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(71) Applicant: **National Institute of Radiological Sciences**
Chiba-shi, Chiba 263-8555 (JP)

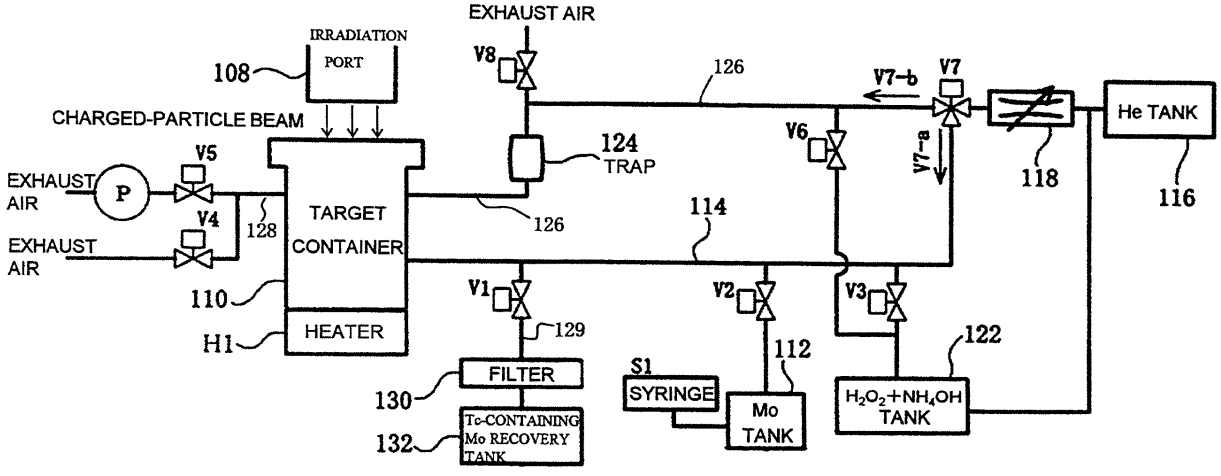
(72) Inventors:
- **NAGATSU, Koutaro**
  Chiba-shi, Chiba 263-8555 (JP)
- **MINEGISHI, Katsuyuki**
  Chiba-shi, Chiba 263-8555 (JP)
- **UCHIDA, Shigeo**
  Chiba-shi, Chiba 263-8555 (JP)
- **TAGAMI, Keiko**
  Chiba-shi, Chiba 263-8555 (JP)

(74) Representative: **Twelmeier Mommer & Partner**
Patent- und Rechtsanwälte
Westliche Karl-Friedrich-Strasse 56-68
75172 Pforzheim (DE)

(54) PROCESS AND DEVICE FOR PRODUCTION OF RADIONUCLIDE USING ACCELERATOR

(57) A target material, which is dissolved or mixed in liquid, is introduced into a target container, and dried inside of the target container to reduce its liquid component. Subsequently, the target material is irradiated with a beam from a particle accelerator. This allows remotely and repeatedly producing a radionuclide such as technetium 99m and molybdenum 99, which are radioactive pharmaceuticals in high demand, using one target container.

Fig. 1



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Description

TECHNICAL FIELD

[0001] The present invention relates to a method for producing a radionuclide using a particle accelerator and an apparatus for producing the radionuclide. Especially, the present invention relates to a method for producing the radionuclide using the particle accelerator and the apparatus for producing the radionuclide that allow remotely and repeatedly producing a radionuclide such as technetium 99m and molybdenum 99, which are radionuclides in high demand as radioactive pharmaceuticals, in one target container.

BACKGROUND ART

[0002] Technetium 99m (Tc-99m with a half-life of six hours), which is used in fields of nuclear medicine and image diagnosis worldwide, has a percentage of equal to or more than 70 percent of radioisotopes used for nuclear medicine, and is a major player. Molybdenum 99 (Mo-99 with a half-life of 66 hours) generates Tc-99m along with decay of Mo-99, and is a radioisotope called a parent nuclide of aforementioned Tc-99m. A commercially available apparatus (a Mo-99/Tc-99m generator) selectively recovers Tc-99m that is generated by adsorbing Mo-99 to a support such as alumina, or by similar method.

