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
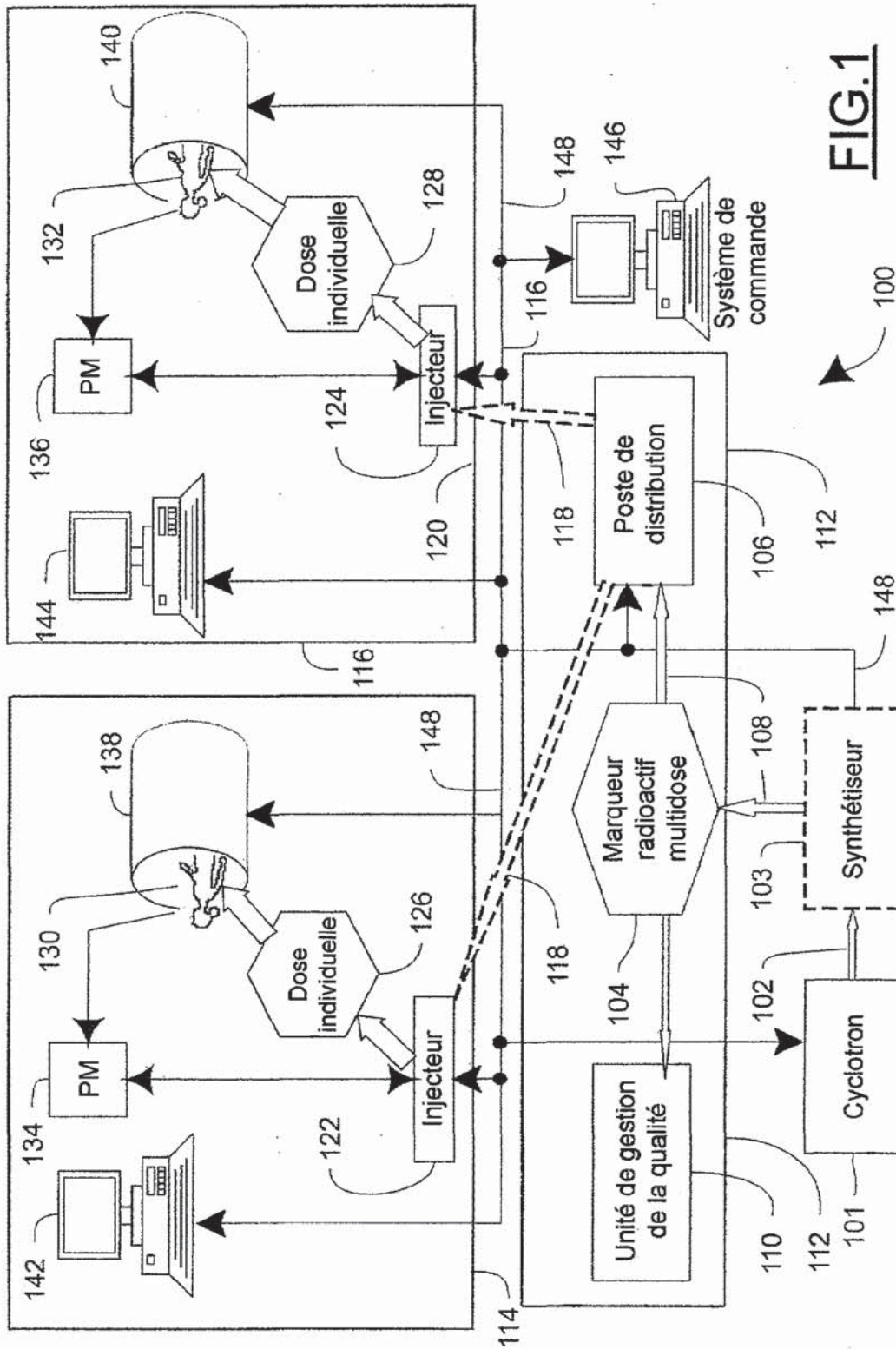
lever (806) le flacon multidose (302) jusque dans un système d'étalonnage (300) de dose du système d'injection (122 ou 124).

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 :
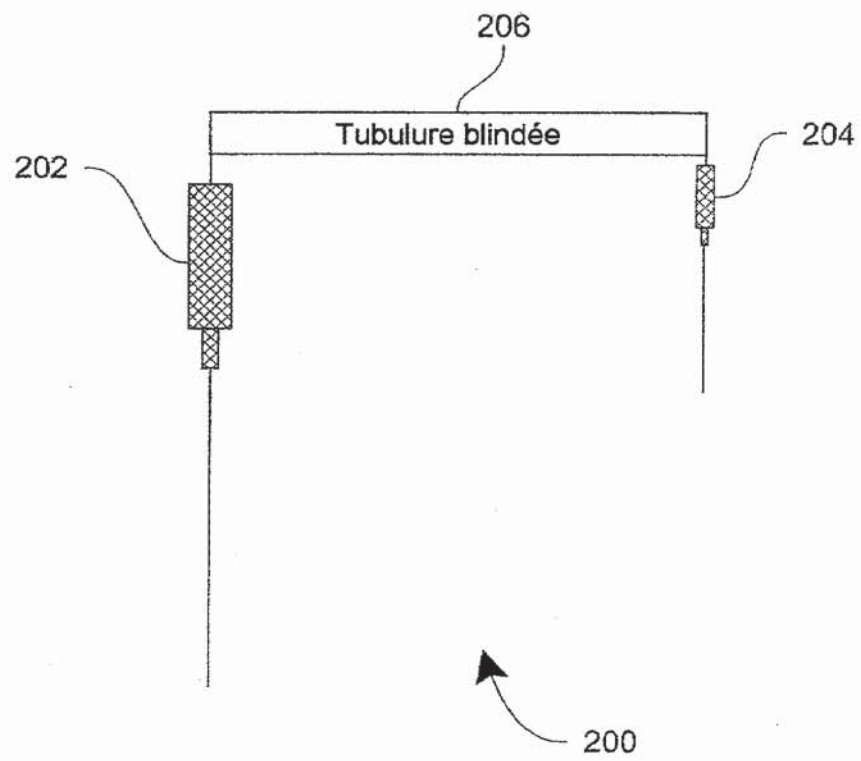
extraire (1002) d'un flacon multidose (302) un dose individuelle (126 ou 128) d'un produit radiopharmaceutique (104) ;

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
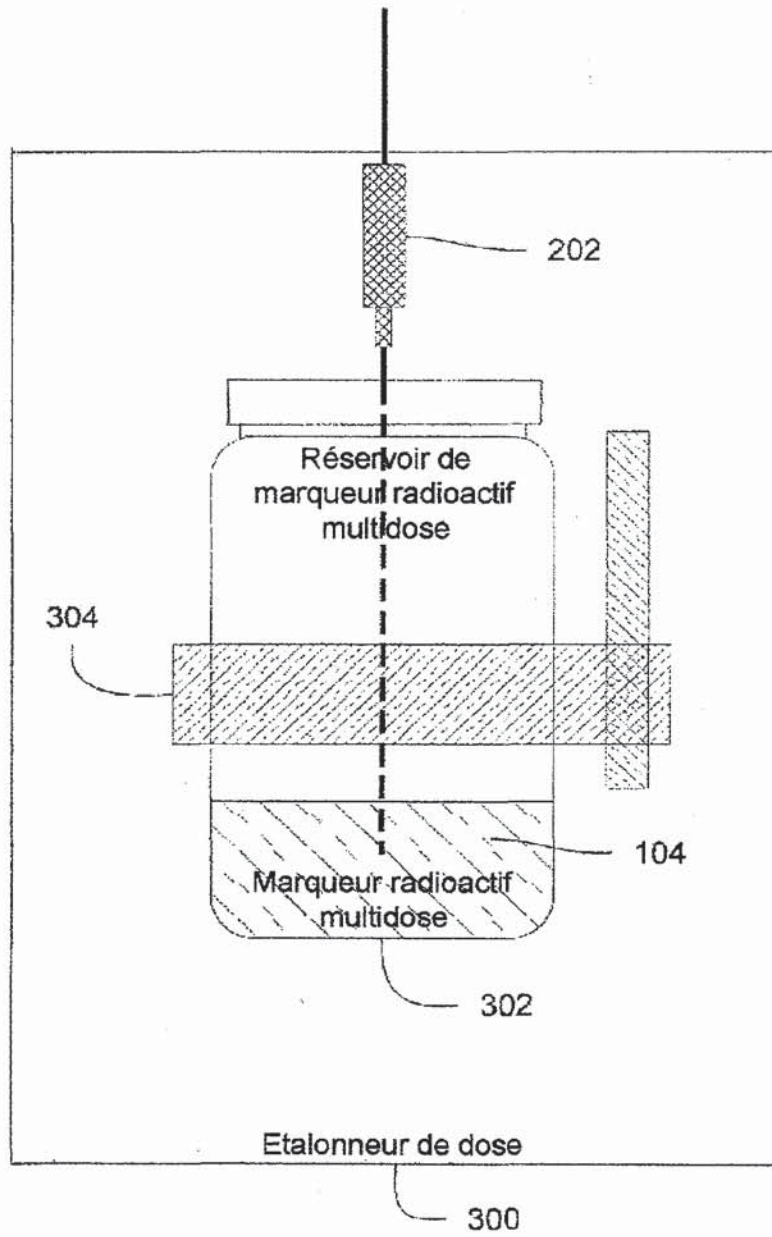
ajouter (1006) une solution saline provenant d'une poche (412) de solution saline et d'une conduite de solution saline dans le flacon (416) de patient via un deuxième robinet d'arrêt (410) à trois voies.
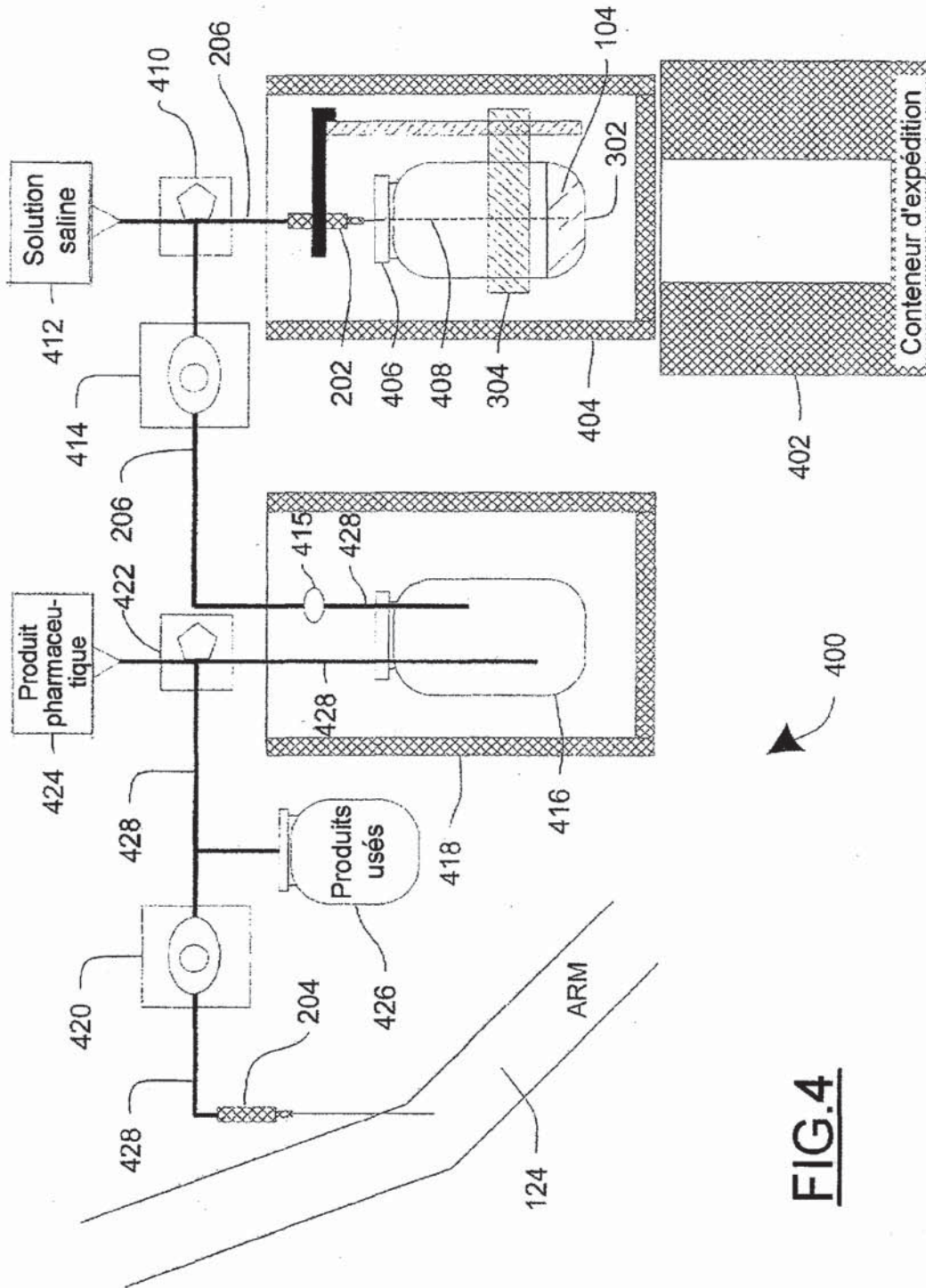
FIG.1

