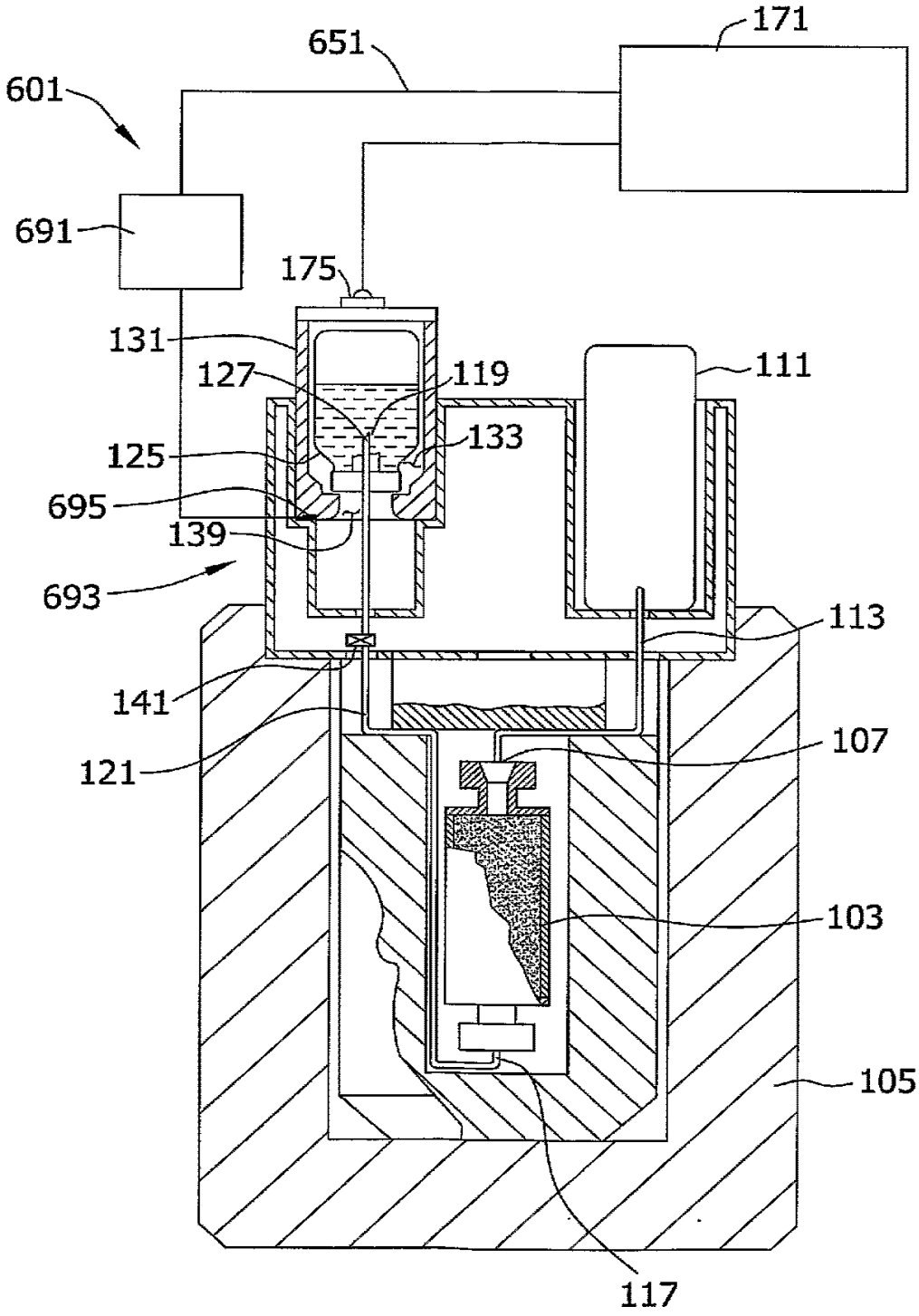
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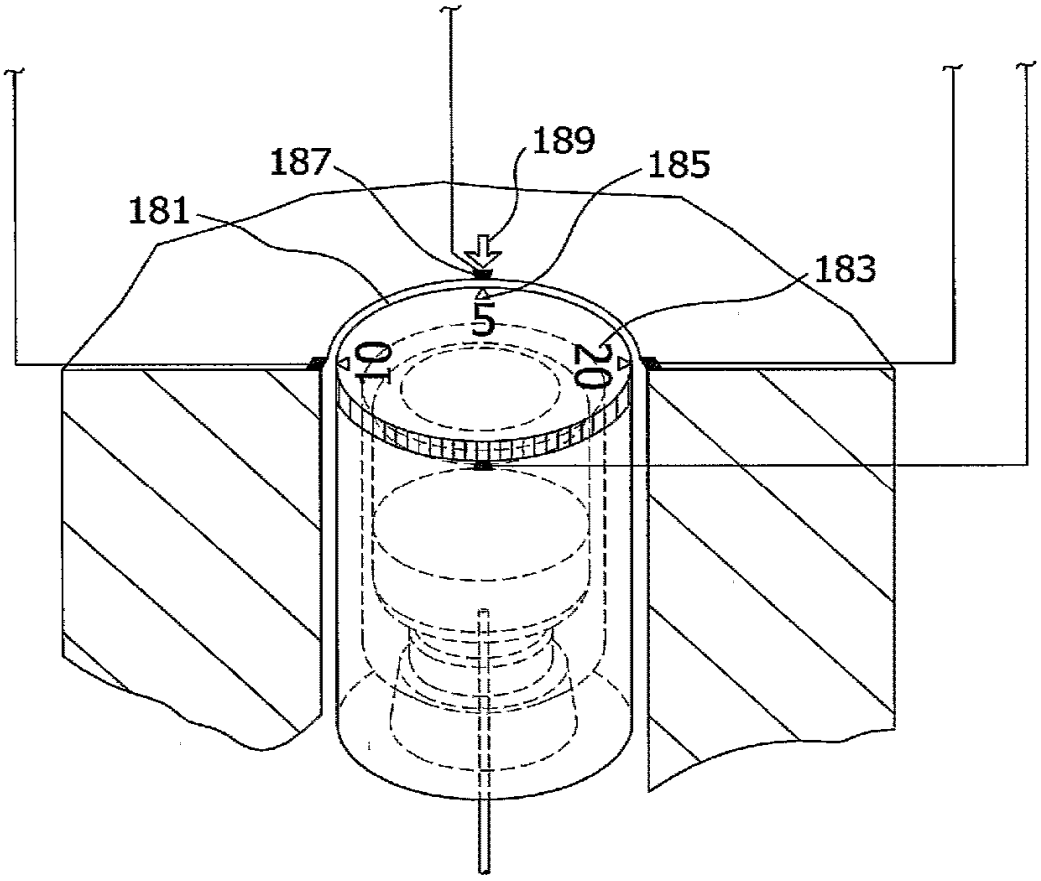
FIG. 8



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(54) Title: SYSTEM AND METHOD FOR ELUTING RADIOISOTOPE TO A CONTAINER DISPOSED OUTSIDE OF A RADIOISOTOPE GENERATOR ASSEMBLY

(57) Abstract: The invention, in one characterization, may be said to be directed to a radiopharmaceutical system that may be utilized in radioisotope elution procedures. In some embodiments, the system may include a radioisotope generator assembly having a radiation shield with a receptacle and a cover disposed over the receptacle. The system may also include a radioisotope generator disposed in the receptacle below the cover. Some embodiments of the system may include an eluate extraction mechanism having an eluate conduit fluidly coupled to a hollow output needle of the radioisotope generator, and a radiation shielded housing disposed outside the radiation shield. The eluate extraction mechanism also may include a hollow needle fluidly coupled to the eluate conduit opposite the radioisotope generator, wherein the hollow needle is disposed inside the radiation shielded housing.

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SYSTEM AND METHOD FOR ELUTING RADIOISOTOPE TO A CONTAINER DISPOSED OUTSIDE OF A RADIOISOTOPE GENERATOR ASSEMBLY

FIELD OF THE INVENTION

[0001] The invention relates generally to the field of nuclear medicine. Specifically, the invention relates to a system and method for eluting a radioisotope from a radioisotope generator to an eluate container disposed outside of an auxiliary shield containing the radioisotope generator.

BACKGROUND

[0002] This section is intended to introduce the reader to various aspects of art that may be related to various aspects of the present invention, which are described and/or claimed below. This discussion is believed to be helpful in providing the reader with background information to facilitate a better understanding of the various aspects of the present invention. Accordingly, it should be understood that these statements are to be read in this light, and not as admissions of prior art.

[0003] Nuclear medicine utilizes radioactive material for diagnostic and therapeutic purposes by injecting a patient with a small dose of the radioactive material, which concentrates in certain organs or biological regions of the patient. Radioactive materials typically used for nuclear medicine include Technetium-99m, Indium-113m, and Strontium-87m among others. Some radioactive materials naturally concentrate toward a particular tissue, for example, iodine concentrates toward the thyroid. However, radioactive materials are often combined with a tagging or organ-seeking agent, which targets the radioactive material for the desired organ or biologic region of the patient. These radioactive materials alone or in combination with a tagging agent may be to as radiopharmaceuticals in the field of nuclear medicine. At relatively lower doses of the radiopharmaceutical, a radiation imaging system (e.g., a gamma camera) provides an image of the organ or biological region that collects the radiopharmaceutical. Irregularities in the image are often indicative of a pathologic condition, such as cancer. Higher doses of the radiopharmaceutical may be used to deliver a therapeutic dose of radiation directly to the pathologic tissue, such as cancer cells.

[0004] A variety of systems are used to generate, enclose, transport, dispense, and administer radiopharmaceuticals. Unfortunately, these systems often use different containers and shielding structures and, thus, the radiopharmaceuticals tend to be repeatedly exchanged from one container to another during the various steps from elution to eventual administration to a patient. In addition, these systems often involve repeated connection and disconnection of components, such as male and female connectors of containers. Unfortunately, the male connectors can be damaged due to misalignment with the corresponding female connectors. For example, hollow needles can be bent, crushed, or

broken due to misalignment with female connectors. As a result, the systems may operate less effectively or become completely useless. If the systems contain radiopharmaceuticals, then the damaged connectors can result in monetary losses, delays with respect to nuclear medicine procedures, and/or undesired exposure of technicians (or other personnel) to radiation.

SUMMARY

[0005] The present invention, in certain embodiments, is directed to removability and replaceability of a hollow needle that pierces an eluate container (e.g., a septum thereof) in a radioisotope elution system. Specifically, in some embodiments, a removable hollow needle may be coupled to a radioisotope generator via an eluate conduit, which in turn may be coupled to an output needle of the radioisotope generator. Instead of directly coupling the eluate container with the output needle of the generator, the removable hollow needle may be used for connections and disconnections with the eluate container. In this manner, the removable hollow needle may reduce the likelihood of damage to the generator output needle, while possibly reducing the cost and downtime associated with any potential damage to the removable hollow needle. In some embodiments, the removable hollow needle may be disposed outside of a radiation shield that is disposed about the radioisotope generator. As such, a user may access and replace the removable hollow needle without opening the radiation shield. Some embodiments of the present invention may enable a user to access and view the eluate container without opening the radiation shield.

[0006] Certain aspects commensurate in scope with the originally claimed invention are set forth below. It should be understood that these aspects are presented merely to provide the reader with a brief summary of certain forms the invention might take and that these aspects are not intended to limit the scope of the invention. Indeed, the invention may encompass a variety of features and aspects that may not be set forth below.

[0007] A first aspect of the invention is directed to a radiopharmaceutical system that includes a radioisotope generator assembly and an eluate extraction mechanism. The radioisotope generator assembly includes a radiation shield having a receptacle, a cover disposed over the receptacle, and a radioisotope generator disposed in the receptacle below the cover. The eluate extraction mechanism includes an eluate conduit fluidly coupled to a hollow output needle of the radioisotope generator, a radiation shielded housing disposed outside the radiation shield, and a hollow needle fluidly coupled to the eluate conduit opposite the radioisotope generator. The hollow needle of the generator is disposed inside the radiation shielded housing of the eluate extraction mechanism. Incidentally, "fluidly coupled" or the like herein refers to a joining of a first component to a second component or to one or more components which may be connected with the second component, or to joining the first component to part of a system that includes the second component so that the molecules of

a substance(s) (such as a liquid or gas) are capable of flowing through the system, including through both the first and second components.

[0008] A second aspect of the invention is directed to an eluate extraction mechanism that includes a radiation shielded housing and an eluate conduit. The eluate conduit has a radioisotope generator end disposed outside the radiation shielded housing and an opposite end disposed inside the radiation shielded housing. The eluate extraction mechanism also includes a hollow injection needle fluidly coupled to the opposite end of the eluate conduit. In addition, the eluate extraction mechanism includes a plunger coupled to the radiation shielded housing movably through a guide structure. The plunger is typically coupled to the hollow injection needle inside the radiation shielded housing.

[0009] Yet a third aspect of the invention is directed to an eluate extraction mechanism that includes a radiation shielded housing and a shielded eluate collection assembly. This shielded eluate collection assembly may be disposed removably inside the radiation shielded housing adjacent a door of the housing. The eluate extraction mechanism includes an eluate conduit having a radioisotope generator end disposed outside the radiation shielded housing and an opposite end disposed inside the radiation shielded housing. In addition, the eluate extraction mechanism includes a hollow needle fluidly coupled to the opposite end of the eluate conduit. The hollow needle may be moved between a connected position and a disconnected position relative to the shielded eluate collection assembly.

[0010] Still a fourth aspect of the invention is directed to a method of using a radiopharmaceutical system. In this method, an eluant is supplied into a radioisotope generator, and a radioisotope is eluted in the radioisotope generator. An eluate (including the radioisotope) is received at an output of the radioisotope generator. This eluate flows from the output through an eluate conduit and a hollow needle that is removably inserted, via movement of a plunger, into an eluate container.

[0011] Various refinements exist of the features noted above in relation to the various aspects of the present invention. Further features may also be incorporated in these various aspects as well. These refinements and additional features may exist individually or in any combination. For instance, various features discussed below in relation to one or more of the specific embodiments may be incorporated into any of the above-described aspects of the present invention alone or in any combination. Again, the brief summary presented above is intended only to familiarize the reader with certain aspects and contexts of the present invention without limitation to the claimed subject matter.

BRIEF DESCRIPTION OF THE FIGURES

[0012] These and other aspects, features, and advantages of the present invention will become better understood when the following detailed description is read with reference to the accompanying figures in which like characters represent like parts throughout the figures, wherein:

[0013] FIG. 1 is a front perspective view of an exemplary embodiment of a radioisotope elution system including an eluate extraction mechanism disposed outside a radioisotope generator assembly, wherein the eluate extraction mechanism is disposed above a cover of an auxiliary shield containing a radioisotope generator, and the eluate extraction mechanism includes a plunger;

[0014] FIG. 2 is a rear perspective view of the radioisotope elution system as illustrated in FIG. 1, further illustrating a door coupled to the eluate extraction mechanism via a hinge;

[0015] FIG. 3 is a cross-sectional side view of the radioisotope elution system as illustrated in FIGS. 1 and 2, further illustrating the eluate extraction mechanism in an open, non-circulating configuration, wherein the door is rotated open and the plunger includes a hollow injection needle uncoupled from an eluate container;

[0016] FIG. 4 is a cross-sectional side view of the radioisotope elution system as illustrated in FIG. 3, further illustrating the eluate extraction mechanism in a closed, circulating configuration, wherein the door is rotated closed and the hollow injection needle is coupled to the eluate container;

[0017] FIG. 5 is a rear perspective view of the radioisotope elution system as illustrated in FIG. 4, further illustrating an open viewing slot in a shielded eluate assembly having the eluate container disposed inside;

[0018] FIG. 6 is a cross-sectional side view of the radioisotope elution system as illustrated in FIG. 5, further illustrating the shielded eluate assembly removed from the eluate extraction mechanism when the hollow injection needle is uncoupled from the eluate container and the door is disposed in an open position;

[0019] FIG. 7 is an exploded cross-sectional side view of the radioisotope elution system as illustrated in FIG. 6, illustrating the hollow injection needle removed from the plunger of the eluate extraction mechanism;

[0020] FIG. 8 is an exploded cross-sectional view of the eluate extraction mechanism as illustrated in FIG. 7, further illustrating details of the hollow injection needle removed from the plunger of the eluate extraction mechanism;

[0021] FIG. 9 is a top perspective view of an exemplary embodiment of the plunger as illustrated in FIG. 8, further illustrating a removable fluid coupling disposed at a bottom side of the plunger;

[0022] FIG. 10 is a bottom perspective view of the plunger as illustrated in FIG. 9;

[0023] FIG. 11 is an exploded perspective view of the plunger as illustrated in FIGS. 9 and 10, further illustrating the removable fluid coupling having a bossed portion or rail exploded laterally from a slot in the bottom side of the plunger;

[0024] FIG. 12 is a side view of an embodiment of the removable fluid coupling as illustrated in FIGS. 9-11;

[0025] FIG. 13 is a bottom view of an embodiment of the plunger as illustrated in FIGS. 9-11, further illustrating the plunger without the removable fluid coupling;

[0026] FIGS. 14 and 15 are rear perspective views of the eluate extraction mechanism as illustrated in FIGS. 1-8, further illustrating an alignment adapter disposed about an eluate conduit of the eluate extraction mechanism;

[0027] FIG. 16 is a flowchart illustrating an exemplary embodiment of a nuclear medicine process using a radiopharmaceutical acquired by the radioisotope elution system as illustrated in FIGS. 1-15;

[0028] FIG. 17 is a block diagram illustrating an exemplary embodiment of a radiopharmacy or system utilizing the radioisotope elution system as illustrated in FIGS. 1-15; and

[0029] FIG. 18 is a block diagram illustrating an exemplary embodiment of a nuclear imaging system utilizing a radiopharmaceutical acquired by the radioisotope elution system as illustrated in FIGS. 1-15.

DETAILED DESCRIPTION OF SPECIFIC EMBODIMENTS

[0030] One or more specific embodiments of the present invention will be described below. In an effort to provide a concise description of these embodiments, all features of an actual implementation may not be described in the specification. It should be appreciated that in the development of any such actual implementation, as in any engineering or design project, numerous implementation-specific decisions must be made to achieve the developers' specific goals, such as compliance with system-related and business-related constraints, which may vary from one implementation to another. Moreover, it should be appreciated that such a development effort might be complex and time consuming, but would nevertheless be a routine undertaking of design, fabrication, and manufacture for those of ordinary skill having the benefit of this disclosure.

[0031] FIGS. 1 and 2 are perspective views of an exemplary embodiment of a radioisotope elution system 10 having an eluate extraction mechanism 12 mounted outside, and specifically on top of, a radioisotope generator assembly 14. The radioisotope generator assembly 14 may include a radiation shielded container or auxiliary shield 16, which may receive and at least substantially enclose a

radioisotope generator 18 and an eluant supply container 20 as discussed below with reference to FIG. 3. The eluate extraction mechanism 12 and the auxiliary shield 16 may include a variety of radiation-shielding materials, such as lead, tungsten, tungsten impregnated plastic and/or another suitable radiation shielding material. The eluate extraction mechanism 12 may be mounted at least partially or entirely outside of the auxiliary shield 16 in a variety of configurations, orientations, and positions, such that an elution process may be performed to output an eluate to a position outside of the auxiliary shield 16. For example, the eluate extraction mechanism 12 may be mounted along a generally horizontal surface on top of a cover 22 that generally closes a receptacle 24 of the auxiliary shield 16. Alternatively, the eluate extraction mechanism 12 may be mounted to the auxiliary shield 16 along a generally vertical surface or a side of the auxiliary shield 16. Alternatively, the eluate extraction mechanism 12 may be mounted separate from the radioisotope generator assembly 14. For example, the eluate extraction mechanism 12 may be disposed next to, above, below, or in a variety of remote locations relative to the radioisotope generator assembly 14, wherein an eluate conduit 52 may couple the eluate extraction mechanism 12 to the radioisotope generator assembly 14 as discussed in further detail below with reference to FIG. 3.

[0032] In the illustrated embodiment of FIGS. 1 and 2, the eluate extraction mechanism 12 may be removably coupled to the cover 22, such that the eluate extraction mechanism 12 can be installed and removed without removing the cover 22 from the receptacle 24. In this manner, the eluate extraction mechanism 12 may improve the containment of radioactivity from the radioisotope generator 18 disposed within the auxiliary shield 16. If the radioisotope generator assembly 14 is not being used for an elution process, then the eluate extraction mechanism 12 may be removed and replaced with a radiation shielded plug that may extend into and/or cover the passage 48 in the cover 22. If an elution process is desired now or in the near future, then the radiation shielded plug may be removed and replaced with the eluate extraction mechanism 12 on or over the cover 22. The eluate extraction mechanism 12 may be removably coupled to the cover 22 by a variety of fasteners and alignment structures. For example, the fasteners may include screws, bolts, or other threaded fasteners. The fasteners also may include latches or tool free connectors, such as snap-fit mechanisms, boss members that mate with keyhole slots, and so forth. The fasteners may also include hinges, adhesives, and compressive or interference fits. Alternatively, the eluate extraction mechanism 12 and the cover 22 may be integrally formed as one structure, which may be mounted on top of the auxiliary shield 16.

[0033] FIG. 3 is a cross-sectional side view of an embodiment of the radioisotope elution system 10 as illustrated in FIGS. 1 and 2, further illustrating the eluate extraction mechanism 12 in an open, non-circulating configuration on top of the radioisotope generator assembly 14. As illustrated, the radioisotope generator assembly 14 may include the auxiliary shield 16 and the radioisotope generator 18 disposed in the receptacle 24 below the cover 22 of the auxiliary shield 16. The radioisotope generator assembly 14 also may include the eluant supply container 20 coupled to one or more hollow

input needles 26 of the radioisotope generator 18. For example, the one or more hollow input needles 26 may pierce a flexible insert 28, such as a rubber material, disposed within a head 30 of the eluant supply container 20. In this manner, the one or more hollow input needles 26 fluidly couple the eluant supply container 20 with an internal radioisotope element, such as molybdenum-99, disposed inside the radioisotope generator 18. The eluant supply container 20 may be disposed entirely or at least substantially inside the auxiliary shield 16 in the receptacle 24 below the cover 22, as illustrated in FIG. 3. Alternatively, the eluant supply container 20 may be disposed at least partially or entirely outside the auxiliary shield 16 in other embodiments of the radioisotope elution system 10. As discussed in further detail below, the eluant supply container 20 may hold a variety of eluants, such as a saline solution, suitable for eluting a radioisotope (e.g., technetium-99m) from the radioisotope generator 18 into the eluate extraction mechanism 12.

[0034] As illustrated in FIG. 3, the eluate extraction mechanism 12 may have a shielded eluate assembly 34 disposed removably inside a radiation shielded housing 36 on top of the cover 22. The illustrated radiation shielded housing 36 may have a variety of shapes and configurations. For example, the radiation shielded housing 36 may have a generally L-shaped or angled structure having a top or elongated housing portion 38 and a bottom housing portion 40.

[0035] The radiation shielded housing 36 also may have a cover alignment member 42 disposed about an opening 44 in a base 46. In certain embodiments, the cover alignment member 42 may improve the alignment of the eluate extraction mechanism 12 with a passage 48 through the cover 22 of the auxiliary shield 16. For example, the base 46 may have a generally flat bottom surface 50, and the cover alignment member 42 may protrude outwardly from the flat surface 50. In view of this protruding characteristic, the cover alignment member 42 may fit or extend at least partially inside or through the passage 48 when the eluate extract mechanism 12 is mounted on the cover 22. In this manner, the cover alignment member 42 may increase the likelihood of proper alignment with the radioisotope generator 18 disposed inside the auxiliary shield 16. For example, the cover alignment member 42 may improve alignment between conduits, hollow needles, and various connections between the eluate extraction mechanism 12 and the radioisotope generator 18.

[0036] Regarding the various fluid connections, the eluate extraction mechanism 12 of FIG. 3, for example, may include an eluate conduit 52 that may pass through the radiation shielded housing 36 and the passage 48 in the cover 22. At one end, the eluate conduit 52 may be coupled with a hollow output needle 54 on the radioisotope generator 18. At an opposite end from the hollow output needle 54, the eluate conduit 52 may be coupled to a plunger 56 movably coupled to the eluate extraction mechanism 12 along a path of travel, e.g., a linear path of vertical motion. For example, the plunger 56 may be moveably disposed in a guide structure or passage 58 within the top or elongated housing portion 38 of the eluate extraction mechanism 12. The plunger 56 also may include a hollow injection needle 60 or

another suitable fluid connector. Thus, the plunger 56 and the hollow injection needle 60 may be jointly moved along a path of travel between a connected position and a disconnection position between the hollow injection needle 60 and an eluate container 74 as discussed in further detail below. The hollow injection needle 60, or other suitable fluid connector, may be removably coupled to the eluate conduit 52 via a releasable fastener 62. For example, the fastener 62 may include a luer connection, a compression fit mechanism, a threaded joint, snap-fit members, latches, or another release mechanism.

[0037] As discussed in detail below, the hollow injection needle 60 may be accessed, removed, serviced, or replaced independent and remote from the hollow output needle 54 on the radioisotope generator 18. Moreover, the coupling of the eluate conduit 52 and the hollow output needle 54 may be maintained during the life or use of a radioisotope generator 18, thereby reducing the likelihood of bending or damaging the hollow output needle 54. Instead, over the course of repeated use of the radioisotope elution system 10, the hollow injection needle 60 may be repeatedly connected and disconnected with the shielded eluate assembly 34. In view of the removability of the hollow injection needle 60, any bending or damage may be easily and cheaply serviced by replacing the needle 60 rather than the entire radioisotope generator 18. Moreover, the hollow injection needle 60 is disposed outside the auxiliary shield 16, such that servicing may be performed without removing the cover 22 and being exposed to radiation from the radioisotope generator 18.

[0038] As further illustrated in FIG. 3, the shielded eluate assembly 34 may be inserted and removed from a region 64 generally below the plunger 56 via a door opening 66 along a side of the top or elongated housing portion 38. The radiation shielded housing 36 also includes a selective access door 68 having a hinge 70 coupled to the elongated housing portion 38 adjacent the door opening 66. Accordingly, radiation shielded housing 36 including the door 68 may provide substantially continuous radioactive shielding about the shielded eluate assembly 34 outside of the auxiliary shield 16, while the door 68 and opening 66 may enable a user to view and selectively access the shielded eluate assembly 34 quickly and easily without opening the auxiliary shield 16. In addition, as discussed below, the shielded eluate assembly 34 may have a variety of features, such as a slot 93 and a door 94, to enable viewing of the extracted eluate. As illustrated in FIG. 3, the door 68 can open and close the door opening 66 for selective access, insertion, and removal of the shielded eluate assembly 34. In other embodiments, the door 68 may be coupled to the radiation shielded housing 36 via a sliding mechanism, a spring-loaded mechanism, a swinging mechanism, or another suitable opening and closing mechanism configured to enable selective access, viewing, insertion, and removal of the shielded eluate assembly 34.

[0039] The shielded eluate assembly 34 as illustrated in FIG. 3 may include an eluate container shield 72 disposed about an eluate container 74, such as an evacuated vial, bottle, or other container in a vacuum condition. The eluate container shield 72 may include a variety of radiation-shielding

materials, such as lead, tungsten, tungsten impregnated plastic and/or another suitable radiation shielding material. The eluate container 74 may include a variety of transparent or translucent materials, such as glass. The eluate container shield 72 may include a cap 76 coupled to a shielded cup structure 78, such that the eluate container 74 may be generally aligned with an opening 80 through the cap 76. The cap 76 may be coupled to the shielded cup structure 78 via threads, an interference fit, a snap-fit mechanism, or another suitable attachment mechanism. The eluate container 74 may be aligned with the opening 80 via a variety of alignment mechanisms, such as an alignment adapter or ring 82 disposed about the eluate container 74 inside the shielded cup structure 78. Alternatively, the opening 80 may have a protruding portion facing downwardly toward a head 84 of the eluate container 74, such that the head 84 may be aligned with the opening 80.

[0040] The eluate extraction mechanism 12 as illustrated in FIG. 3 may also include a variety of alignment mechanisms to improve alignment of the shielded eluate assembly 34 relative to the hollow injection needle 60 coupled to the plunger 56. For example, the eluate extraction mechanism 12 may include one or more alignment members or tabs 86 along the base 46 of the radiation shielded housing 84. The alignment members or tabs 86 may increase the likelihood that the shielded eluate assembly 34 fits snugly between the tab 86 and the door 68 when the door 68 is closed over the door opening 66. In addition to the snug fit, the alignment members or tabs 86 may position a center of the head 84 (and longitudinal axis) of the eluate container 74 with a longitudinal axis of the hollow injection needle 60 and the direction of motion of the plunger 56. In this manner, the hollow injection needle 60 may be connected and disconnected in a generally centered and straight direction into and out of the eluate container 74, thereby reducing the likelihood of bending or damaging the hollow injection needle 60. Again, a variety of fasteners, alignment mechanisms, containers, and configurations of the eluate extraction mechanism 12 may be employed to elute a radioisotope to the shielded eluate assembly 34 generally outside the confines of the radioisotope generator assembly 14.

[0041] FIG. 4 is a cross-sectional side view of and embodiment of the radioisotope elution system 10 as illustrated in FIG. 3, further illustrating the eluate extraction mechanism 12 disposed in a closed, fluidly coupled configuration with the radioisotope generator assembly 14. As illustrated by arrow 88, the door 68 has been rotated about the hinge 70 to close the door opening 66, such that the shielded eluate assembly 34 may be snuggly fit between the alignment tab 86 and the door 68. In this manner, the alignment tab 86 and the door 68 can secure and align the opening 80 in the eluate container shield 72 in a generally centered position with the hollow injection needle 60 of the plunger 56. In addition, the head 84 of the eluate container 74 may be generally aligned or centered with the opening 80 and the hollow injection needle 60 via the alignment adapter or ring 82 disposed about the eluate container 74 inside the shielded cup structure 78. With the eluate container 74 generally aligned or centered with the hollow injection needle 60, the plunger 56 may be depressed downwardly as indicated by arrow 90 to

pierce the hollow injection needle 60 into the eluate container 74 through a flexible insert 92, such as a rubber material, in the head 84 of the eluate container 74.

[0042] In certain embodiments, the eluate container 74 may be in vacuum, such that the pressure differential between the eluant supply container 20 and the eluate container 74 facilitates circulation of the eluant 32 through the radioisotope generator 18 and out through the eluate conduit 52 into the eluate container 74. As the eluant 32, e.g., a saline solution, circulates through the radioisotope generator 18, the circulating eluant 32 generally washes out or elutes a radioisotope, e.g., Technetium-99m. For example, one embodiment of the radioisotope generator 18 includes a radiation shielded outer casing (e.g., lead shell) that encloses a radioactive parent, such as molybdenum-99, adsorbed to the surfaces of beads of alumina or a resin exchange column. Inside the radioisotope generator 18, the parent molybdenum-99 transforms, with a half-life of about 67 hours, into metastable technetium-99m. The daughter radioisotope, e.g., technetium-99m, is generally held less tightly than the parent radioisotope, e.g., molybdenum-99, within the radioisotope generator 18. Accordingly, the daughter radioisotope, e.g., technetium-99m, can be extracted or washed out with a suitable eluant, such as an oxidant-free physiologic saline solution. The eluate output from the radioisotope generator 18 into the eluate container 74 generally includes the eluant 32 and the washed out or eluted radioisotope from within the radioisotope generator 18. Upon receiving the desired amount of eluate within the eluate container 74, the plunger 56 may be withdrawn outwardly from the shielded eluate assembly 34, such that the circulation and output of eluate is terminated. As discussed in further detail below, the extracted daughter radioisotope can then, if desired, be combined with a tagging agent to facilitate diagnosis or treatment of a patient (e.g., in a nuclear medicine facility).

[0043] After or during the elution process, the door 68 may be rotated open to view the level or amount of eluate collected within the eluate container 74. For example, the eluate container shield 72 may include one or more viewing windows or openings to enable a user to view the quantity of eluate within the container 74. FIG. 5 is a rear perspective view of an embodiment of the radioisotope elution system 10 of FIG. 4, further illustrating the eluate extraction mechanism 12 with the plunger 56 depressed and the door 68 opened to enable viewing of the eluate through a viewing window or slot 93 in the shielded cup structure 78 of the shielded eluate assembly 34. The slot 93, if included, also may be removably covered by a door 94 disposed along the outer walls of the shielded cup structure 78. In certain embodiments, the door 94 may include a sliding door, a rotating door, a sleeve disposed about the shielded eluate assembly 34, or another suitable mechanism for opening and closing the viewing window or slot 93.

[0044] FIG. 6 is a cross-sectional side view of an embodiment of the elution system 10 of FIGS. 3 and 4, further illustrating the plunger 56 withdrawn in an upward direction as indicated by arrow 96, the door 68 opened in a counterclockwise direction as indicated by arrow 98, and the shielded eluate

assembly 34 withdrawn from the eluate extraction mechanism 12 in an outward direction as indicated by arrow 100. In certain embodiments, the shielded eluate assembly 34 may be a radiopharmaceutical dosing assembly, such that one or more doses of the radioisotope may be extracted directly into a syringe or other container for delivery to a hospital or other medical facility. In other words, the eluate extraction mechanism 12 may reduce the number of shielded containers involved in the radiopharmaceutical preparation process within a radiopharmacy. For example, the eluate extraction mechanism 12 may eliminate the use of a shielded eluate container configured to fit within the passage 48 in the cover 22 and/or with the top side of the radioisotope generator 18 inside the auxiliary shield 16. Thus, the eluate extraction mechanism 12 enables output of the eluate directly into the shielded eluate assembly 34, which may then be used to prepare one or more radiopharmaceutical doses without first transferring the eluate to another shielded container assembly.