[0003] As a method for producing technetium 99m using a particle accelerator, a method where a target is irradiated with charged particles, specifically, isotopically enriched molybdenum 100 (Mo-100) is irradiated with a proton beam has been studied. However, a result at a practical level (for example, a large amount of radioactivity is provided enough for medical use, or a set of apparatus is validated for medical use) has not been reported.

[0004] The present invention is a method for producing Tc-99m or Mo-99 by nuclear reaction of ^{100}Mo (p,2n) ^{99m}Tc or ^{100}Mo (p,pn) ^{99}Mo using charged particles obtained from a particle accelerator. Therefore, prior art of a general method using a particle accelerator is validated. In any cases, yield (radioactivity) at a practical level is not obtained, and evaluation has ended with conceptual examination or validation.

[0005] That is, Non-Patent Document 1 discloses generation amounts of Tc-99m and Mo-99 that are estimated in the case where Mo-100 is irradiated with a proton beam in the 68-8 MeV energy range, and Non-Patent Document 2 discloses generation amounts of Tc-99m and Mo-99 that are estimated in the case where Mo-100 is irradiated with a proton beam in the 22-10 MeV energy range. It is disclosed that both the nuclides are obtained in yield corresponding to energy. However, a specific irradiation method or any configuration of apparatus is not disclosed. The Non-Patent Documents are prior literatures for tentative examination that explore what is called feasibility, and are reports on investigation of physical phenomenon.

[0006]

Non-Patent Document 1: Lagunas-solar, M.C. et al. (1991) Cyclotron production of NCA 99mTc and 99Mo. An alternative non-reactor supply source of instant 99mTc and 99Mo----99mTc generators. Appl. Radiat. Isot. 42(7), 643-657

Non-Patent Document 2: Beaver, J.E. and Hupf, H.B. (1971) Production of 99mTc on a medical cyclotron: A feasibility study. J. Nucl. Med. 12(11), 739-741

DISCLOSURE OF THE INVENTION

PROBLEMS TO BE SOLVED BY THE INVENTION

[0007] Irradiating Mo-100 with a proton beam generates Mo-99 and/or Tc-99m corresponding to incident energy, which is known since early times. However, any production using charged particles is not performed even now. This may be because there is no production apparatus that handles a large amount of radioactive material generated after the irradiation without exposure. Specifically, the target material employs molybdenum or molybdenum compound, which is solid. Therefore, when preparation in the target container, extraction after irradiation, or similar process is performed, means for easily performing these operations is not available. Unlike a general operation, these operations are performed under environment with high radiation. In view of this, it is required to ensure safety for the operator from exposure and contamination, which is extremely difficult to be achieved. Usually, production of a radioisotope using a solid target employs a remote controlled and automated industrial robot, or an exposure reduction measure that is a combination of a barrier and a manipulator. However, for example, installation of these facility and equipment costs considerably, and a skilled operator is needed for operations of the manipulator. High specifications are required in economic and technical aspects.

[0008] Therefore, it is strongly requested to establish a method for producing a radioisotope using a solid target at

low-price with facilitated operation.

[0009] The present invention has been made to solve the above-described problems, and it is an object of the present invention to establish a specific structure and operation method of irradiation that are applicable when irradiation of molybdenum 100 is performed in order to practically produce technetium 99m and/or molybdenum 99.

SOLUTIONS TO THE PROBLEMS

[0010] The inventors attempted to solve by dissolving molybdenum as a target material in an appropriate solvent, drying this target material so as to transform the liquid into solid before irradiation. In the irradiation, using a target (molybdenum solution) in a liquid state is possible. However, the liquid absorbs beam energy. This consequently interferes with sufficient nuclear reaction of the molybdenum target. Therefore, this method significantly reduces expected yields of Tc-99m or Mo-99. The present invention removes liquid from the target material before the irradiation, and increases the density of the molybdenum target in an incident beam path, thus obtaining theoretical yields of the nuclear reaction.

[0011] The present invention is made based on the aforementioned knowledge. The present invention is a method for producing a radionuclide using a particle accelerator. The method includes: introducing a target material, which is dissolved or mixed in a liquid, into a target container, reducing liquid component by drying inside of the target container, and irradiating a beam from a particle accelerator.

[0012] Here, the method may dry the target material inside of the target container to deposit solid component of the target material. The target material is dissolved or mixed in the liquid and introduced into the target container.

[0013] The solid component deposited inside of the target container may have a thickness of 0.1 to 5 mm in an incident beam path from the particle accelerator.