FIG.2

206

Tubulure blindée

202

204

200

FIG.3

202

Réservoir de
marqueur radioactif
multidose

304

104

Marqueur radioactif
multidose

302

Etalonneur de dose

300

FIG.4

FIG.5

Unité de gestion de la qualité — 110

204

520

518

516

514

TABLE

Pousse-seringue

512

206

509

502

503

Cible de cyclotron

Pompe

415

404

206

508

506

504

FIG.6

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      │ ── 804
│   flacon multidose  │
└─────────────────────┘                    ┌─────────────────────┐
          │                    802 ──      │   Mettre en marche  │
          │                                │     l'ordinateur    │
          ▼                                └─────────────────────┘
┌─────────────────────┐  ── 806                      │
│  Lever le flacon multidose │                        │
│ jusque dans l'étalonneur de dose │                  │
└─────────────────────┘                               │
          │                                            │
          ▼                                            ▼
          └──────────────────────────────────────────┘
                             │
                             ▼
```

↖ ── 800

2867084

FIG.9

```
┌─────────────────────────────────┐
│  Installer le flacon de patient  │────── 902
└─────────────────────────────────┘
                 │
                 ▼
┌─────────────────────────────────┐
│   Installer l'aiguille de sortie │────── 904
└─────────────────────────────────┘
                 │
                 ▼
┌─────────────────────────────────┐
│     Insérer l'aiguille de sortie │────── 906
│     dans le flacon de patient    │
└─────────────────────────────────┘
                 │
                 ▼
┌─────────────────────────────────┐
│     Placer le flacon de patient  │────── 908
│     dans l'étalonneur de dose    │
└─────────────────────────────────┘
                 │
                 ▼
┌─────────────────────────────────┐
│     Installer le robinet d'arrêt │────── 910
└─────────────────────────────────┘
                 │
                 ▼
┌─────────────────────────────────┐
│        Installer la tubulure     │────── 912
│          intraveineuse           │
└─────────────────────────────────┘
                 │
                 ▼
┌─────────────────────────────────┐
│        Installer l'aiguille      │────── 914
│          intraveineuse           │
└─────────────────────────────────┘
                 │
                 ▼
┌─────────────────────────────────┐
│         Fixer la poche de        │────── 916
│          solution saline         │
└─────────────────────────────────┘
```

900

FIG.10

```
┌─────────────────────────────────┐
│ Extraire une dose individuelle du│──── 1002
│ flacon multidose pour la faire   │
│ entrer dans le flacon de patient │
└─────────────────────────────────┘
                │
                ▼
          ◇ Activité de la ◇
          ◇ dose individuelle = ◇──── 1004
          ◇ activité manquante ◇
          ◇         ?         ◇
                │ Oui
                │      ┌──── 1006
                ▼
        ┌─────────────────┐
        │   Ajouter la    │
        │ solution saline │
        └─────────────────┘
                │
                ▼
          ◇ Vérifier la dose ◇──── 1008
          ◇ avec l'ordinateur ◇
          ◇        ?        ◇
                │
                ▼
    ┌──────────────────────────────┐
    │ Enregistrer l'activité de la dose │──── 1010
    └──────────────────────────────┘
                │
                ▼
    ┌──────────────────────────────┐
    │  Injecter la dose dans le patient │──── 1012
    └──────────────────────────────┘
                │
                ▼
    ┌──────────────────────────────┐
    │ Chasser de la solution saline │──── 1014
    │ dans la tubulure du patient   │
    └──────────────────────────────┘
                │
                ▼
    ┌──────────────────────────────┐
    │   Débrancher les tubulures    │──── 1016
    └──────────────────────────────┘
                │
                ▼
    ┌──────────────────────────────┐
    │ Mettre la tubulure du patient et │──── 1018
    │ le robinet d'arrêt dans l'étalonneur │
    └──────────────────────────────┘
                │
                ▼
    ┌──────────────────────────────┐
    │      Mesurer l'activité       │──── 1020
    │      dans l'étalonneur        │
    └──────────────────────────────┘
                │
                ▼
    ┌──────────────────────────────┐
    │ Enregistrer l'activité de la dose │──── 1022
    └──────────────────────────────┘
```

1000

2867084

FIG.11