[0045] FIG. 7 is an exploded cross-sectional side view of an embodiment of the radioisotope elution system 10 of FIG. 6, further illustrating the removability and replaceability of various components including the hollow injection needle 60 of the eluate extraction mechanism 12. In addition, FIG. 8 is an exploded cross-sectional side view of an embodiment of the eluate extraction mechanism 12, further illustrating the removability and replaceability of the hollow injection needle 60. As illustrated, if the hollow injection needle 60 becomes damaged, bent, clogged, or inoperable during an elution process, then the hollow injection needle 60 may be removed and replaced with another needle 60 to ensure proper circulation of fluids through the elution system 10 into the shielded eluate assembly 34. The eluate extraction mechanism 12 and the removable hollow injection needle 60 may increase the life and operational efficiency of the radioisotope generator assembly 14, for example, by substantially reducing the likelihood of an inoperable generator assembly 14 that may be caused by damage to the hollow output needle 54 coupled to the radioisotope generator 18, among other reasons.

[0046] In other words, after making the initial connection between the hollow output needle 54 of the radioisotope generator 18 and the eluate conduit 52 of the eluate extraction mechanism 12, the connections and disconnections with the eluate container 74 may be made with the plunger 56 and the hollow injection needle 60 rather than the hollow output needle 54. For example, each time an amount of eluate is desired from the radioisotope generator 18, the hollow injection needle 60 may be inserted into the eluate container 74 and then removed after the amount of eluate is collected in the container 74. However, the eluate conduit 52 may remain continuously coupled to the hollow output needle 54 of the radioisotope generator 18 during each elution process. Therefore, any likelihood of potential damage to the eluate output connectors (e.g., hollow needles) may be moved away from the radioisotope generator 18 to the eluate extraction mechanism 12. Any potential damage to hollow injection needle 60 can be easily and cheaply addressed by replacing the hollow injection needle 60, whereas the relatively lower potential for damage to the hollow output needle 54 may be addressed by replacing the entire radioisotope generator 18. For these reasons, the removability and replaceability of the hollow

injection needle 60 may reduce downtime, costs, and difficulty in repairing the system 10 in the event of damage to the eluate output connectors.

[0047] FIGS. 9-13 are various views of an embodiment of the plunger 56, further illustrating connection mechanisms for the eluate conduit 52 and the hollow injection needle 60. FIGS. 9 and 10 are top and bottom perspective views of the plunger 56 illustrating a removable fluid coupling 57 that may be removably coupled to a bottom side 59 of the plunger 56. As illustrated in FIGS. 9 and 10, the removable fluid coupling 57 may include an eluate conduit connector 61 extending laterally from the coupling 57, such that the eluate conduit 52 can fit securely and removably about the connector 61. The illustrated eluate conduit connector 61 also may include a variety of raised and lowered portions, such as a series of rings 63, to resist separation between the eluate conduit 52 (e.g., a flexible tube) and the connector 61. In the illustrated embodiment, the connector 61 is oriented at about 90 degrees relative to the hollow injection needle 60. However, the connector 61 may be oriented at a variety of angles in other embodiments of the plunger 56. The hollow injection needle 60 may be generally aligned with a centerline 65 of the plunger 56, such that the needle 60 can be inserted and removed in a straight direction relative to the centerline of the eluate container 74. In certain embodiments, the hollow injection needle 60 may be removably coupled to the removable fluid coupling 57. Alternatively, the hollow injection needle 60 may be an integral portion of the removable fluid coupling 57. In either embodiment, the hollow injection needle 60 may be quickly removed and inexpensively replaced if the needle 60 becomes damaged during use.

[0048] For example, turning to FIG. 11, the plunger 56 may include a slot 67 (e.g., a T-shaped slot) to receive a bossed portion or rail 69 (e.g., a T-shaped head) of the removable fluid coupling 57. As illustrated in FIG. 11, the slot 67 may include a narrow outer opening 71 leading into an enlarged inner channel 73. Similarly, the bossed portion 69 may include a narrow inner portion 75 leading to an enlarged outer portion 77. FIG. 12 is a side view of the removable fluid coupling 57, further illustrating the geometry of the portions 75 and 77. As indicated by arrow 79 in FIG. 11, the fluid coupling 57 may removably couple with the plunger 56 by laterally or horizontally moving the bossed portion or rail 69 into the slot 67. In this manner, the fluid coupling 57 may be vertically interlocked with the plunger 56. In addition, the top of the bossed portion or rail 69 may include a detent 81 to interlock removably with a protrusion 83 inside the slot 67, as illustrated in FIGS. 11 and 13. In certain embodiments, the detent 81 illustrated in FIG. 11 may be a concave recess, and the protrusion 83 illustrated in FIG. 13 may be a convex protrusion or ball-shaped portion. FIG. 13 is a bottom view of the plunger 56 illustrating an embodiment of the protrusion 83 positioned toward the interior or center of the plunger 56. At this interior position, the protrusion 83 may engage the detent 81 as the bossed portion or rail 69 of the removable fluid coupling 57 slides into the slot 67 of the plunger 56. In certain embodiments, the protrusion 83 and the detent 81 may snap-fit together, thereby removably securing the bossed portion or rail 69 in a lateral or horizontal direction relative to the slot 67. In this manner, a user may quickly

install, remove, and replace the removable fluid coupling 67 relative to the slot 67 and rail 69 via the vertical interlocking between the slot 67 and rail 69 and the horizontal interlocking between the detent 81 and protrusion 83. In other embodiments, the removable fluid coupling 67 may be coupled to the plunger 56 via threads, latches, pin and grooves, and so forth.

[0049] Referring again to FIG. 11, the plunger 56 may include one or more guiding rails 85, which may extend vertically lengthwise along the exterior of the plunger 56. These guiding rails 85 may have a generally rectangular geometry or another suitable geometry, which slides lengthwise along a mating portion of the guide structure or passage 58 within the radiation shielded housing 36. In this manner, the guiding rails 85 may ensure proper alignment of the hollow injection needle 60 relative to the eluate container 74 and, also, ensure proper positioning of the eluate conduit connector 61 relative to the eluate conduit 52. However, other embodiments of the plunger 56 may employ a variety of alternative alignment mechanisms.

[0050] FIGS. 14 and 15 are perspective views of an embodiment of the eluate extraction mechanism 12, further illustrating alignment features that may facilitate alignment with the radioisotope generator assembly 14. As illustrated, the radiation shielding housing 84 has a generally L-shaped or 90 degree elbow-shaped geometry. However, any other suitable shapes, structures, or geometries are within the scope of the disclosed system. Moreover, the cover alignment member 42 may have a variety of shapes and configurations to facilitate alignment of the eluate extraction mechanism 12 and the eluate conduit 52 with the radioisotope generator assembly 14. For example, the cover alignment member 42 may have an elongated portion 102, such as an alignment adapter, that may be configured to fit and align with the passage 48 in the cover 22 and a top portion of the radioisotope generator 18. The elongated portion 102 may be an integral part of the eluate extraction mechanism 12 or the elongated portion 102 may be a removable structure having a suitable fastener, such as threads, latches, or snap-fit members, among other fasteners. In addition, the conduit 52 may be at least partially rigid (or rigidly supported) to facilitate the connection and alignment with the hollow output needle 54 of the radioisotope generator 18. For example, the eluate conduit 52 may be supported along most of its length by the alignment portion 102, such that the eluate conduit 52 may be generally centered with the hollow output needle 54 of the radioisotope generator 18 during insertion and removal of the eluate extraction mechanism 12 relative to the cover 22. However, a variety of mounting mechanisms and alignment devices may be utilized with the eluate extraction mechanism 12.

[0051] FIG. 16 is a flowchart illustrating an exemplary nuclear medicine process utilizing the radioactive isotope produced by the elution system 10 illustrated with reference to FIGS. 1-15. As illustrated, the process 104 begins by providing a radioactive isotope for nuclear medicine at block 106. For example, block 106 may include eluting technetium-99m from the radioisotope generator 18 illustrated and described in detail above. At block 108, the process 104 proceeds by providing a

tagging agent (e.g., an epitope or other appropriate biological directing moiety) adapted to target the radioisotope for a specific portion, e.g., an organ, of a patient. At block 110, the process 104 then proceeds by combining the radioactive isotope with the tagging agent to provide a radiopharmaceutical for nuclear medicine. In certain embodiments, the radioactive isotope may have natural tendencies to concentrate toward a particular organ or tissue and, thus, the radioactive isotope may be characterized as a radiopharmaceutical without adding any supplemental tagging agent. At block 112, the process 104 then may proceed by extracting one or more doses of the radiopharmaceutical into a syringe or another container, such as a container suitable for administering the radiopharmaceutical to a patient in a nuclear medicine facility or hospital. At block 114, the process 104 proceeds by injecting or generally administering a dose of the radiopharmaceutical into a patient. After a pre-selected time, the process 104 proceeds by detecting/imaging the radiopharmaceutical tagged to the patient's organ or tissue (block 116). For example, block 116 may include using a gamma camera or other radiographic imaging device to detect the radiopharmaceutical disposed on or in or bound to tissue of a brain, a heart, a liver, a tumor, a cancerous tissue, or various other organs or diseased tissue.

[0052] FIG. 17 is a block diagram of an exemplary system 118 for providing a syringe having a radiopharmaceutical disposed therein for use in a nuclear medicine application. As illustrated, the system 118 includes the radioisotope elution system 10 previously described with regard to FIGS. 1-15. The system 118 also includes a radiopharmaceutical production system 120, which functions to combine a radioisotope 122 (e.g., technetium-99m solution acquired through use of the radioisotope elution system 10) with a tagging agent 124. In some embodiment, this radiopharmaceutical production system 120 may refer to or include what are known in the art as "kits" (e.g., Technescan® kit for preparation of a diagnostic radiopharmaceutical). Again, the tagging agent may include a variety of substances that are attracted to or targeted for a particular portion (e.g., organ, tissue, tumor, cancer, etc.) of the patient. As a result, the radiopharmaceutical production system 120 produces or may be utilized to produce a radiopharmaceutical including the radioisotope 122 and the tagging agent 124, as indicated by block 126. The illustrated system 118 may also include a radiopharmaceutical dispensing system 128, which facilitates extraction of the radiopharmaceutical into a vial or syringe 130. In certain embodiments, the various components and functions of the system 118 are disposed within a radiopharmacy, which prepares the syringe 130 of the radiopharmaceutical for use in a nuclear medicine application. For example, the syringe 130 may be prepared and delivered to a medical facility for use in diagnosis or treatment of a patient.

[0053] FIG. 18 is a block diagram of an exemplary nuclear medicine imaging system 132 utilizing the syringe 130 of radiopharmaceutical provided using the system 118 of FIG. 12. As illustrated, the nuclear medicine imagining system 132 includes a radiation detector 134 having a scintillator 136 and a photo detector 138. In response to radiation 140 emitted from a tagged organ within a patient 142, the scintillator 136 emits light that is sensed and converted to electronic signals by the photo detector 138.

Although not illustrated, the imaging system 132 also can include a collimator to collimate the radiation 140 directed toward the radiation detector 134. The illustrated imaging system 132 also includes detector acquisition circuitry 144 and image processing circuitry 146. The detector acquisition circuitry 144 generally controls the acquisition of electronic signals from the radiation detector 134. The image processing circuitry 146 may be employed to process the electronic signals, execute examination protocols, and so forth. The illustrated imaging system 132 also includes a user interface 148 to facilitate user interaction with the image processing circuitry 146 and other components of the imaging system 132. As a result, the imaging system 132 produces an image 150 of the tagged organ within the patient 142. Again, the foregoing procedures and resulting image 150 directly benefit from the radiopharmaceutical produced by the elution system 10 as illustrated and described with reference to FIGS. 1-15.

[0054] When introducing elements of the present invention or various embodiments thereof, the articles "a", "an", "the", and "said" are intended to mean that there are one or more of the elements. The terms "comprising", "including", and "having" are intended to be inclusive and mean that there may be additional elements other than the listed elements. Moreover, the use of "top", "bottom", "above", "below" and variations of these terms is made for convenience, but does not require any particular orientation of the components.

[0055] While the invention may be susceptible to various modifications and alternative forms, specific embodiments have been shown by way of example in the figures and have been described in detail herein. However, it should be understood that the invention is not intended to be limited to the particular forms disclosed. Rather, the invention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention as defined by the following appended claims.

CLAIMS:

1. A radiopharmaceutical system, comprising:

a radioisotope generator assembly, comprising:

a radiation shield having a receptacle and a cover disposed over the receptacle; and

a radioisotope generator disposed in the receptacle below the cover; and

an eluate extraction mechanism, comprising:

an eluate conduit fluidly coupled to a hollow output needle of the radioisotope generator;

a radiation shielded housing disposed outside the radiation shield; and

a hollow needle fluidly coupled to the eluate conduit opposite the radioisotope generator wherein the hollow needle is disposed inside the radiation shielded housing.

2. The radiopharmaceutical system of claim 1, wherein the eluate conduit is disposed at least mostly within the radiation shield and the radiation shielded housing.

3. The radiopharmaceutical system of claim 1, wherein the hollow needle is mounted along a path of movement within the radiation shielded housing.

4. The radiopharmaceutical system of claim 1, further comprising an eluate container, wherein the eluate container is disposed removably inside the radiation shielded housing adjacent a door.

5. The radiopharmaceutical system of claim 4, wherein the radiation shielded housing comprises an alignment member disposed adjacent the eluate container opposite the door.

6. The radiopharmaceutical system of claim 1, further comprising an eluate container, wherein the eluate container is disposed inside an eluate container shield comprising a radiation shielding material, wherein the eluate container shield comprises an eluate container viewing window.

7. The radiopharmaceutical system of claim 1, further comprising an eluate container, wherein the eluate container is disposed inside an eluate container shield comprising a radiation shielding material, wherein an alignment adapter is disposed between the eluate container and the eluate container shield.

8. The radiopharmaceutical system of claim 1, wherein the radiation shielded housing is mounted on top of the cover.

9. The radiopharmaceutical system of claim 8, wherein the radiation shielded housing comprises an alignment portion disposed at least partially into a passage in the cover.

10. The radiopharmaceutical system of claim 9, wherein the eluate conduit extends through the alignment portion and the passage.

11. The radiopharmaceutical system of claim 1, wherein the hollow needle is coupled to a plunger via a releasable fastener.

12. The radiopharmaceutical system of claim 11, wherein the releasable fastener comprises a luer connector.

13. The radiopharmaceutical system of claim 1, comprising an eluant supply container fluidly coupled to the radioisotope generator.

14. The radiopharmaceutical system of claim 13, wherein the eluant supply container is disposed inside the radiation shield.

15. An eluate extraction mechanism, comprising:

a radiation shielded housing;

an eluate conduit having a radioisotope generator end disposed outside the radiation shielded housing and an opposite end disposed inside the radiation shielded housing;

a hollow injection needle fluidly coupled to the opposite end of the eluate conduit; and

a plunger coupled to the radiation shielded housing movably through a guide structure, wherein the plunger is coupled to the hollow injection needle inside the radiation shielded housing.

16. The eluate extraction mechanism of claim 15, wherein the hollow injection needle comprises a release mechanism.

17. The eluate extraction mechanism of claim 15, wherein the plunger has a path of travel including a connected position and a disconnected position between the hollow injection needle and an eluate container disposed inside the radiation shielded housing.

18. The eluate extraction mechanism of claim 17, wherein the eluate container is disposed removably inside the radiation shielded housing adjacent a door.

19. The eluate extraction mechanism of claim 17, wherein the eluate container is disposed inside an eluate container shield comprising a radiation shielding material, wherein the eluate container shield comprises a viewing window and the eluate container comprises a transparent or translucent material.

20. The eluate extraction mechanism of claim 15, wherein the eluate extraction mechanism comprises a generator alignment portion protruding from a base of the radiation shielded housing.

21. An eluate extraction mechanism, comprising:

a radiation shielded housing comprising a door;

a shielded eluate collection assembly disposed removably inside the radiation shielded housing adjacent the door;

an eluate conduit having a radioisotope generator end disposed outside the radiation shielded housing and an opposite end disposed inside the radiation shielded housing; and

a hollow needle fluidly coupled to the opposite end of the eluate conduit, wherein the hollow needle includes a connected position and a disconnected position relative to the shielded eluate collection assembly.

22. The eluate extraction mechanism of claim 21, comprising an actuator disposed through the radiation shielded housing and coupled to the hollow needle.

23. The eluate extraction mechanism of claim 21, wherein the shielded eluate collection assembly comprises an eluate container disposed inside an eluate container shield comprising a radiation shielding material, wherein the eluate container shield comprises a viewing window and the eluate container comprises a transparent or translucent material.

24. The eluate extraction mechanism of claim 21, wherein the eluate extraction mechanism comprises a generator alignment portion protruding from a base of the radiation shielded housing.

25. A method of using a radiopharmaceutical system, the method comprising:

supplying an eluant into a radioisotope generator;

eluting a radioisotope in the radioisotope generator;

receiving an eluate at an output of the radioisotope generator; and

flowing the eluate from the output along an eluate conduit to a hollow needle that is removably inserted into an eluate container via a plunger.

26. The method of claim 25, wherein flowing comprises transferring the eluate through a radiation shield disposed about the radioisotope generator and directly into a radiation shielded housing disposed outside the radiation shield, wherein the radiation shielded housing is disposed about the eluate container, the hollow needle, and at least a portion of the plunger.

27. The method of claim 25, comprising maintaining a continuous connection between the output and the eluate conduit during connections and disconnections between the hollow needle and the eluate container.

28. The method of claim 25, comprising enabling selective viewing of the eluate within the eluate container via a window.

29. The method of claim 25, comprising enabling selective access to the eluate container via a door.

30. The method of claim 25, comprising guiding the plunger along a path of movement between an engaged position and a disengaged position with the eluate container.

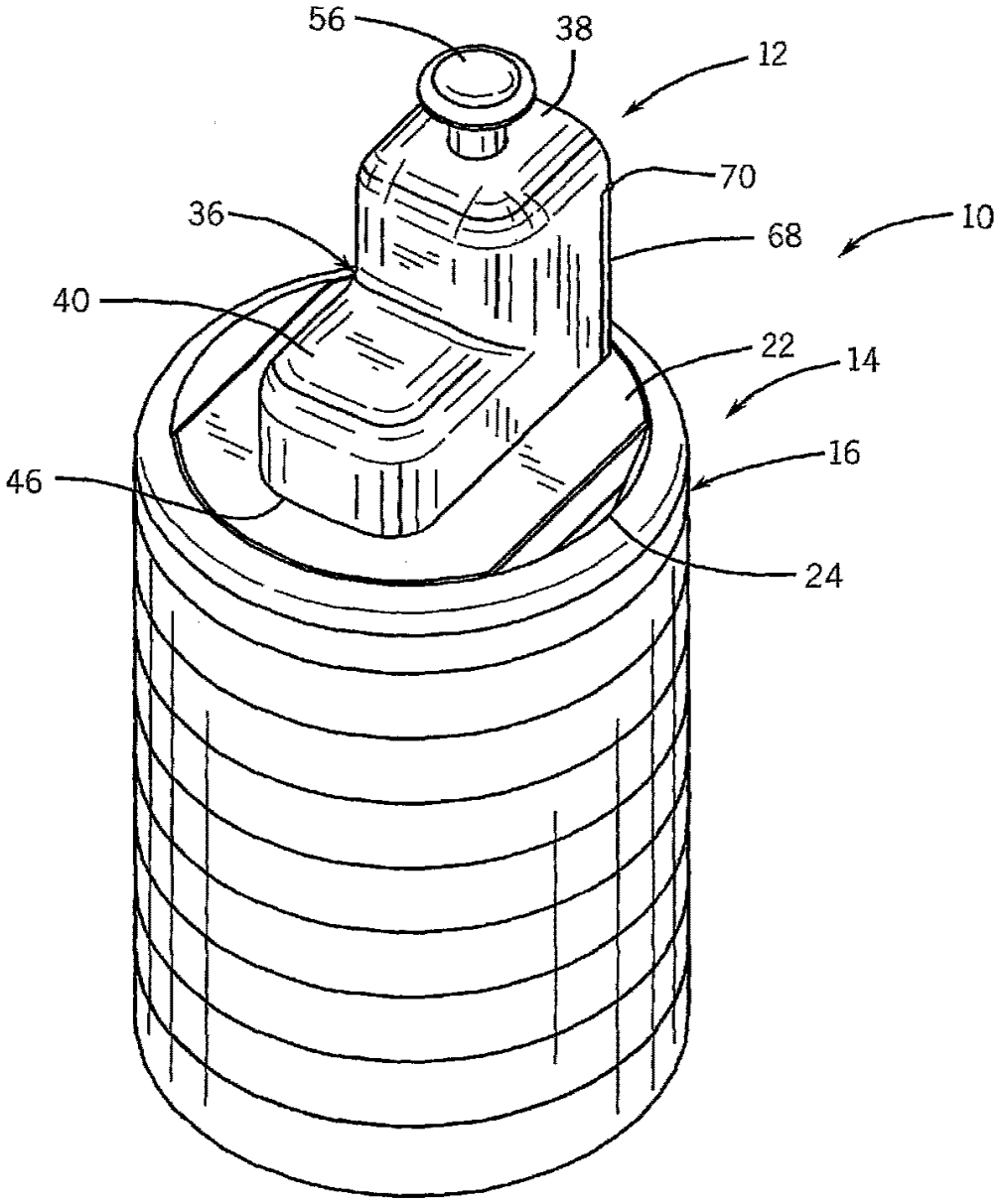

FIG. 1

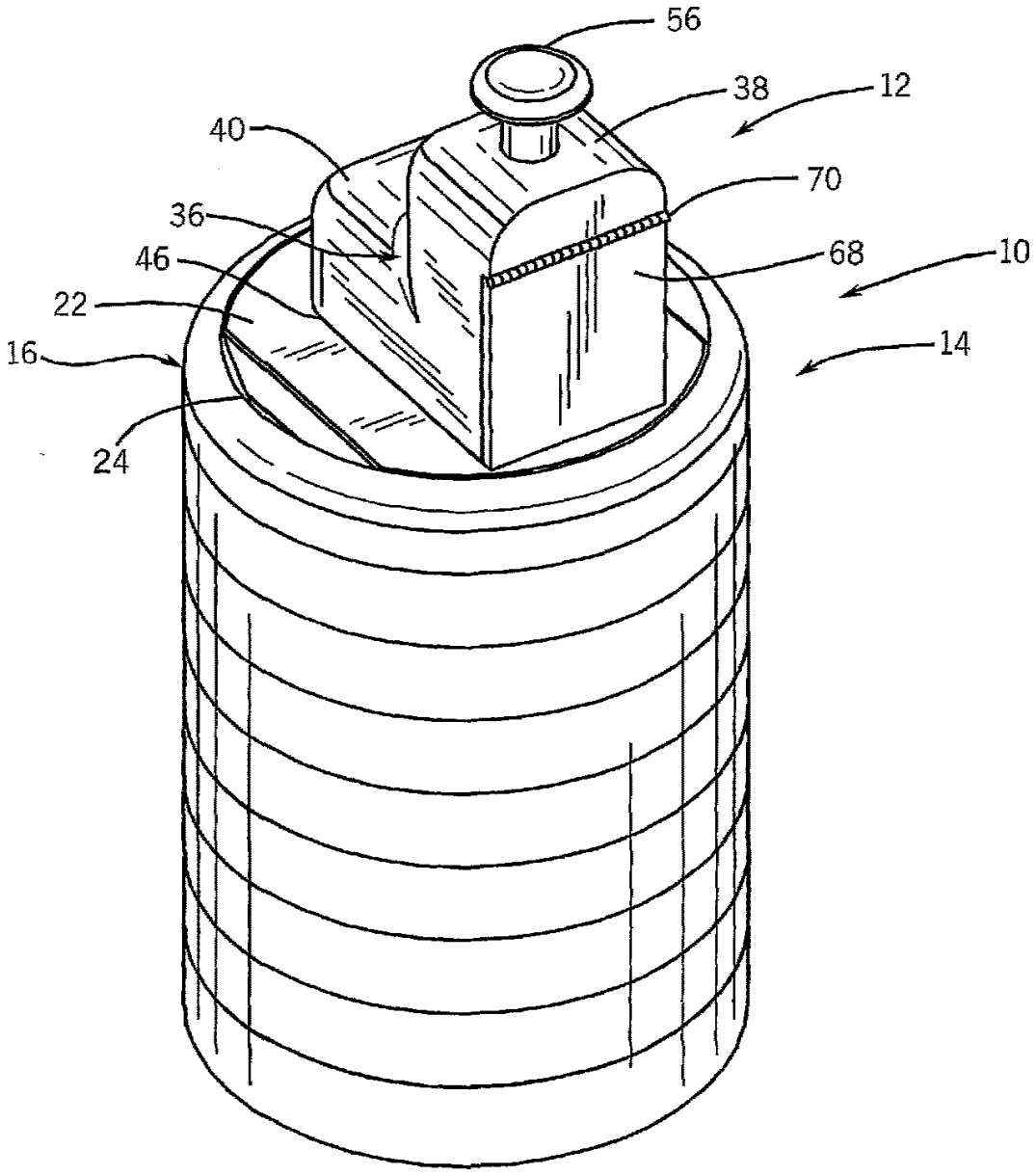

FIG. 2

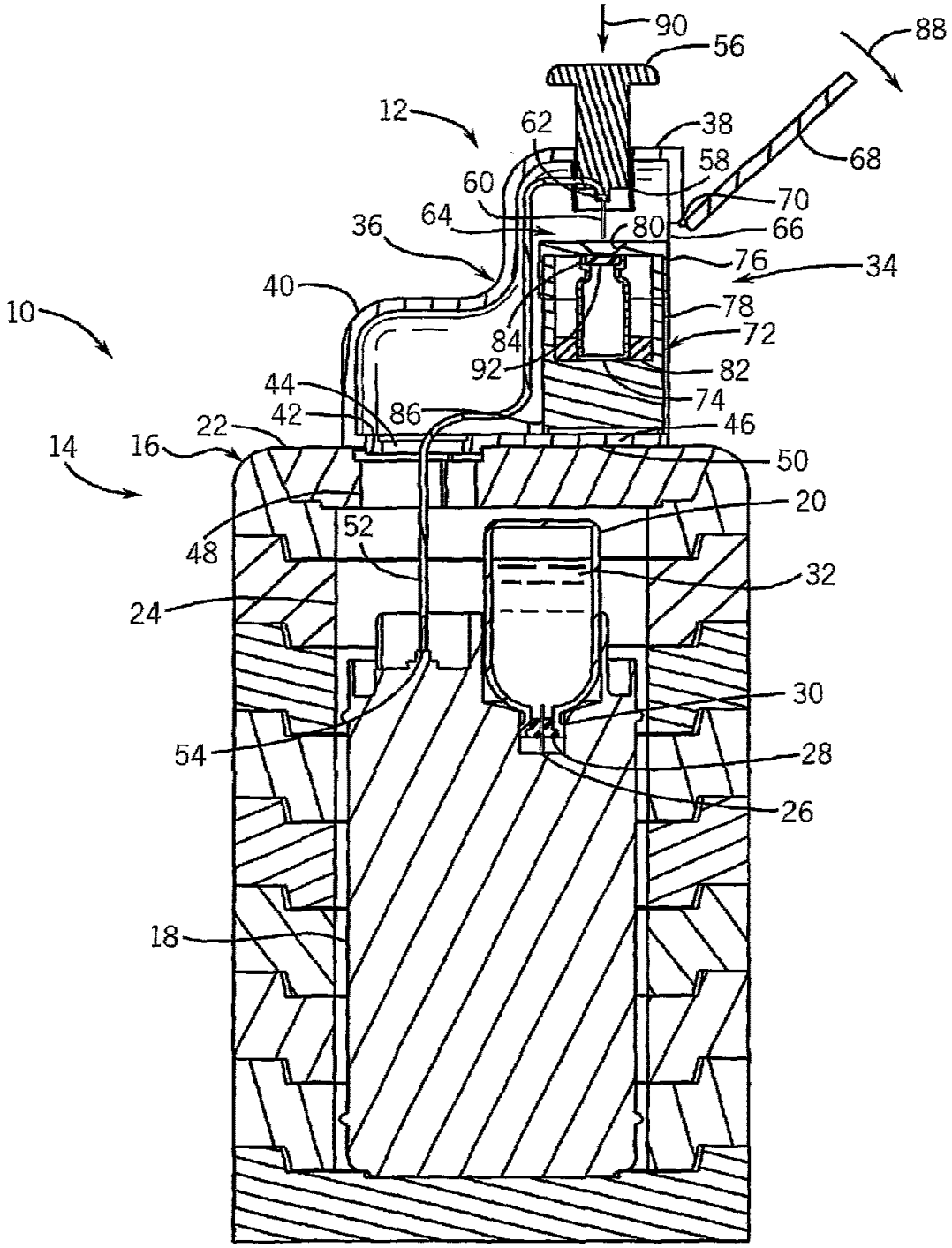
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FIG. 3

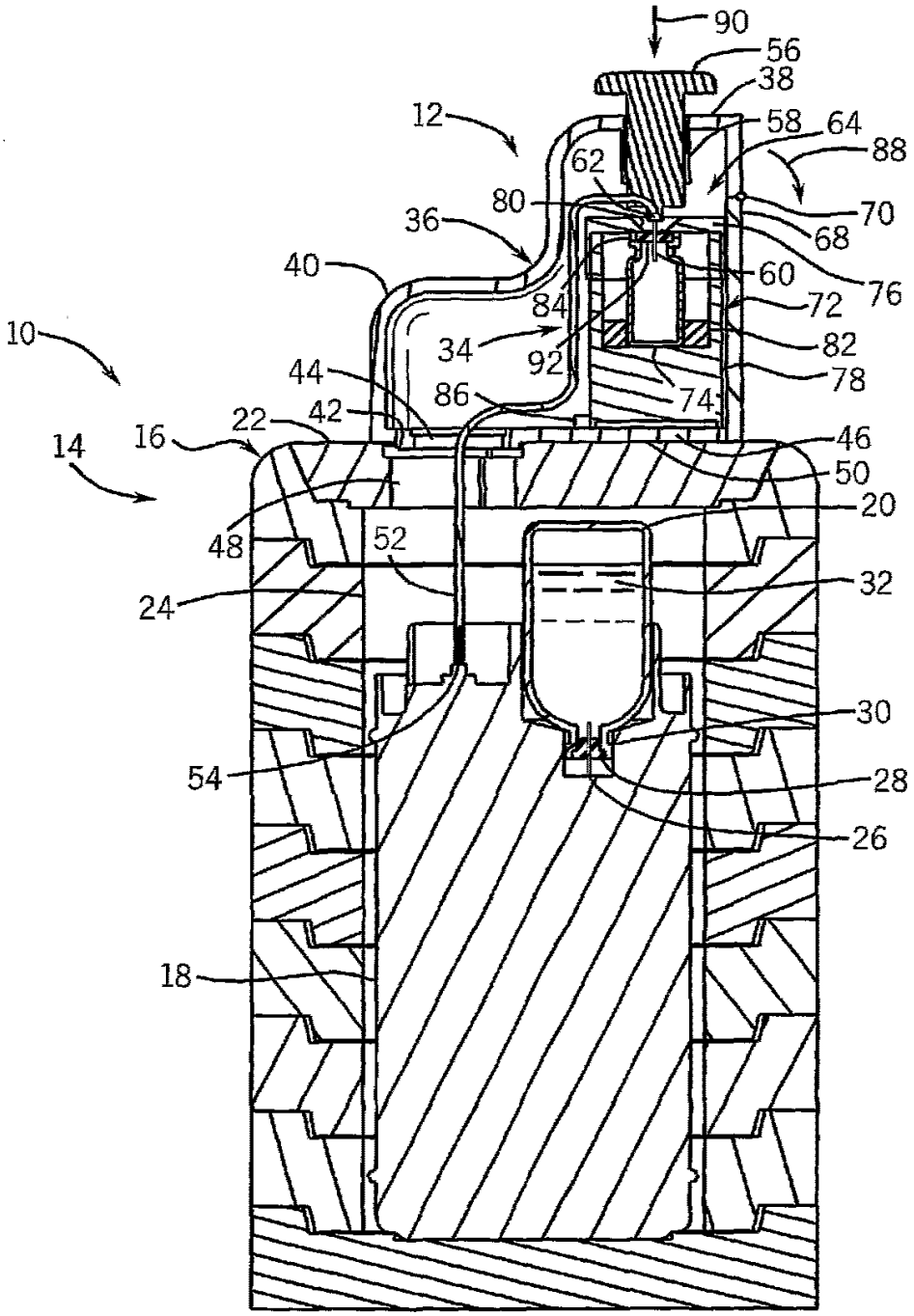
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FIG. 4