[0014] The drying may be performed by at least one of heating, introducing drying gas, and exhausting air.

[0015] A temperature inside of the target container at the drying may be equal to or more than 100°C.

[0016] The drying may use a gas, the gas being one of helium, hydrogen, or carbon monoxide.

[0017] The gas used for the drying may be introduced into the target container such that the gas passes through the target material. The target material is dissolved or mixed in the liquid, introduced into the target container, and accumulated at a lower portion of the target container.

[0018] Liquid may be introduced into the target container after the irradiation of beam terminates. The target material is again dissolved or mixed in the liquid. The liquid is then extracted from the target container.

[0019] The liquid extracted from the target container may be recovered without disposal.

[0020] The target material may be molybdenum 100, the beam may be a proton beam at 40-9 MeV, and a radionuclide to be produced may be technetium 99m and/or molybdenum 99.

[0021] The target material to be introduced into the target container may be molybdenum oxide dissolved in an ammonia solution.

[0022] A hydrogen peroxide solution may be added to the ammonia solution.

[0023] The temperature at drying may be from 200 to 650°C.

[0024] The liquid may be an ammonia solution and/or a hydrogen peroxide solution.

[0025] The present invention also provides a method for producing a radionuclide using a particle accelerator. The method includes: introducing liquid into a target container when extracting a target material from the target container after the target material is irradiated with a beam from the particle accelerator; dissolving or mixing the target material in the liquid; and extracting the target material from the target container.

[0026] The present invention also provides an apparatus for producing a radionuclide using a particle accelerator. The apparatus includes: a target container, means for introducing a target material into the target container where the target material is dissolved or mixed in a liquid, drying means for drying an inside of the target container to reduce liquid component, and means for irradiating the target container with a beam from the particle accelerator.

[0027] Here, the drying means may dry the target material inside of the target container to deposit solid component. The target material is dissolved or mixed in the liquid and introduced into the target container.

[0028] The drying means may include at least one of heating means, gas supplying means, and exhausting means.

[0029] The target container may include a metal thin film, the metal thin film sealing the target container and allowing the beam to pass through. The metal thin film is cooled.

[0030] The apparatus may further include: means for introducing liquid into the target container after irradiation of the beam terminates; and means for dissolving or mixing the target material in the liquid again, and extracting the target material from the target container.

[0031] The present invention may further include means for recovering liquid extracted from the target container without disposal.

[0032] The means for recovering may include a filter disposed in a middle of a pipe.

[0033] The present invention also provides an apparatus for producing a radionuclide using a particle accelerator by extracting a target material from a target container after the target material is irradiated with a beam from the particle

accelerator. The apparatus includes means introducing liquid into the target container, dissolving or mixing the target material in the liquid, and extracting the target material from the target container.

EFFECTS OF THE INVENTION

[0034] The present invention allows production of Tc-99m using molybdenum as a target, which has not been reported in the past. Additionally, this allows remotely performing all processes needed for production. This eliminates occupational exposure of an operator. This ensures production where aspects of safety and health are considered.

[0035] This allows quickly extracting the target material from the target container, and repeatedly performing the production using one target container. This also allows extracting even a radionuclide with a short half-life without any problem.

BRIEF DESCRIPTION OF THE DRAWINGS

[0036]

FIG 1 is a conduit line map illustrating a configuration according to a first embodiment of the present invention.
FIG. 2 is a cross-sectional view illustrating a target container used in the first embodiment.
FIG 3 is a flowchart illustrating a procedure of the first embodiment.
FIG. 4 is a cross-sectional view of a target container, which is used in a second embodiment of the present invention, taken along the line IV-IV of FIG 5.
FIG. 5 is a side view of FIG 4 viewed in an arrow direction V.

DESCRIPTION OF PREFERRED EMBODIMENTS

[0037] Embodiments of the present invention will be described in detail by referring to the accompanying drawings.