```
┌─────────────────────────┐
│   Recevoir une demande   │ ── 1102
│    de matière de cible   │
└─────────────────────────┘
            │
            ▼
┌─────────────────────────┐
│  Déterminer la production │ ── 1104
│    de matière de cible   │
└─────────────────────────┘
            │
            ▼
┌─────────────────────────┐
│ Envoyer des instructions de │ ── 1106
│ production de matière de cible │
└─────────────────────────┘
            │
            ▼
┌─────────────────────────┐
│ Envoyer des instructions de │ ── 1108
│ distribution de matière de cible │
└─────────────────────────┘
```

1100

Ordinateur distant 1228

NIC 1234

1226

Enceinte

NIC 1232

Alimentation électrique 1238

1230

WAN

SAN 1236

1240

1224

Enceinte

1212

1222

Afficheur

1202

Processeur 1204

RAM 1206

ROM 1208

Mémoire externe 1210

COMM 1216

1214

Internet

1218

Clavier

Dispositif de pointage 1220

FIG.12

1200

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

		Also published as:
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Inventor(s):	JACKSON MARK ALAN; DHAWALE PARITOSH JAYANT; LARA HERMAN RODRIGO; BRUSSERMANN MICHAEL; KETZSCHER ULRICH	JP2005326398 (A) DE102005010154 (A1)
Applicant(s):	GEN ELECTRIC [US]	**Cited documents:**
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	US2003004463 (A1) EP0310148 (A2) US5885216 (A)
- european:	G21G4/08; G21F5/018; G21H5/02	
Application number:	FR20050001689 20050218	
Priority number(s):	US20040792683 20040302	

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.
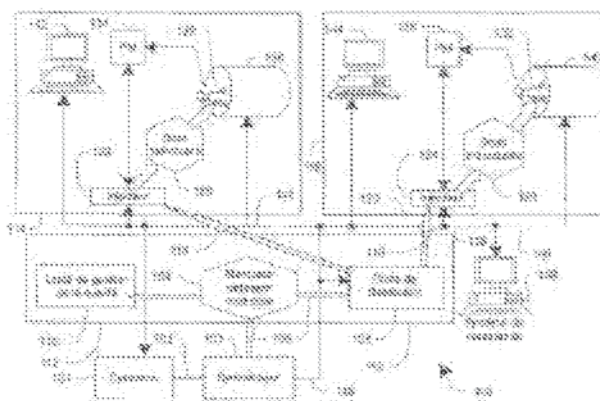
Data supplied from the *esp@cenet* database — Worldwide

(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
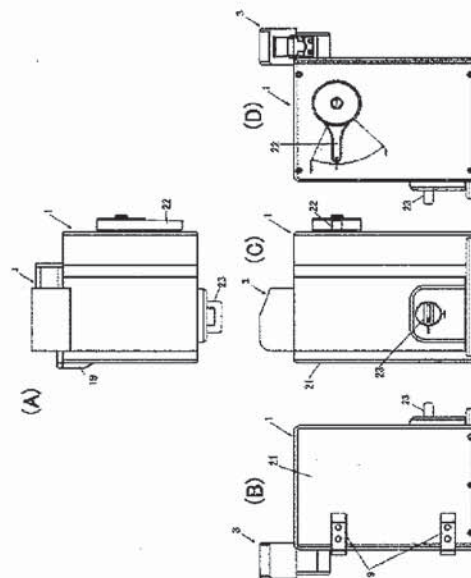
【特許請求の範囲】
【請求項1】
放射線を遮蔽する遮蔽材を全面に有し開閉可能で内部に液状放射性医薬剤を充填されたバイアルを収納できる遮蔽キャビネットと、前記遮蔽キャビネットの内部に設けられ、前記バイアルの上部のゴム栓に穿刺される薬剤針と、これらの薬剤針を、遮蔽キャビネットの外部からの力により、前記ゴム栓に向かって針の方向に沿って昇降させる昇降機構と、前記遮蔽キャビネットの内部に収納されるシリンジに連通し前記薬剤針に連通するチューブと、遮蔽キャビネットの外部からの力により、前記シリンジのプランジャを引いて吸引を行う吸引動作機構と、を有することを特徴とする放射性薬剤吸引装置。

【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に記載の放射性薬剤吸引装置。

【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、鉛又はタング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、^{99m}Tc、^{123}I、^{131}I、^{201}Tl、^{67}Ga、^{51}Cr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13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。
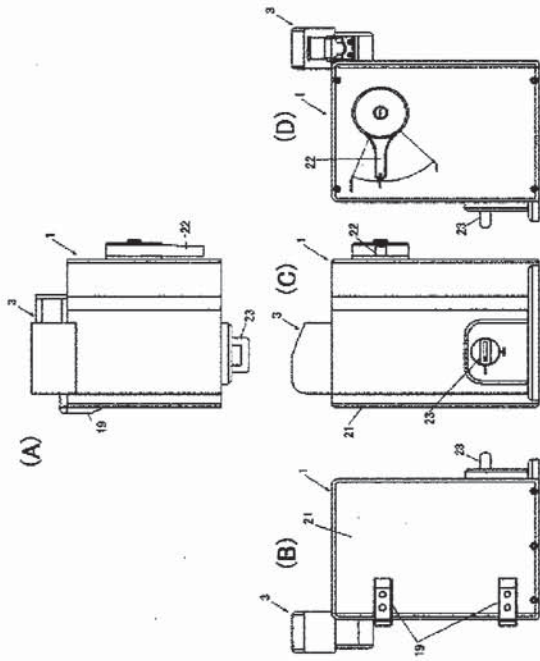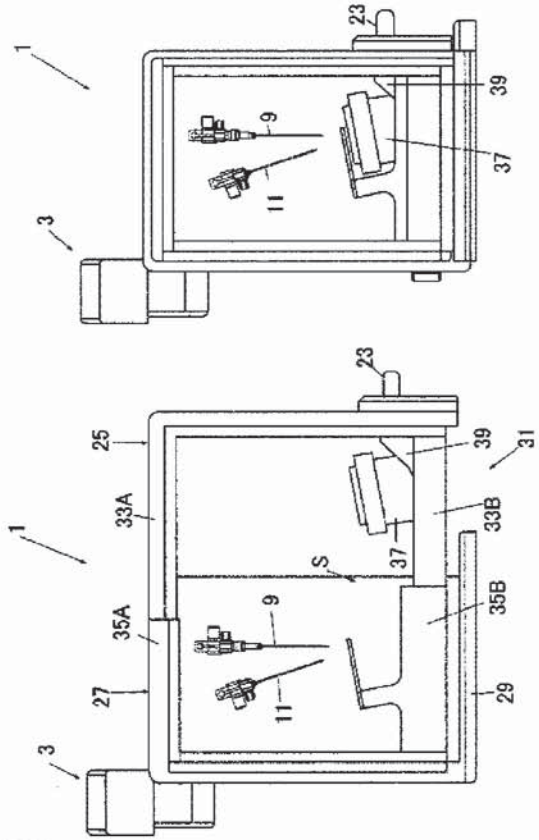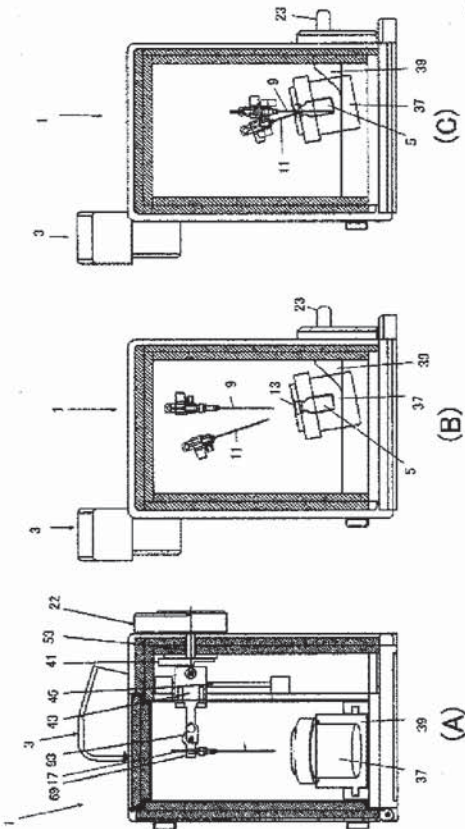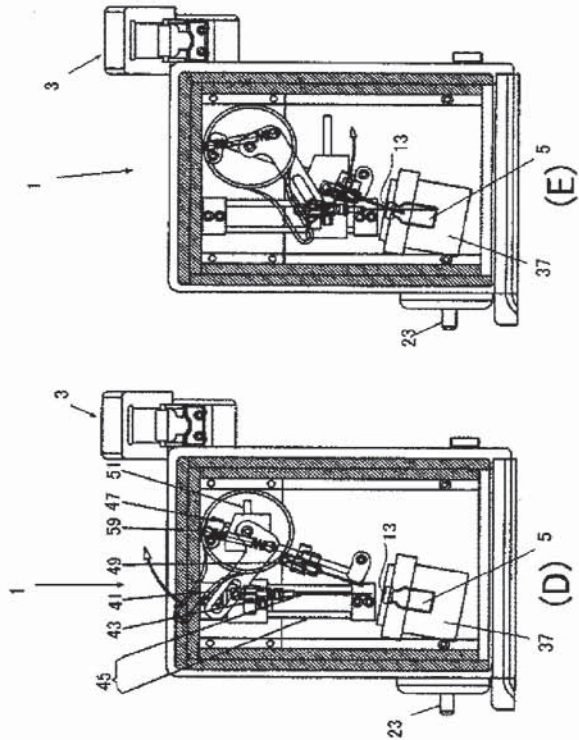
【図1】

【図2】

【図3】

【図4】

【図5】
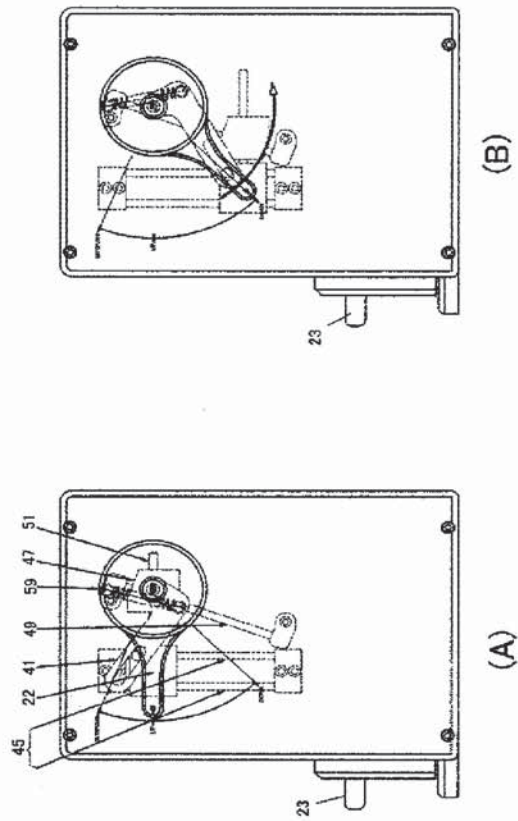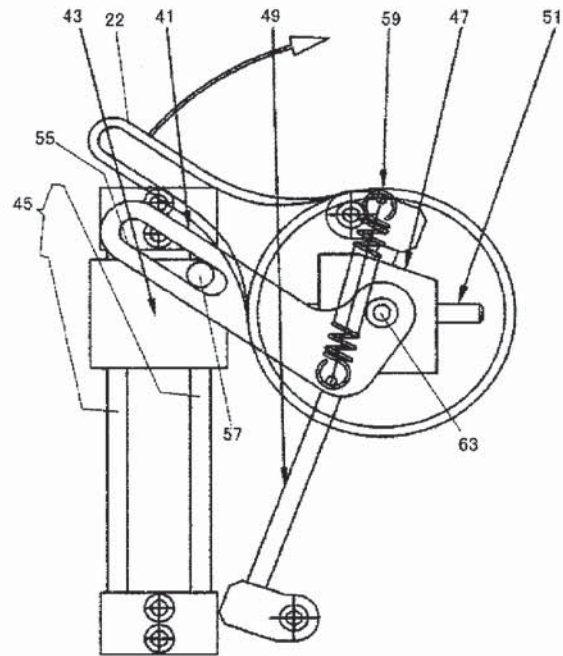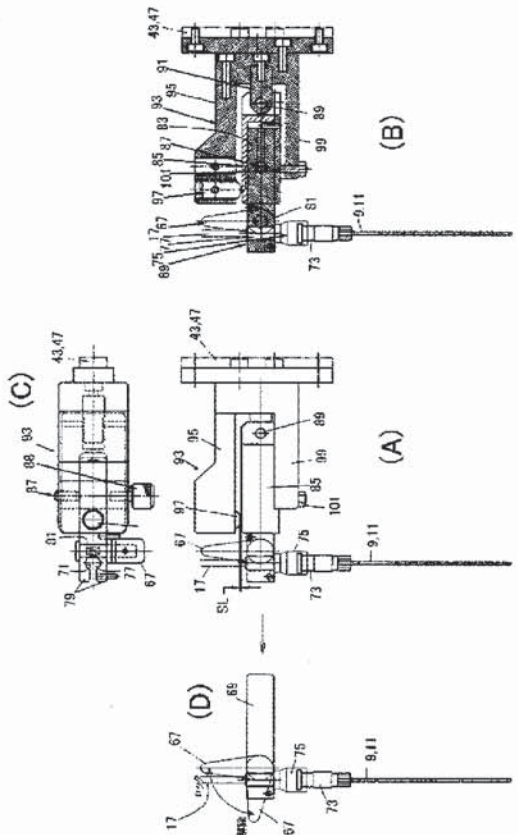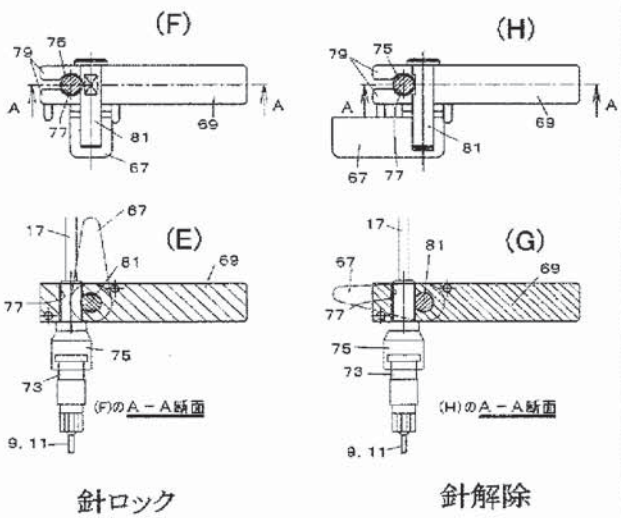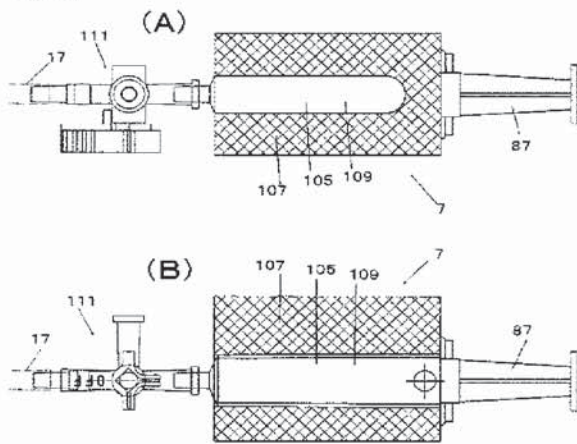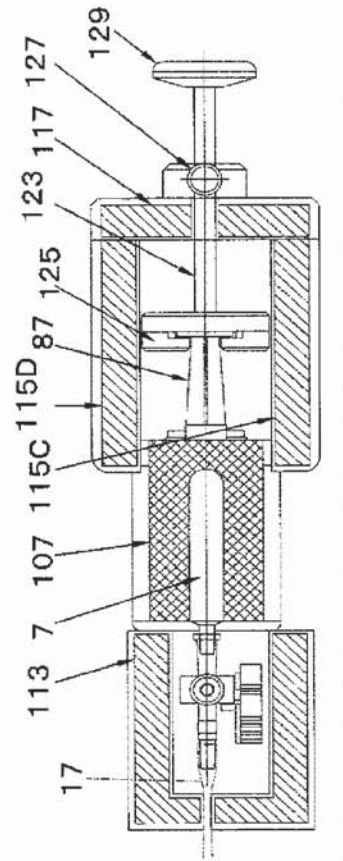
（B）

（A）

【図6】

【図7】

（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)

(B)

【図10】

EUROPEAN PATENT OFFICE

Patent Abstracts of Japan

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.
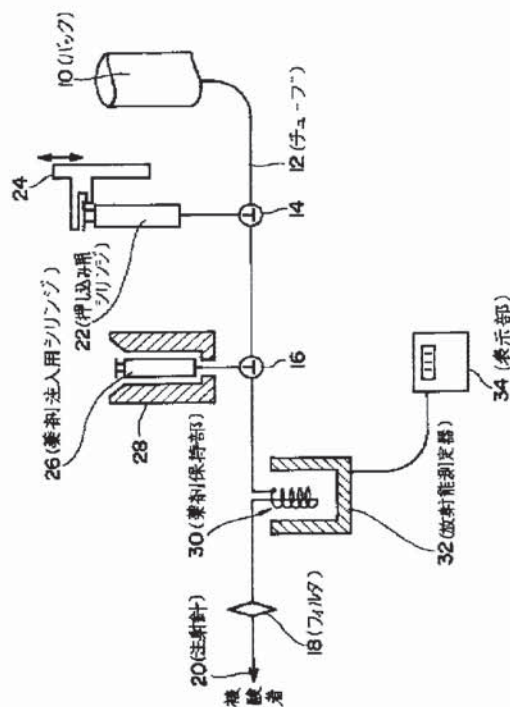
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(54)【発明の名称】 放射性液体の注入方法及び装置

(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人方法。
【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、木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、木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。

【０ ０ ２ ６】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。

【０ ０ ２ ７】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。

【０ ０ ２ ８】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。

【０ ０ ２ ９】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。

【０ ０ ３ ０】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。

【０ ０ ３ １】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。

【０ ０ ３ ２】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。

【０ ０ ３ ３】

【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

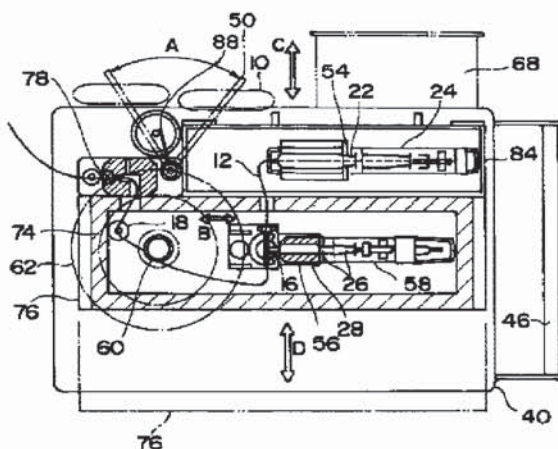【図２】本発明の具体的な構成例である第２実施形態を示す、正面から見た縦断面図

【図３】同じく上面から見た横断面図

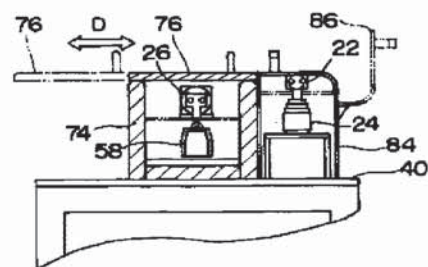【図４】同じく右側面から見た縦断面図

【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３）

（図４）

【図1】
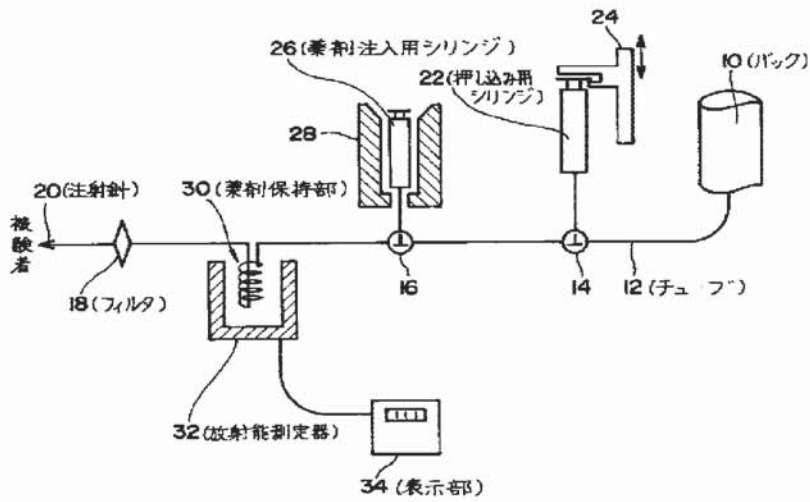
【図2】
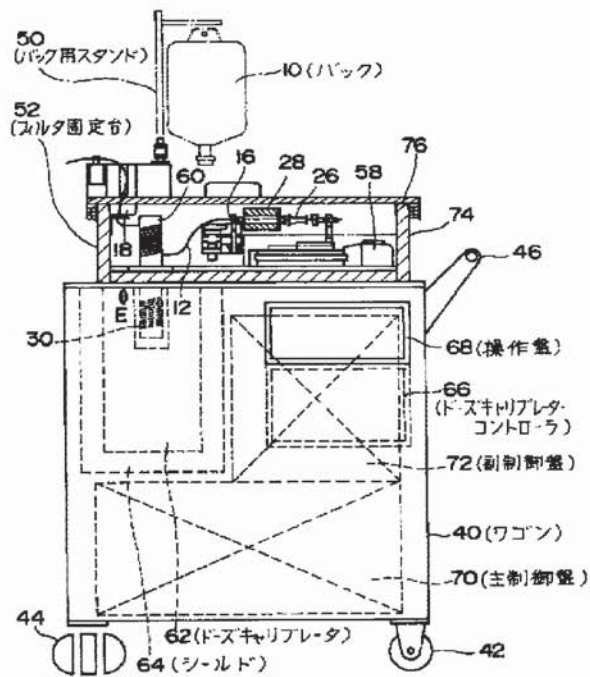
【図5】
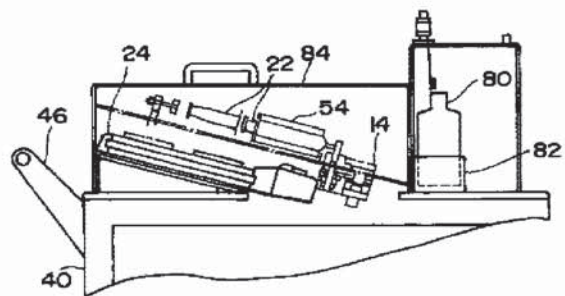
フロントページの続き

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　　　械工業株式会社新居浜製造所内

EUROPEAN PATENT OFFICE

Patent Abstracts of Japan

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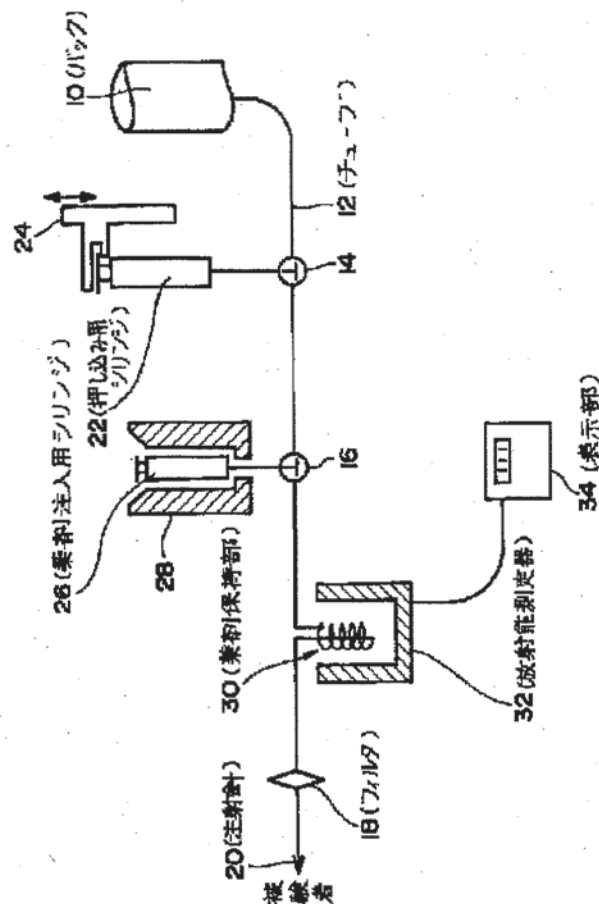PUBLICATION DATE : 19-12-00

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:	6276284
Application Number:	12137356
International Application Number:	
Confirmation Number:	7360
Title of Invention:	SHIELDING ASSEMBLIES FOR INFUSION SYSTEMS
First Named Inventor/Applicant Name:	Charles R. Quirico
Customer Number:	22859
Filer:	Elisabeth Lacy Belden
Filer Authorized By:	
Attorney Docket Number:	56782.1.5
Receipt Date:	16-OCT-2009
Filing Date:	11-JUN-2008
Time Stamp:	14:26:54
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_56782-1-5.pdf	861910 ef6e06d924843b208bfea71bbd2b73302f96f01f	no	5

Warnings:
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2	Foreign Reference	WO9956117A1.pdf	1299254 021d516ba323664bf4eaa2984a9680b3f8779f83	no	31

Warnings:

Information:

3	Foreign Reference	WO2005002971A1.pdf	786004 74ebc85658451adab8f3d793213966aec617ac54	no	22

Warnings:

Information:

4	Foreign Reference	WO2006129301A2.pdf	8063321 ca5d9340c1342351071eb4c9a28f631424ab8dac	no	152

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Information:

5	Foreign Reference	WO2008037939A2.pdf	930500 5a5a97f3d408d70cb7716dcbdd4e6f91e3cd74d6	no	18

Warnings:

Information:

6	Foreign Reference	WO2008082966A2.pdf	6042906 e68c5721046494ae068a4203d7fd457dbdc5dba2	no	158

Warnings:

Information:

7	Foreign Reference	EP0160303A2.pdf	1600444 a1d4f192673b0413e221e8d53cf8298f7e894755	no	42

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Information:

8	Foreign Reference	EP0310148A2.pdf	940420 d65761328c609b56b84279ae9a8fbcc9784b741a	no	20

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Information:

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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11	Foreign Reference	JP2006325826A.pdf	751423 6499fff7b8d76ffc068e84c28c4819d0a3c8d 698	no	18

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12	Foreign Reference	JP2006325826Abstract.pdf	205713 f3bac4c407c20dc79a9f509eed83cf2af3d8c cc2	no	1

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13	Foreign Reference	JP2000350783A.pdf	250118 9299a2273b04952054d73dfdf73ee437361 2caa0	no	5

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14	Foreign Reference	JP2000350783Abstract.pdf	205893 7c72b781cd4e5ab680721cefd817693c231 0ace9	no	1

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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