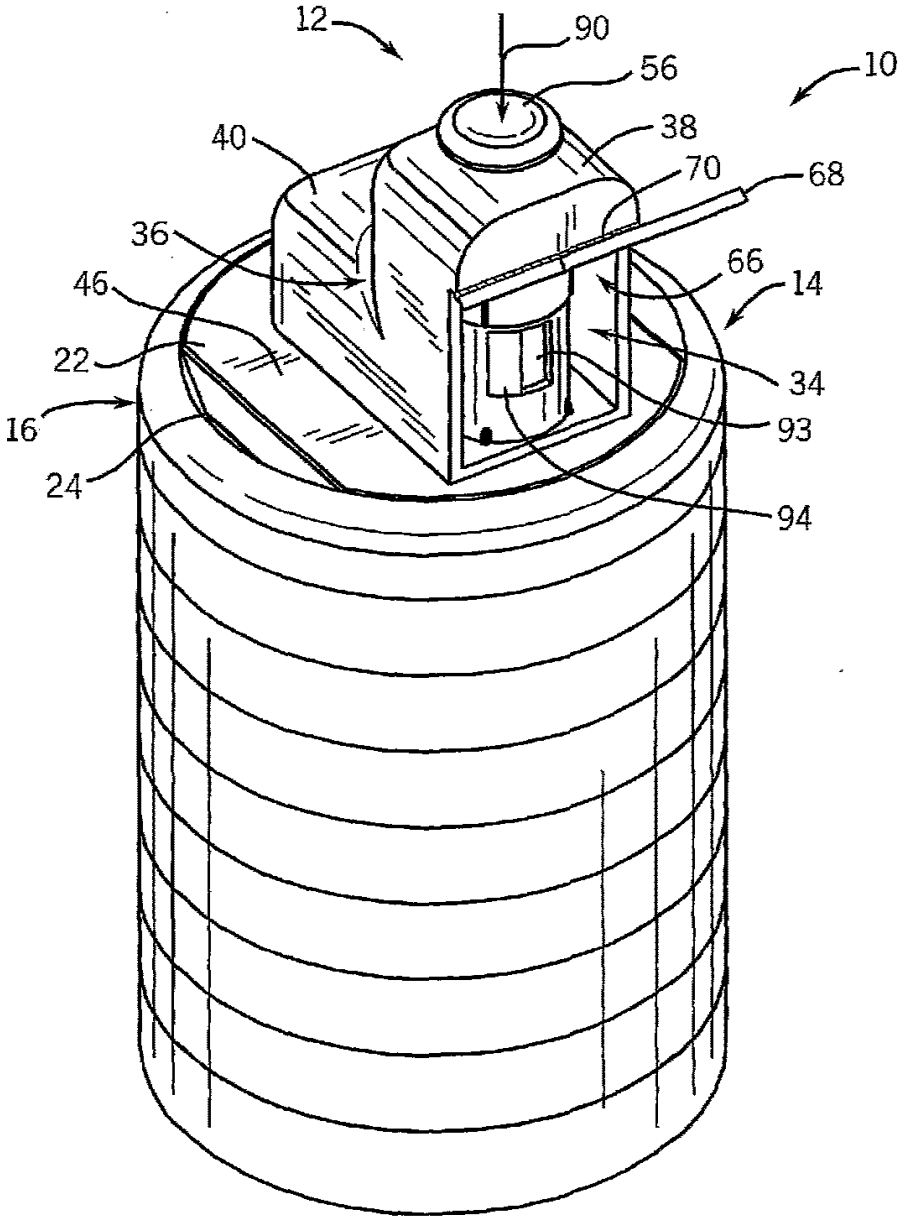

FIG. 5

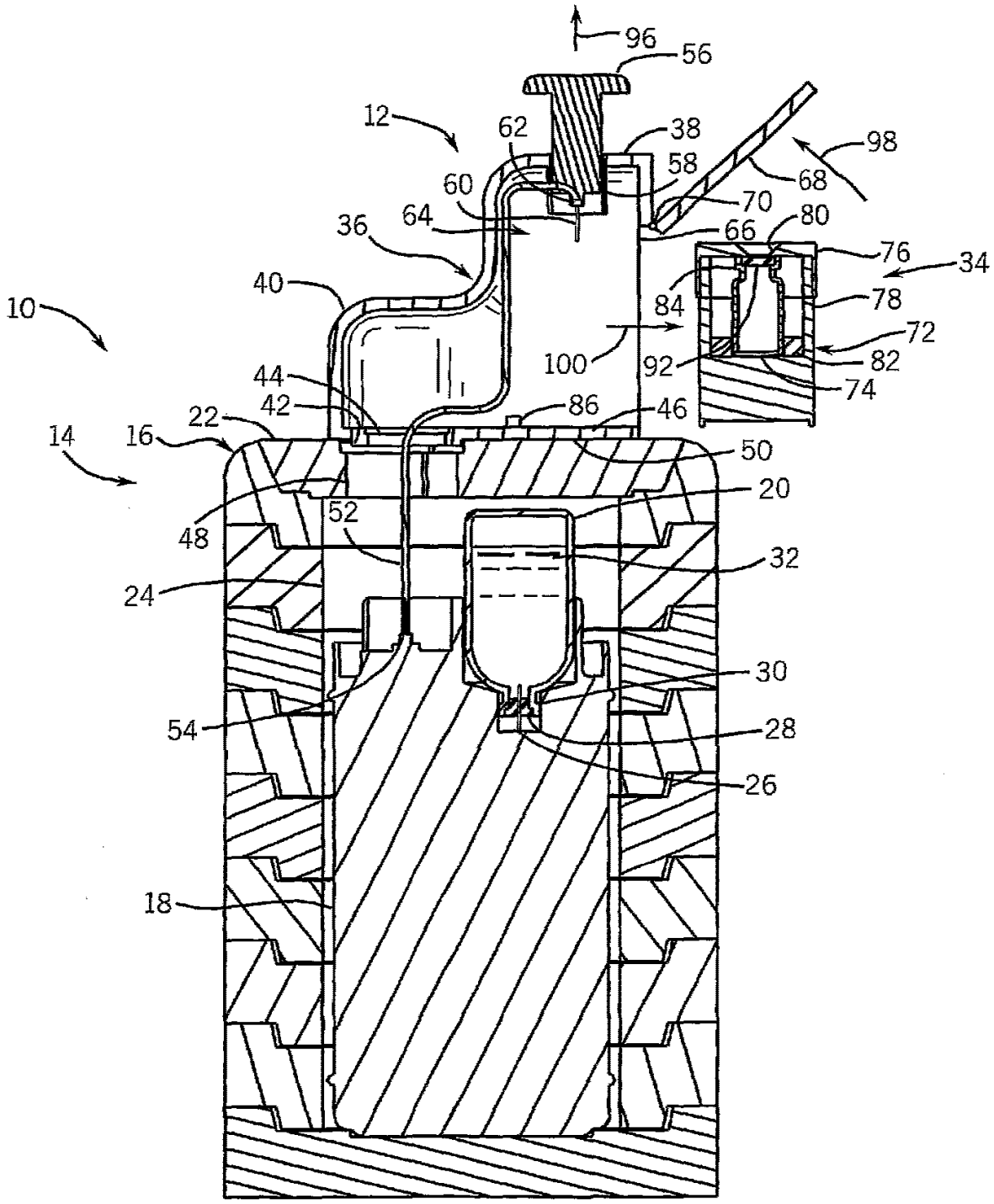
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FIG. 6

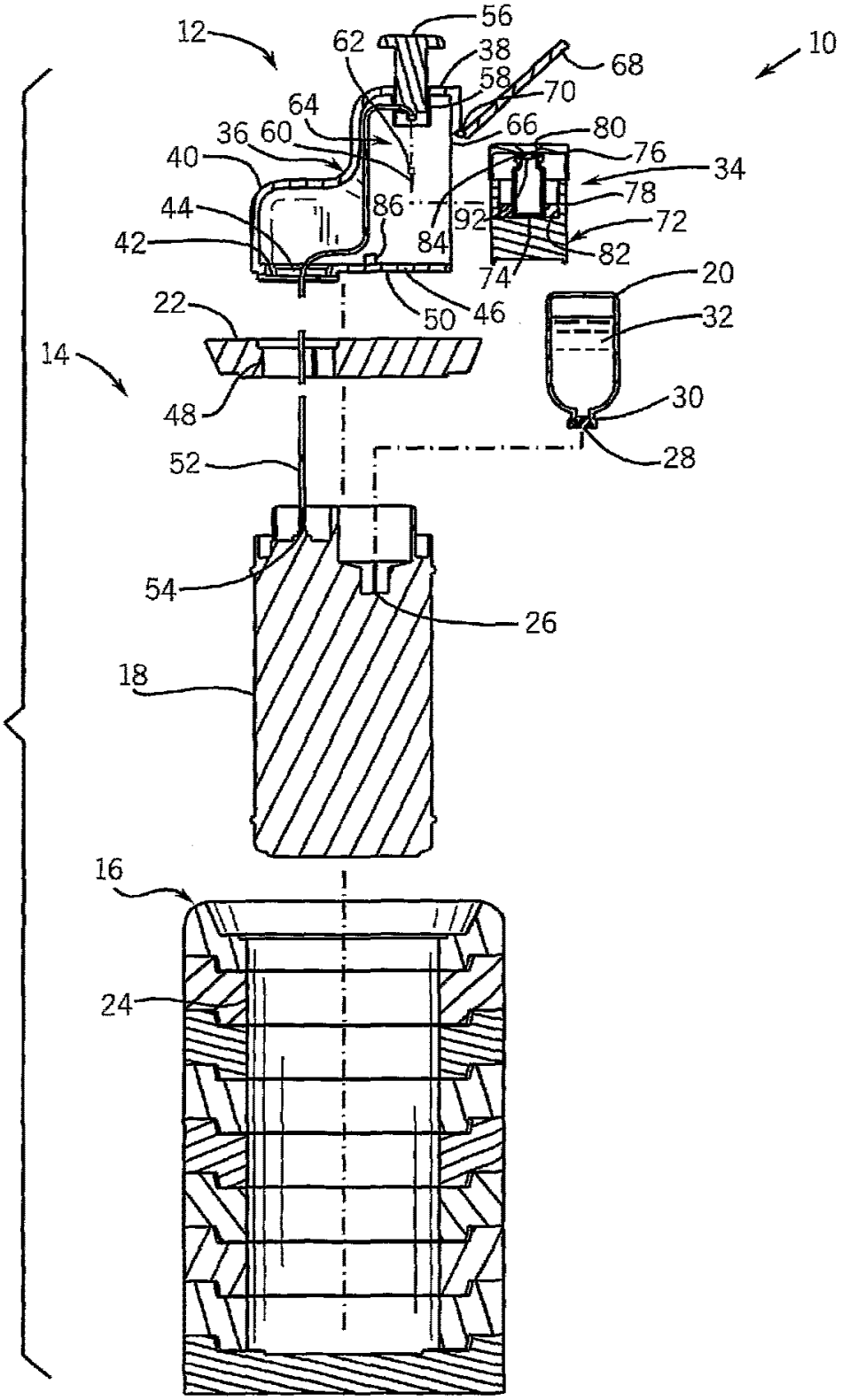
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FIG. 7

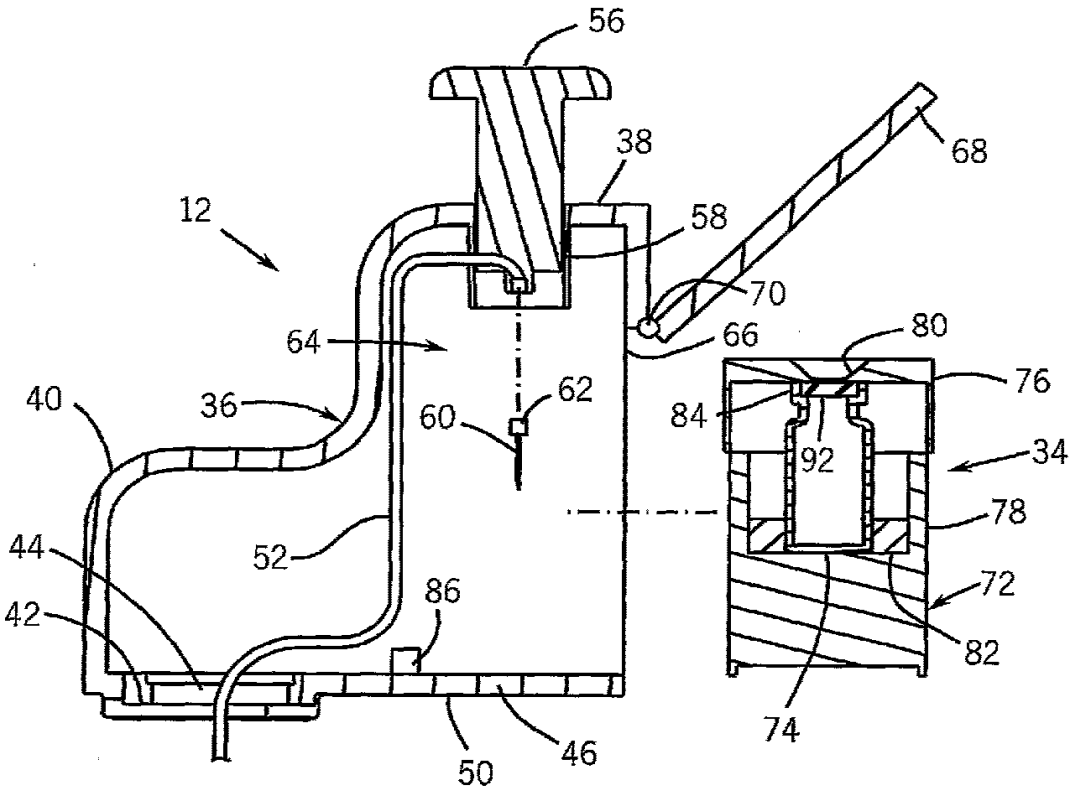
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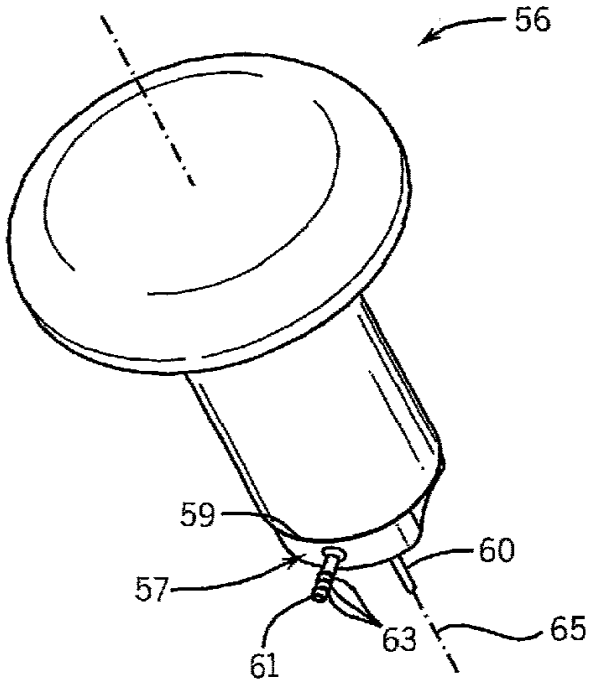
FIG. 8

FIG. 9



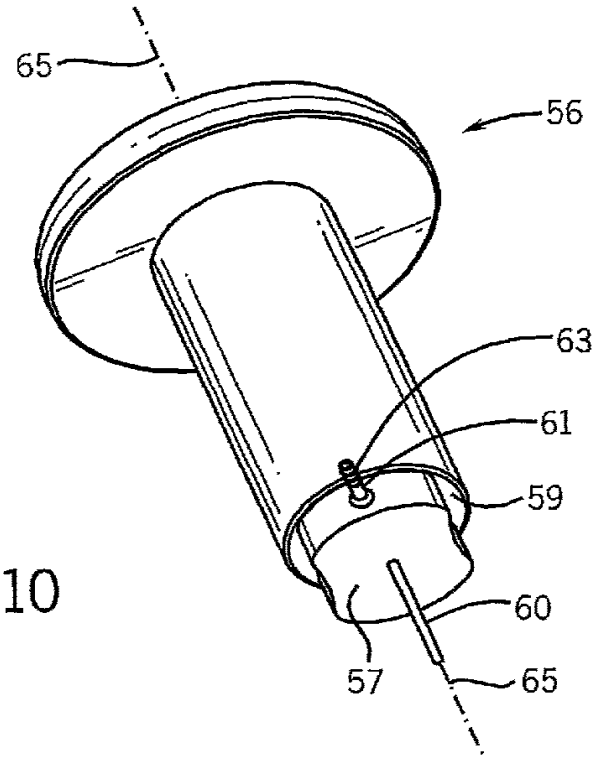


FIG. 10

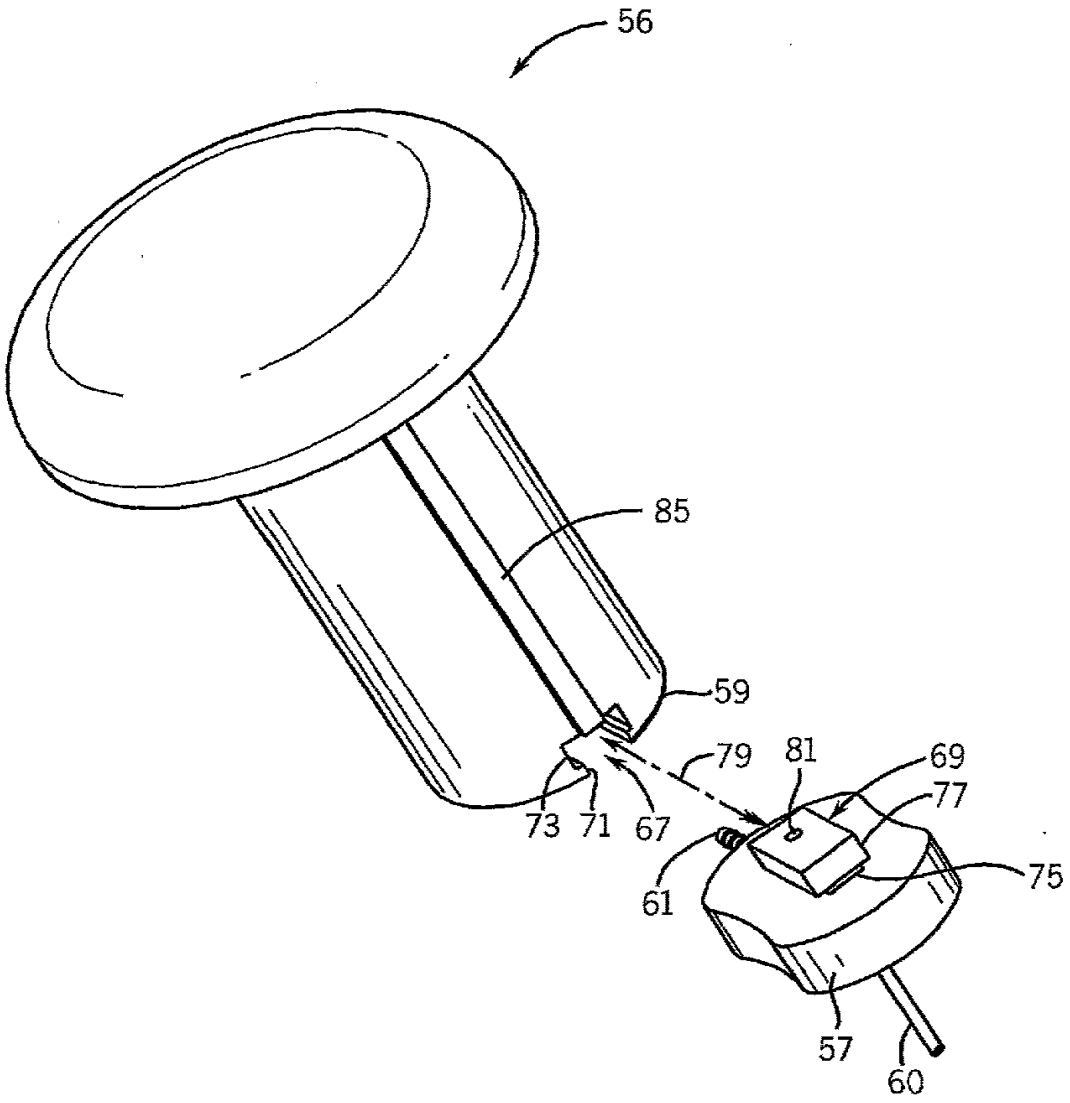


FIG. 11

FIG. 12

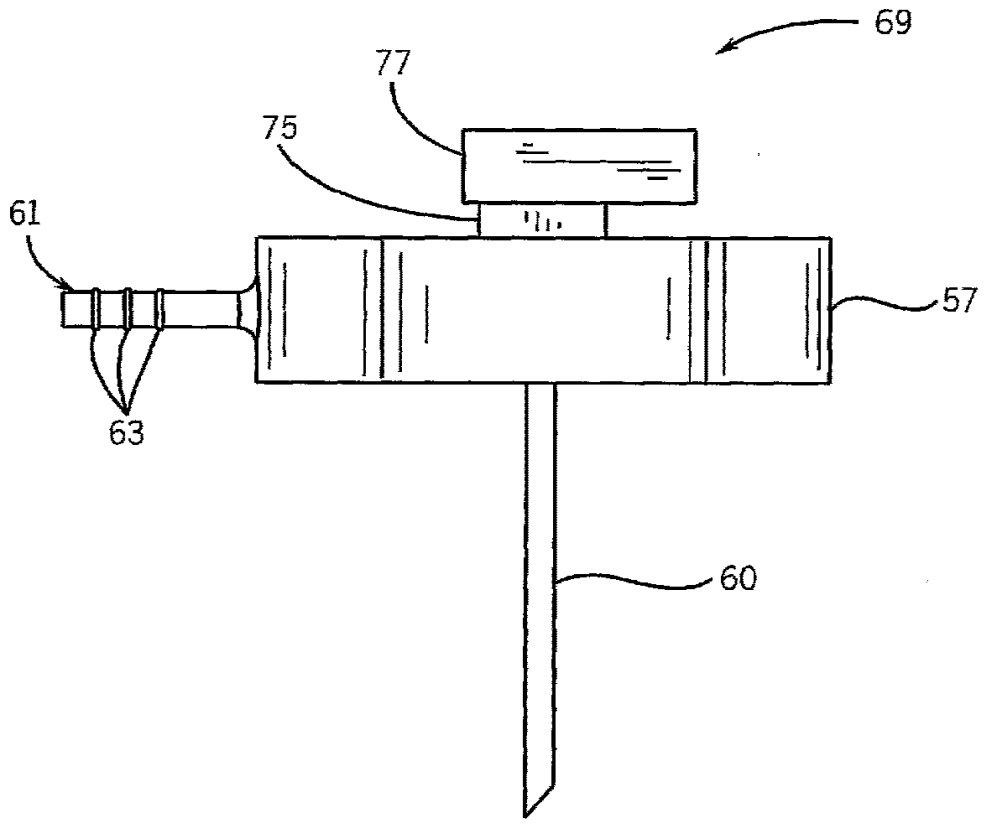


FIG. 13

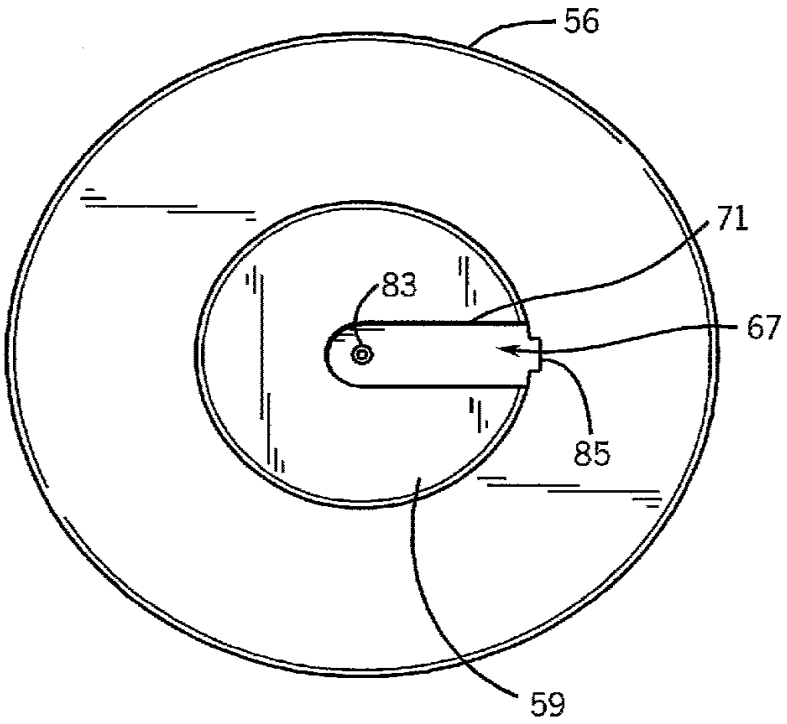
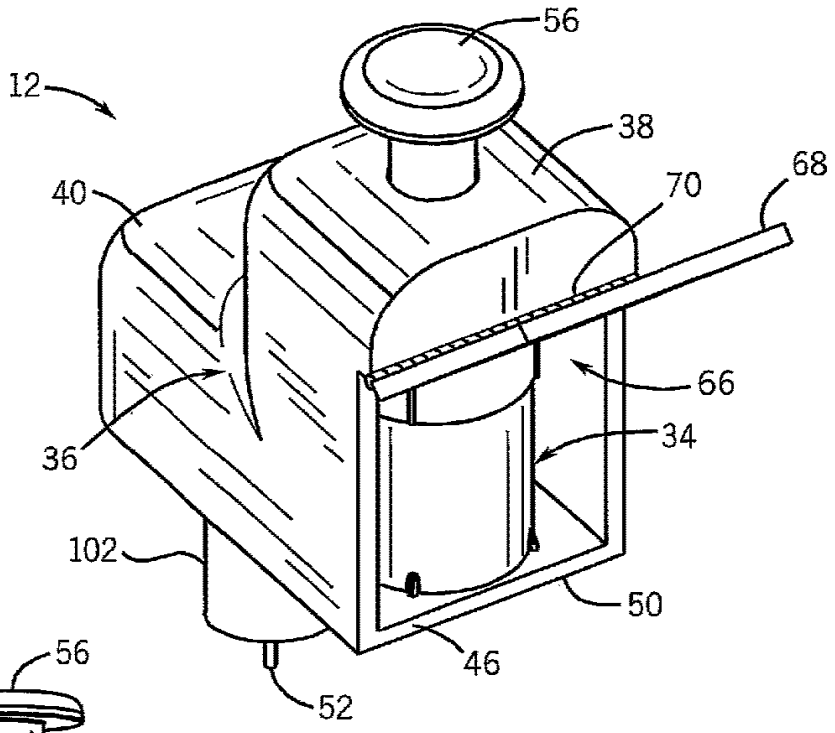


FIG. 14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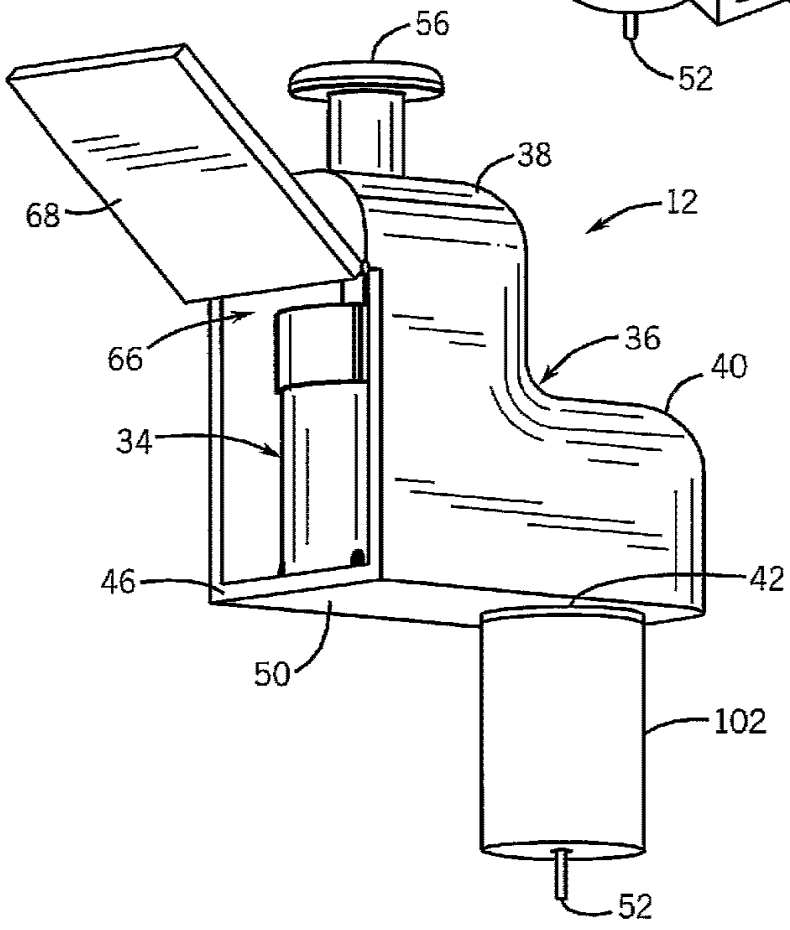
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FIG. 15

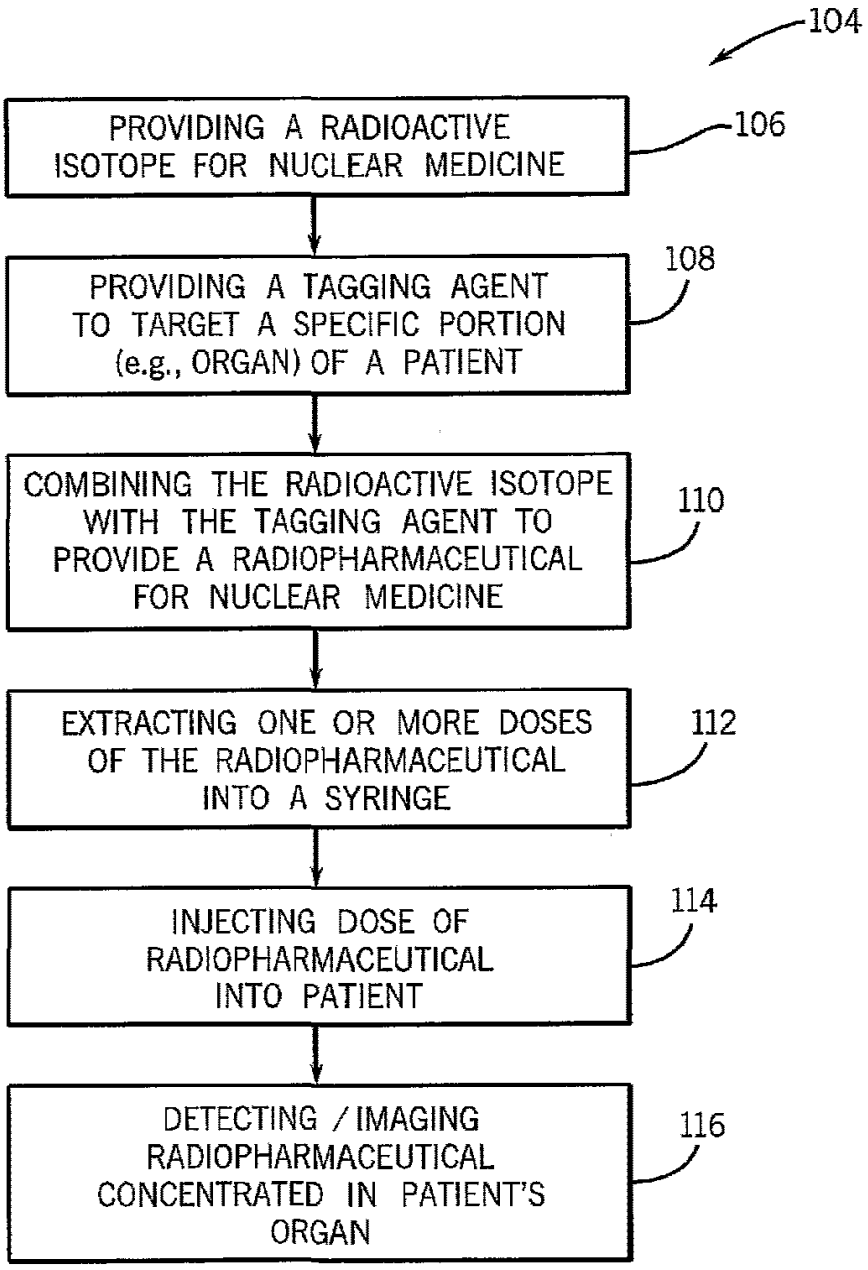
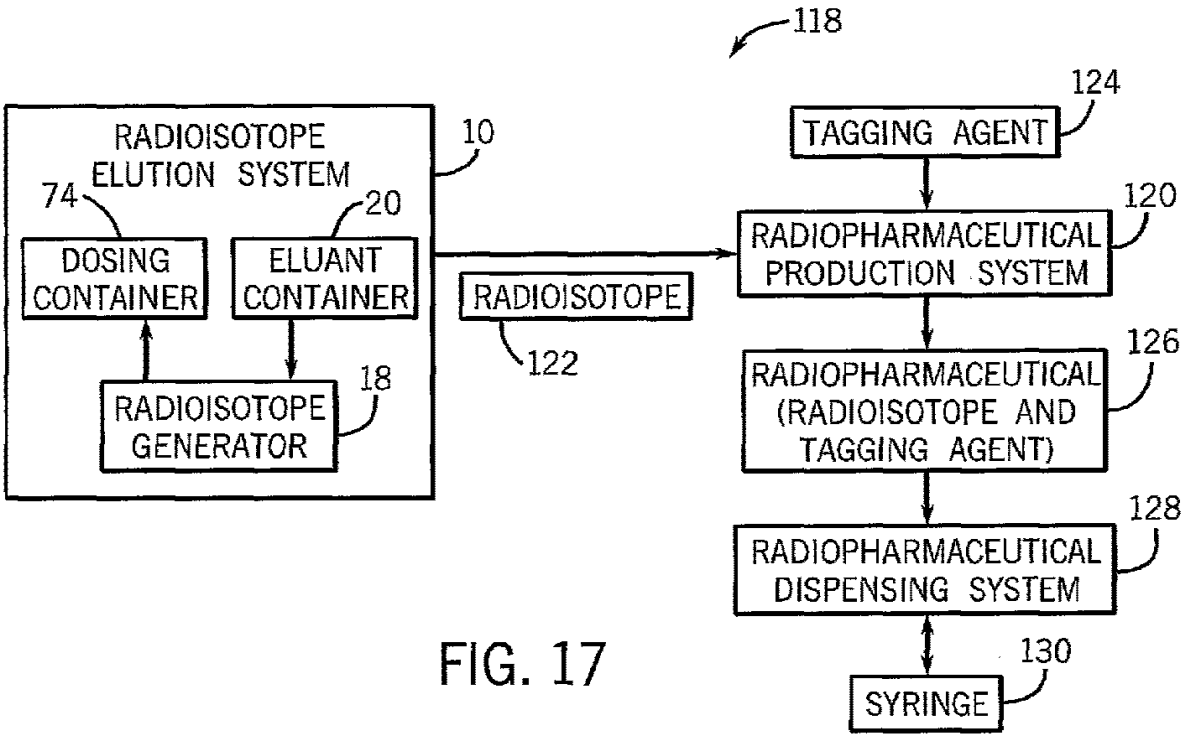