[0038] A first embodiment of the present invention includes, as illustrated in FIG. 1, a target container 110, a target solution (Mo) tank 112, a syringe S1, a heater H1 for heating, a helium (He) tank 116, a flow rate controller 118, a decompression pump (such as a vacuum pump) P, a solvent mixture (H_2O_2 + NH_4OH) tank 122, a valve V3, a three-way diversion valve V7, a solution trap 124, a valve V6, a valve V1, a filter 130, a Tc-containing Mo recovery tank 132, valves V1 to V8, and pipes 114, 126, 128, and 129. The target container 110 is, for example, vertically irradiated with a charged particle (here, proton) beam from a particle accelerator irradiation port 108. The particle accelerator irradiation port 108 is means for irradiation of the beam from a particle accelerator (not shown). The target solution (Mo) tank 112 stores a target material (Mo) that dissolves in or is mixed with liquid (referred to as target solution). The syringe S 1 is means for extruding the target solution from the Mo tank 112 to the pipe 114 and introducing the target solution into the target container 110. The heater H1 is drying means that dries the target solution inside the target container 110 until the irradiation of the proton beam is not affected, and reduces liquid component such that solid component is deposited. The He tank 116, the flow rate controller 118, and the decompression pump P supply inert gas for drying (also used for pressure source of liquid transportation) such as helium gas. The decompression pump P is used for vaporizing and enhancing exhaust air. The solvent mixture (H_2O_2 + NH_4OH) tank 122 stores a solvent for recovery such as H_2O_2 + NH_4OH. The valve V3 is means for extruding the solvent for recovery inside the H_2O_2 + NH_4OH tank 122 using such as a syringe (not shown) to the pipe 114 after the irradiation of proton beam terminates, so as to introduce the solvent for recovery into the target container 110. The three-way diversion valve V7 selects a flow path V7-a, a flow path V7-b, and a closed path of helium gas. The solution trap 124 is disposed in the middle of the pipe 126 from the target container 110, and allows overflow of the solution from the target container 110. The valve V6 is means for introducing the solvent for recovery, which is introduced from the H_2O_2+NH_4OH tank 122 using a syringe (not shown) or similar member, to the target container 110 from the solution trap 124 and the pipe 126, so as to clean the target container 110. The valve V 1 is means for extracting liquid from the inside of the target container 110, and for recovering the liquid without disposal. The filter 130 is disposed in the middle of the recovery pipe 129 to inhibit solid content of the recovered material from obstructing the subsequent pipe inside. Here, the valves except the valve V7 are one directional opening and closing valve.

[0039] Molybdenum solution used as the target solution is obtained by dissolving or mixing molybdenum oxide (MoO_3 is preferred.) in 10 to 30% ammonia solution. In order to enhance dissolution, 10 to 30% hydrogen peroxide solution may be added. In this case, it is preferred that solution composition be as follows.

25% ammonia solution : 30% hydrogen peroxide solution = 1 : 1 to 1 : 2

[0040] As illustrated in FIG. 2 in detail, the target container 110 includes a target chamber 110C and a heating/cooling portion 110D. The target chamber 110C is separated from an irradiation port 110A side by a metal thin film 110B, and the target solution is introduced into the target chamber 110C so as to process irradiation of charged particles. The heating/cooling portion 110D includes the heater H1 to heat and cool the target chamber 110C. Additionally, at the irradiation port 110A side of the metal thin film 110B, a cooling chamber 110F that is partitioned with a vacuum diaphragm 110E and the metal thin film 110B to flow fluid (here, helium gas) for cooling the metal thin film 110B. In the drawing, a reference numeral 110G denotes a port that is coupled to the pipe 114 and the recovery pipe 129. A reference numeral 110H denotes a port that is coupled to the pipe 126 where the solution trap 124 is disposed. A reference numeral 110I denotes a port that is coupled to the pipe 128 where the valves V4 and V5 are disposed. A reference numeral 110J denotes a cooling He gas inlet port. A reference numeral 110K denotes a cooling He gas outlet port. A reference numeral 110L denotes a cooling water inlet port. A reference numeral 110M denotes a cooling water outlet port.

[0041] The target chamber 110C is made, for example, in a columnar shape with an inner diameter of 10 to 20 mm and a depth of 20 to 100 mm, and may employ material of aluminum, gold, or platinum. The preferred material is aluminum, which is low-price. Considering corrosion resistance, it is possible to employ gold or platinum. The metal thin film 110B, which allows the beam from the particle accelerator to pass through so as to irradiate the target material with the beam, similarly employs material. The metal thin film 110B is preferred to have a thickness of, for example, 10 to 500 μm, especially, 10 to 100 μm corresponding to the beam energy. A portion of a flange 110N, which needs air tightness, includes an O-ring 110P made of stainless steel or heat-resistant silicon. The metal thin film 110B maintains air tightness by a pressing force of the flange 110N. This should not be construed in a limiting sense.