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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
12/137,356	06/11/2008	Charles R. Quirico	56782.1.5

CONFIRMATION NO. 7360
NEW OR REVISED PPD NOTICE

22859
INTELLECTUAL PROPERTY GROUP
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MINNEAPOLIS, MN 55402

OC000000037850956

NOTICE OF NEW OR REVISED PROJECTED PUBLICATION DATE

The above-identified application has a new or revised projected publication date. The current projected publication date for this application is 12/24/2009. If this is a new projected publication date (there was no previous projected publication date), the application has been cleared by Licensing & Review or a secrecy order has been rescinded and the application is now in the publication queue.

If this is a revised projected publication date (one that is different from a previously communicated projected publication date), the publication date has been revised due to processing delays in the USPTO or the abandonment and subsequent revival of an application. The application is anticipated to be published on a date that is more than six weeks different from the originally-projected publication date.

More detailed publication information is available through the private side of Patent Application Information Retrieval (PAIR) System. The direct link to access PAIR is currently http://pair.uspto.gov. Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

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DEPARTMENT OF DEFENSE
ACCESS ACKNOWLEDGEMENT / SECRECY ORDER RECOMMENDATION
FOR PATENT APPLICATION

Application Serial No: DP12137356   Filing Date: Date Referred: 06/25/2008

I hereby acknowledge that the Department of Defense reviewers has inspected this application in administration of 35 USC 181 on behalf of the Agencies/Commands specified below. DoD reviewers will not divulge any information from this application for any purpose other than administration of 35 USC 181.

Defense Agency	Recommendation	Reviewer Name	Date Reviewed
Army	Secrecy Not Recommended	Linda Lewis	09/08/2008

Type of Recommendations:	*SNR: Secrecy Not Recommended*
	SR: Secrecy Recommended
	NC: No Comment

Instructions to Reviewers:
1. All DoD personnel reviewing this application will be listed on this form regardless of whether they are making a secrecy order recommendation.

2. This form will be forwarded to USPTO once all assigned DoD entities have provided their secrecy order recommendation.

Time for Completion of Review:
Pursuant to 35 USC 184, the subject matter of this application may be filed in a foreign country for the purpose of filing a patent application without a license anytime after the expiration of six (6) months from filing date unless the application becomes the subject of a secrecy order.

The USPTO publishes patent application at 18 months from the earliest claimed filing date. The USPTO will delay the publication of a patent application made available to a defense agency under 35 USC 181 until no earlier than 6 months from the filing date or 90 days from the date of referral to that agency. This application will be cleared for publication 6 months from the filing date or 90 days from the above Date Referred, whichever is later, unless a response is provided to the USPTO regarding the necessary recommendations as to the imposition of a secrecy order.

DoD Completion of Review: Final
Forwarded to USPTO: 09/04/2009   By: Oksana Nesterczuk

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	12137356
	Filing Date	2008-06-11
	First Named Inventor	Charles R. Quirico
	Art Unit	3763
	Examiner Name	
	Attorney Docket Number	56782.1.5

U.S.PATENTS

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	3774036		1973-11-20	Gerhart	
	2	3997784		1976-12-14	Picunko, et al.	
	3	4286169		1981-08-25	Rossem	
	4	4625118		1986-11-25	Kriwetz et al.	
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	6	4755679		1988-07-05	Wong	
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	8	5039863		1991-08-13	Matsuno et al.	

	INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	12137356		
		Filing Date	2008-06-11		
		First Named Inventor	Charles R. Quirico		
		Art Unit	3763		
		Examiner Name			
		Attorney Docket Number	56782.1.5		

	9	5258906		1993-11-02	Kroll et al.	
	10	5274239		1993-12-28	Lane et al.	
	11	5475232		1995-12-12	Powers et al.	
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	13	5739508		1998-04-14	Uber, III	
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	18	6626862	B1	2003-09-30	Duchon et al.	
	19	6767319	B2	2004-07-27	Reilly et al.	

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	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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FOREIGN PATENT DOCUMENTS — Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	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]

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Not for submission under 37 CFR 1.99)

Application Number	12137356
Filing Date	2008-06-11
First Named Inventor	Charles R. Quirico
Art Unit	3763
Examiner Name	
Attorney Docket Number	56782.1.5

	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	12137356
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☒ 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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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(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

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Background of the invention

The present invention relates to a device and a method for dispensing a radioac-
tive liquid to a destination. In particular, the invention relates to the problem of ac-
curately dispensing a well-determined dose of radioactivity, e.g., for injection to a
15   living body.

In a number of medical applications, it is necessary to deliver a radiopharmaceuti-
cal 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
20   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
25   which can be absorbed by certain cells in the brain or in other organs. The con-
centration of the accumulated radiopharmaceutical in a specific body part will often
depend on factors of diagnostic interest, such as cell metabolism or other physio-
logical or biochemical processes. Thus, such processes can be imaged in a non-
invasive fashion by determining the spatio-temporal distribution of radioactivity
30   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 (pro-
ton-rich) radionuclide. The most common radionuclides (radioisotopes) for use

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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.

5

The most common therapeutic uses of radiopharmaceuticals are the ^{131}I therapies in thyroid diseases.