104
PROVIDING A RADIOACTIVE ISOTOPE FOR NUCLEAR MEDICINE
106
PROVIDING A TAGGING AGENT TO TARGET A SPECIFIC PORTION (e.g., ORGAN) OF A PATIENT
108
COMBINING THE RADIOACTIVE ISOTOPE WITH THE TAGGING AGENT TO PROVIDE A RADIOPHARMACEUTICAL FOR NUCLEAR MEDICINE
110
EXTRACTING ONE OR MORE DOSES OF THE RADIOPHARMACEUTICAL INTO A SYRINGE
112
INJECTING DOSE OF RADIOPHARMACEUTICAL INTO PATIENT
114
DETECTING / IMAGING RADIOPHARMACEUTICAL CONCENTRATED IN PATIENT'S ORGAN
116

FIG. 16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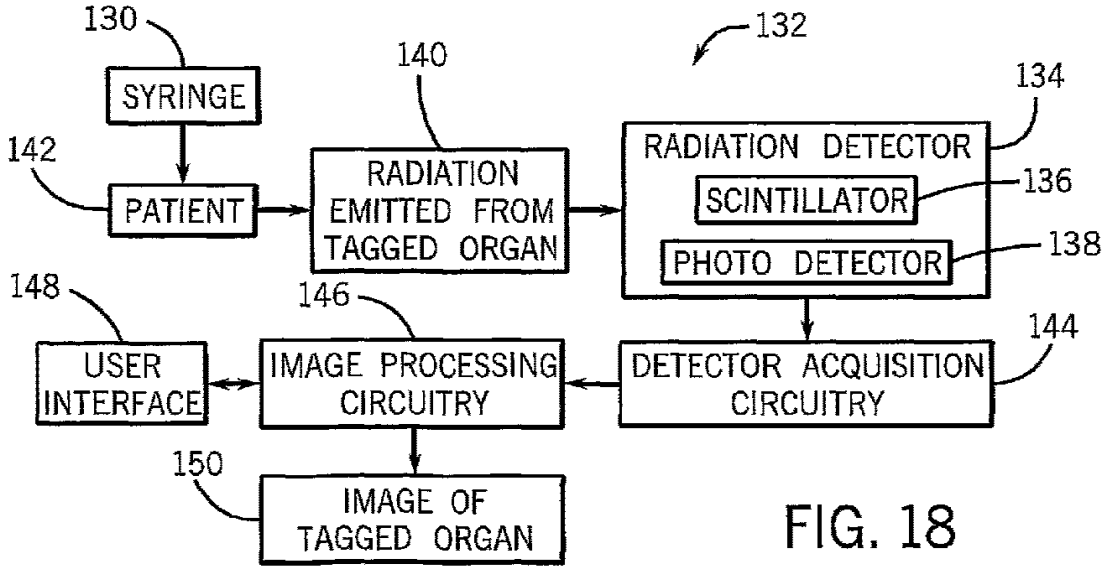
RADIOISOTOPE ELUTION SYSTEM
10
74
20
DOSING CONTAINER
ELUANT CONTAINER
RADIOISOTOPE GENERATOR
18
RADIOISOTOPE
122
TAGGING AGENT
124
RADIOPHARMACEUTICAL PRODUCTION SYSTEM
120
RADIOPHARMACEUTICAL (RADIOISOTOPE AND TAGGING AGENT)
126
RADIOPHARMACEUTICAL DISPENSING SYSTEM
128
SYRINGE
130

FIG. 17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SYRINGE
140
132
134
142
PATIENT
RADIATION EMITTED FROM TAGGED ORGAN
RADIATION DETECTOR
SCINTILLATOR
136
PHOTO DETECTOR
138
148
146
USER INTERFACE
IMAGE PROCESSING CIRCUITRY
DETECTOR ACQUISITION CIRCUITRY
144
150
IMAGE OF TAGGED ORGAN

FIG. 18

Electronic Acknowledgement Receipt

EFS ID:	4275676
Application Number:	12137363
International Application Number:	
Confirmation Number:	7372
Title of Invention:	INFUSION SYSTEM CONFIGURATIONS
First Named Inventor/Applicant Name:	Charles Quirico
Customer Number:	22859
Filer:	Elisabeth Lacy Belden
Filer Authorized By:	
Attorney Docket Number:	56782.1.6
Receipt Date:	12-NOV-2008
Filing Date:	11-JUN-2008
Time Stamp:	16:30:56
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_6_IDS.pdf	616875 a2bdb45f97619e8a97b2f264ec891f9259ccbfb7	no	5

Warnings:	
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2	Foreign Reference	56782_1_EP0102121A1.pdf	513030 2ed3206792c3e4b85d5ea5ac7e216731e1a30015	no	19
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National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
12/137,363	06/11/2008	3763	2040	56782.1.6	36	4

CONFIRMATION NO. 7372

22859
INTELLECTUAL PROPERTY GROUP
FREDRIKSON & BYRON, P.A.
200 SOUTH SIXTH STREET
SUITE 4000
MINNEAPOLIS, MN 55402

FILING RECEIPT

Date Mailed: 06/24/2008

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

Applicant(s)

Charles Quirico, Residence Not Provided;
Ernest Balestracci, Residence Not Provided;
Dan D. Darst, Residence Not Provided;
Eric J. Krause, Residence Not Provided;
Vishal N. Lokhande, Residence Not Provided;
Jake Childs, Residence Not Provided;

Assignment For Published Patent Application

BRACCO DIAGNOSTICS, INC., Princeton, NJ

Power of Attorney: None

Domestic Priority data as claimed by applicant

Foreign Applications

If Required, Foreign Filing License Granted: 06/23/2008

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 12/137,363**

Projected Publication Date: To Be Determined - pending completion of Missing Parts

Non-Publication Request: No

Early Publication Request: No

Title

INFUSION SYSTEM CONFIGURATIONS

Preliminary Class

604

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4158).

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
12/137,363	06/11/2008	Charles Quirico	56782.1.6

CONFIRMATION NO. 7372

22859
INTELLECTUAL PROPERTY GROUP
FREDRIKSON & BYRON, P.A.
200 SOUTH SIXTH STREET
SUITE 4000
MINNEAPOLIS, MN 55402

FORMALITIES LETTER

OC000000030633545

Date Mailed: 06/24/2008

NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

FILED UNDER 37 CFR 1.53(b)

Filing Date Granted

Items Required To Avoid Abandonment:

An application number and filing date have been accorded to this application. The item(s) indicated below, however, are missing. Applicant is given **TWO MONTHS** from the date of this Notice within which to file all required items and pay any fees required below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

- The oath or declaration is missing.
  A properly signed oath or declaration in compliance with 37 CFR 1.63, identifying the application by the above Application Number and Filing Date, is required.
  Note: If a petition under 37 CFR 1.47 is being filed, an oath or declaration in compliance with 37 CFR 1.63 signed by all available joint inventors, or if no inventor is available by a party with sufficient proprietary interest, is required.

The application is informal since it does not comply with the regulations for the reason(s) indicated below.

The required item(s) identified below must be timely submitted to avoid abandonment:

- Replacement drawings in compliance with 37 CFR 1.84 and 37 CFR 1.121(d) are required. The drawings submitted are not acceptable because:
  - Numbers, letters, and reference characters on the drawings must measure at least 0.32 cm (1/8 inch) in height. See Figure(s) 5A-10.
  - The drawings submitted to the Office are not electronically reproducible because portions of figures 4-10 are missing and/or blurry.

Applicant is cautioned that correction of the above items may cause the specification and drawings page count to exceed 100 pages. If the specification and drawings exceed 100 pages, applicant will need to submit the required application size fee.

The applicant needs to satisfy supplemental fees problems indicated below.

The required item(s) identified below must be timely submitted to avoid abandonment:

- To avoid abandonment, a surcharge (for late submission of filing fee, search fee, examination fee or oath or declaration) as set forth in 37 CFR 1.16(f) of $**130** for a non-small entity, must be submitted with the missing items identified in this notice.

SUMMARY OF FEES DUE:

Total additional fee(s) required for this application is $**130** for a non-small entity
- $**130** Surcharge.

Replies should be mailed to:

Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

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https://sportal.uspto.gov/authenticate/AuthenticateUserLocalEPF.html

For more information about EFS-Web please call the USPTO Electronic Business Center at **1-866-217-9197** or visit our website at http://www.uspto.gov/ebc.

If you are not using EFS-Web to submit your reply, you must include a copy of this notice.

/mduong/

Office of Data Management, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

PTO/SB/14 (07-07)
Approved for use through 06/30/2010. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	56782.1.6
	Application Number	
Title of Invention	INFUSION SYSTEM CONFIGURATIONS	

The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.
This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.

Secrecy Order 37 CFR 5.2

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

Applicant Information:

Applicant 1 Remove

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Charles		Quirico	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City		State/Province		Country of Residence [i]	

Citizenship under 37 CFR 1.41(b) [i]

Mailing Address of Applicant:

Address 1	
Address 2	

City		State/Province	
Postal Code		Country [i]	

Applicant 2 Remove

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Ernest		Balestracci	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City		State/Province		Country of Residence [i]	

Citizenship under 37 CFR 1.41(b) [i]

Mailing Address of Applicant:

Address 1	
Address 2	

City		State/Province	
Postal Code		Country [i]	

Applicant 3 Remove

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Dan	D.	Darst	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City		State/Province		Country of Residence [i]	

PTO/SB/14 (07-07)
Approved for use through 06/30/2010. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	56782.1.6
	Application Number	
Title of Invention	INFUSION SYSTEM CONFIGURATIONS	

Citizenship under 37 CFR 1.41(b) i					
Mailing Address of Applicant:					
Address 1					
Address 2					
City		**State/Province**			
Postal Code		**Country**i			

Applicant 4 Remove

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Eric	J.	Krause	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City		**State/Province**		**Country of Residence** i	

Citizenship under 37 CFR 1.41(b) i	
Mailing Address of Applicant:	
Address 1	
Address 2	

City		**State/Province**	
Postal Code		**Country**i	

Applicant 5 Remove

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Vishal	N.	Lokhande	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City		**State/Province**		**Country of Residence** i	

Citizenship under 37 CFR 1.41(b) i	
Mailing Address of Applicant:	
Address 1	
Address 2	

City		**State/Province**	
Postal Code		**Country**i	

Applicant 6 Remove

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Jake		Childs	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City		**State/Province**		**Country of Residence** i	

Citizenship under 37 CFR 1.41(b) i	

PTO/SB/14 (07-07)
Approved for use through 06/30/2010. OMB 0651-0032
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	56782.1.6
	Application Number	
Title of Invention	INFUSION SYSTEM CONFIGURATIONS	

Mailing Address of Applicant:			
Address 1			
Address 2			
City		**State/Province**	
Postal Code		**Country**[i]	

All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the **Add** button. Add

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below. For further information see 37 CFR 1.33(a).

☐ **An Address is being provided for the correspondence Information of this application.**

Customer Number	22859		
Email Address		Add Email	Remove Email

Application Information:

Title of the Invention	INFUSION SYSTEM CONFIGURATIONS		
Attorney Docket Number	56782.1.6	**Small Entity Status Claimed**	☐
Application Type	Nonprovisional		
Subject Matter	Utility		
Suggested Class (if any)		**Sub Class (if any)**	
Suggested Technology Center (if any)			
Total Number of Drawing Sheets (if any)	23	**Suggested Figure for Publication (if any)**	

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S. C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32).
Enter either Customer Number or complete the Representative Name section below. If both sections are completed the Customer Number will be used for the Representative Information during processing.

Please Select One:	◉ Customer Number	○ US Patent Practitioner	○ Limited Recognition (37 CFR 11.9)
Customer Number	22859		

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	56782.1.6
	Application Number	
Title of Invention	INFUSION SYSTEM CONFIGURATIONS	

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, or 365(c) or indicate National Stage entry from a PCT application. Providing this information in the application data sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78(a)(2) or CFR 1.78(a)(4), and need not otherwise be made part of the specification.

Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)

Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the **Add** button. Add

Foreign Priority Information:

This section allows for the applicant to claim benefit of foreign priority and to identify any prior foreign application for which priority is not claimed. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55(a).

Remove

Application Number	Country [i]	Parent Filing Date (YYYY-MM-DD)	Priority Claimed
			○ Yes ◉ No

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button. Add

Assignee Information:

Providing this information in the application data sheet does not substitute for compliance with any requirement of part 3 of Title 37 of the CFR to have an assignment recorded in the Office.

Assignee 1 Remove

If the Assignee is an Organization check here. ☒			
Organization Name	Bracco Diagnostics, Inc.		
Mailing Address Information:			
Address 1	107 College Road East		
Address 2			
City	Princeton	**State/Province**	NJ
Country [i]	US	Postal Code	08540
Phone Number		Fax Number	
Email Address			

Additional Assignee Data may be generated within this form by selecting the **Add** button. Add

Signature:

A signature of the applicant or representative is required in accordance with 37 CFR 1.33 and 10.18. Please see 37 CFR 1.4(d) for the form of the signature.

Signature	/Charles D. Segelbaum/	Date (YYYY-MM-DD)	2008-06-11

PTO/SB/14 (07-07)
Approved for use through 06/30/2010. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	56782.1.6
	Application Number	
Title of Invention	INFUSION SYSTEM CONFIGURATIONS	

First Name	Charles D.	Last Name	Segelbaum	Registration Number	42138

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

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9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

INFUSION SYSTEM CONFIGURATIONS

RELATED APPLICATIONS

[01] The present application is related to the following commonly assigned utility patent applications, all of which are filed concurrently herewith and all of which are hereby incorporated by reference in their entireties: Practitioner Docket No. 56782.1.5, entitled: SHIELDING ASSEMBLIES FOR INFUSION SYSTEMS; Practitioner Docket No. 56782.1.7, entitled: INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE; and Practitioner Docket No. 56782.1.8, entitled: CABINET STRUCTURES SUPPORTING INFUSION SYSTEMS.

TECHNICAL FIELD

[02] The present invention pertains to configurations of systems that generate and infuse radiopharmaceuticals, and, more particularly, to the routing of infusion circuit tubing lines.

BACKGROUND

[03] Nuclear medicine employs radioactive material for therapy and diagnostic imaging. Positron emission tomography (PET) is one type of diagnostic imaging, which utilizes doses of radiopharmaceutical, for example, generated by elution within a radioisotope generator, that are injected, or infused into a patient. The infused dose of radiopharmaceutical is absorbed by cells of a target organ, of the patient, and emits radiation, which is detected by a PET scanner, in order to generate an image of the organ. An example of a radioactive isotope, which may be used for PET, is Rubidium-82 (produced by the decay of Strontium-82); and an example of a radioisotope generator, which yields a saline solution of Rubidium-82, via elution, is the CardioGen-82® available from Bracco Diagnostics Inc. (Princeton, NJ).

[04] Whether the half-life of a particular radioactive isotope, employed by a radiopharmaceutical, is relatively short or long, a patient undergoing a nuclear imaging procedure is not typically exposed to a significant amount of radiation. However those personnel, whose job it is to set up and maintain radiopharmaceutical infusion systems, and to administer doses therefrom, are subject to more frequent and prolonged exposures to radiation. Therefore, shielding assemblies, which provide a radiation barrier to protect these personnel from excessive exposure to radiation sources, are an important component of radiopharmaceutical generators and infusion systems. These shielding assemblies are typically formed with lead sidewalls, the bulk and weight of which can pose difficulties for the personnel who regularly set up disposable tubing lines for the infusion circuit of the infusion system. These lines should be routed into and out from compartments of the shielding assembly without kinking or crushing the lines. Thus, there is a need for new infusion system configurations and assemblies that facilitate this task.

BRIEF DESCRIPTION OF THE DRAWINGS

[05] The following drawings are illustrative of particular embodiments of the present invention and therefore do not limit the scope of the invention. The drawings are not to scale (unless so stated) and are intended for use in conjunction with the explanations in the following detailed description. Embodiments of the present invention will hereinafter be described in conjunction with the appended drawings, wherein like numerals denote like elements.

[06] Figure 1A is a first perspective view of an infusion system, according to some embodiments of the present invention.

[07] Figure 1B is another perspective view of a portion of a cabinet structure of the system shown in Figure 1A, according to some embodiments.

[08] Figure 1C is a second perspective view of the system shown in Figure 1A, according to some embodiments.

[09] Figure 1D is a schematic of an infusion circuit, according to some embodiments of the present invention.

[10] Figure 2A is a perspective view of a shielding assembly for an infusion system, such as that shown in Figures 1A-C, according to some embodiments of the present invention.

[11] Figure 2B is a perspective view of a framework of the system, according to some embodiments, with an enlarged detailed view of a component of the system, according to some embodiments.

[12] Figure 3A is another perspective view of the shielding assembly shown in Figure 2A.

[13] Figure 3B is a perspective view of the infusion circuit, shown in Figure 1C, configured and routed, according to some embodiments.

[14] Figure 3C is a perspective view of a disposable infusion circuit subassembly, according to some embodiments.

[15] Figure 3D is a frame for the subassembly shown in Figure 3C, according to some embodiments.

[16] Figure 4 is a main menu screen shot from an interface of a computer, which may be included in systems of the present invention, according to some embodiments.

[17] Figure 5A is a schematic showing a first group of successive screen shots from the computer interface, according to some embodiments.

[18] Figure 5B is a pair of screen shots from the computer interface, which provide indications related to eluant volume levels in a reservoir of the system, according to some embodiments.

[19] Figure 5C is a schematic showing a second group of successive screen shots from the computer interface, according to some embodiments.

[20] Figure 6 is a schematic showing a third group of successive screen shots from the computer interface, according to some embodiments.

[21] Figures 7A-C are schematics showing a fourth group of successive screen shots from the computer interface, according to some embodiments.

[22] Figures 8A-B are schematics showing a fifth group of successive screen shots from the computer interface, according to some embodiments.

[23] Figures 9A-C are schematics showing a sixth group of successive screen shots from the computer interface, according to some embodiments.

[24] Figure 10 is a schematic showing a seventh group of successive screen shots from the computer interface, according to some embodiments.

DETAILED DESCRIPTION

[25] The following detailed description is exemplary in nature and is not intended to limit the scope, applicability, or configuration of the invention in any way. Rather, the following description provides practical illustrations for implementing exemplary embodiments. Utilizing the teaching provided herein, those skilled in the art will recognize that many of the examples have suitable alternatives that can be utilized.

[26] Figure 1A is a first perspective view of an infusion system 10, according to some embodiments of the present invention, wherein system 10 is shown supported by a cabinet structure, which includes a platform 113 (seen better in Figure 2B) and a shell 13; shell 13 extends upward from a skirt 11, that surrounds platform 113, to surrounds an interior space in which a portion of infusion system 10 is contained (-seen in Figure 1C). Shell may be formed from panels of injection-molded polyurethane fitted together according to methods known to those skilled in the art. Figure 1A illustrates the cabinet structure of system 10 including a grip or handle 14, which extends laterally from shell 13, in proximity to an upper surface 131 thereof, and a post 142, which extends upward from shell 13, and to which a work surface, or tray 16 and a computer 17 are, preferably, attached, via an ergonomic, positionable mount. According to some embodiments, computer 17 is coupled to a controller of system 10, which is mounted within the interior space surrounded by shell 13, and a monitor 172 of computer 17 not only displays indications of system operation for a user of system 10, but also serves as a device for user input (e.g. touch screen input). However, according to alternate embodiments, another type of user input device, known to those skilled in the art, may be employed by computer 17. Other types of user input devices may included, for example, a keyboard, a series of control buttons or levers, a

barcode reader (or other reader of encoded information), a scanner, a computer readable medium containing pertinent data, etc. The user input device may be mounted on the cabinet structure of system 10, as shown, or may be tethered thereto; alternatively the user input device may be remote from system 10, for example, located in a separate control room. According to some additional embodiments, another user input device, for example, in addition to a touch screen of computer 17, may be remote from system 10 and used to start and stop infusions. Operation of system 10, which is facilitated by computer 17, will be described below, in conjunction with Figures 4-9C.

[27] Figure 1A further illustrates two pairs of wheels 121, 122, mounted to an underside of platform 113, to make system 10 mobile; handle 14 is shown located at an elevation suitable for a person to grasp in order to maneuver system 10, from one location for another, upon pairs of wheels 121, 122. According to some preferred embodiments, one or both pairs of wheels 121, 122, are casters, allowing for rotation in a horizontal plane (swivel), in order to provide additional flexibility for maneuvering system 10 in relatively tight spaces.

[28] Figure 1B is a perspective view of a portion of system 10, on a side 111 of the cabinet structure, which is in proximity to wheels 121. Figure 1B illustrates a lever or pedal 125, which is located for activation by a foot of the person, who grasps handle 14 to maneuver system 10. In a neutral position, pedal 125 allows wheels 121, 122 to rotate, and, if embodied as casters, to swivel freely. Pedal 125 may be depressed to a first position which prevents a swiveling of wheels 122, according to those embodiments in which wheels 122 are casters, and may be further depressed to brake wheels 121, 122 from rolling and swiveling, upon reaching a desired location. Figure 1B further illustrates a rear access panel 174, for example, providing access to circuit boards of the aforementioned controller contained within the interior space surrounded shell 13, an optional lock 184, to secure panel 174, a power jack 118, for connecting system 10 to a power source, and a printer 117 for providing documentation of each patient infusion carried out by system 10, and of system quality control test results. In some embodiments, system 10 may further include one or more additional

connectors, or ports (not shown), which allow system 10 to be coupled to, for communication with, other devices used for nuclear imaging procedures.

[29] Figure 1A further illustrates upper surface 131 of shell 13 including several openings 133, 135, 139 formed therein. Figure 1C is a partially exploded perspective view of system 10, wherein a removable access panel 132 is shown as a contoured portion of upper surface 131, which, when exposed, by lifting away a bin 18, that mates therewith, may be removed from another opening 137 formed in upper surface 131. Figure 1C also provides a better view of another panel 134 which may be lifted away from opening 139. According to the illustrated embodiment, openings 139 and 137 provide a user of system 10 with independent access to separate portions of infusion system 10, which are contained within shell 13, for example, to set up and maintain system 10; and openings 133 and 135 provide passageways for tubing lines to pass through shell 13. Figure 1C further illustrates an optional switch 102, which in case of an emergency, may be activated to abort function of system 10. With reference to Figures 1A and 1C, it may be appreciated that an arrangement of features formed in upper surface 131 of shell 13, in conjunction with bin 18, tray 16 and computer 17, provide a relatively ergonomic and organized work area for technical personnel who operate system 10.

[30] Turning now to Figure 1D, a schematic of an infusion circuit 300, which may be incorporated by system 10, is shown. Figure 1D illustrates circuit 300 generally divided into a first part 300A, which includes components mounted outside shell 13, and a second part 300B, which includes components mounted within the interior space surrounded by shell 13. (Parts 300A and 300B are delineated by dotted lines in Figure 1D.) Figure 1D further illustrates second part 300B of circuit 300 including a portion contained within a shielding assembly 200, which is designated schematically as a dashed line. Some embodiments of shielding assembly 200 will be described in greater detail, in conjunction with Figures 2A-B and 3A-B, below.

[31] According to the illustrated embodiment, circuit 300 includes an eluant reservoir 15, for example, a bag, bottle or other container, containing saline as the eluant, which is shown hanging from a post, or hanger 141 above upper surface 131 of shell 13 in Figure 1A; a syringe pump 33, for pumping the eluant from reservoir 15, and a pressure syringe 34, for monitoring pumping pressure; a filter 37, which may also serve as a bubble trap, for the pumped eluant; a radioisotope generator 21, through which the filtered eluant is pumped to create a radioactive eluate, for example an eluate carrying Rubidium-82 that is generated by the decay of Strontium-82, via elution, within a column of generator 21; and an activity detector 25, for measuring the activity of the eluate discharged from generator 21, in order to provide feedback for directing the flow of the eluate, via a divergence valve 35WP, either to a waste bottle 23 or through a patient line 305p, for example, to inject a dose of the radiopharmaceutical eluate into a patient. With reference back to Figure 1A, patient line 305p is shown extending out from shell 13, through opening 135, to a distal end thereof, which, according to some embodiments, includes a filter. Patient line 305p may be coupled to another line that includes a patient injection needle (not shown). Alternatively, patient line 305p may be coupled to another line (not shown), which extends from a source of another active substance, for example, a stress agent; the other line is coupled to the line that includes the patient injection needle, in order to permit injection of the additional active substance. Figure 1D illustrates an eluant tubing line 301 coupled to reservoir 15 and to pump 33, and, with reference to Figures 1A-B, it may be appreciated that opening 133 provides the passageway for tubing line 301 to enter the interior space surrounded by shell 13. According to some preferred embodiments, opening 133 includes a grommet-type seal that prevents leakage of eluant, which may spill from reservoir 15, into the interior space through opening 133, while allowing a user to assemble tubing line 301 through opening 133. Likewise opening 135, which provides a passageway for patient line 305p, may include a grommet-type seal.

[32] Figure 1D further illustrates another eluant tubing line 302 coupled to pump 33 and a divergence valve 35BG, which may either direct pumped eluant through a tubing line 304, to generator 21, or direct the pumped eluant through a by-pass tubing line 303, directly to patient line 305p. Divergence valve 35BG, as well as divergence valve 35WP, which directs eluate from an eluate tubing line 305 either to a waste line 305w or to patient line 305p, may each be automatically operated by a corresponding servomotor (not shown), coupled to the controller (not shown) of system 10, which controller receives feedback from activity detector 25. When system 10 is operating for automatic infusion, to deliver a dose of radiopharmaceutical to a patient, for example, Rubidium-82 for diagnostic imaging, divergence valve 35BG is initially set to direct eluant to generator 21 and divergence valve 35WP is set to direct eluate from generator into waste bottle 23, until activity detector 25 detects the desired activity of the eluate, at which time the feedback from activity detector 25 causes the controller to direct the corresponding servo-motor to re-set valve 35WP for diverting the flow of eluate into patient line 305p. According to some embodiments, once a prescribed volume of the eluate has passed through patient line 305p, the controller directs the corresponding servomotor to re-set divergence valve 35BG for diverting the flow of eluant through by-pass line 303 and into patient line 305p in order to flush, or push any eluate remaining in patient line 305p into the patient. According to some embodiments, the controller may also direct the corresponding servomotor to re-set divergence valve 35WP back toward waste bottle 23, prior to the flush through by-pass line 303, in order to prevent back flow of eluant, through line 305, toward generator 21.

[33] With further reference to Figure 1D, it may be appreciated that shielding assembly 200 encloses those portions of circuit 300 from which radioactive radiation may emanate, with the exception of that portion of patient line 305p, which must extend out from shielding assembly 200 in order to be coupled to the patient for injection, or in order to be coupled to shielded sample vials, as will be described below. Thus, technical personnel, who operate system 10, are protected from radiation by shielding assembly 200, except at those times when

an infusion is taking place, or when quality control tests require collection of eluate into sample vials. During infusions and quality control test sample collection, all technical personnel are typically in another room, or otherwise distanced from system 10, in order to avoid exposure to radiation during the infusion, and, according to some preferred embodiments of the present invention, system 10 includes at least one means for informing technical personnel that an infusion is about to take place or is taking place. With reference back to Figures 1A and 1C, system 10 is shown including a light projector 100, mounted on post 142. According to the illustrated embodiment, projector 100, projects a light signal upward, for maximum visibility, when pump 33 is pumping eluant and elution is taking place within generator 21, or at all times when pump 33 is pumping eluant. According to some embodiments, the light signal flashes on and off when the eluate is being diverted from generator 21 into waste bottle 23, and the light signal shines steadily when the eluate is being diverted through patient line 305p, or visa versa. According to other embodiments, a projector 100 shines a light having a first color, to indicate that eluate is being diverted to waste bottle 23, and then shines a light having a second, different color, to indicate that eluate is being directed to patient line 305p for infusion. Light projector 100 may further project a more rapidly flashing light, for example, for approximately five seconds, once a peak bolus of radioactivity is detected in the eluate, to provide further information to technical personnel. Alternative means of informing technical personnel that an infusion is taking place may also be incorporated by system 10, for example, including audible alarms or other types of visible or readable signals that are apparent at a distance from system, including in the control room.

[34] When maintenance of system 10 requires the emptying waste bottle 23, relatively easy access to waste bottle 23 is provided through opening 139 in top surface 131 of shell 13. It should be noted that technical personnel are preferably trained to empty waste bottle 23 at times when the eluate, contained in waste bottle 23, has decayed sufficiently to ensure that the radioactivity thereof has fallen below a threshold to be safe. Opening 139 is preferably located at an elevation of

between approximately 2 feet and approximately 3 feet; for example, opening 139 may be at an elevation of approximately 24 inches, with respect to a lower surface of platform 113, or at an elevation of approximately 32 inches, with respect to a ground surface upon which wheels 121, 122 rest. According to the illustrated embodiment, opening 139 is accessed by lifting panel 134; just within opening 139, a shielded lid or door 223 (Figure 2A) may be lifted away from a compartment of shielding assembly 200 that contains waste bottle 23. With further reference to Figure 1C, it may be appreciated that opening 137 provides access to other portions of circuit 300 for additional maintenance procedures, such as changing out generator 21 and/or other components of circuit 300, as will be described below.

[35] Figures 1A and 1C further illustrate a pair of relatively shallow external recesses 190, which are formed in upper surface 131 of shell 13, for example, in order to catch any spills from infusion system; one of recesses 190 is shown located in proximity to post, or hanger 141, which holds reservoir 15, and in proximity to opening 133, through which tubing line 301 passes. Another recess 192 is shown formed in upper surface 131; a width and depth of recess 192 may accommodate storage of technical documentation associated with infusion system 10, for example, a technical manual and/or maintenance records, or printouts from printer 117 (Figure 1B). With reference to Figure 1C, upper surface 131 of shell 13 is shown to also include additional recesses 101, which are each sized to hold a shielded test vial, which contains samples from infusion system 10, for example, for breakthrough testing and/or calibration, which will be described in greater detail, below. Additional receptacles 180 are shown formed in bin 18, on either side of a handle 182, which facilitates removal of bin 18 away from shell 13. Technical personnel may, thus, conveniently transport bin 18 to a storage area for a collection of supplies, for example, sharps, gloves, tubing lines, etc..., into one or more receptacles 180 thereof, and/or to a waste container where separate receptacles 180 of bin 18 may be emptied of waste, such as packaging for the aforementioned supplies, for example, deposited therein during infusion procedures.

[36] Figure 2A is a perspective view of shielding assembly 200, according to some embodiments of the present invention. With reference to Figures 1C and 2A, together, it may be appreciated that opening 137, in upper surface 131 of shell 13, provides access to a lid or door 221 of a sidewall 201 of shielding assembly 200, which sidewall 201 encloses a compartment sized to contain a radioisotope generator of system 10, for example, generator 21, previously introduced. According to the illustrated embodiment, opening 137 and door 221 are located at a lower elevation, for example, with respect to platform 113, than are opening 139 and lid 223, which provide access to the compartment being formed by a sidewall 203 of shielding assembly 200 to contain waste bottle 23, as previously described. When panel 132 is separated from shell 13, and door 221 opened, generator 21 may be lifted out from an opening 231 (Figure 3A) which mates with door 221 of sidewall 201. A weight of generator 21, which includes its own shielding, may be between approximately 23 and approximately 25 pounds, thus, according to some preferred embodiments of the present invention, the elevation of each of openings 137 and 231, with respect to the lowermost portion of the cabinet structure, is between approximately 1 foot and approximately 2 feet, in order to facilitate an ergonomic stance for technical personnel to lift generator 21 out from the compartment. According to an exemplary embodiment, when shielding assembly 200 is contained in the cabinet structure of Figure 1A , openings 137 and 231 are located at an elevation of approximately 12 inches, with respect to the lower surface of platform 113, or at an elevation of approximately 19 inches, with respect to the ground surface upon which wheels 121, 122 rest. Figure 1C further illustrates access panel 132 including a security lock 138, which mates with a framework 19 of system 10, shown in Figure 2B, in order to limit access to generator 21.