[0042] The aforementioned target solution is introduced from a bottom portion or a side surface of the target container 110. When the solution is introduced, the pump, the syringe, and similar member may be used. The amount of solution to be introduced is preliminarily determined as an amount that allows molybdenum compound to have a thickness of 0.1 to 5 mm in a beam path after deposition. In order to obtain practical yields, in the case where an incoming proton beam energy is 18 MeV, for example, area density of molybdenum is assumed to be equal to or more than about 450 mg/cm^2. However, needed area density is not limited since the area density strongly depends on incident energy.

[0043] As means for drying the solution and reducing liquid component, heating is performed with a heating element such as the heater H1 that is secured to an outer periphery, for example, on the bottom portion of the target container 110. Here, a temperature is set to about 100 to 700°C inside the target container 110, more preferably, 200 to 650°C. Additionally, gas is sent to the inside of the target container so as to enhance discharge of water vapor. When the discharge of water vapor terminates, molybdic acid ammonium salt is deposited. Further, continuing heating decomposes this compound into molybdenum oxide, ammonia gas, and water. At this time, ammonia gas and water are discharged to the outside of the target container together with introduced gas. Consequently, crystal of molybdenum oxide alone is disposed on the bottom face of the target container.

[0044] The introduced gas is preferred to employ helium gas since the helium gas does not provide a nuclear reaction product when the helium gas remains inside the target container. Alternatively, it is preferred that hydrogen or carbon monoxide be introduced to reduce the aforementioned molybdenum oxide. This is because the crystal obtained by the reduction increases in content of molybdenum per unit volume, and this increases nuclear reaction efficiency. This consequently increases yield of Tc-99m or Mo-99 to be obtained.

[0045] As described above, the target material introduced into the target container as liquid is prepared as solid by drying and hardening. This ensures effective irradiation. Drying and hardening are performed at least to extent of allowable influence of absorption of the beam energy due to the remaining liquid.

[0046] Partial volatilization (sublimation) of molybdenum oxide may occur due to heat generation at irradiation. Therefore, the top of the target container is sealed with the metal thin film 110B, and cooled using helium gas or similar gas. This consequently allows excessive sublimate to be deposited on the thin film, thus preventing raw material loss.

[0047] During irradiation, the target container may be a sealing type or an open type. The open type target container prevents increase in pressure caused by heat generation at irradiation. This allows irradiation without damaging the target container.

[0048] Here, the target container 110 includes the plurality of outlets and inlets.

1. An upper hole functions as an exhaust outlet at injection of solution. This consequently does not increase in pressure.
2. At heating and drying, the upper hole is coupled to the vacuum pump P in a negative pressure system. Rather, the pressure becomes lower than air pressure in spite of heating.
3. At irradiation, temperature increases due to heat generation of the beam. However, an expansion chamber that increases and decreases in storage capacity corresponding to increase and decrease in internal pressure is disposed in a passage communicating with the upper hole. This keeps balancing the pressure with air pressure. Accordingly, there is no problem with soundness of the metal thin film 110B. Damage caused by pressure does not occur at least.

[0049] After the irradiation terminates, ammonia solution is introduced into the target container, and molybdenum oxide that is irradiated for about 5 to 10 minutes is redissolved. Instead of introducing ammonia solution, mixed solution that is mixed with ammonia solution and hydrogen peroxide solution is introduced. This allows molybdenum oxide to redissolve more easily. To enhance dissolution, mixing and similar process by warming and introducing gas is performed.

[0050] As liquid to be introduced, the ammonia solution with a mass concentration of 10 to 30% and the hydrogen peroxide solution with a mass concentration of 10 to 30% are assumed to be used. Their liquid measures depend on a shape of target container. Liquid measure corresponding to 20 to 80% of the volume is introduced. With increasing solution, this increases in efficiency of dissolving and recovering Tc-99m and Mo-99, which have possibility of being attached on a wall surface of the target container in a wide range.