10   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

15   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

20   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

25   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.

30

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,

5 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

10 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

15 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

20 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

25 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

30 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
5   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
10   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
15   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
20   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
25   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,
30   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,

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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;

Detailed description of the invention

Fig. 1 shows, in a highly schematic manner, a device for dispensing a radioactive

10   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 surround-
ings from radioactivity originating from the vial 2, the vial 2 is placed inside a shield

15   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 clos-
ing off vial 2, extends from the inside of vial 2 through a first peristaltic precision

20   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 me-
tering 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 sec-

25   ond peristaltic precision pump P2 to the valve V1. The valve V1 is operable to con-
nect 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

30   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.

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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

10   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

15   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

20   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 illus-

25   trative 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

30   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

9

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.

5   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
10   a step 940, it is decided whether another injection shall be performed. If yes, op- eration 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:
15   the desired activity Ar to be injected to the patient, and the estimated concentra- tion 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.

20   The initialisation period 910 comprises the following steps:
Step 911 (Initial filling of radiopharmaceutical to point C): In a first step, the com- plete 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
25   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
30   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 radio- pharmaceutical 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

5   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

10   line 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.

15

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

20   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

25   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:

30   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
5   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.

10   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.

15

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
20   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
25   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
30   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 il-lustrated 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 con-
5   nect 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 ac-tivity 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
10   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.
15

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
20   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 radio-pharmaceutical (to the same or a different patient) is required, operation continues
25   by repeating the calibration and delivery phases 920 and 930. Otherwise, opera-tion 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
30   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 meter-ing 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.

5   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

10   be delivered to the patient. This is because during the actual delivery of the radio-pharmaceutical 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

15   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.

20   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 compo-

25   nents 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

30   coil shape with nine windings and a diameter of 3.5 cm, made from fluoro-ethylene-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 typi-
5   cally 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.

10 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
15   section 8 of tubing is large enough to hold at the same time all volumes of radio-pharmaceutical 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
20   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
25   during the (predetermined) time needed for the dispensing procedure.

The inventive device and method are not only useful for delivering a radiopharma-ceutical 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
30   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

15

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 informa-tion to the controller 13.

5   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

10   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 me-

15   tering 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.

20

List of reference signs

	P1	first pump
	P2	second pump
	V1	first valve
25	V2	second valve
	a, b, c	connections of first valve
	d, e, f	connection of second valve
	A	inlet of radiopharmaceutial
30	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
5	2	vial
	3	shield
	4	tubing
	5	saline container
	6	tubing
10	7	tubing
	8, 8'	metering section
	9	dose calibrator
	10	tubing
	11	injection needle
15	12	waste
	13	controller
	21, 22, 23	volumes of radiopharmaceutical
20	31	sliding element

Claims

5   1.   Device for dispensing a radioactive liquid (1) to a destination (11), com-
            prising

            -     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