[37] Figures 1C and 2A further illustrate a lid or a door 225 of another sidewall 205 (Figure 3A) of shielding assembly 200, which encloses another compartment that is accessible through opening 137 of shell 13, and which is located adjacent the compartment enclosed by sidewall 201. Each of doors 221, 225 are shown being attached by a corresponding hinge H, and another door 227 is shown

attached to sidewall 203 by another hinge H. Figure 2A illustrates each of lid 223 and doors 221, 225, 227 including a handle 232, 212, 252 and 272, respectively, for moving lid 223 and doors 221, 225, 227, in order to provide access to the corresponding compartments, which can be seen in Figures 3A-B. Figure 2A further illustrates optional thumb screws 290, one securing lid 223 to sidewall 203 and another securing door 221 to sidewall 201, or other means for securing the doors, which are known to those skilled in the art, may be incorporated. Each sidewall 201, 203, 205 and the corresponding lid/door 223, 221, 225, 227 thereof may be individually cast from 3% antimony lead, or from other known shielding materials, and then assembled together according to methods known to those skilled in the art.

[38] According to the illustrated embodiment, doors 221, 225 are hinged to open in an upward direction, per arrows D and C, and, with reference back to Figure 1C, a latch component 191 is provided to hold each of doors 221, 225 in an opened position, thereby, preventing doors 221, 225 from falling closed, which could pinch/crush fingers of technical personnel and/or tubing lines of circuit 300, when in the midst of a maintenance procedure. Figure 2B is a perspective view of framework 19 of the cabinet structure of system 10, according to some embodiments, to which latch component 191 is mounted; Figure 2B includes an enlarged detailed view of latch component 191, according to some embodiments. Figure 2B illustrates latch component 191 including a first pin 193, corresponding to door 225, and a second pin 195, corresponding to door 221; each pin 193, 195 includes a lever end 193A, 193B, respectively, and a holding end 193B, 195B, respectively. An edge of each door 221, 225, upon opening of doors 221, 225, may push past the holding end 195B, 193B of the corresponding pin 195, 193, in a first direction, per arrow F, and then may rest against a respective side S95 and S93 of each end 195B, 193B, until the corresponding lever end 195A, 193A is rotated in a counter-clockwise direction, per arrow cc, thereby moving the corresponding holding end 193B, 195B to make way for the closing of doors 221, 225. Doors 221, 225 being held by latch component 191 in an open position may be seen in Figure 3A.

[39] With further reference to Figure 2A, according to some preferred embodiments of the present invention, an edge of door 225 overlaps door 221 to prevent door 221 from being opened, per arrow D, if door 225 is not opened, per arrow C; and an edge of door 227 overlaps an edge of door 225 to prevent door 225 from being opened if door 227 is not opened, per arrow B; and an edge of lid 223 overlaps door 227 to prevent door 227 from being opened if lid 223 is not opened, per arrow A. Thus, access to the compartment enclosed by sidewall 201 and containing generator 21 is only systematically allowed through a sequential opening of lid 223 and doors 227, 225, 221, since, when generator 21 is replaced it is typically desirable to also replace those portions of circuit 300 which are shielded behind lid 223 and doors 227, 225. The routing of these portions of circuit 300 will be described in conjunction with Figures 3A-C.

[40] Figure 3A is another perspective view of shielding assembly 200, according to some embodiments of the present invention. In Figure 3A, lid 223 and doors 221, 225, and 227 are opened to provide a view into openings 233, 235 and 231 of sidewalls 203, 205 and 201, respectively, and into a passageway 207, which is formed in sidewall 203, opposite the compartment, which contains waste bottle 23. Passageway 207 is shown extending vertically along sidewall 203 and having a grooved extension 213 formed in a perimeter surface of opening 233. An optional retaining member 237, for example, formed from an elongate strip of resilient plastic having a generally c-shape cross-section, is shown being mounted along a length of passageway 207 to hold lines 305w and 305p in place within passageway 207. Figure 3A further illustrates a pair of passageways 251b and 251g, which are formed as grooves in a portion of sidewall 205, and another pair of passageways 215i and 215o, which are formed as grooves in a portion of sidewall 201. A routing of portions of tubing circuit 300 (Figure 1D) through passageways 207, 251b, 251c, 215i and 215o is shown in Figure 3B.

[41] Figure 3B illustrates tubing line 304 being routed through passageways 251g and 215i, eluate tubing line 305 being routed through passageway 215o, and both waste line 305w and patient line 305p being routed along passageway 207. Waste line 305w further extends through grooved extension 213 to waste bottle

23, and patient line 305p further extends outward from shielding assembly 200, for example, to extend out through opening 135 in upper surface 131 of shell 13 (Figure 1A). According to the illustrated embodiment, each passageway formed in shielding assembly 200, by being accessible along a length thereof, can facilitate a relatively easy routing of the corresponding tubing line therethrough, when the corresponding lid/door is open, and a depth of each passageway prevents pinching and/or crushing of the corresponding tubing line routed therethrough, when the corresponding lid/door is closed down thereover.

[42] Figure 3A further illustrates sidewall 205 including a valve actuator receptacle 253, into which divergence valve 35WP is mounted, to be controlled by one of the servomotors (not shown) of system 10, and an opening 325 for activity detector 25. Activity detector 25 is mounted in a shielded well 255 that extends downward from opening 325 (shown in Figure 3B), and, with reference to Figure 3B, tubing line 305 passes over opening 325 so that detector 25 can detect an activity of the eluate, which passes therethrough. According to some embodiments, the positioning, within the compartment enclosed by sidewall 205, of the components of the portion of infusion circuit 300 which are shown routed therein, is facilitated by providing the components mounted in a frame 39 as a disposable subassembly 390, an embodiment of which is illustrated by Figures 3C-D.

[43] Figure 3C is a perspective view of subassembly 390, and Figure 3D is a perspective view of frame 39. According to the embodiment illustrated by Figure 3D, frame 39 is formed from mating trays 39A, 39B, for example, formed from a thermoformed plastic, which fit together to capture, therebetween, and hold, in fixed relation to a perimeter edge of frame 39, divergence valve 35WP and portions of eluant tubing line 304, by-pass tubing line 303, eluate tubing line 305, waste line 305w and patient line 305p. Figure 3C illustrates the perimeter edge divided into a first side 391, a second side 392, opposite first side 391, a third side 393, extending between first and second sides 391, 392, and a fourth side 394, opposite third side 393. Although Figure 3D shows trays 39A, 39B individually formed for fitting together, according to alternate embodiments,

mating trays of frame 39 may be parts of a continuous sheet of plastic folded over on itself.

[44] According to the illustrated embodiment, an end 404A, of eluant line 304, and an end 403, of by-pass line 303 extend from third side 393 of frame 39 to couple with divergence valve 35BG and an upstream section of eluant tubing line 302. Figure 3C further illustrates an opposite end 404B of eluant line extending from first side 391 of frame 39, alongside a similarly extending end 405 of eluate line 305, and ends 406 and 407 of patient line 305p and waste line 305w, respectively, extending from second side 392 of frame 39. Although ends 406, 407 are shown extending upward from tray 39a, as they would within shielding assembly 200, it should be appreciated that the tubing lines of circuit 300 are preferably flexible and would drop down under their own weight rather than extending upward, as shown, if not supported. Referring back to Figure 1D, in conjunction with Figure 3C, it can be seen that fittings are provided for coupling subassembly 390 into circuit 300: a first fitting 311 couples the section of eluant line 302 to filter 37; a second fitting 312 couples eluant line 304 to an inlet port of generator 21; a third fitting 313, which may incorporate a check valve, couples eluate line 305 to an outlet port of generator 21; a fourth fitting 314 couples waste line 305w to waste bottle 23; and a fifth fitting 315 couples patient line 305p to an extension thereof, which extends outside shell 13 (designated by the dotted line). Each of the fittings 311, 312, 313, 314, 315 may be of the Luer type, or any other suitable type that is known to those skilled in the art.

[45] As previously mentioned, when generator 21 is replaced, it is typically desirable to also replace those portions of circuit 300 which are shielded behind lid 223 and doors 227, 225, and, in those instances wherein system 10 is moved to a new site each day, these portions may be replaced daily. Thus, according to the illustrated embodiment, these portions are conveniently held together by frame 39, as subassembly 390, in order to facilitate relatively speedy removal and replacement, while assuring a proper assembly orientation, via registration with features formed in sidewall 205 (Figure 3A), for example: registration of divergence valve 35WP with valve actuator receptacle 253, registration of tubing

line ends 403 and 404A with passageways 251b and 251g, respectively, registration of tubing line ends 404B and 405 with passageways 215i and 215o, respectively, and registration of tubing line ends 406 and 407 with passageway 207.

[46] With further reference to Figure 3B, other portions of tubing circuit 300 are shown. Figure 3B illustrates eluant tubing line 301 extending from reservoir 15, outside of shell 13 (Figure 1A), to syringe pump 33, which is mounted to an actuating platform 433. According to the illustrated embodiment, platform 433 is actuated by another servomotor (not shown) of system 10, which is controlled by the controller and computer 17 of system 10, to cause a plunger of pump 33 to move, per arrow I, so as to draw in eluant, from reservoir 15, through tubing line 301, and then to cause the plunger to move in the opposite direction so as to pump the eluant, through tubing line 302, to either generator 21 or to by-pass line 303. Although the illustrated embodiment includes syringe pump 33, other suitable pumps, known to those skilled in the art, may be substituted for pump 33, in order to draw eluant from reservoir 15 and to pump the eluant throughout circuit 300. Although not shown, it should be appreciated that divergence valve 35BG is fitted into another valve actuating receptacle mounted within shell 13 and coupled to yet another servomotor (not shown) of system 10.

[47] Figure 3B further illustrates a filter holder 317 that is mounted alongside an interior surface of shell 13 to hold filter 37 (Figure 1D) of tubing line 302. Filter holder 317, like frame 39 for subassembly 390, may be formed from a thermoformed plastic sheet; holder 317 may have a clam-shell structure to enclose filter 37 in an interior space, yet allow tubing line 302, on either side of filter 37, to extend out from the interior space, in between opposing sides of the clam-shell structure. Holder 317 is shown including an appendage 307 for hanging holder 317 from a structure (not shown) inside shell 13.

[48] Turning now to Figures 4-9C details concerning computer-facilitated operation of system 10 will be described, according to some embodiments of the present invention. As previously mentioned, and with reference back to Figure 1A, computer 17 of system 10 includes monitor 172, which, preferably, not only

displays indications of system operation to inform a user of system 10, but is also configured as a touch screen to receive input from the user. It should be understood that computer 17 is coupled to the controller of system 10, which may be mounted within the interior space surrounded by shell 13. Although Figure 1A shows computer 17 mounted to post 142 of system 10, for direct hardwiring to the controller of system 10, according to some alternate embodiments, computer 17 is coupled to the controller via a flexible lead that allows computer 17 to be positioned somewhat remotely from those portions of system 10, from which radioactive radiation may emanate; or, according to some other embodiments, computer 17 is wirelessly coupled, for example, via two-way telemetry, to the controller of system 10, for even greater flexibility in positioning computer 17 away from radioactive radiation.

[49] According to some preferred embodiments, computer 17 is pre-programmed to guide the user, via monitor 172, through procedures necessary to maintain system 10, to perform quality control tests on system 10, and to operate system 10 for patient infusions, as well as to interact with the user, via the touch-screen capability of monitor 172, according to preferred embodiments, in order to track volumes of eluant and eluate contained within system 10, to track a time from completion of each elution performed by system 10, to calculate one or more system parameters for the quality control tests, and to perform various data operations. It should be understood that screen shots shown in Figures 4-9C are exemplary in nature and are presented to provide an outline of some methods of the present invention in which computer 17 facilitates the aforementioned procedures, without limiting the scope of the invention to any particular computer interface format.

[50] Figure 4 is a screen shot of a main menu 470, which is presented by computer 17 on monitor 172, according to some embodiments. Main menu 470 includes a listing of each computer-facilitated operation that may be selected by the user, once the user has logged on.

[51] Figure 5A is a schematic showing a series of screen shots which includes a log in screen 570. After the user enters the appropriate information into data entry fields of log in screen 570, computer 17 presents a request for the user to confirm the volume of eluant that is within reservoir 15 (e.g. saline in saline bag), via a screen 571, and then brings up main menu 470. According to some embodiments, when the user touch-selects the data entry fields of screen 570 or 571, or of any of the other screens presented herein, below, a virtual keyboard is displayed for touch-select data entry into the selected data entry field; alternately, computer 17 may be augmented with another type of device for user data entry, examples of which include, without limitation, a peripheral keyboard device, a storage medium (i.e. disk) reader, a scanner, a barcode reader (or other reader of encoded information), a hand control (i.e. mouse, joy stick, etc...).

[52] If the user determines that the volume of eluant/saline is insufficient, the user selects a menu item 573, to replace the saline bag, which leads computer 17 to prompt the user to enter a quantity of saline contained by the new saline bag, via a screen 574. Thus, computer 17 uses either the confirmed eluant/saline volume, via screen 571, or the newly entered eluant/saline volume, via screen 574, as a baseline from which to track depletion of reservoir volume, via activations of pump 33, in the operation of system 10. With reference to Figure 5B, during the operation of system 10, when computer 17 detects that the eluant reservoir/saline bag has been depleted to a predetermined volume threshold, computer 17 warns the user, via a screen 577. If the user has disregarded screen 577 and continues to deplete the saline bag, computer 17 detects when the saline bag is empty and provides indication of the same to the user, via a screen 578. To replenish the reservoir/saline bag, the user may either refill the reservoir/bag or replace the empty reservoir/bag with a full reservoir/bag. According to some embodiments, system 10 automatically precludes any further operation of the system until the reservoir is replenished.

[53] In addition to tracking the volume of eluant in reservoir 15, computer 17 also tracks a volume of the eluate which is discharged from generator 21 into waste bottle 23. With reference to Figure 5C, an item 583 is provided in main menu

470, to be selected by the user when the user empties waste bottle 23. When the user selects item 583, computer 17 presents a screen 584, by which the user may effectively command computer 17 to set a waste bottle level indicator to zero, once the user has emptied waste bottle 23. Typically, the user, when powering up system 10 for operation, each day, will either empty waste bottle 23, or confirm that waste bottle 23 was emptied at the end of operation the previous day, and utilize screen 584 to set the waste bottle level indicator to zero. Thus, computer 17, can track the filling of waste bottle 23 via monitoring of the operation of pump 33 and divergence valve 35WP, and provide an indication to the user when waste bottle 23 needs to be emptied, for example, via presentation of screen 584, in order to warn the user that, unless emptied, the waste bottle will overflow. According to some embodiments, system 10 automatically precludes any further operation of the system until the waste bottle is emptied.

[54] In addition to the above maintenance steps related to eluant and eluate volumes of system 10, the user of system 10 will typically perform quality control tests each day, prior to any patient infusions. With reference to Figure 6, according to preferred methods, prior to performing the quality control tests (outlined in conjunction with Figures 7A-C and 8A-B), the user may select an item 675 from main menu 470, in order to direct system 10 to wash the column of generator 21. During the generator column wash, which is performed by pumping a predetermined volume of eluant, for example, approximately 50 milliliters, through generator 21 and into waste bottle 23, computer 17 provides an indication, via a screen 676, that the wash is in progress. Also, during the generator column wash, the system may provide a signal to indicate that eluate it being diverted to waste bottle 23, for example, light projector 100 (Figure 1C) may project a flashing light signal, as previously described.

[55] Figure 6 further illustrates a screen 677, which is presented by computer 17 upon completion of the column wash, and which provides an indication of a time lapse since the completion of the wash, in terms of a time countdown, until a subsequent elution process may be effectively carried out. While screen 677 is

displayed, system 10 may be refilling, from reservoir 15, pump 33, which has a capacity of approximately 55 milliliters, according to some embodiments. According to some preferred embodiments of the present invention, computer 17 starts a timer once any elution process is completed and informs the user of the time lapse, either in terms of the time countdown (screen 677), or in terms of a time from completion of the elution, for example, as will be described in conjunction with Figure 7B. According to an exemplary embodiment, wherein generator 21 is the CardioGen-82® that yields a saline solution of Rubidium-82, produced by the decay of Strontium-82, via the elution, a time required between two effective elution processes is approximately 10 minutes.

[56] Once the appropriate amount of time has lapsed, after the elution process of generator column wash, a first quality control test may be performed. With reference to Figure 7A, the user may select, from main menu 470, an item 773A, which directs computer 17 to begin a sequence for breakthrough testing. In conjunction with the selection of item 773A, the user attaches a needle to an end of patient line 305p and inserts the needle into to a test vial, for the collection of an eluate sample therefrom, and, according to Figure 7A, computer 17 presents a screen 774, which instructs the user to insert the test vial into a vial shield, which may be held in recess 101 of shell 13 (Figure 1C).

[57] Figure 7A further illustrates a subsequent screen 775, by which computer 17 receives input, from the user, for system 10 to start the breakthrough elution, followed by a screen 776, which provides both an indication that the elution is in progress and an option for the user to abort the elution. As previously described, the system may provide a signal to indicate that elution is in progress, for example, light projector 100 (Figure 1C) may project a flashing light signal during that portion of the elution process when eluate is diverted from generator 21 through waste line 305w and into waste bottle 23, and then a steady light signal during that portion of the elution process when the eluate is diverted from generator 21 through patient line 305p and into the test vial, for example, once activity detector 25 detects a dose rate of approximately 1.0 mCi/sec in the eluate discharged from generator 21. Another type of light signal, for example,

the more rapidly flashing light, as previously described, may be projected when a peak bolus of radioactivity is detected in the eluate.

[58] Upon completion of the elution process for breakthrough testing, computer 17 presents a screen 777, shown in Figure 7B, which, like screen 677, provides an indication of a time lapse since the completion of the elution, but now in terms of a time since completion of the breakthrough elution process. When the user transfers the vial containing the sample of eluate into a dose calibrator, to measure the activity of the sample, the user may make a note of the time lapse indicated on screen 777. With further reference to Figure 7B, once the user has received the activity measure from the dose calibrator, the user proceeds to a screen 778, which includes data entry fields for the activity measure and the time between that at which the dose calibrator measured the activity of the sample and that at which the elution was completed. The user may enter the data via the touch-screen interface of monitor 172, or via any of the other aforementioned devices for user data entry. According to some alternate embodiments, computer 17 may receive the data, electronically, from the dose calibrator, either via wireless communication or a cable connection.

[59] After the data is entered by the user, computer 17 presents screen 779, from which the user moves back to main menu 470 to perform a system calibration, for example, as will be described in conjunction with Figures 8A-B, although the breakthrough testing is not completed. With reference back to Figure 7A, an item 773B is shown, somewhat faded, in main menu 470; item 773B may only be effectively selected following the completion of steps for item 773A, so as to perform a second stage of breakthrough testing. In the second stage, the breakthrough of the sample of eluate collected in the test vial for the breakthrough testing is measured, at a time of approximately 60 minutes from the completion of the elution that produced the sample. With reference to Figure 7C, after the user has selected item 773B from main menu 470, in order to direct computer 17 to provide breakthrough test results, a screen 781 is displayed. Screen 781 includes, for reference, the values previously entered by the user in screen 778, along with another pair of data entry fields into which the user is

instructed to enter the breakthrough reading of the sample at 60 minutes and the background radiation reading, respectively. After the user enters this remaining information, as described above, computer 17 may calculate and then display, on a screen 782, the breakthrough test results. According to the illustrated embodiment, computer 17 also displays on screen 782 pre-programmed allowable limits for the results, so that the user may verify that the breakthrough test results are in compliance with acceptable limits, before moving on to a patient infusion. According to some embodiments, system 10 will not allow an infusion if the results exceed the acceptable limits, and may present a screen explaining that the results are outside the acceptable limits; the screen may further direct the user to contact the generator supplier, for example, to order a replacement generator.

[60] With reference to Figure 8A, during the aforementioned 60 minute time period, while waiting to complete the breakthrough testing, the user may perform calibration by selecting item 873 from main menu 470. Upon selection of item 873, computer 17 presents a screen 874, which instructs the user to insert a new test vial into an elution vial shield. In addition to placing the vial in the shield, the user, preferably, replaces patient line 305p with a new patient line, and then attaches a needle to the end of the new patient line for insertion into the test vial, in order to collect an eluate sample therefrom. After performing these steps, the user may move to screen 875, wherein a plurality of data entry fields are presented; all or some of the fields may be filled in with pre-programmed default parameters, which the user has an option to change, if necessary. Once the user confirms entry of desired parameters for the calibration, the user may enter a command, via interaction with a subsequent screen 876, to start the calibration elution.

[61] With reference to Figure 8B, after computer 17 starts the elution process, a screen 87 informs the user that the calibration elution is in progress and provides an option to abort the elution. As previously described, the system may provide an indication that elution is in progress, for example, light projector 100 (Figure 1C) may project a flashing light signal during that portion of the elution process

when eluate is diverted from generator 21 through waste line 305w and into waste bottle 23, and then a steady light signal during that portion of the elution process when activity detector 25 has detected that a prescribed dose rate threshold is reached, for example, 1.0 mCi/sec, and the eluate is being diverted from generator 21, through the new patient line, and into the test vial. Another type of light signal, for example, the more rapidly flashing light, as previously described, may be projected when a peak bolus of radioactivity is detected in the eluate. Upon completion of the elution process for calibration, computer 17 presents a screen 878, which provides an indication of a time lapse since the completion of the elution, in terms of a time since completion of the calibration elution process. When the user transfers the vial containing the sample of eluate into the dose calibrator, to measure the activity of the sample, the user may make a note of the time lapse indicated on screen 878. With further reference to Figure 8B, once the user has received the activity measure from the dose calibrator, the user proceeds to a screen 879, which includes data entry fields for the activity measure and the time, with respect to the completion of elution, at which the dose calibrator measured the activity of the sample. Once the data is input by the user, as described above, computer calculates a calibration coefficient, or ratio, and presents the ratio on a screen 880. According to Figure 8B, screen 880 further provides an indication of a desirable range for the calibration ratio and presents an option for the user to reject the calculated ratio, in which case, the user may instruct computer 17 to recalculate the ratio.

[62] With reference to Figure 9A, upon completion of the above-described quality control tests, the user may select an item 971, from main menu 470, in order to direct system 10 to begin a procedure for the generation and automatic infusion of a radiopharmaceutical into a patient. As previously described, system 10 infuses the patient with the radiopharmaceutical so that nuclear diagnostic imaging equipment, for example, a PET scanner, can create images of an organ of the patient, which absorbs the radiopharmaceutical, via detection of radioactive radiation therefrom. According to Figure 9A, upon selection of item 971, computer 17 presents a screen 972 which includes a data entry field for a

patient identification number. This identification number that is entered by the user is retained by computer 17, in conjunction with the pertinent system parameters associated with the patient's infusion. After the user enters the patient identification number, computer 17 directs, per a screen 973, the user to attach a new patient line and to purge the patient line of air. A subsequent screen 974 presented by computer 17 includes data entry fields by which the user may establish parameters for the automatic infusion; all or some of the fields may be filled in with pre-programmed default parameters, which the user has an option to change, if necessary.

[63] With reference to Figure 9B, if pump 33 does not contain enough eluant/saline for the patient infusion, computer 17 will present a warning, via a screen 901, which includes an option for the user to direct the refilling of pump 33, via a subsequent screen 902. Once pump 33 has been filled, computer 17 presents an indication to the user, via a screen 903. According to some embodiments, if the user does not re-fill pump 33, yet attempts to proceed with an infusion, system 10 will preclude the infusion and present another screen, that communicates to the user that no infusion is possible, if the pump is not refilled, and asking the user to refill the pump, as in screen 901. When pump 33 contains a sufficient volume of eluant for the patient infusion, computer 17 presents a screen 975, which is shown in Figure 9C, and allows the user to enter a command for system 10 to start the patient infusion. During the infusion, computer 17 provides the user with an indication that the infusion is in process and with a option for the user to abort the infusion, via a screen 976. As previously described, the system may provide an indication that an elution is in progress, for example, light projector 100 (Figure 1C) may project a flashing light signal during that portion of the elution process when eluate is diverted from generator 21 through waste line 305w and into waste bottle 23, and then a steady light signal during that portion of the elution process when activity detector 25 has detected that a prescribed dose rate threshold is reached, for example, 1.0 mCi/sec, and the eluate is being diverted from generator 21, through the new patient line for infusion into the patient. Another type of light signal, for example,

the more rapidly flashing light, previously described, may be projected when a peak bolus of radioactivity is detected in the eluate. At the completion of the infusion, a screen 977 is displayed by computer 17 to inform the user of the completion of the infusion and a time since the completion. Computer 17 also displays a summary of the infusion, per screen 978.

[64] Printer 117 (Figure 1B) may be activated to print out a hard copy of the infusion summary, on which the patient identification number and pertinent system parameters are also printed, for reference. Alternatively, or in addition, according to some embodiments, the summary of the infusion, which includes the patient identification number and pertinent system parameters, may be downloaded onto a computer readable storage device to be transferred to one or more remote computers and/or automatically transferred thereto, via wireless communication or a cable connection. The one or more remote computers may be included, for example, in a hospital information system, and/or an inventory system, and/or a billing system, and/or in a medical imaging system. With reference back to Figure 9A the user may select an item 995, from main menu 470, in order have system 10 perform data operations, such as, archiving a data base of patient infusion information and quality control test results, transmitting patient infusion summary records to USB mass storage devices, and various types of data filtering, for example, according to date ranges and/or patient identification numbers, for example, to search for a particular set of data and/or to compile a summary report of related sets of data.

[65] Turning now to Figure 10, an item 981 for computer-facilitated purging of the tubing lines of system 10 is shown included in main menu 470. When a user selects item 981, computer 17 guides the user to select either an air purge or a saline purge. The direction provided by computer 17 is not explicitly laid out herein, for a saline purge, as procedures for saline purging should be readily apparent to those skilled in the art, with reference to the schematic of infusion circuit 300 shown in Figure 1D. A saline purge of circuit 300 is desired to assure that all the air is removed from circuit 300 when a new generator and/or a new complete or partial tubing set is installed. An air purge of the tubing lines of

circuit 300 may be performed after removing reservoir 15, by-passing generator 21, by connecting tubing line 304 to tubing line 305, and coupling patient line 305p to a vial, for example, as is directed by the computer interface, in screens 983 and 984 shown in Figure 10. The air purge is desirable for blowing out the tubing lines, thereby removing all remaining eluant and eluate, prior to installing a new generator and/or prior to transporting system 10 from one site to another. If generator 21 is not depleted and will be used in system 10 at the new site, it is important to by-pass the generator prior to purging the tubing lines of circuit 300 with air, so that air is not blown across the generator, since air through generator 21 may compromise both the function and the aseptic nature of generator 21.

[66] According to preferred embodiments, once the user has followed the instructions presented in screens 983 and 984 and selects to start the air purge, for example, via screen 985, computer 17 directs the controller of system 10 to carry out a complete air purge, in which pump 33 and divergence valves 35BG and 35WP are automatically controlled. The automated air purge preferably includes the following steps, which may be best understood with reference to tubing circuit 300 in Figure 1D: pumping any remaining volume of eluant left in pump 33, through lines 302, 304, 305 and 305w, to waste bottle 23; refilling pump 33 with air and pumping the air through lines 302, 304, 305 and 305w, into waste bottle 23 (lines 304 and 305 have been previously connected directly to one another, in order to by-pass generator 21; if generator 21 is depleted and will be replaced with a new generator, pumping air through generator 21 may be acceptable); refilling pump 33 with air and then pumping a portion of the air through lines 302, 304, 305 and 305p, into the vial, and then a remaining portion of the air through lines 302, 304, 303 and 305p, into the vial. With reference to Figure 1D and the previous description of divergence valves 35BG, 35WP, it should be understood how divergence valves 35BG, 35WP are automatically controlled to carry out the above steps.

[67] The purge operations, which are facilitated by selecting item 981 from main menu 470, may also be accessed via the selection of an item 991 for generator setup. When the user selects item 991, computer 17 may present an option for

guidance in removing an old, depleted, generator and a set of tubing lines, prior to installing the new generator, or an option to just be guided in the installation of the new generator.

[68] In the foregoing detailed description, the invention has been described with reference to specific embodiments. However, it may be appreciated that various modifications and changes can be made without departing from the scope of the invention as set forth in the appended claims.

We claim:

1. An infusion system comprising:

a cabinet structure including a shell defining an interior space thereof;

an eluant source;

a shielding assembly located within the interior space of the cabinet structure, the shielding assembly including a sidewall defining a plurality of compartments and providing a barrier to radioactive radiation for the compartments, the shielding assembly further including a corresponding plurality of doors, each door, when open, providing access to the corresponding compartment via an opening in the sidewall, and, when closed, providing further barrier to radioactive radiation for the corresponding compartment;

a radioisotope generator contained within a first compartment of the plurality of compartments of the shielding assembly;

an eluant line coupled to the eluant source and to the generator, the eluant line extending from the eluant source to the generator, through the shielding assembly, at a first location between the sidewall and a first door of the plurality of doors, which corresponds to the first compartment;

an eluate line coupled to the generator and extending out from the first compartment and into a second compartment of the plurality of compartments of the shielding assembly, at a second location between the sidewall and both the first door and a second door of the plurality of doors, which corresponds to the second compartment, the second compartment being located immediately adjacent the first compartment;

a patient line coupled to the eluate line, within the second compartment, the patient line extending out from the second compartment at a third location between the sidewall and the second door, and out from the interior space through an opening in the shell of the cabinet structure.

2. The system of claim 1, wherein:
the eluant source comprises a reservoir and a pump;
the reservoir is mounted to the cabinet structure outside the interior space defined by the shell and the pump is mounted within the interior space;
the eluant line includes a first segment coupled to the reservoir and to the pump and a second segment coupled to the pump and to the generator; and
the first segment of the eluant line extends from the reservoir to the pump through another opening in the shell of the cabinet structure.

3. The system of claim 2, wherein at least one of the openings in the shell of the cabinet structure includes a grommet-type seal surrounding the corresponding line that extends therethrough.

4. The system of claim 1, further comprising:
a bypass flush line coupled to the eluant source and coupled to the patient line, within the second compartment;
wherein the flush line extends from the eluant source to the patient line, through the shielding assembly at a fourth location between the sidewall and the second door.

5. The system of claim 1, wherein the eluant line includes a filter, the filter being mounted within the interior space of the cabinet structure.

6. The system of claim 1, further comprising:
a filter holder mounted within the interior space of the cabinet structure; and
wherein the eluant line includes a filter, the filter being housed in the holder.

7. The system of claim 1, further comprising:

a waste bottle contained within a third compartment of the plurality of compartments of the shielding assembly; and

a waste line coupled to the eluate line, within the second compartment, and coupled to the waste bottle, within the third compartment;

wherein the waste line extends out from the second compartment at the third location.

8. The system of claim 7, wherein the waste line extends into the third compartment at a fourth location, the fourth location being between the sidewall and a third door of the plurality of doors, which corresponds to the third compartment.

9. The system of claim 7, wherein:

the plurality of compartments of the shielding assembly further includes a fourth compartment located immediately adjacent the second compartment and the third compartment;

the waste line extends from the second compartment directly into the fourth compartment at the third location, the third location also being between the sidewall and a fourth door of the plurality of doors, which corresponds to the fourth compartment; and

the waste line extends from the fourth compartment directly into the third compartment at a fourth location, the fourth location being between the sidewall and a third door of the plurality of doors, which corresponds to the third compartment.

10. The system of claim 9, further comprising a retaining member mounted within the fourth compartment to hold the waste line in place within the fourth compartment.

11. The system of claim 9, wherein:

the patient line extends from the second compartment directly into the fourth compartment at the third location; and

the patient line extends out from the fourth compartment at a fifth location, the fifth location being between the sidewall and the fourth door.

12. The system of claim 11, further comprising a retaining member mounted within the fourth compartment to hold the waste line and the patient line in place within the fourth compartment.

13. The system of claim 1, wherein:

the plurality of compartments of the shielding assembly further includes a third compartment located immediately adjacent the second compartment;

the patient line extends from the second compartment directly into the third compartment at the third location, the third location also being between the sidewall and a third door of the plurality of doors, which corresponds to the third compartment; and

the patient line extends out from the third compartment at a fourth location, the fourth location being between the sidewall and the third door.

14. The system of claim 13, further comprising a retaining member mounted within the third compartment to hold the patient line in place within the third compartment.

15. The system of claim 1, wherein the opening in the shell of the cabinet structure includes a grommet-type seal surrounding the patient line extending therethrough.

16. A shielding assembly for an infusion system, the shielding assembly comprising:

a sidewall defining a plurality of compartments and providing a radioactive radiation barrier for the compartments;

a first passageway formed in an upper surface of a first portion of the sidewall, the first portion of the sidewall defining a first compartment of the plurality of compartments, the first compartment being sized to contain a radioisotope generator of the infusion system, and the first passageway being sized to accommodate routing of an eluate line from the generator;

a second passageway formed along a second portion of the sidewall, the second portion of the sidewall extending upward relative to the first portion of the sidewall and defining a second compartment of the plurality of compartments, the second compartment being sized to accommodate a waste bottle of the infusion system and the second compartment being located on a side of the second portion of the sidewall that is opposite the second passageway, and the second passageway being sized to accommodate routing of at least one extension of the eluate line from the generator.

17. The shielding assembly of claim 16, wherein the upper surface of the first portion of the sidewall extends about a perimeter of an opening into the first compartment.