[0051] Subsequently, redissolution liquid of molybdenum oxide where Tc-99m or Mo-99 is dissolved is transported to the outside of the target container by a pressurized gas such as helium gas or similar gas. At this time, molybdenum oxide or similar element that is not completely dissolved in the aforementioned process may obstruct the recovery pipe. Thus, the filter 130 is disposed immediately after the target container. Removing these elements allows stabilized solution transportation. The filter 130 in the middle of this pipe may employ a commercial product with a hole diameter of equal to or more than 0.22 μm. The hole diameter is not limited insofar as the pipe is not obstructed. While filter material is preferred to employ, especially, quartz, polypropylene, or Teflon (registered trademark), the filter material is not limited.

[0052] The recovered solution is subsequently purified, for example, using ion-exchange resin to obtain Tc-99m as a target. At this time, liquid that has passed through the ion-exchange resin is trapped, and used in the next production. The trapped liquid has a composition with the same content as that of liquid to be prepared before irradiation. This allows directly using the trapped liquid in the next production without special purification.

[0053] A description will be given of an operational procedure of the embodiment below by referring to FIG 2 and FIG. 3.

[1. Preparation of target]

[0054] The target solution (ammonium molybdenum oxide) is introduced from the port 110G to the target chamber 110C via the valve V2 and the valve V 1 (Step 100). At this time, the valve V4 is opened as an exhaust path.

[0055] Subsequently, the heater H1, which is attached to the target container, heats the target container 110 and dries the solution (Step 110). At this time, helium gas is introduced via the valve V7-a and the pipe 114 while the flow rate controller 118 performs flow rate control. This enhances drying inside the target chamber, and exhausts air from the port 110I via the valve V5 and the vacuum pump P in this order. At this time, the helium gas may be introduced from the port 110H. However, the helium gas, which is introduced from the port 110G, is preferred to be introduced into the target container to prevent clogging. Because this prevents the target material, which is mixed with the liquid and accumulated at the lower portion of the target container 10, from passing through the port 110G, flowing backward to the pipe passage 114, becoming solid in the middle of the passage, and causing the clogging. While temperature inside the target container 110 at drying is assumed to be 100 to 700°C, the temperature is preferred to be equal to or more than 250°C that is a temperature where ammonia in addition to water is removed as vapor.

[0056] After drying is performed for an appropriate period (Step 120), preparation terminates with cooling of temperature of the target container down to approximately a room temperature (Step 130). At this time, flowing cooling water from the port 110L to the port 110M is possible as forced cooling. After termination of preparation, all the paths are shut off.

[2. Irradiation]

[0057] The proton beam passes through the metal thin film 110B and is irradiated to the bottom portion of the target chamber 110C (Step 140). The irradiation is performed such that a range of proton beam energy on the target is 9-40 MeV. In production of technetium-99m, the range is preferred to be, especially, 15-22 MeV. In order to suppress increase in inner pressure of the target container due to heat generation at irradiation, the valve V8 is opened to prevent damage on the target container, especially, on the metal thin film 110B. Additionally, helium gas flows from the port 110J to the port 110K so as to cool the vacuum partition wall 110E and the metal thin film 110B while cooling water also flows from the port 110L to the port 110M so as to cool the bottom portion of the target container 110, which is performed by proton beam irradiation and especially reaches a high temperature.

[3. Recovery]

[0058] After performing the irradiation for an appropriate period (for example, several hours), generated technetium 99m is recovered. Recovery agent employs solution as follows.

30% ammonia solution : 30% hydrogen peroxide solution = 1 : 1

After introduction from the port 110G to the target container 110 via the valve V3 and the pipe 114 in this order, the helium gas is introduced from the port 110G via the pipe 114. Subsequently, stirring inside the target is performed (Step 150). The valve V8 is opened as a helium gas exhaust path. Additionally, the heater H1 heats the target container 110. The aforementioned procedure enhances dissolution of irradiated molybdenum oxide. At this time, in order to allow the solution from flowing out of the target container, the solution trap 124 and/or an auxiliary tank are/is disposed between the valve V8 and the target container 110. Additionally, the valve V8 may have an open end where the expansion chamber is disposed.

[0059] After a lapse of a certain period of time (for example, 5 to 10 minutes), the valve V8 is closed. Subsequently, helium gas is supplied from the port 110H to the target container 110 via the valve V7-b, the pipe 126, and the solution trap 124 in this order. Subsequently, the target solution is allowed to pass through the recovery pipe 129 and the filter 130 from the valve V1 through the port 110G. Consequently, the target solution is recovered in the Tc-containing Mo recovery tank 132 (Step 160).