10   -   an activity metering unit (9) operable to determine a level of radioac-
            tivity 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).

15

    2.   Device according to claim 1, characterized in that said first valve means
            (V1) are adapted for remote operation and that said device further com-
            prises a control unit (13) receiving signals from said activity metering unit
            (9) and controlling operation of said first valve means (V1) between at
20   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).

25

    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).

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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);

5   -   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

10   -   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

15   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);

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-        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);

25

-        with said activity metering unit (9), measuring the reference level of radioactivity (A2) present in said metering section (8);

30   -   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

5

-       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:

10

-       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);

15

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

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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)

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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

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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);

24

- 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);

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- 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

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- 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);

15

- 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

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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 sec-

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tion (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

30

(Am) to said metering section (8);

25

-      measuring a level of radioactivity (A2) present in said metering sec-
tion (8);

-      based upon the measured level of radioactivity (A2), calculating the
concentration of radioactivity (Cs) in said source of radioactive liquid (5);

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

10   -   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).
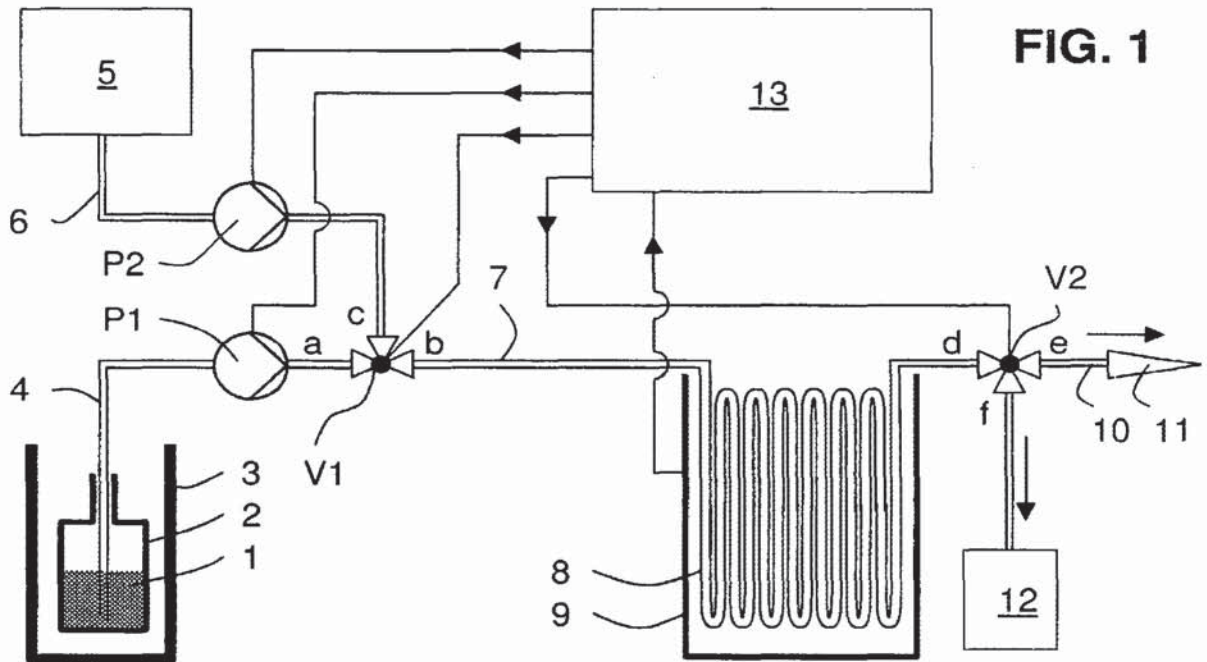
FIG. 1
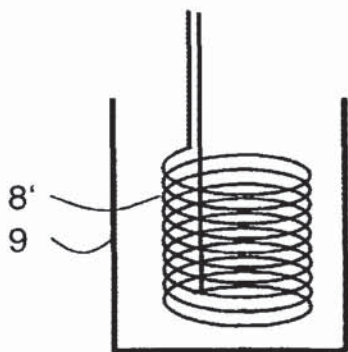
FIG. 2

FIG. 3A

FIG. 3B

FIG. 4

FIG. 5

FIG. 6

FIG. 7

FIG. 8
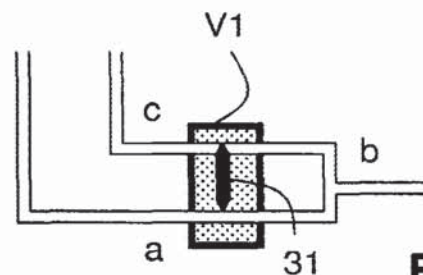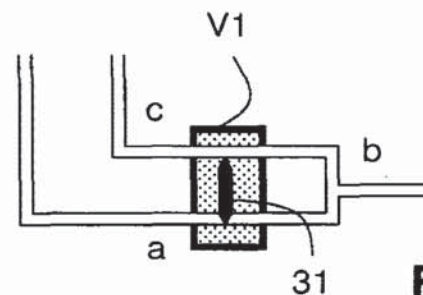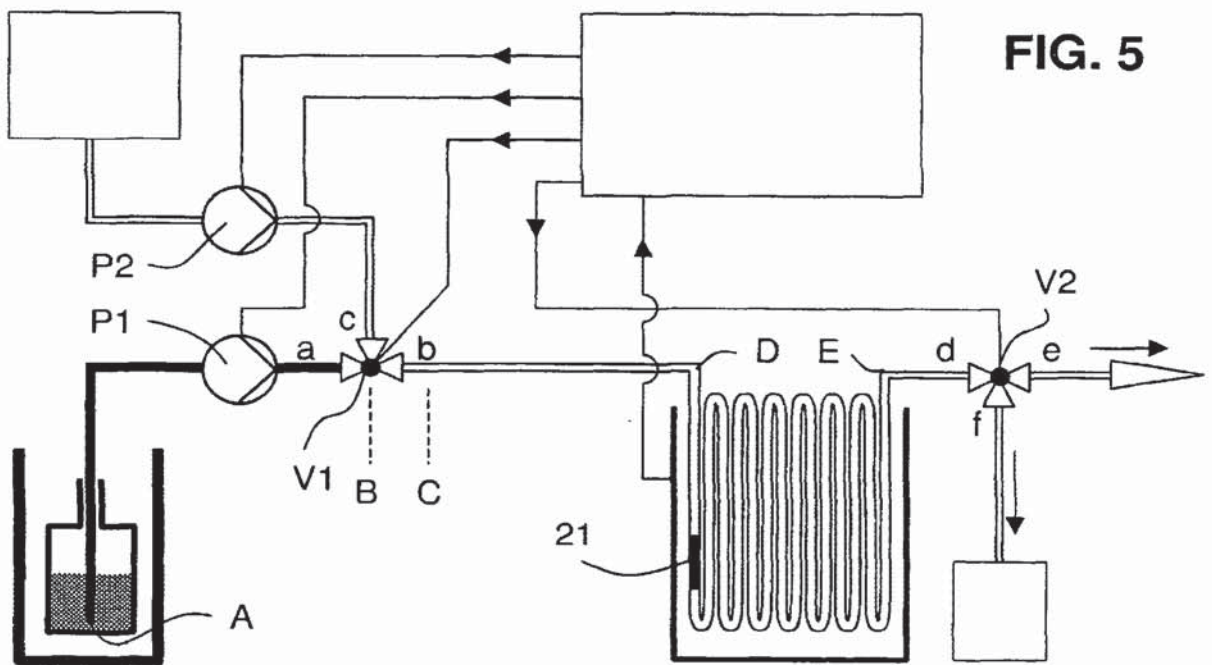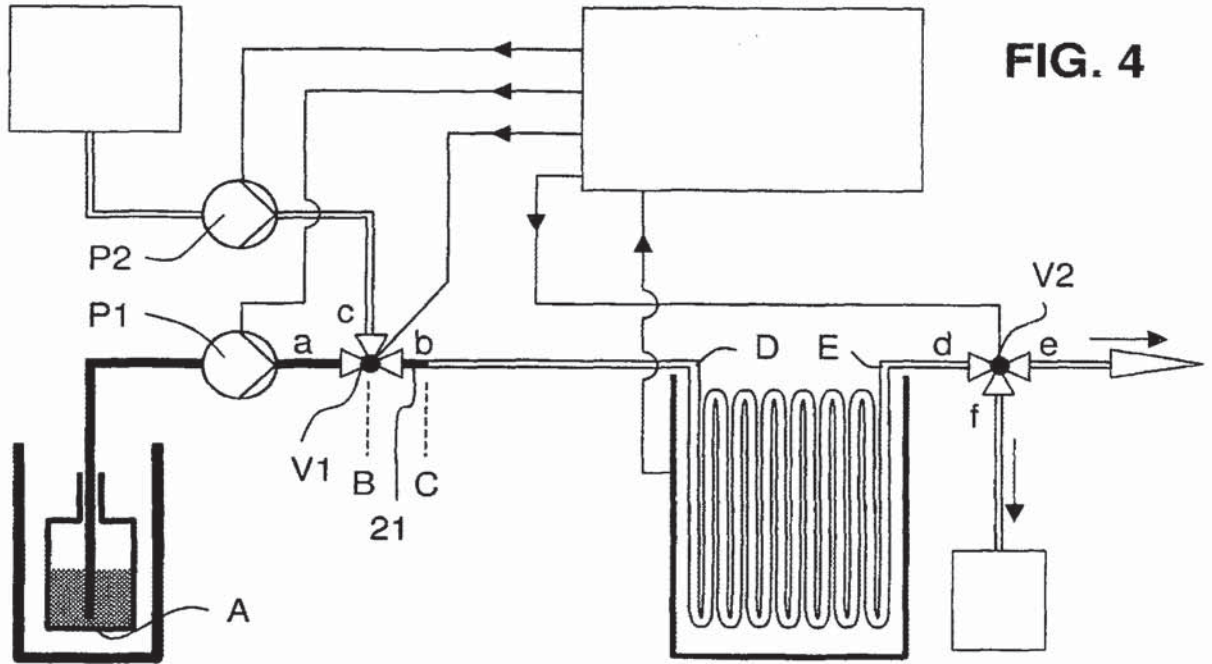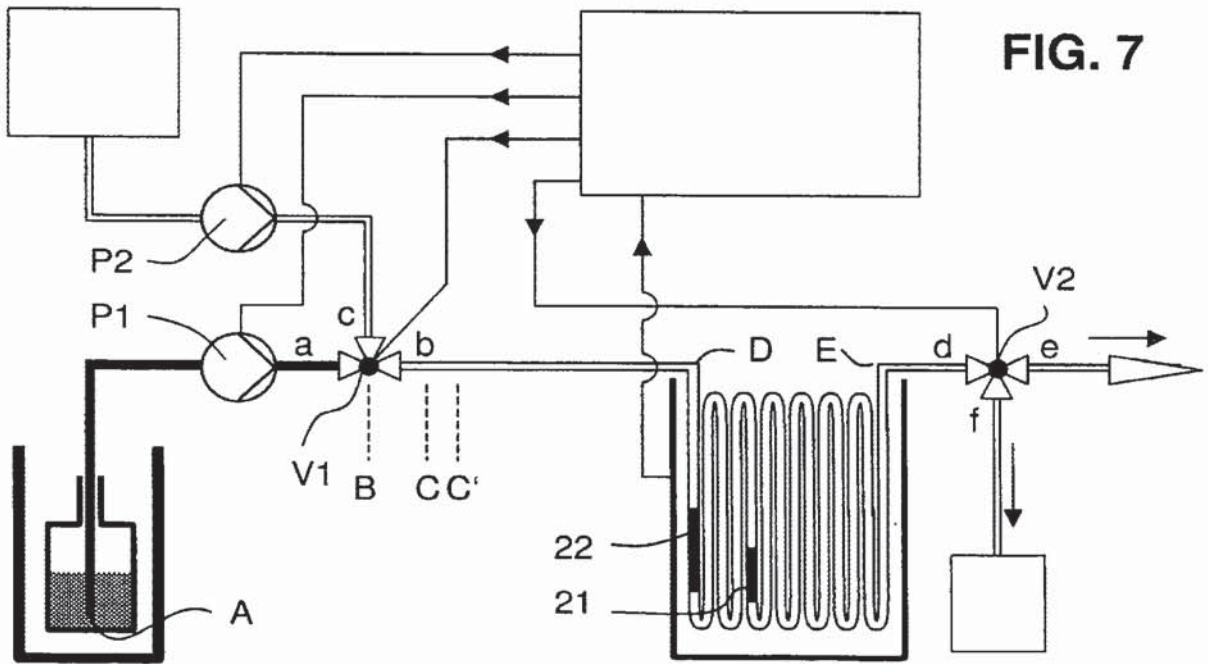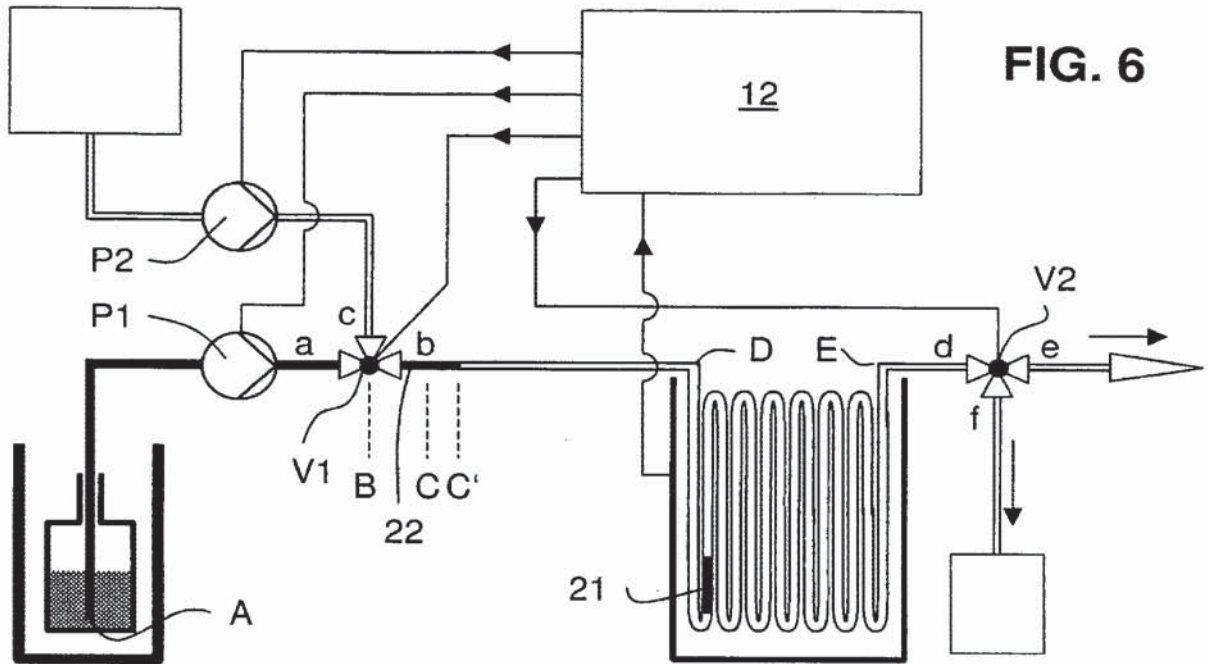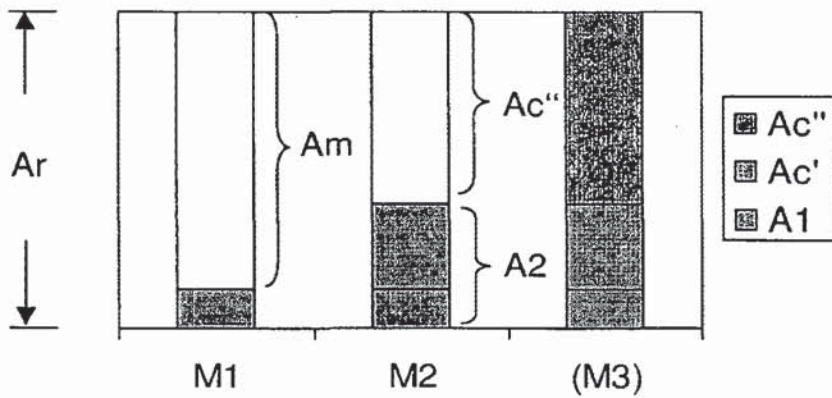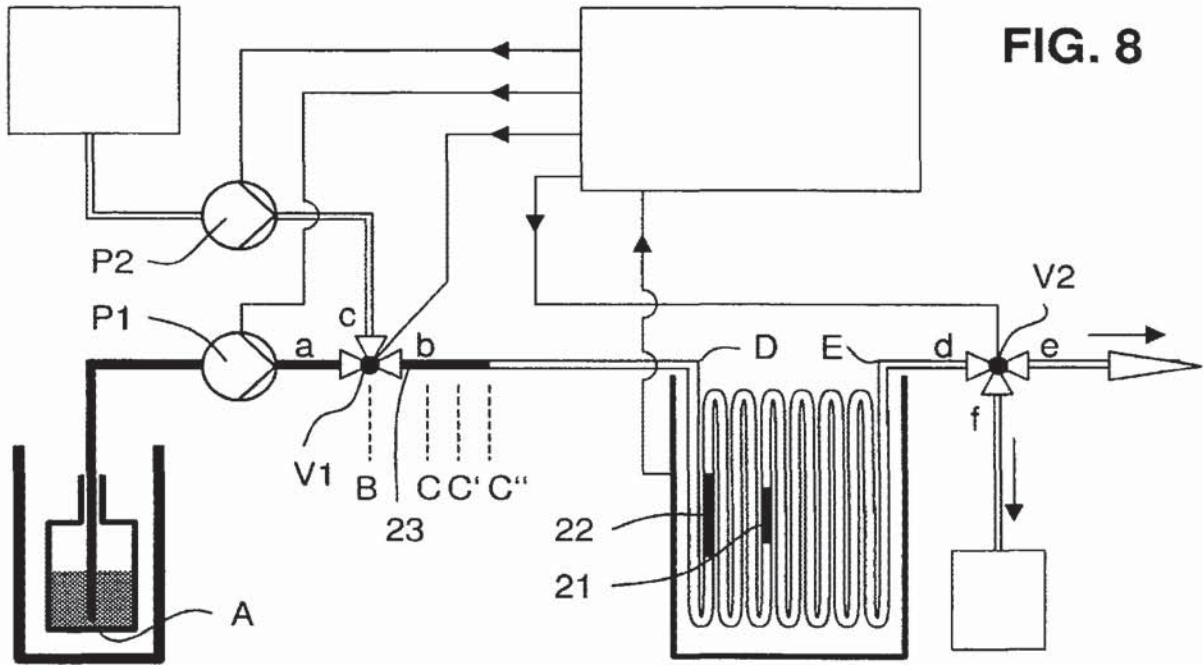
FIG. 10

FIG. 9

INTERNATIONAL SEARCH REPORT

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 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	Authorized officer Schultz, O

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

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

Form PCT/ISA/210 (continuation of second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

| 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.

Form PCT/ISA/210 (continuation of first sheet (2)) (January 2004)

INTERNATIONAL SEARCH REPORT

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
JP 2002306609	A	22-10-2002	NONE		
JP 2000350783	A	19-12-2000	NONE		
EP 0486283	A	20-05-1992	CA	2055297 A1	14-05-1992
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US 2003004463	A1	02-01-2003	US	2004260143 A1	23-12-2004
			US	2003216609 A1	20-11-2003

Electronic Acknowledgement Receipt

EFS ID:	5704505
Application Number:	12137356
International Application Number:	
Confirmation Number:	7360
Title of Invention:	SHIELDING ASSEMBLIES FOR INFUSION SYSTEMS
First Named Inventor/Applicant Name:	Charles R. Quirico
Customer Number:	22859
Filer:	Elisabeth Lacy Belden
Filer Authorized By:	
Attorney Docket Number:	56782.1.5
Receipt Date:	15-JUL-2009
Filing Date:	11-JUN-2008
Time Stamp:	15:46:39
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_5_IDS4.pdf	999570 44e4dec466c322a1a62ee84747afa2e2761b4228	no	6

Warnings:
Information:

2	Foreign Reference	56782_1_WO2006007750A1. pdf	751592	no	35
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	12137356
	Filing Date	2008-06-11
	First Named Inventor	Charles R. Quirico
	Art Unit	3763
	Examiner Name	
	Attorney Docket Number	56782.1.5

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number: 12137356 Filing Date: 2008-06-11 First Named Inventor: Charles R. Quirico Art Unit: 3763 Examiner Name: Attorney Docket Number: 56782.1.5

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	12137356
	Filing Date	2008-06-11
	First Named Inventor	Charles R. Quirico
	Art Unit	3763
	Examiner Name	
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Signature	/Elisabeth Lacy Belden/	Date (YYYY-MM-DD)	2009-05-20
Name/Print	Elisabeth Lacy Belden	Registration Number	50,751

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(54) Title: A RUBIDIUM GENERATOR FOR CARDIAC PERFUSION IMAGING AND METHOD OF MAKING AND MAINTAINING SAME
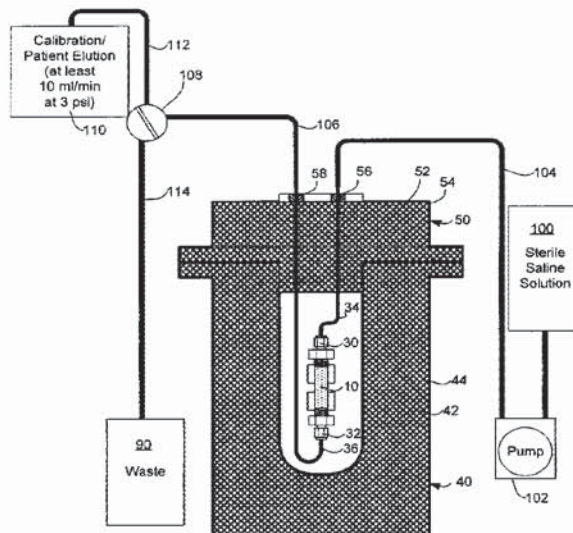
(57) Abstract: An $^{82}Sr/^{82}Rb$ generator column is made using a fluid impervious cylindrical container having a cover for closing the container in a fluid tight seal, and further having an inlet for connection of a conduit for delivering a fluid into the container and an outlet for connection of 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.

A RUBIDIUM GENERATOR FOR CARDIAC PERFUSION

IMAGING AND METHOD OF MAKING AND

MAINTAINING SAME

TECHNICAL FIELD

5   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

10   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 15   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 20   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 25 ^{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

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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.

5   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
10   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,
15   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
20   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
25   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