18. The shielding assembly of claim 16, wherein the second passageway extends to an upper surface of the second portion of the sidewall, the upper surface of the second portion extending about a perimeter of an opening into the second compartment.

19. The shielding assembly of claim 16, further comprising a retaining member mounted within the second passageway to hold the at least one extension of the eluate line in place within the second passageway.

20. The shielding assembly of claim 16, further comprising:

a third compartment defined by a third portion of the sidewall, the third compartment extending between the first passageway and the second passageway and being sized to hold a portion of an infusion circuit of the infusion system;

wherein the portion of the infusion circuit includes the eluate line, a patient line and a waste line, the patient line and the waste line being coupled to the eluate line within the third compartment; and

the at least one extension of the eluate line includes the patient line and the waste line.

21. The shielding assembly of claim 20, further comprising a third passageway formed in an edge of the third compartment, the third passageway being sized to accommodate routing of an eluant line from an eluant source of the infusion system.

22. The shielding assembly of claim 21, further comprising a fourth passageway formed in the upper surface of the first portion of the sidewall and extending alongside the first passageway, the fourth passageway being sized to accommodate routing of the eluant line to the generator.

23. The shielding assembly of claim 16, further comprising a third passageway formed in the upper surface of the first portion of the sidewall, the third passageway being sized to accommodate routing of an eluant line from an eluant source of the infusion system to the generator.

24. The shielding assembly of claim 23, wherein the third passageway extends alongside the first passageway

25. A shielding assembly for an infusion system, the shielding assembly comprising:

a sidewall defining plurality of compartments and providing a radioactive radiation barrier for the compartments;

a first passageway formed in an upper surface of a first portion of the sidewall, the first portion of the sidewall defining a first compartment of the plurality of compartments, the first compartment being sized to contain a radioisotope generator of the infusion system, and the first passageway being sized to accommodate routing of an eluate line from the generator; and

a second compartment defined by a second portion of the sidewall, the second compartment being sized to hold a portion of an infusion circuit of the infusion system and extending immediately adjacent to the first passageway, and the infusion circuit being an extension of the eluate line from the generator.

26. The shielding assembly of claim 25, further comprising a second passageway formed in an edge of the second compartment, the second passageway being sized to accommodate routing of an eluant line from an eluant source of the infusion system.

27. The shielding assembly of claim 26, further comprising a third passageway formed in the upper surface of the first portion of the sidewall and extending alongside the first passageway, the third passageway being sized to accommodate routing of the eluant line to the generator.

28. The shielding assembly of claim 25, further comprising a second passageway formed in the upper surface of the first portion of the sidewall, the second passageway being sized to accommodate routing of an eluant line from an eluant source of the infusion system to the generator.

29. A disposable infusion circuit subassembly for an infusion system, the assembly comprising:

an eluate line;

a patient line;

a waste line;

a valve member coupling the patient line and the waste line to the eluate line; and

a support frame including a perimeter edge, the support frame holding the valve member and a portion of each of: the eluate line, the patient line and the waste line in approximately fixed relation with respect to the perimeter edge;

wherein the perimeter edge of the support frame is sized to fit within a compartment of a shielding assembly of the infusion system; and

an end of each of the eluate line, the patient line and the waste line extends out from the perimeter edge.

30. The subassembly of claim 29, wherein the end of the eluate line extends out from a first side of the perimeter edge of the support frame, and the end of each of the patient line and the waste line extends out from a second side of the perimeter edge, the second side being opposite the first side.

31. The subassembly of claim 29, further comprising:

an eluant line; and

wherein the support frame further holds a portion of the eluant line in approximately fixed relation with respect to the perimeter edge of the support frame;

opposing ends of the eluant line extend out from the perimeter edge; and

the portion of the eluant line extends between the opposing ends of the eluant line.

32. The subassembly of claim 31, wherein

the end of the eluate line extends out from a first side of the perimeter edge of the support frame, and the end of each of the patient line and the waste line extends out from a second side of the perimeter edge, the second side being opposite the first side;

a first of the opposing ends of the eluant line extends out from a third side of the perimeter edge, the third side extending between the first side and the second side; and

a second of the opposing ends of the eluant line extends out from the first side of the perimeter edge.

33. The subassembly of claim 29, further comprising:

a bypass line coupled to the patient line; and

wherein the support frame further holds a portion of the bypass line in approximately fixed relation with respect to the perimeter edge of the support frame; and

an end of the bypass line extends out from the perimeter edge.

34. The subassembly of claim 33, wherein:

the end of the eluate line extends out from a first side of the perimeter edge of the support frame, and the end of each of the patient line and the waste line extends out from a second side of the perimeter edge, the second side being opposite the first side; and

the end of the bypass line extends out from a third side of the perimeter edge, the third side extending between the first side and the second side.

35. The subassembly of claim 29, wherein the support frame exposes and orients the valve member for interlocking with a valve actuator receptacle within the compartment of the shielding assembly.

36. The subassembly of claim 29, wherein the support frame is formed from at least one thermoformed plastic sheet.

ABSTRACT

Infusion system configurations and assemblies facilitate routing of infusion circuit tubing lines. Tubing lines are routed into and out from compartments of a shielding assembly for the infusion system, at locations which prevent kinking and/or crushing of the lines, and/or provide for ease in assembling the circuit. A plurality of the lines may be held together by a support frame to form a disposable infusion circuit subassembly, that can further facilitate routing of the lines.

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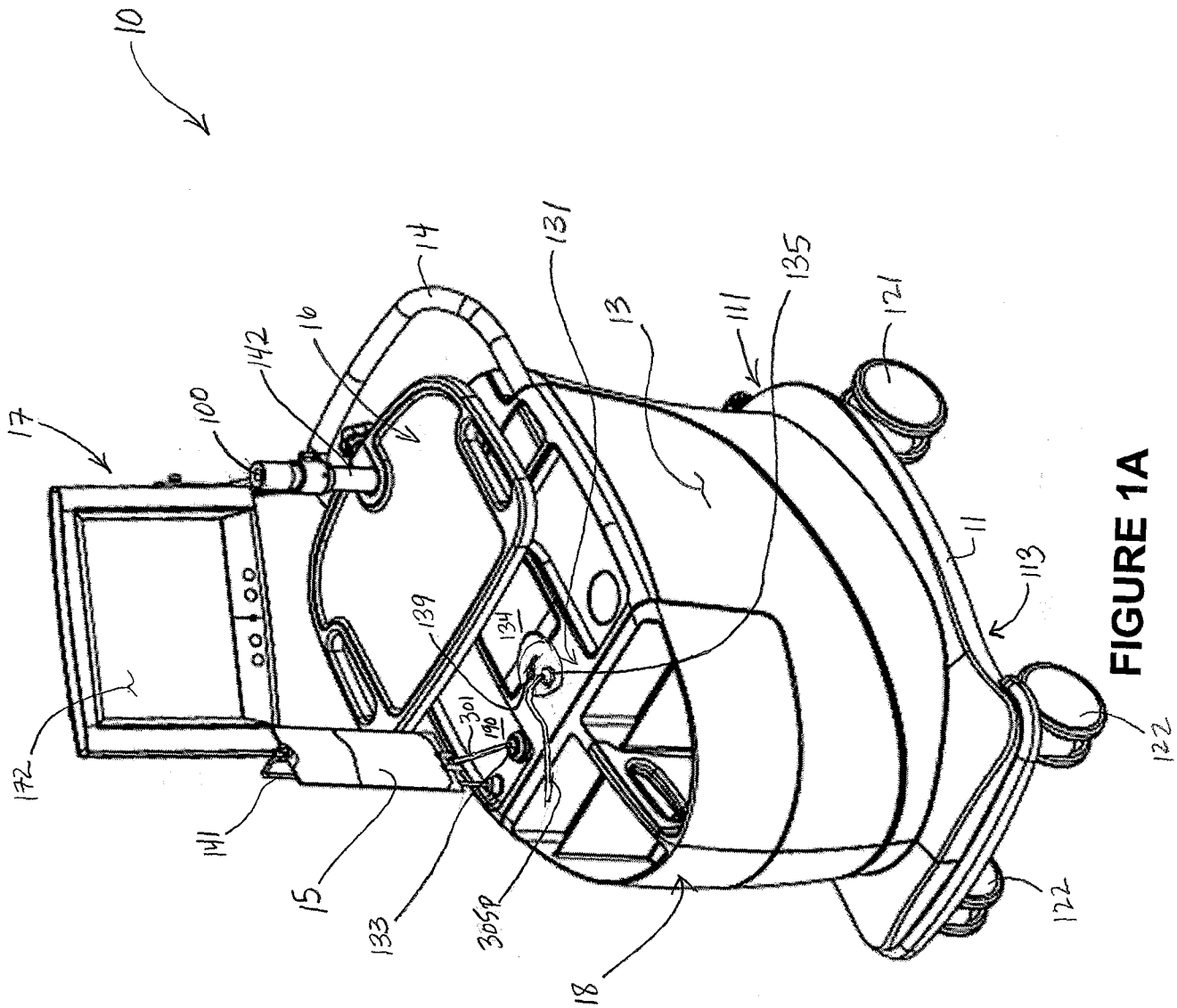
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FIGURE 1A

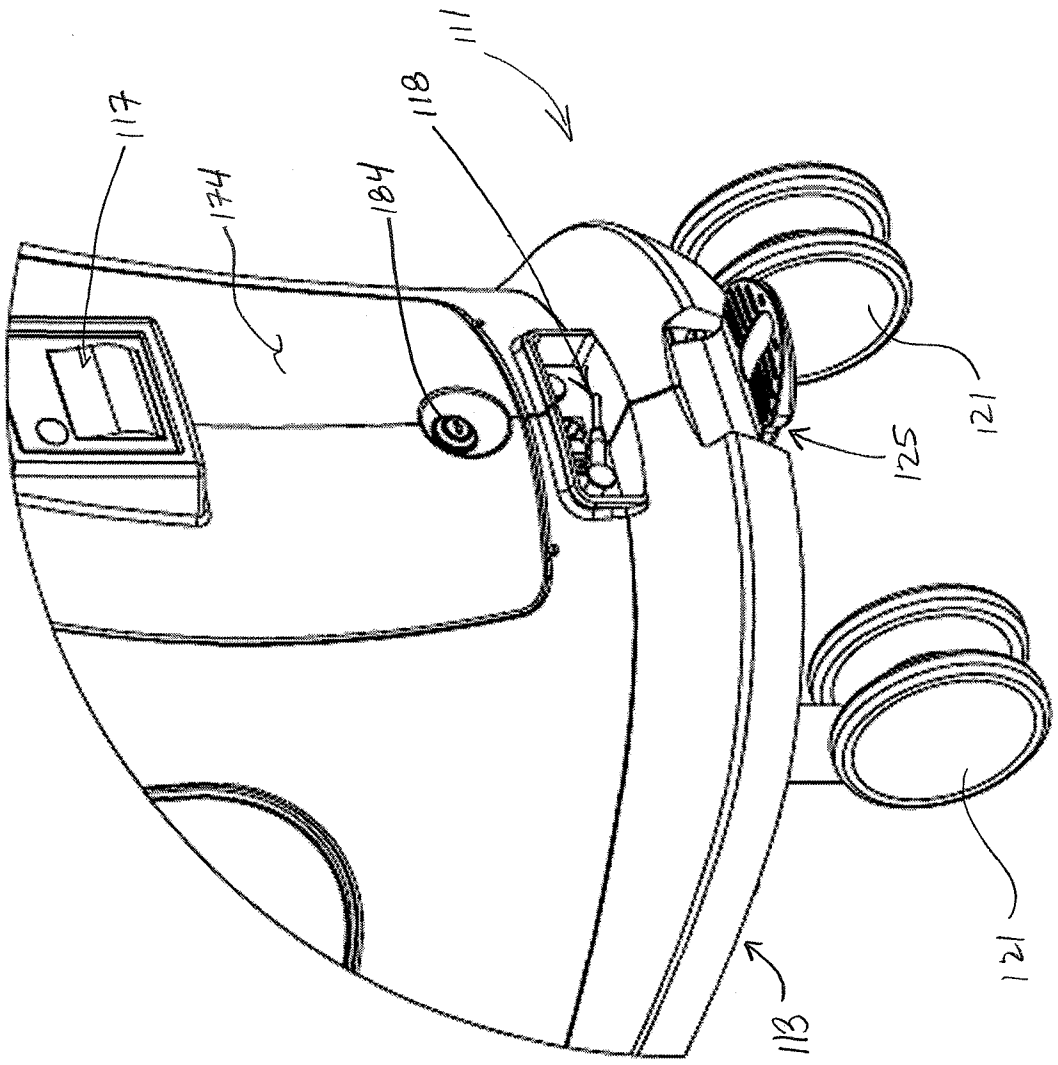

FIGURE 1B

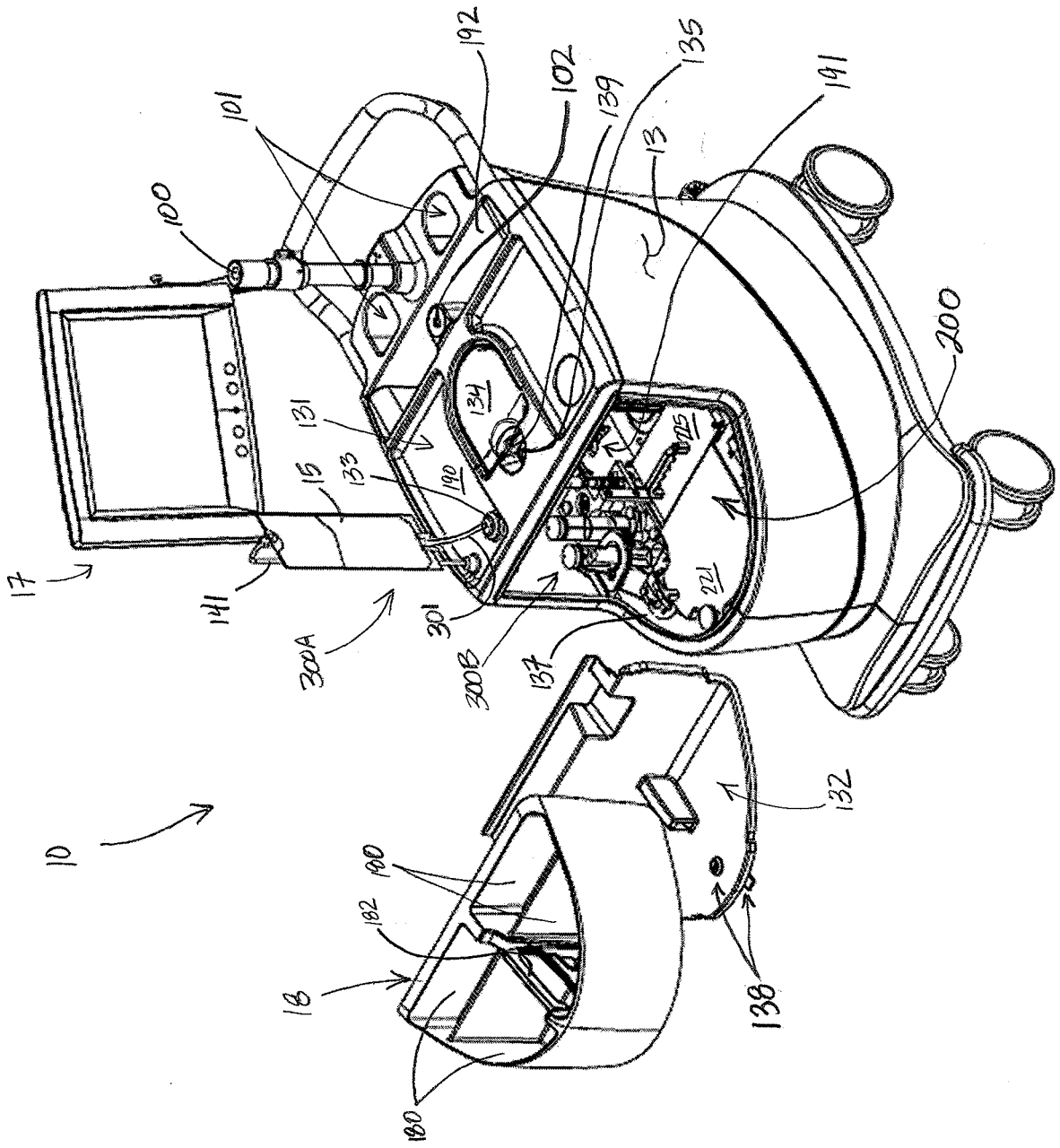
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FIGURE 1C

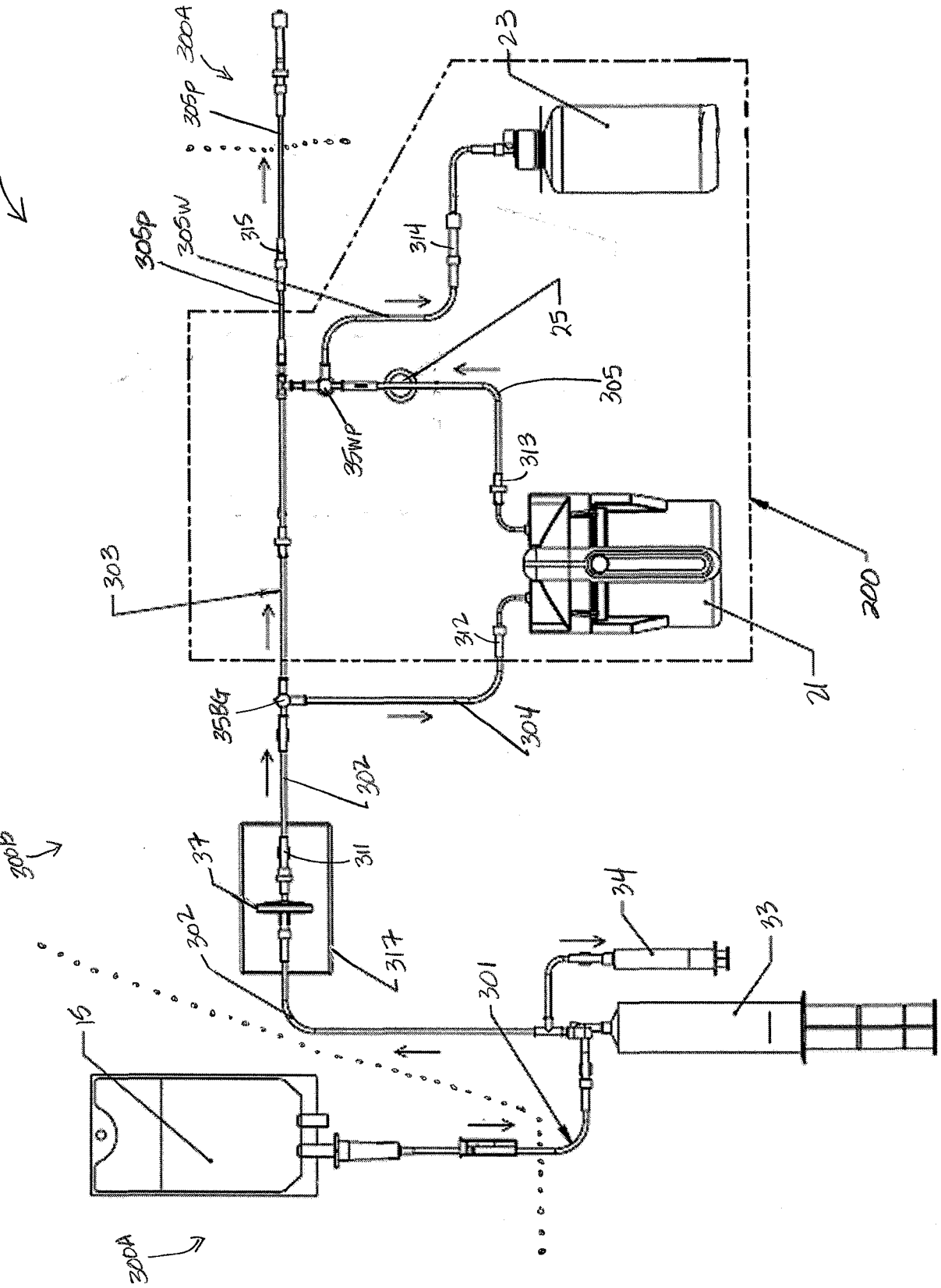
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FIGURE 1D

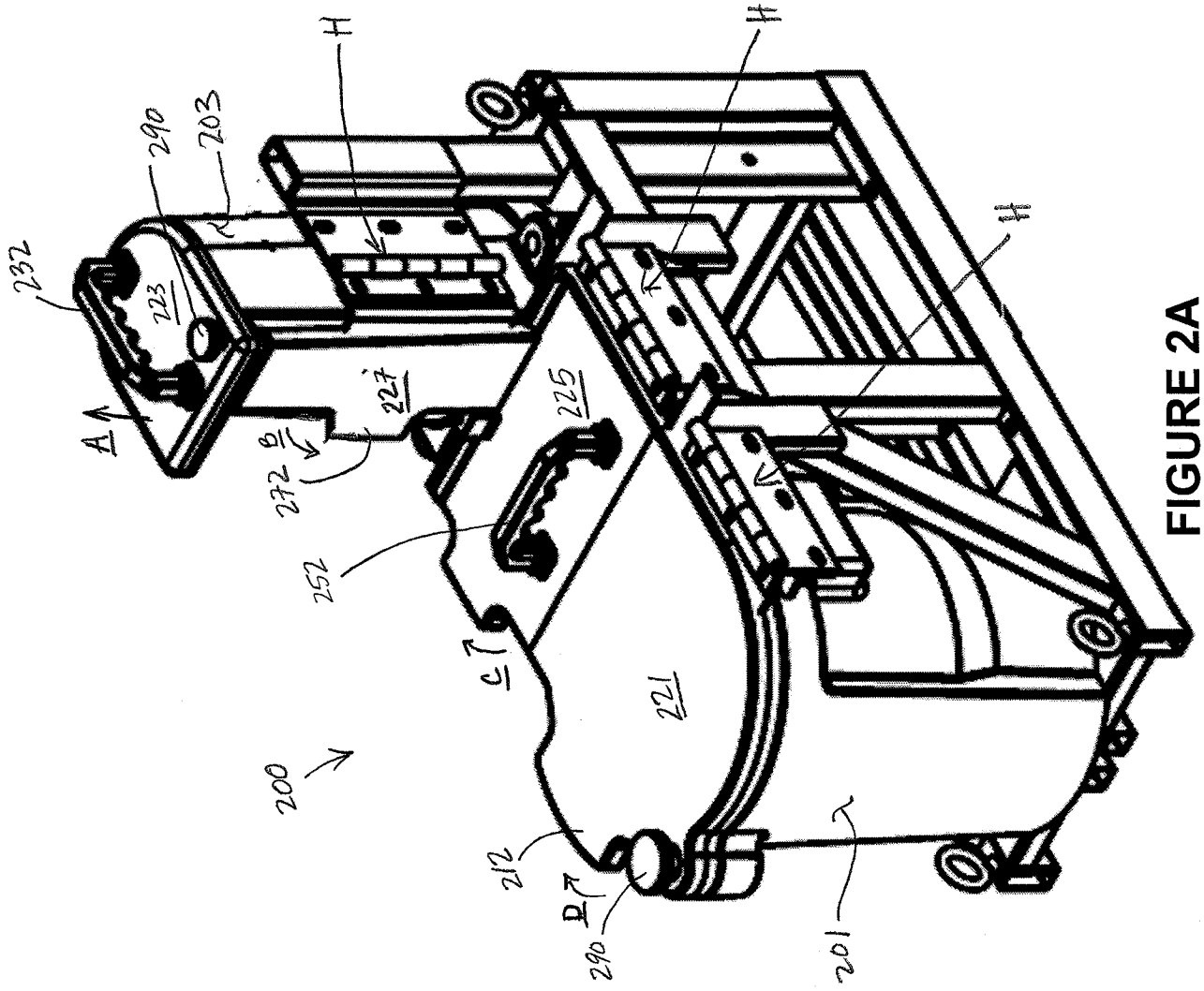


FIGURE 2A

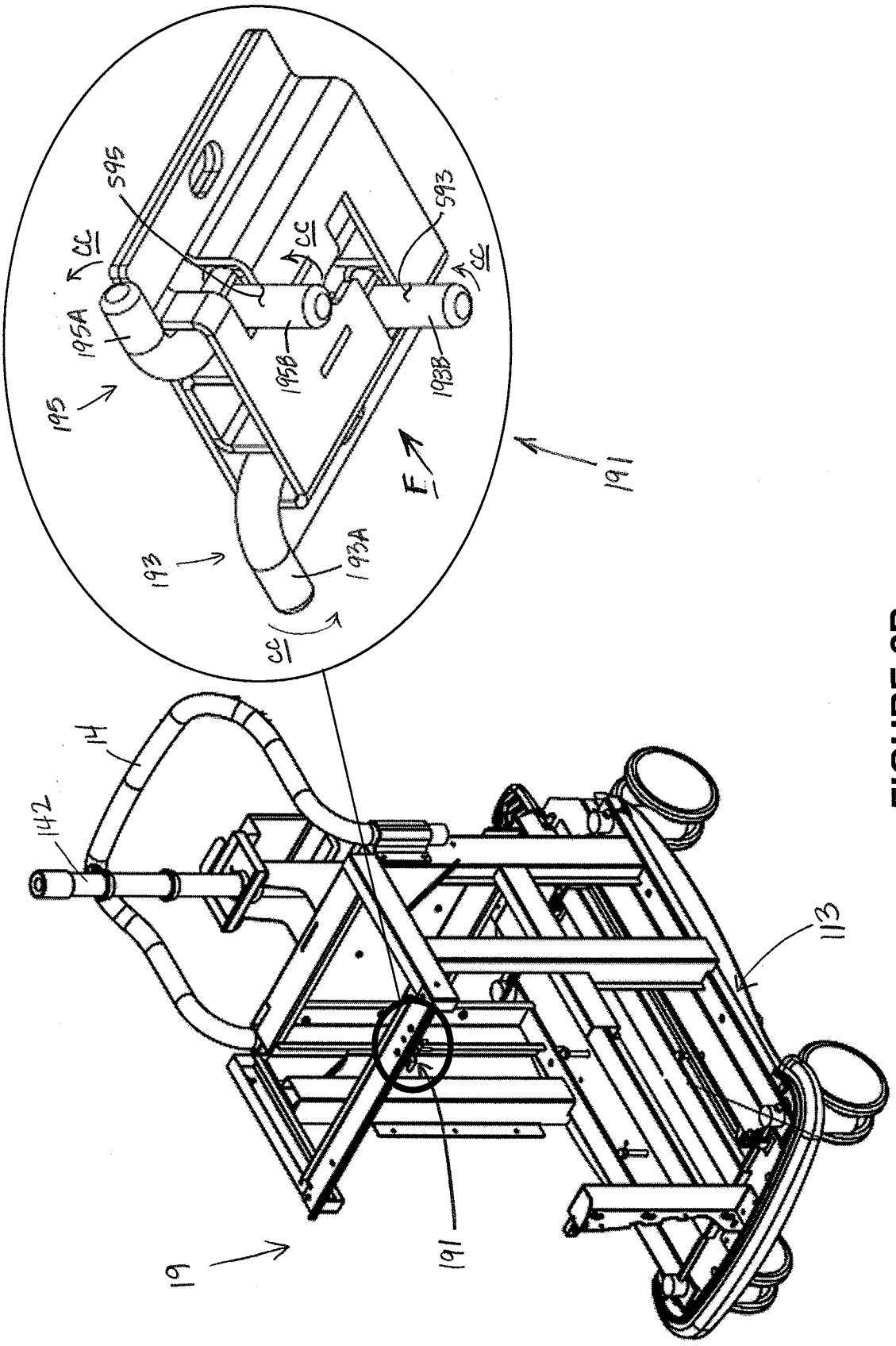
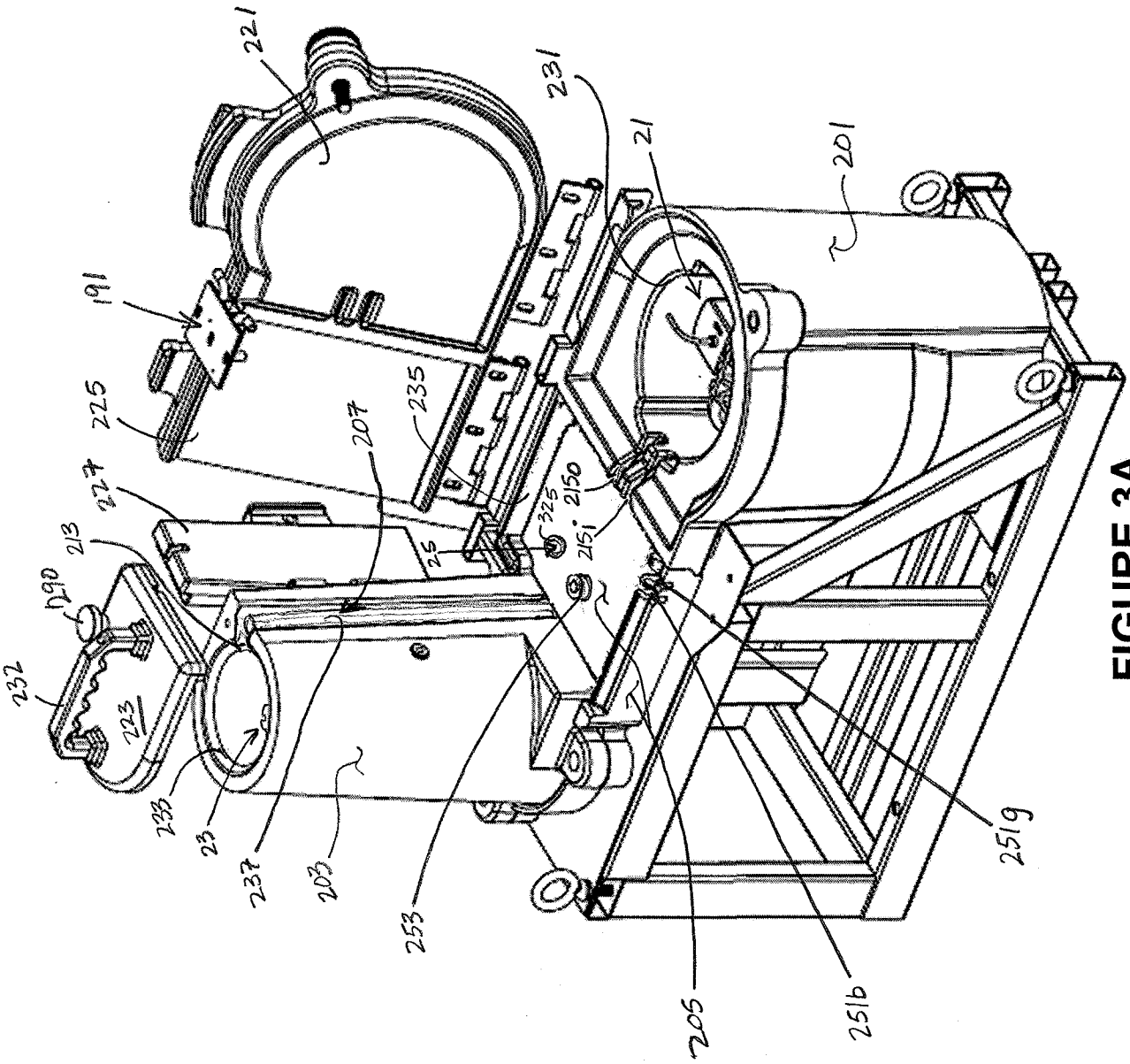