[0060] Subsequently, in order to recover residue attached on the inside of the target container and on the recovery pipe 129, the following solution is employed.

30% ammonia solution : 30% hydrogen peroxide solution = 1 : 1

The solution is introduced from the port 110H into the target container 110 via the valve V6 and the solution trap 124 in this order (Step 170). At this time, the exhaust path as the valve V4 is opened.

[0061] Subsequently, after the valve V4 is closed, helium gas is supplied via the pipe 126, and the residue is recovered in the Tc-containing Mo recovery tank 132 with a procedure similar to the aforementioned procedure (Step 180).

[0062] As described above, a sequence of the procedure completes a remote produce of technetium 99m.

[0063] The next production does not need special operation in addition to the operation described here, and is achieved by the preparation described in [1. Preparation of target]. At this time, the solution recovered in the Tc-containing Mo recovery tank 132 may be reused. In this case, the solution introduced into the target container is a combination of molybdenum, ammonia solution, and hydrogen peroxide solution. The respective components are slightly increased or decreased due to influence of remaining residue in the recovery process in Step 170. This variation is within an expected range. This variation is cancelled by preparation and recovery. The target container and the metal thin film, which are used at the previous irradiation, may be repeatedly reused as they are (without cleaning and a similar process).

[0064] Next, a description will be given of a second embodiment where the particle accelerator performs irradiation of the proton beam in the horizontal direction. This embodiment is as illustrated in FIG. 4 (a cross-sectional view taken along the line IV-IV of FIG 5) and FIG. 5 (a side view viewed in an arrow direction V). The metal thin film 110B is obliquely disposed with respect to the beam path. This embodiment employs a target container 110' where the metal thin film 110B is irradiated with the proton beam in the horizontal direction, which differs from the first embodiment. A portion of the target container in FIG. 4 illustrates a cross-sectional surface taken along the line IV-IV of FIG 5. While the target container has an inner shape of a columnar shape in the first embodiment, the target container is formed in a cone shape with a flat apex in the second embodiment for ease of fabrication. In configuration and operation, this embodiment is otherwise similar to the first embodiment. Like reference numerals designate corresponding or identical elements, and therefore such elements will not be further elaborated here.

[0065] While in the aforementioned embodiments, a target material is, for example, introduced and recovered using the combination of the helium gas and the air exhausting device (the vacuum pump P), means for introducing or discharging the target material is not limited to this. Another general liquid transportation means such as a pump and a syringe may be used. Liquid may be transported by liquid transportation means disposed in a position distant from the target containers 110 and 110'.

[0066] While in the aforementioned embodiments, molybdenum 99 and technetium 99m are produced from molybdenum 100, a type of target material, a type of nuclide to be produced, types of solvents used at the same time, and a type of beam are not limited. For example, assume that a radionuclide to be produced is ${}_{Z}{}^{A}$Product, a target material is ${}_{Z-1}{}^{A}$Target (here, "A" denotes an atomic weight, and "Z" denotes an atomic number), and a proton beam is used for production using nuclear reaction of ${}_{Z-1}{}^{A}$Target (p, x) ${}_{Z}{}^{A}$Product. At this time, an elementary substance, oxide, hydroxide, fluoride, chloride, bromide, iodide, hydrochloride, nitrate, nitrite, hydrosulfate, sulfide, hydride of ${}_{Z-1}{}^{A}$Target, and hydrate of these can be used.

[0067] The solvent may have any solubility. That is, any solvent may be used insofar as solvent can be suspended in mobile phase without being dissolved. For example, while an elemental metal of Mo (fine powder) does not dissolve in

organic solvent such as alcohol, acetone, or similar solvent, this elemental metal can be transported into inside of the target container by these solvents as a mobile phase. Before irradiation, the organic solvent can be easily vaporized. Thus, an object of this production is accomplished. In this description, expression of being dissolved in liquid includes being mixed with liquid, and coexistence of both substances.

[0068] Any ammonia solution concentration and molybdenum oxide concentration are possible. Additionally, in order to improve solubility, hydrogen peroxide solution may be added as needed. At this time, any hydrogen peroxide solution concentration is possible.

[0069] At drying, temperature is preferred to be equal to or more than 100°C inside the target container. Additionally, the temperature is preferred to be 200 to 650°C where ammonia can be vaporized. However, the temperature is not limited to this. While a thickness of a generated crystal is preferred to be 0.1 to 5 mm in the incident beam path, the thickness is not limited to this.