30   exchange material filling the container, the ion exchange

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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).

5   **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:

10   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;

15   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
20   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
25   numerals.

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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
5   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
10 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
15 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
20 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
25 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
30 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 (

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$SnO_2.xH_2O$, 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
5 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
10 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
15 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
20 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
25 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
30 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
5   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
10   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
15   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
20   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
25   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
30   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

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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
5   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
10 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
15 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
20 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
25 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
30 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

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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
5   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
10   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
15   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
20   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
25   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
30   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
5   (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
10   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
15   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
20   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
25   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
30   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 5   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 10   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.

15   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 20   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.

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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.
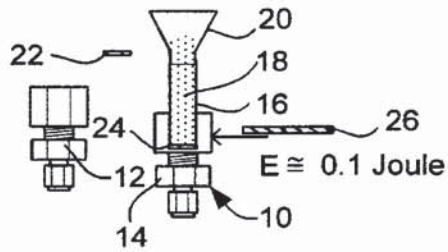
FIG. 1
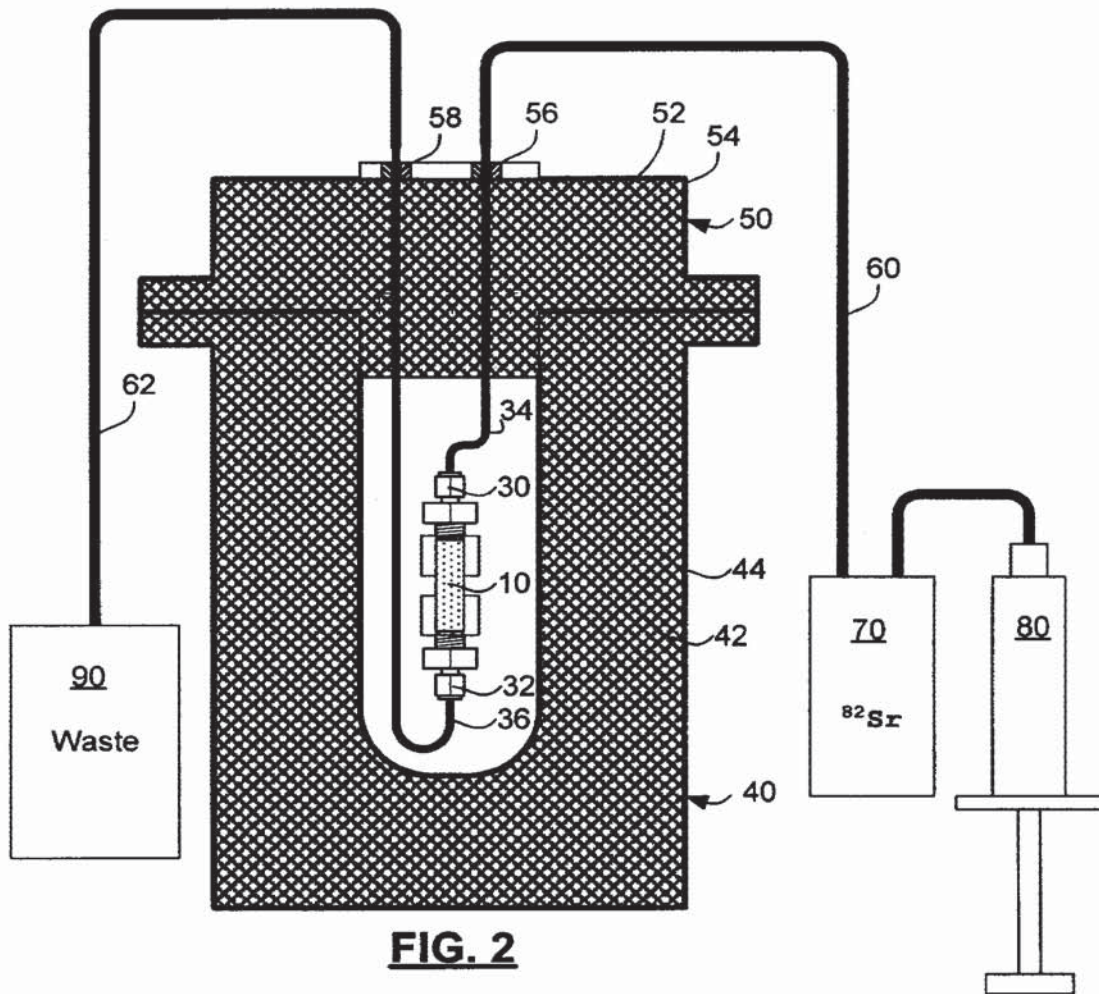
FIG. 2
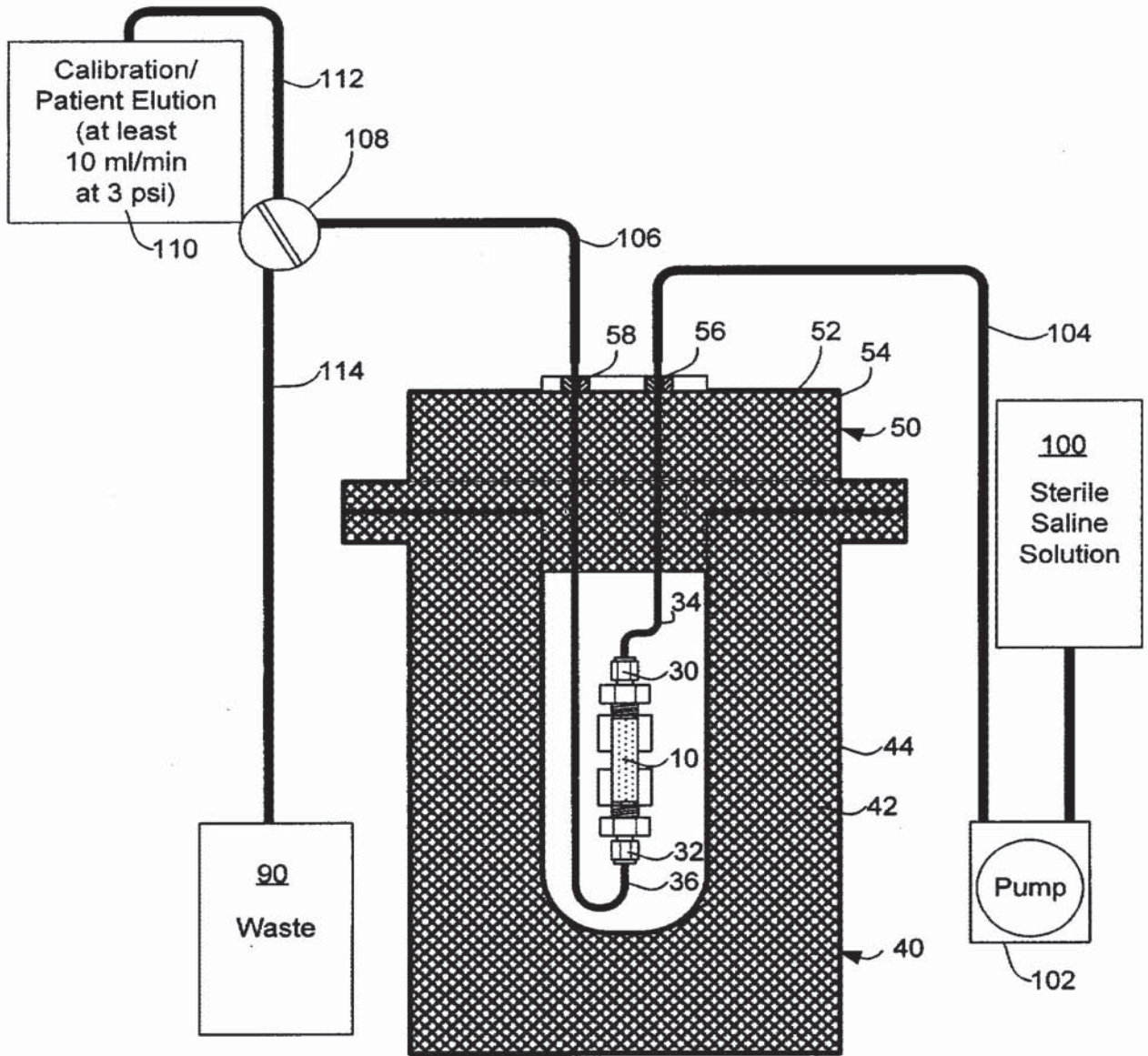
FIG. 3
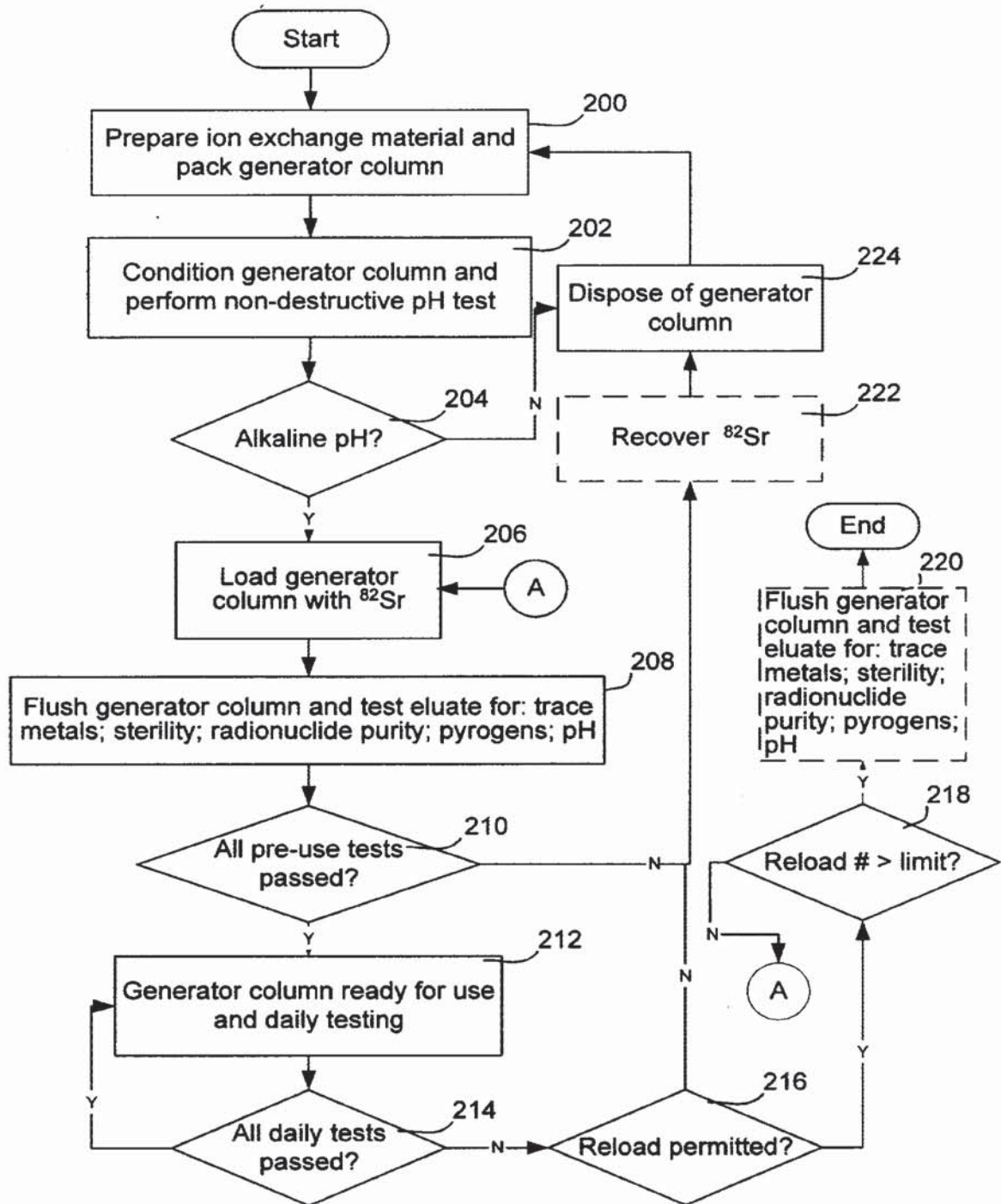
FIG. 4

4/4
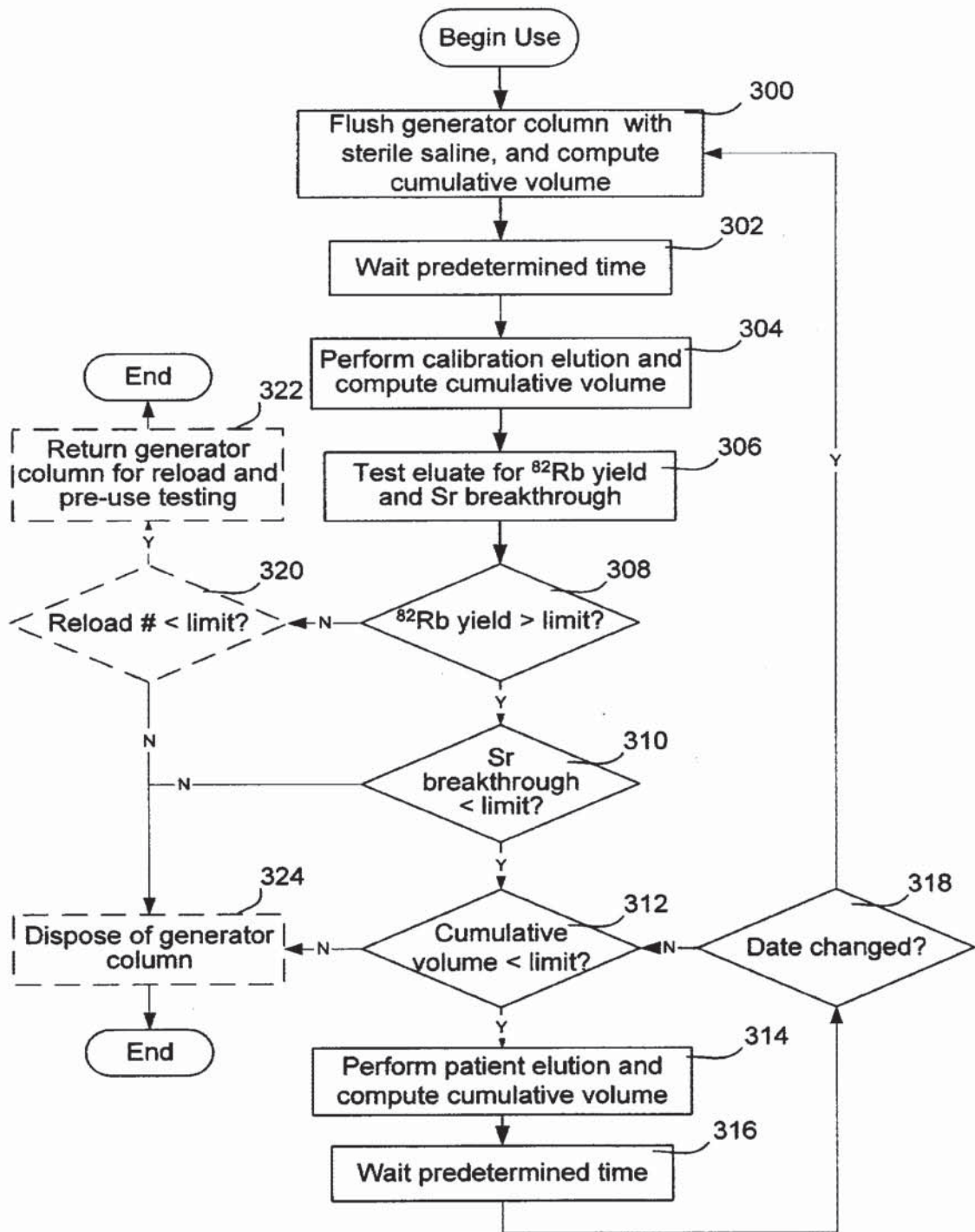
FIG. 5

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 Y	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 * Whole document *	1-20 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 :	"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
"A"	document defining the general state of the art which is not considered to be of particular relevance	"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
"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)	"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
"O"	document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 13 April 2007 (13-04-2007)	Date of mailing of the international search report 17 April 2007 (17-04-2007)
Name and mailing address of the ISA/CA 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	Authorized officer Pierre Cuerrier 819- 997-4379

Form PCT/ISA/210 (second sheet) (April 2005)   Page 2 of 4

INTERNATIONAL SEARCH REPORT

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

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		SE7809128 A	11-10-1979
US3935884	03-02-1976	NONE	
US2845136	29-07-1958	NONE	
US3164980	12-01-1965	NONE	

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(54) Title: RUBIDIUM ELUTION SYSTEM CONTROL

(57) Abstract: A method of controlling an $^{82}Sr/^{82}Rb$ elution system having a generator valve for proportioning a flow of saline solution between an $^{82}Sr/^{82}Rb$ generator and a bypass line coupled to an outlet of the generator such that saline solution traversing the bypass line will merge with eluted saline solution emerging from the generator to provide an active saline solution. During each elution run, a plurality of successive concentration parameter values are obtained at predetermined intervals. Each concentration parameter value is indicative of a respective instantaneous activity concentration of the active saline solution. Respective error values between each concentration parameter value and a target activity concentration value of the elution run are computed. Error data based on a plurality of the computed error values is accumulated. Between successive elution runs, at least one performance parameter of the elution system is adjusted based on the accumulated error data.

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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

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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

5   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

10   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

15   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

20   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

25   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

30   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

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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

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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

5   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

10   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

15   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

20   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

25   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;

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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.

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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
5   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
10   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
15   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
20   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
25   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
30   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

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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 5   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 10   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 15   (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 20   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 25   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 30   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

5   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-

10 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

15 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

20 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

25 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

30 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,

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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

5   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

10 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

15 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,

20 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

25 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

30 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

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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
5   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
10   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
15   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
20   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
25   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
30   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

5   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

10   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

15   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

20   (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

25   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.

30   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).

5   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 10   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 15   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), 20   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 25   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 30   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
5 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"
10 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
15 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
20 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 $C_M(t)$
25 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
30 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

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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
5   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
10 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
15 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.

20   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
25 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.

30   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

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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

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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
5 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.

10   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
15 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
20 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
25 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
30 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
5 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
10 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
15 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
20 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
25 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
30 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
5   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
10   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.

15   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
20   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
25   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
30   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,
5   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
10 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
15 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
20 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
25 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
30 concentration. In particular, the instantaneous activity detected by the dose calibrator during the calibration elution is the convolution of the activity concentration

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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

5   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

10   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

15   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

20   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

25   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

30   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
5   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
10 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.
15 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
20 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
25 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
30 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
5   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
10 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
15 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
20 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
25 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
30 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.