FIGURE 2B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2516

FIGURE 3A

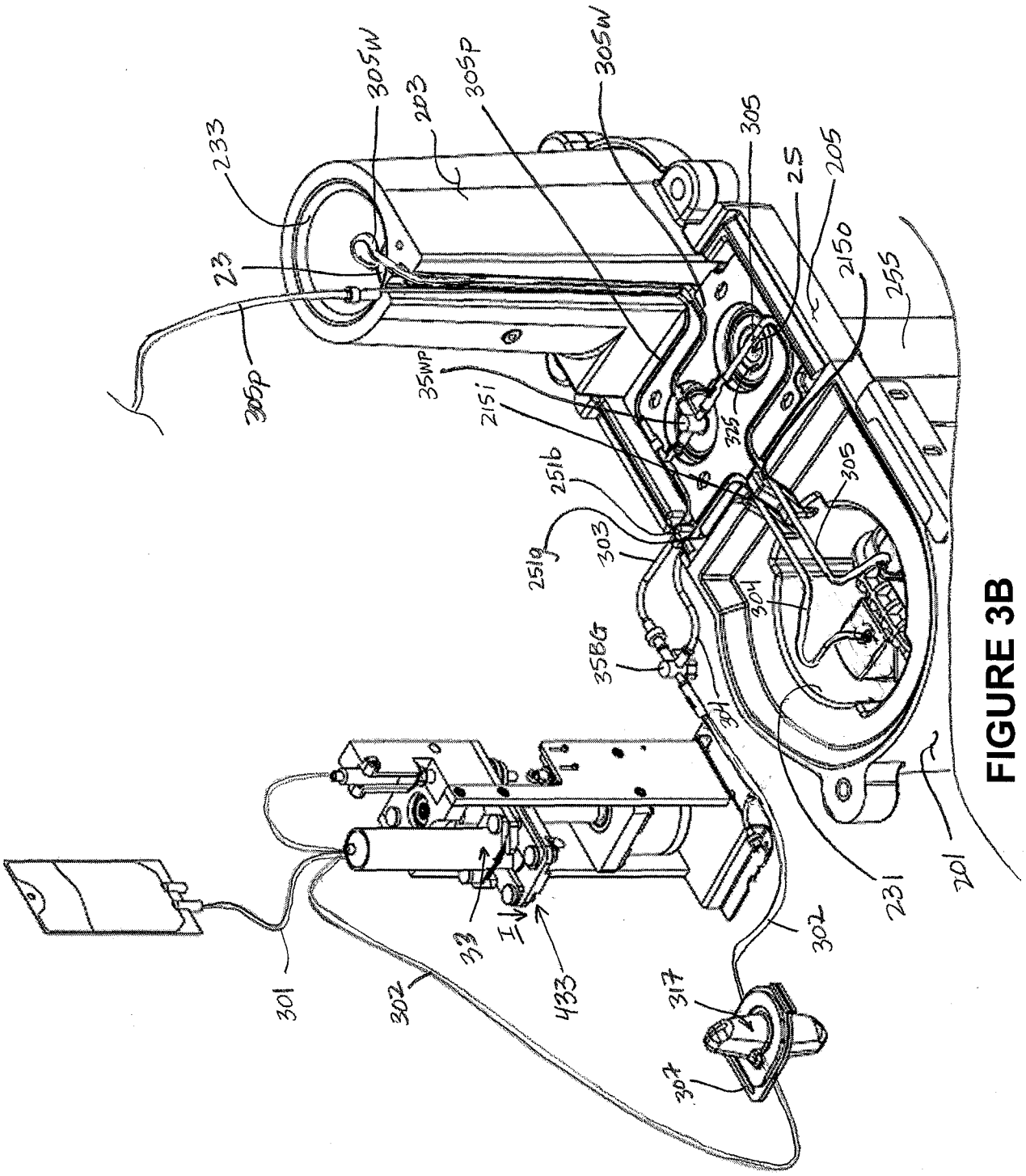
305W
203
305P
305W
233
23
305
25
205
2150
255
305p
35WP
215i
325
306
2516
2519
303
304
35BG
231
201
301
302
33
I
433
317
307
302

FIGURE 3B

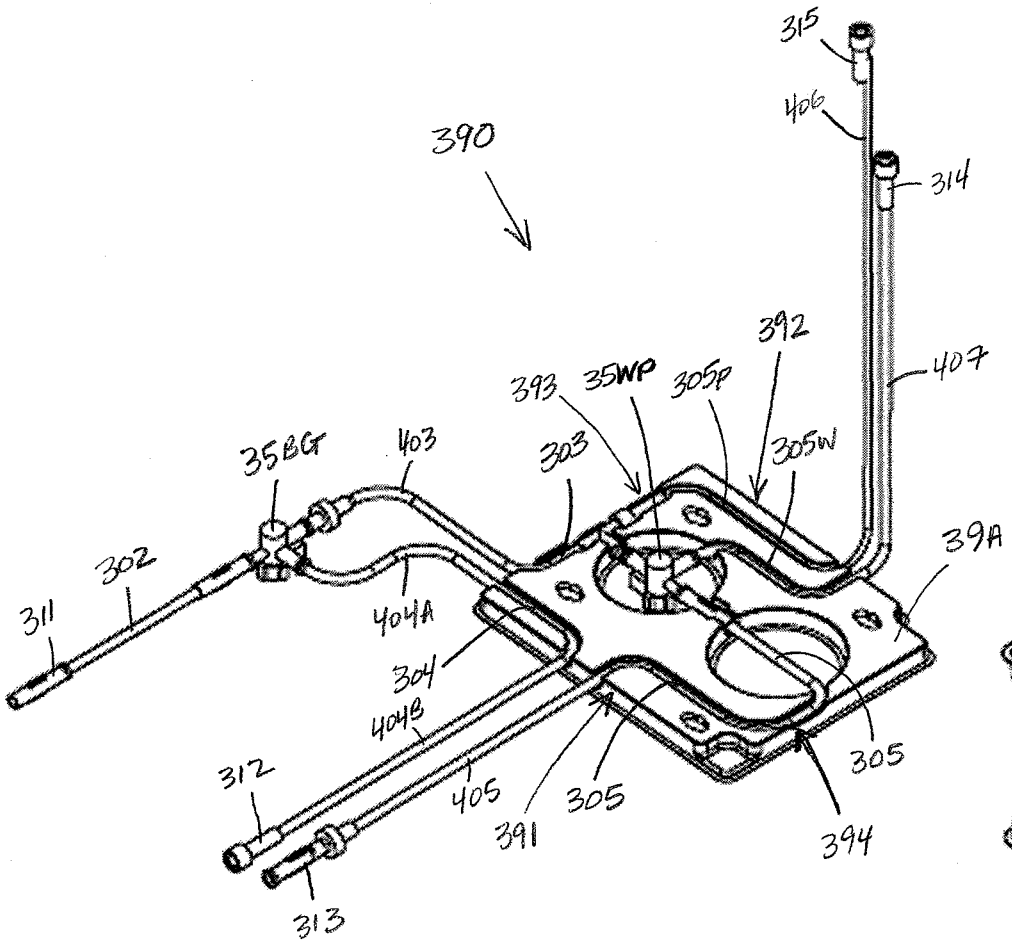

FIGURE 3C

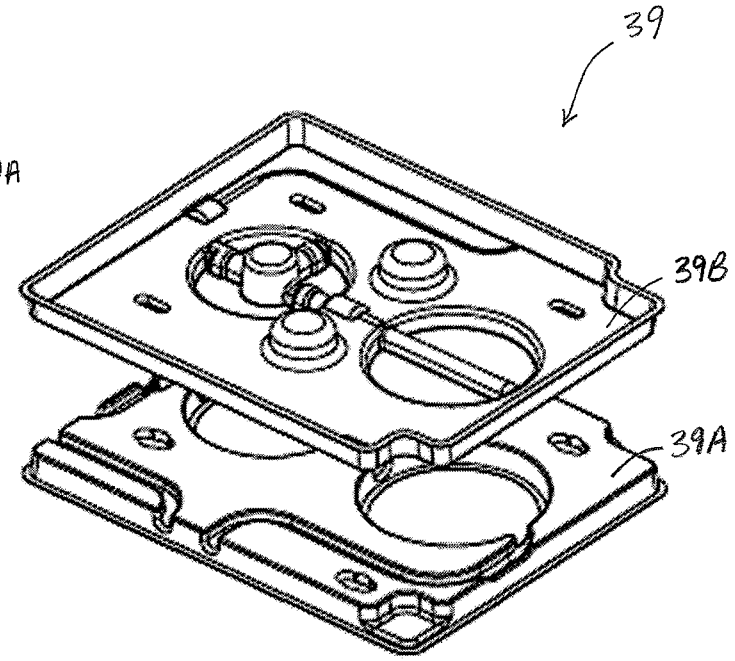

FIGURE 3D

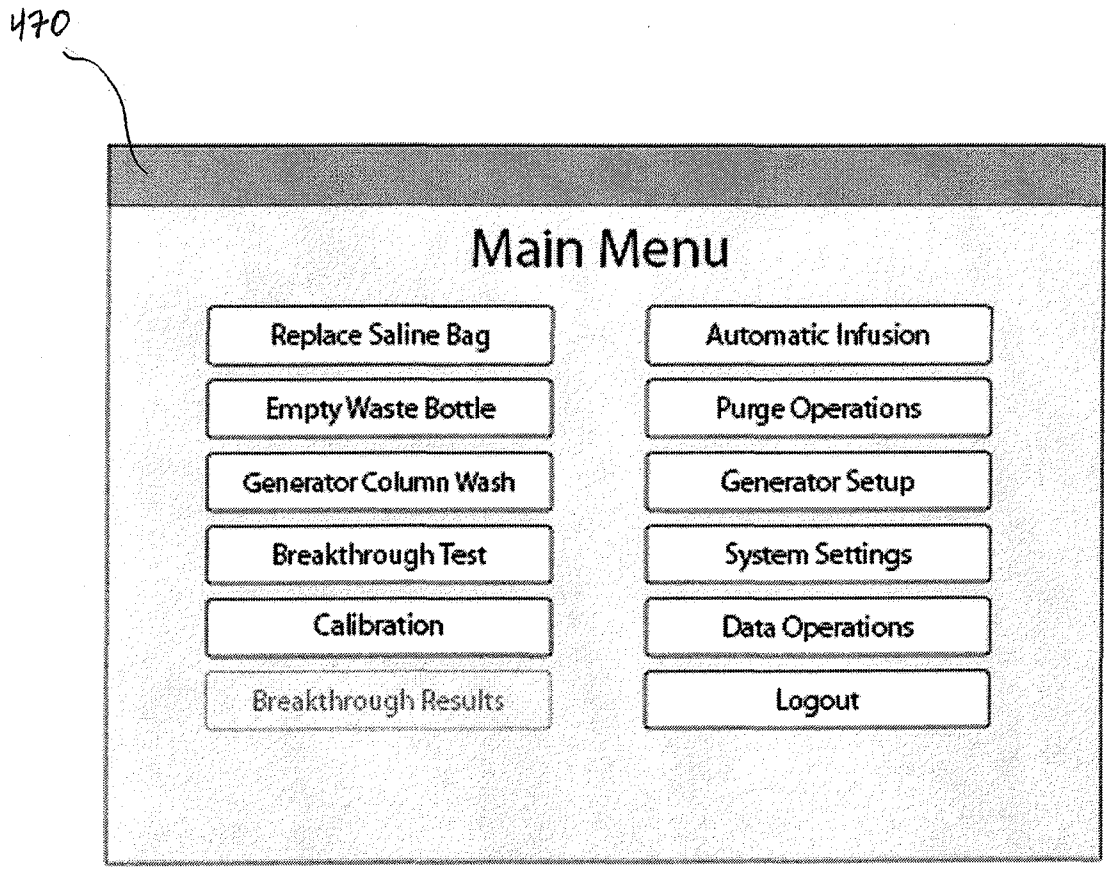
470
Main Menu
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout

FIGURE 4

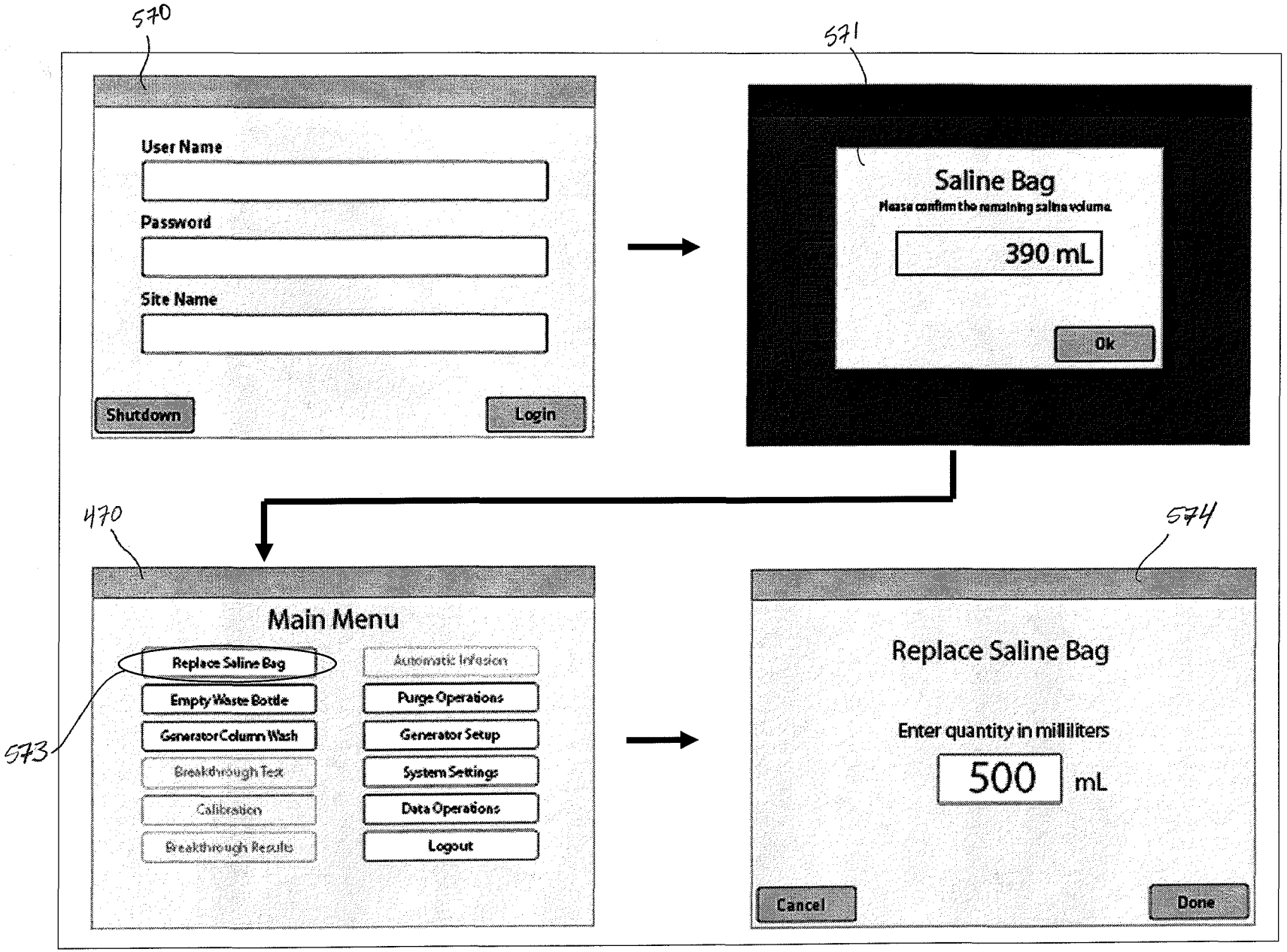
570
User Name
Password
Site Name
Shutdown
Login
571
Saline Bag
Please confirm the remaining saline volume.
390 mL
Ok
470
Main Menu
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
573
574
Replace Saline Bag
Enter quantity in milliliters
500
mL
Cancel
Done

FIGURE 5A

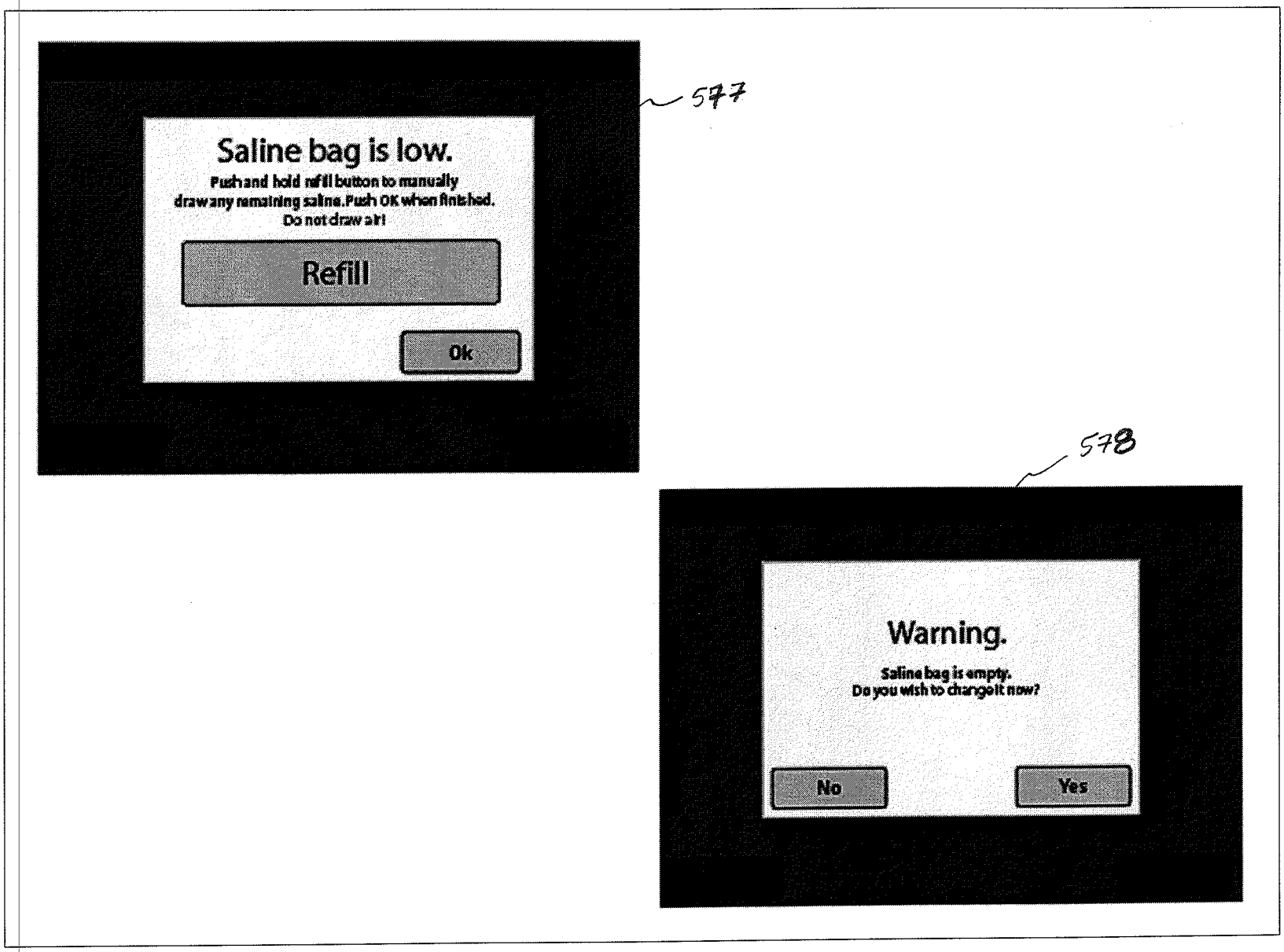
577
Saline bag is low.
Push and hold refill button to manually draw any remaining saline. Push OK when finished.
Do not draw air!
Refill
Ok
578
Warning.
Saline bag is empty.
Do you wish to change it now?
No
Yes

FIGURE 5B

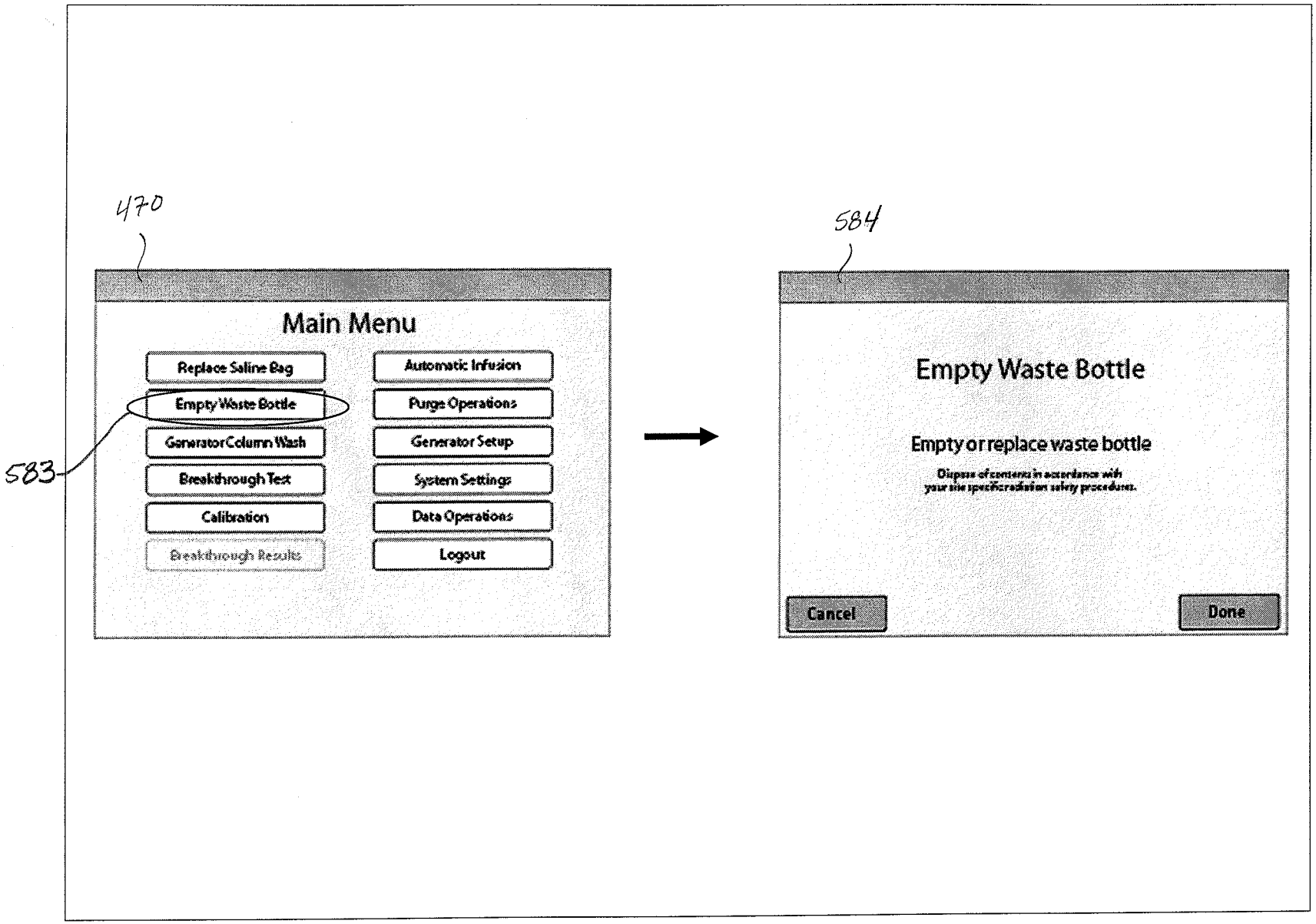
470
Main Menu
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
583
584
Empty Waste Bottle
Empty or replace waste bottle
Cancel
Done

FIGURE 5C

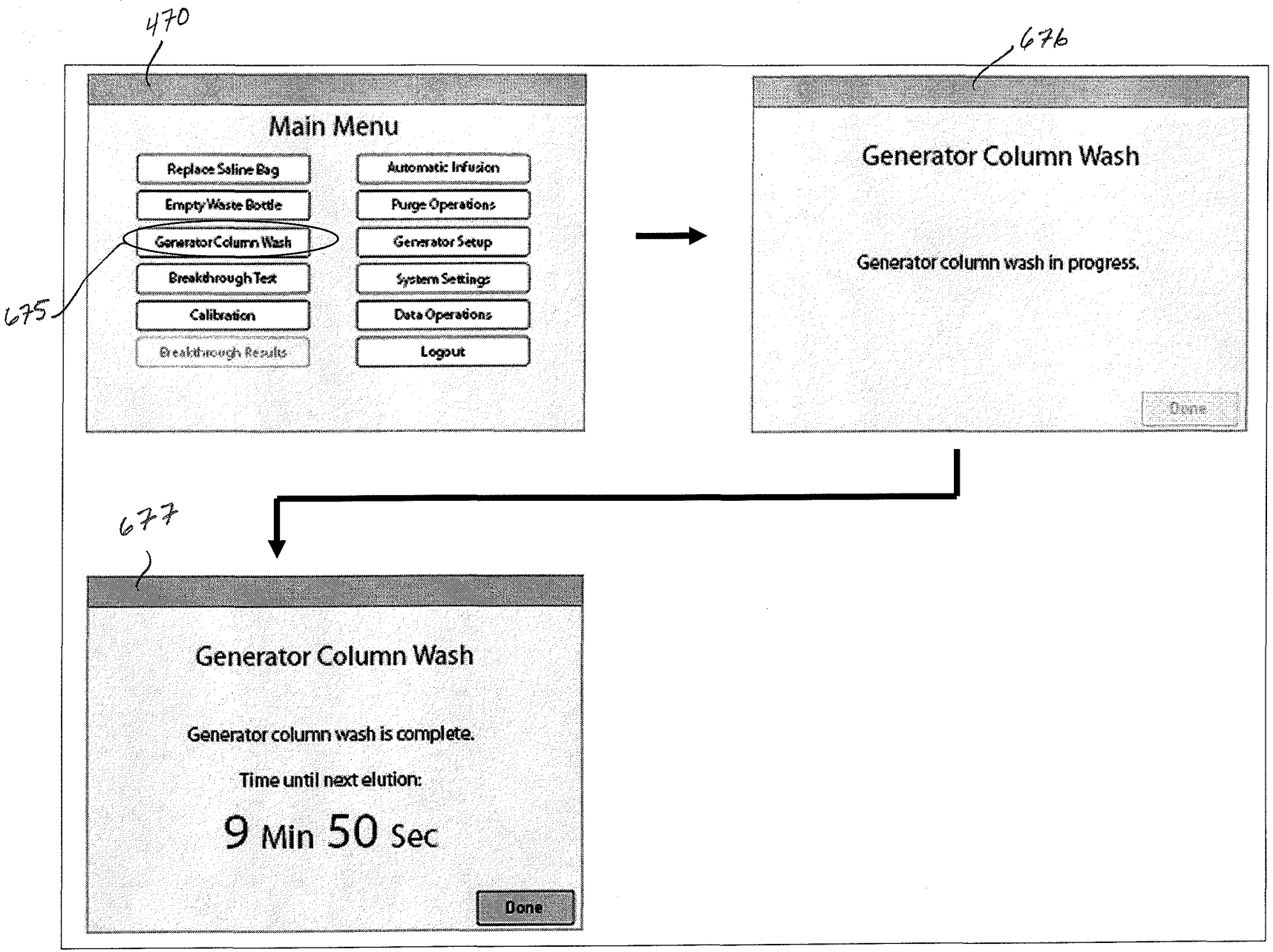
470
Main Menu
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
675
676
Generator Column Wash
Generator column wash in progress.
Done
677
Generator Column Wash
Generator column wash is complete.
Time until next elution:
9 Min 50 Sec
Done

FIGURE 6

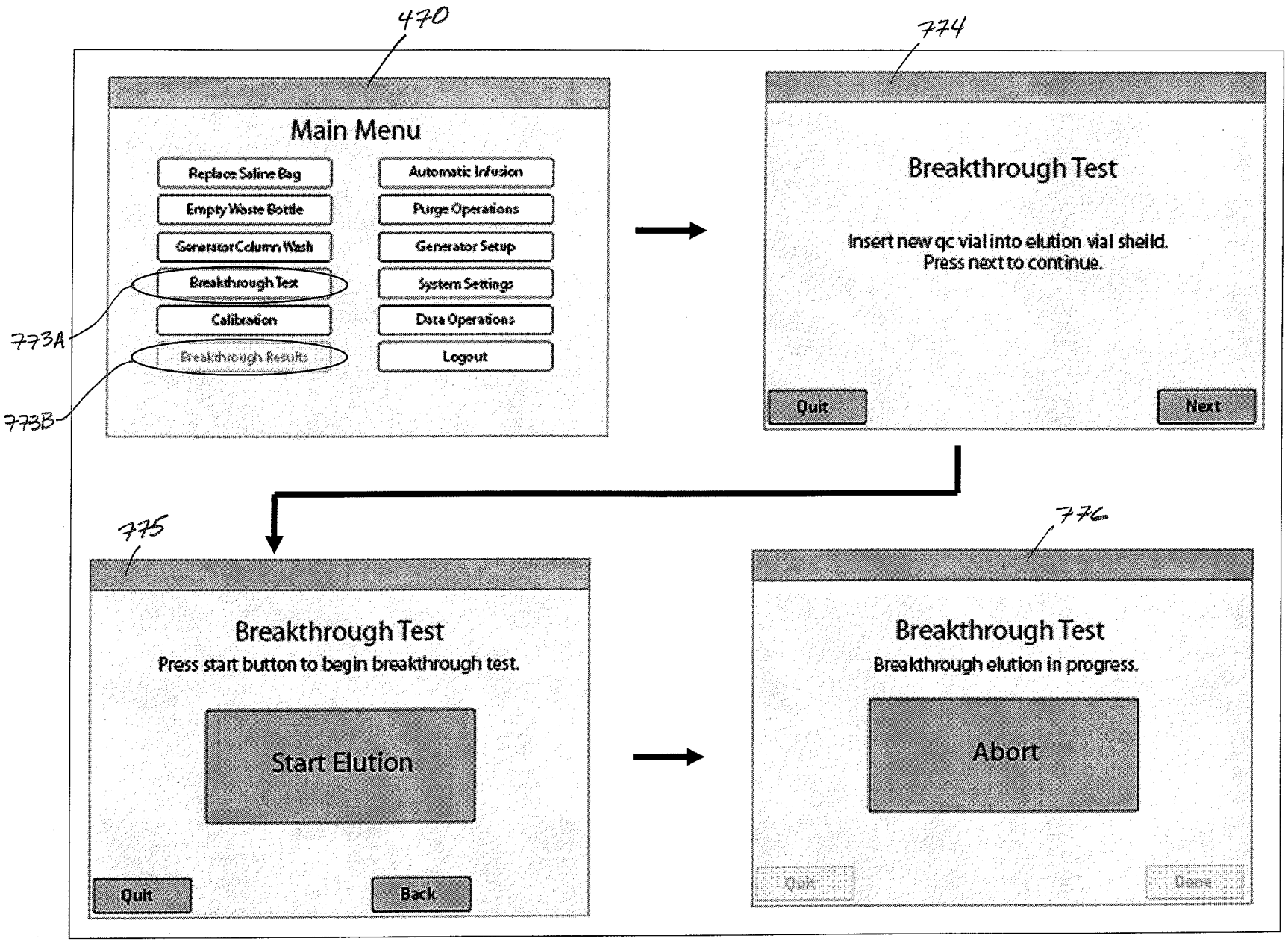
470
Main Menu
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
773A
773B
774
Breakthrough Test
Insert new qc vial into elution vial sheild.
Press next to continue.
Quit
Next
775
Breakthrough Test
Press start button to begin breakthrough test.
Start Elution
Quit
Back
776
Breakthrough Test
Breakthrough elution in progress.
Abort
Quit
Done

FIGURE 7A

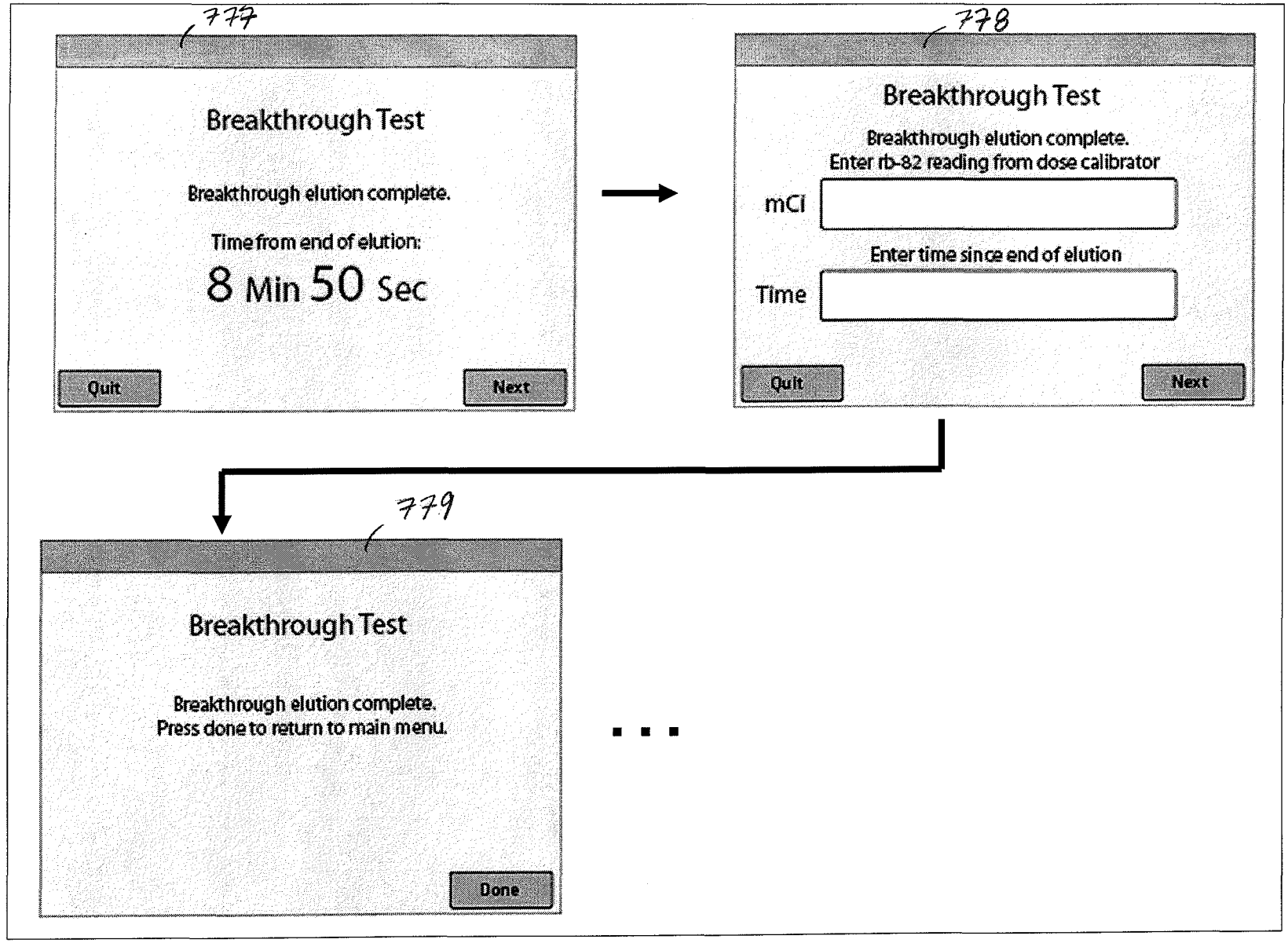
777
Breakthrough Test
Breakthrough elution complete.
Time from end of elution:
8 Min 50 Sec
Quit
Next
778
Breakthrough Test
Breakthrough elution complete.
Enter rb-82 reading from dose calibrator
mCi
Enter time since end of elution
Time
Quit
Next
779
Breakthrough Test
Breakthrough elution complete.
Press done to return to main menu.
Done
. . .

FIGURE 7B

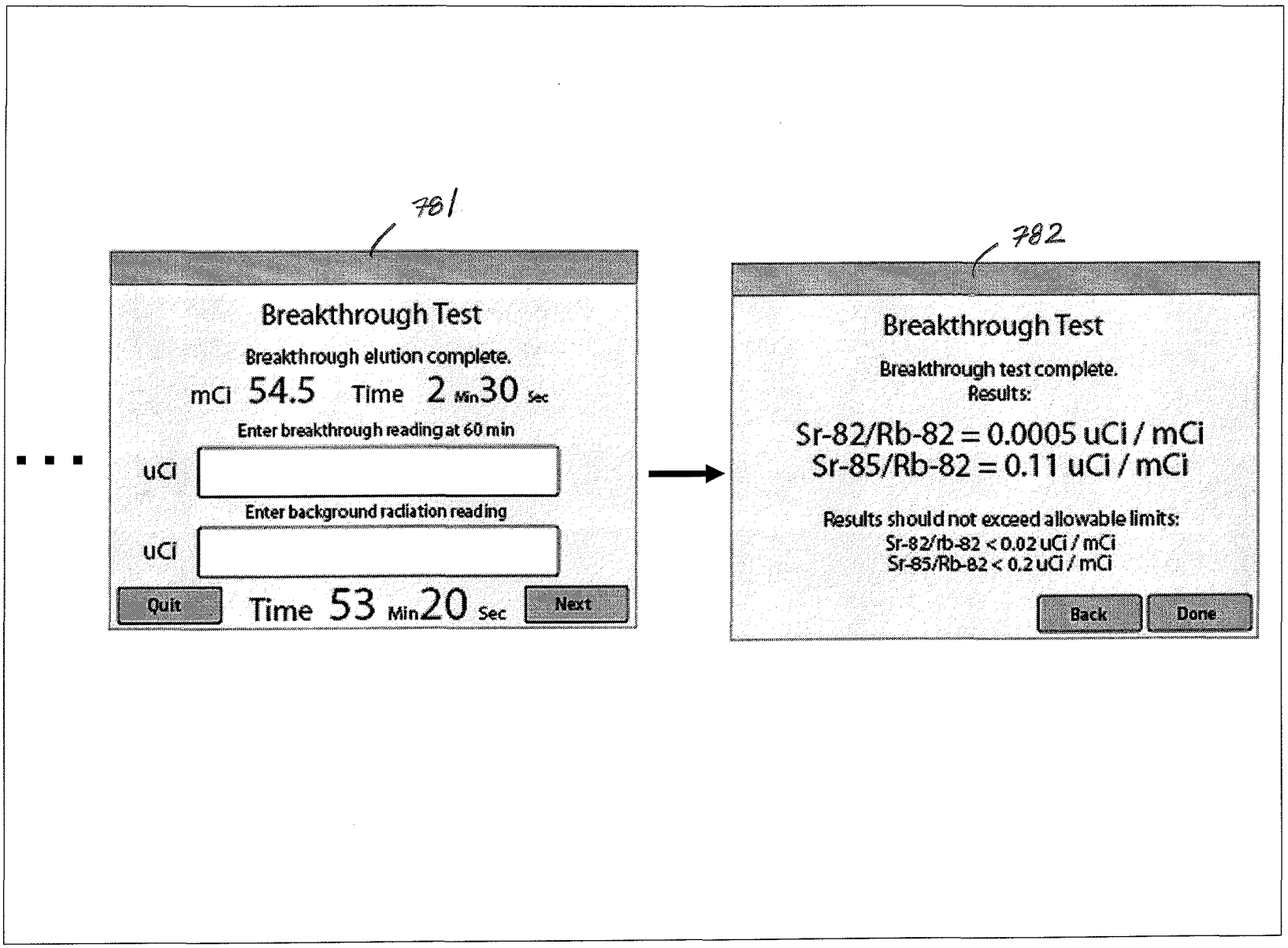
781
Breakthrough Test
Breakthrough elution complete.
mCi 54.5 Time 2 Min 30 Sec
Enter breakthrough reading at 60 min
uCi
Enter background radiation reading
uCi
Quit
Time 53 Min 20 Sec
Next
782
Breakthrough Test
Breakthrough test complete.
Results:
Sr-82/Rb-82 = 0.0005 uCi / mCi
Sr-85/Rb-82 = 0.11 uCi / mCi
Results should not exceed allowable limits:
Sr-82/Rb-82 < 0.02 uCi / mCi
Sr-85/Rb-82 < 0.2 uCi / mCi
Back
Done

FIGURE 7C

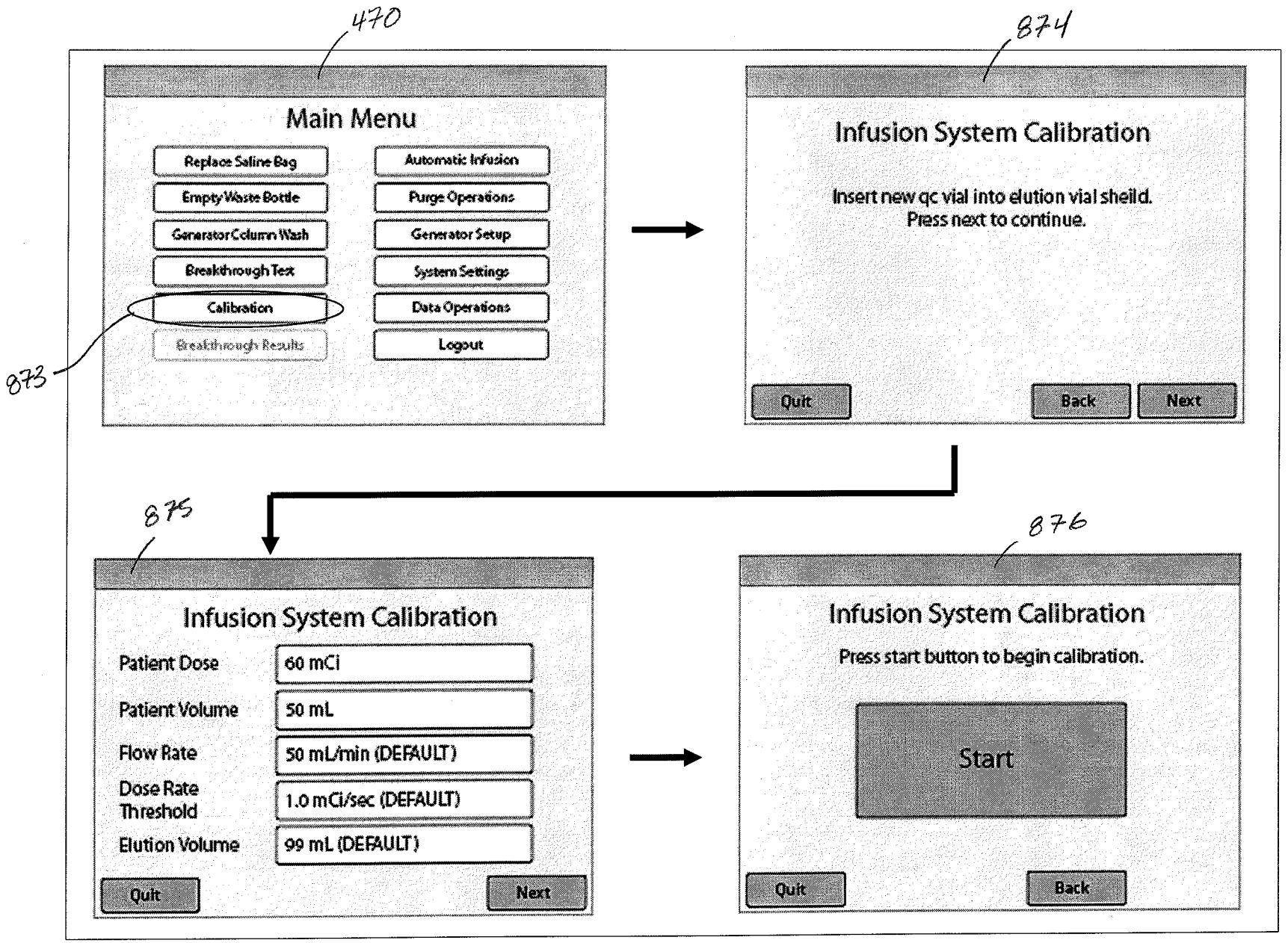
470
Main Menu
Replace Saline Bag
Automatic Infusion
Empty Waste Bottle
Purge Operations
Generator Column Wash
Generator Setup
Breakthrough Test
System Settings
Calibration
Data Operations
Breakthrough Results
Logout
873
874
Infusion System Calibration
Insert new qc vial into elution vial sheild.
Press next to continue.
Quit
Back
Next
875
Infusion System Calibration
Patient Dose
60 mCi
Patient Volume
50 mL
Flow Rate
50 mL/min (DEFAULT)
Dose Rate Threshold
1.0 mCi/sec (DEFAULT)
Elution Volume
99 mL (DEFAULT)
Quit
Next
876
Infusion System Calibration
Press start button to begin calibration.
Start
Quit
Back

FIGURE 8A

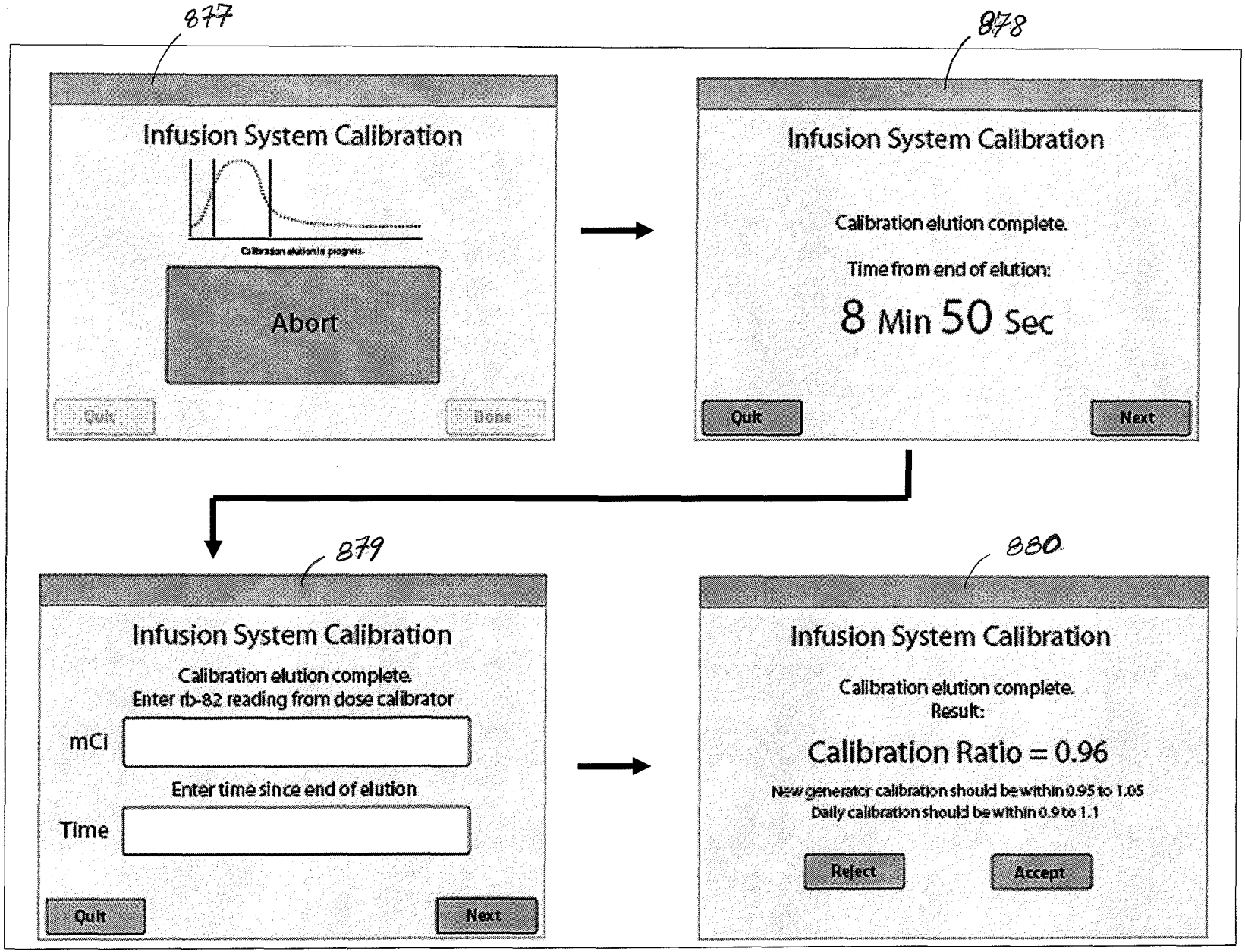
877
Infusion System Calibration
Abort
Quit
Done
878
Infusion System Calibration
Calibration elution complete.
Time from end of elution:
8 Min 50 Sec
Quit
Next
879
Infusion System Calibration
Calibration elution complete.
Enter rb-82 reading from dose calibrator
mCi
Enter time since end of elution
Time
Quit
Next
880
Infusion System Calibration
Calibration elution complete.
Result:
Calibration Ratio = 0.96
New generator calibration should be within 0.95 to 1.05
Daily calibration should be within 0.9 to 1.1
Reject
Accept

FIGURE 8B

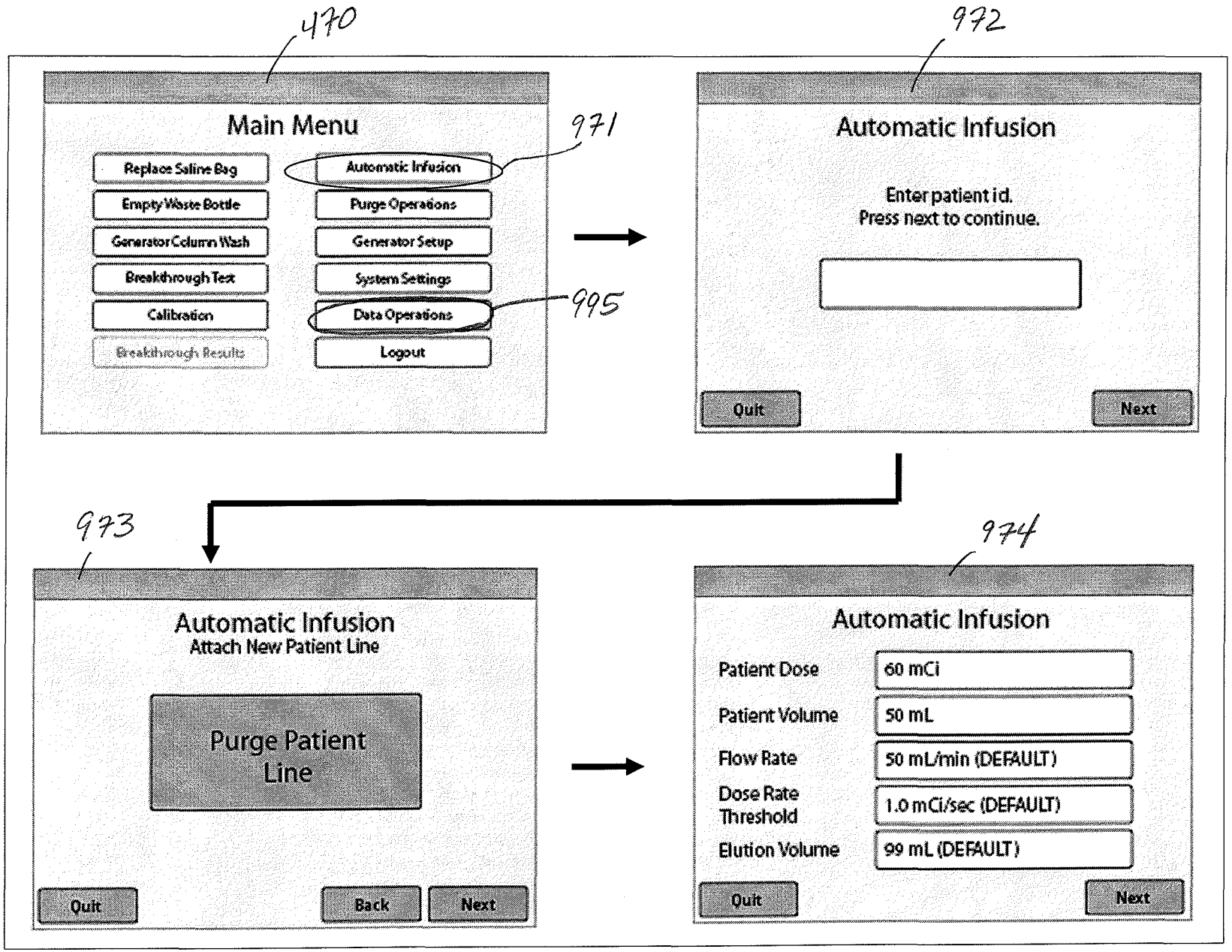
470
Main Menu
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
971
995
972
Automatic Infusion
Enter patient id.
Press next to continue.
Quit
Next
973
Automatic Infusion
Attach New Patient Line
Purge Patient Line
Quit
Back
Next
974
Automatic Infusion
Patient Dose
60 mCi
Patient Volume
50 mL
Flow Rate
50 mL/min (DEFAULT)
Dose Rate Threshold
1.0 mCi/sec (DEFAULT)
Elution Volume
99 mL (DEFAULT)
Quit
Next

FIGURE 9A

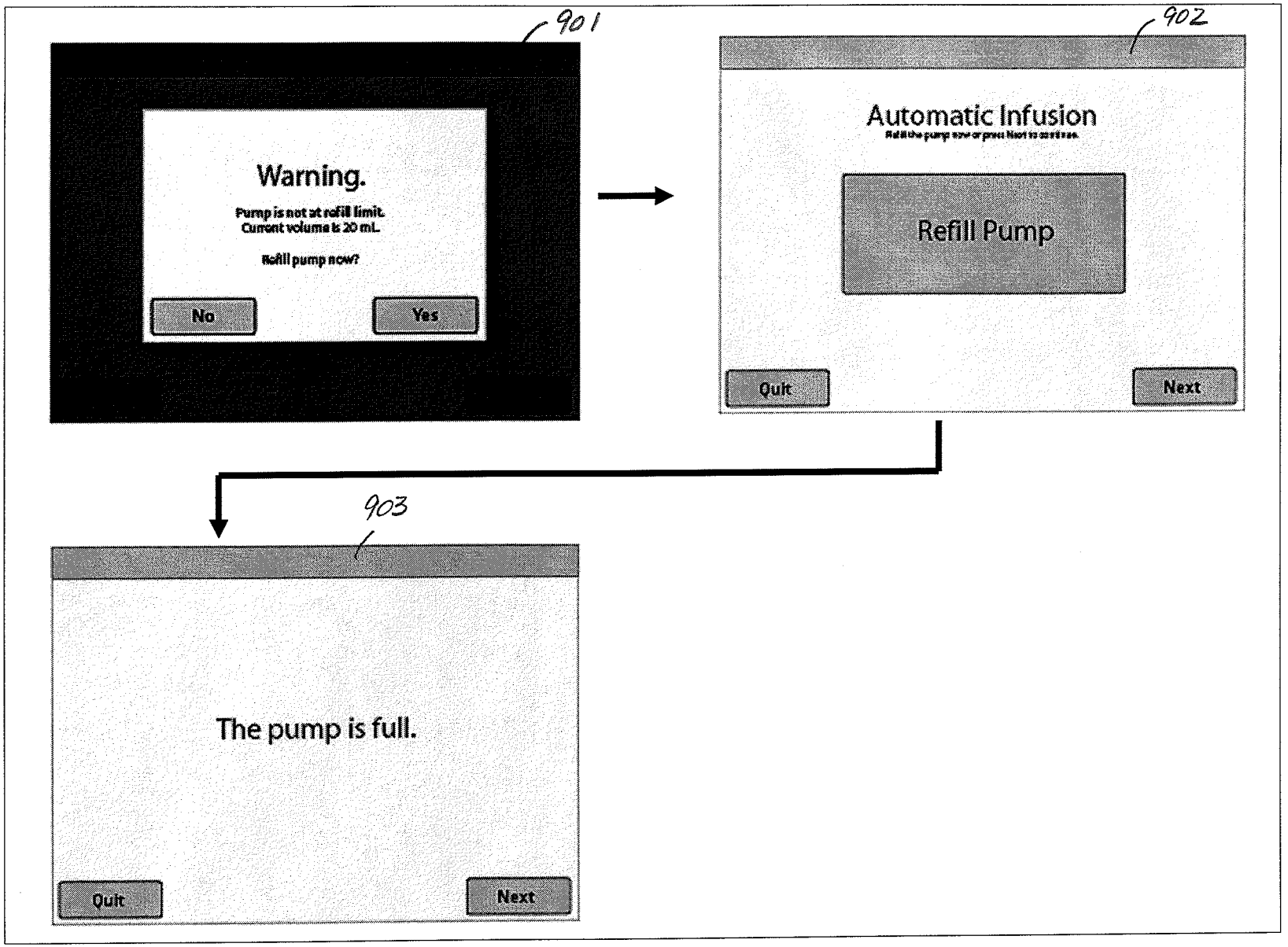
901
Warning.
Pump is not at refill limit.
Current volume is 20 mL.
Refill pump now?
No
Yes
902
Automatic Infusion
Refill the pump now or press Next to continue.
Refill Pump
Quit
Next
903
The pump is full.
Quit
Next

FIGURE 9B

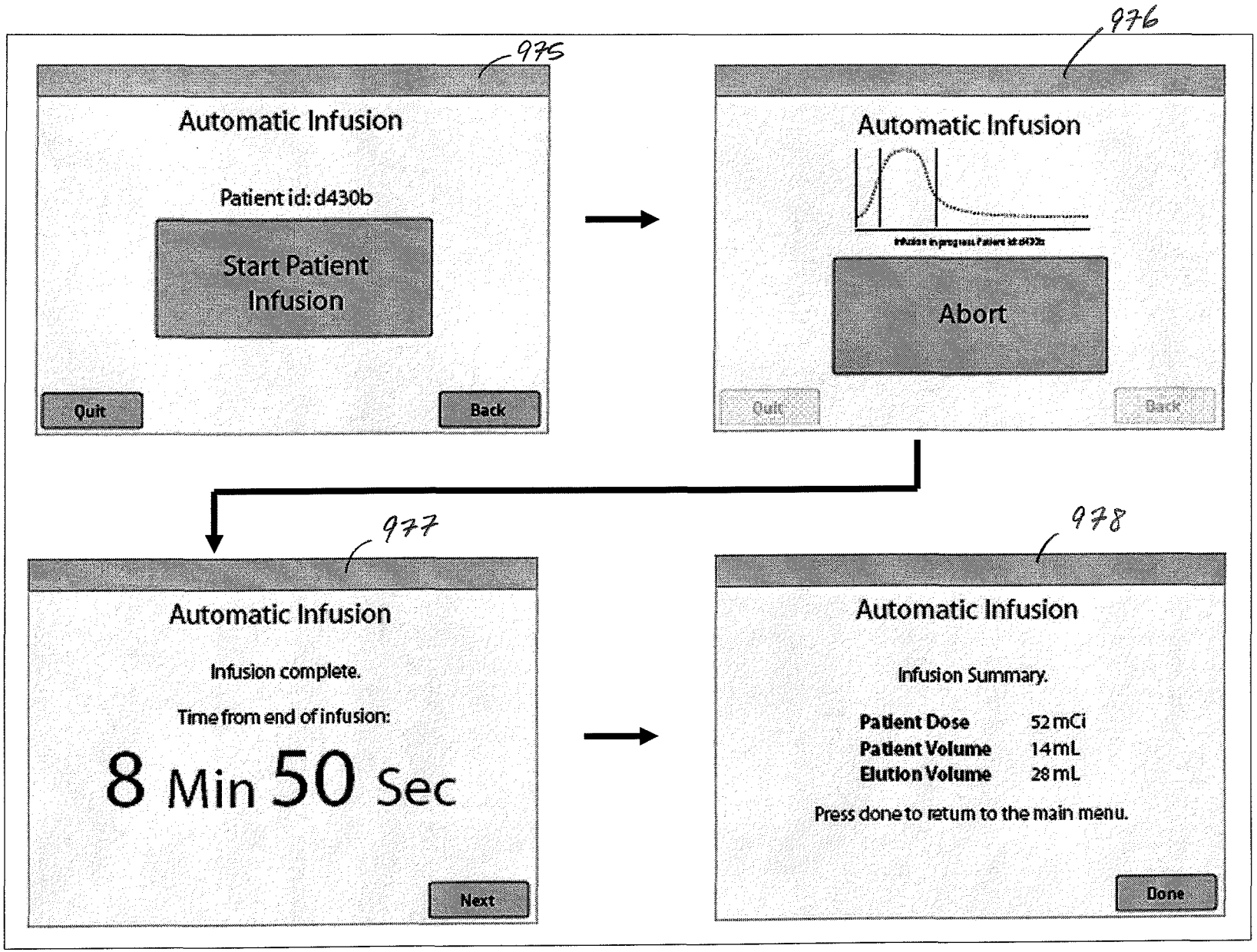
975
Automatic Infusion
Patient id: d430b
Start Patient Infusion
Quit
Back
976
Automatic Infusion
Abort
Quit
Back
977
Automatic Infusion
Infusion complete.
Time from end of infusion:
8 Min 50 Sec
Next
978
Automatic Infusion
Infusion Summary.
Patient Dose 52 mCi
Patient Volume 14 mL
Elution Volume 28 mL
Press done to return to the main menu.
Done

FIGURE 9C

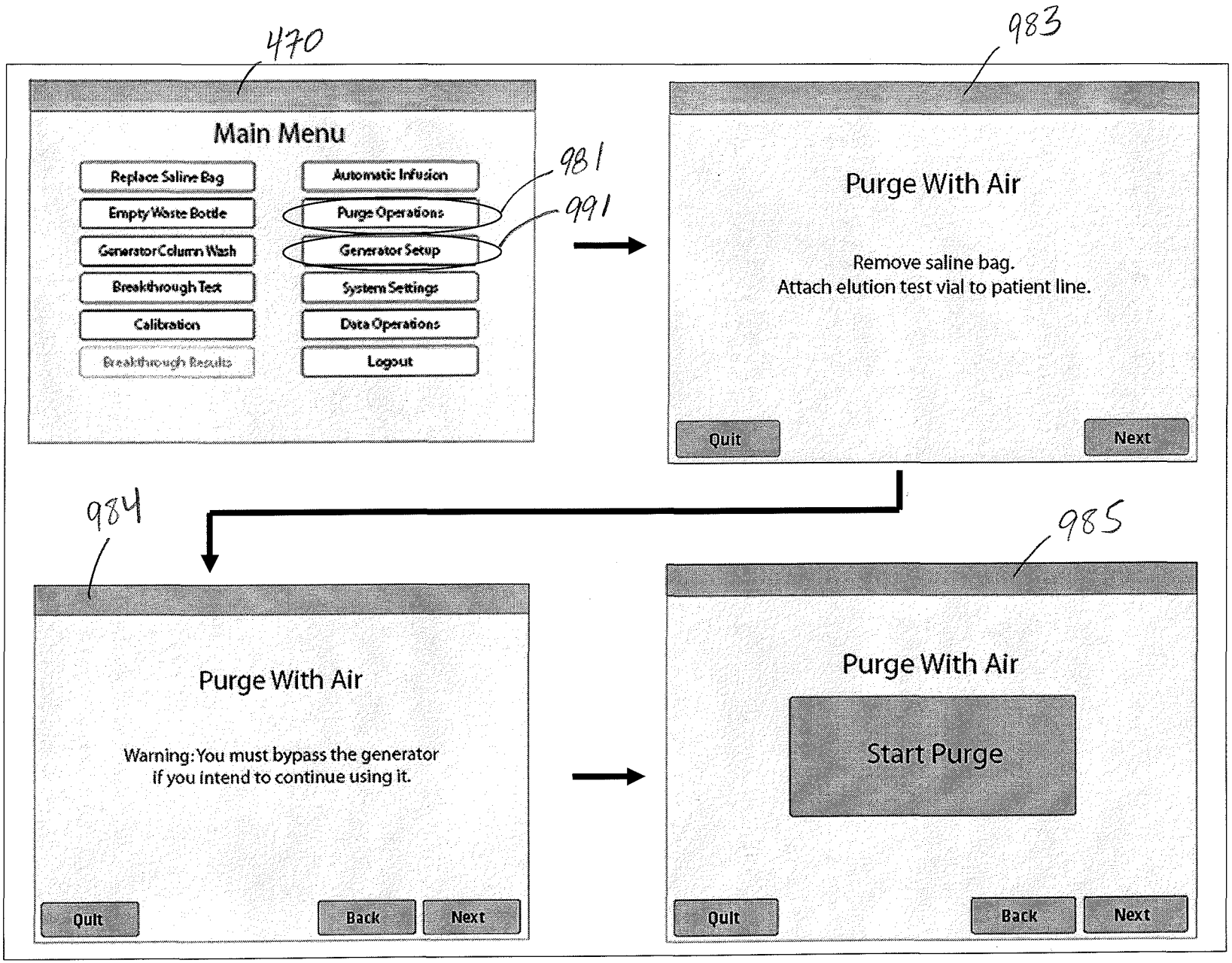
470
Main Menu
Replace Saline Bag
Automatic Infusion
Empty Waste Bottle
Purge Operations
Generator Column Wash
Generator Setup
Breakthrough Test
System Settings
Calibration
Data Operations
Breakthrough Results
Logout
981
991
983
Purge With Air
Remove saline bag.
Attach elution test vial to patient line.
Quit
Next
984
Purge With Air
Warning: You must bypass the generator
if you intend to continue using it.
Quit
Back
Next
985
Purge With Air
Start Purge
Quit
Back
Next

FIGURE 10

Electronic Patent Application Fee Transmittal

Application Number:	
Filing Date:	
Title of Invention:	INFUSION SYSTEM CONFIGURATIONS
First Named Inventor/Applicant Name:	Charles Quirico
Filer:	Charles D. Segelbaum
Attorney Docket Number:	56782.1.6

Filed as Large Entity

Utility Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Utility application filing	1011	1	310	310
Utility Search Fee	1111	1	510	510
Utility Examination Fee	1311	1	210	210
Pages:				
Claims:				
Claims in excess of 20	1202	16	50	800
Independent claims in excess of 3	1201	1	210	210
Miscellaneous-Filing:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**2040**

Electronic Acknowledgement Receipt

EFS ID:	3440373
Application Number:	12137363
International Application Number:	
Confirmation Number:	7372
Title of Invention:	INFUSION SYSTEM CONFIGURATIONS
First Named Inventor/Applicant Name:	Charles Quirico
Customer Number:	22859
Filer:	Charles D. Segelbaum
Filer Authorized By:	
Attorney Docket Number:	56782.1.6
Receipt Date:	11-JUN-2008
Filing Date:	
Time Stamp:	18:17:12
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$2040
RAM confirmation Number	3781
Deposit Account	
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes) /Message Digest	Multi Part /.zip	Pages (if appl.)

1	Application Data Sheet	56782_1_6_ApplicationDataSheet.pdf	1284273 b7e40ce86833c8fdf1966abe84effa67f4684b80	no	6
Warnings:					
Information:					
2		56782_1_6_Application.pdf	190633 6f212722655f71babe87e0286a80ab21502541d9	yes	37
	Multipart Description/PDF files in .zip description				
	Document Description		**Start**	**End**	
	Specification		1	27	
	Claims		28	36	
	Abstract		37	37	
Warnings:					
Information:					
3	Drawings-only black and white line drawings	56782_1_5_6_7_8_Drawings.pdf	3090157 51f728353556654064c53570776bc61a122bc41f	no	23
Warnings:					
Information:					
4	Fee Worksheet (PTO-06)	fee-info.pdf	8523 4403d10203f809d59976199ddd5c2a061dd25565	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	4573586		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/06 (12-04)

Filing Date: 06/11/08

Approved for use through 7/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 12/137,363

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY FEE ($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	310
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	510
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	210
TOTAL CLAIMS (37 CFR 1.16(i))	36 minus 20 =	16	X$ 25		OR	X$50	800
INDEPENDENT CLAIMS (37 CFR 1.16(h))	4 minus 3 =	* 1	X$105			X$210	210
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $260 ($130 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR						
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))			185			370	
			TOTAL			TOTAL	2040

* If the difference in column 1 is less than zero, enter "0" in column 2.

APPLICATION AS AMENDED – PART II

AMENDMENT A		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))					N/A		OR	N/A	
						TOTAL ADD'T FEE		OR	TOTAL ADD'T FEE	

AMENDMENT B		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)	OR	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))					N/A		OR	N/A	
						TOTAL ADD'T FEE		OR	TOTAL ADD'T FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

1. 16. 25. 29.