[0070] While gas used at drying is preferred to be helium, hydrogen, or carbon monoxide, the gas is not limited to these.

[0071] The extraction of solution may employ pressurized feeding by a pressure gas, vacuuming by a syringe, or a similar method.

[0072] Additionally, in order to enhance dissolution of molybdenum oxide, a heating device and a gas supplying device may be combined.

[0073] Also, the number of target containers is not limited to one. A plurality of target containers may be used to continuously perform production by irradiation of beam in series. The beam of the irradiation is not limited to a proton beam. Also, the target material is not limited to solid. The target material may be preliminary liquefied.

INDUSTRIAL APPLICABILITY

[0074] The present invention is applicable to production for a radiopharmaceutical that is used for image diagnosis in fields of radiology and nuclear medicine.

DESCRIPTION OF REFERENCE SIGNS

[0075]

108	particle accelerator irradiation port
110 and 110'	target container
110B	metal thin film
110C	target chamber
110D	heating/cooling portion
H 1	heater
110E	vacuum diaphragm
110F	cooling quality
112	target solution (Mo) tank
114, 126, and 128	pipe passage
122	solvent mixture (H_2O_2+NH_4OH) tank
116	helium (He) tank
P	vacuum (decompression) pump
126 and 128	pipe
129	recovery pipe
130	filter
132	Tc-containing Mo recovery tank

Claims

1. A method for producing a radionuclide using a particle accelerator, comprising:

   introducing a target material into a target container, the target material being dissolved or mixed in a liquid;
   reducing liquid component by drying inside of the target container; and
   irradiating a beam from the particle accelerator.

2. The method for producing the radionuclide using the particle accelerator according to claim 1, further comprising:

drying the target material inside of the target container, the target material being dissolved or mixed in the liquid, the target material being introduced into the target container; and
depositing solid component of the target material.

3. The method for producing the radionuclide using the particle accelerator according to claim 2 or 3, wherein the solid component deposited inside of the target container has a thickness of 0.1 to 5 mm in an incident beam path from the particle accelerator.

4. The method for producing the radionuclide using the particle accelerator according to claim 2, wherein the drying is performed by at least one of heating, introducing drying gas, and exhausting air.

5. The method for producing the radionuclide using the particle accelerator according to claim 5, wherein a temperature inside of the target container at the drying is equal to or more than 100°C.

6. The method for producing the radionuclide using the particle accelerator according to claim 4 or 5, wherein the drying uses a gas, the gas being one of helium, hydrogen, or carbon monoxide.

7. The method for producing the radionuclide using the particle accelerator according to claim 4 or 5, wherein the gas used for the drying is introduced into the target container such that the gas passes through the target material, the target material being dissolved or mixed in the liquid, introduced into the target container, and accumulated at a lower portion of the target container.

8. The method for producing the radionuclide using the particle accelerator according to any one of claims 1 to 7, wherein after the irradiation of beam terminates, liquid is introduced into the target container, the target material is again dissolved or mixed in the liquid, and the liquid is extracted out of the target container.

9. The method for producing the radionuclide using the particle accelerator according to claim 8, wherein the liquid extracted from the target container is recovered without disposal.

10. The method for producing the radionuclide using the particle accelerator according to any one of claims 1 to 9, wherein the target material is molybdenum 100, the beam is a proton beam at 40-9 MeV, and a radionuclide to be produced is technetium 99m and/or molybdenum 99.

11. The method for producing the radionuclide using the particle accelerator according to claim 10, wherein the target material to be introduced into the target container is molybdenum oxide dissolved in an ammonia solution.

12. The method for producing the radionuclide using the particle accelerator according to claim 11, wherein a hydrogen peroxide solution is added to the ammonia solution.

13. The method for producing the radionuclide using the particle accelerator according to claim 11 or 12, wherein the temperature at drying is from 200 to 650°C.

14. The method for producing the radionuclide using the particle accelerator according to claim 8, wherein the liquid is an ammonia solution and/or a hydrogen peroxide solution.

15. A method for producing a radionuclide using a particle accelerator, comprising:

Introducing a liquid into a target container when extracting a target material from the target container after the target material is irradiated with a beam from the particle accelerator; and
dissolving or mixing the target material in the liquid; and
extracting the target material from the target container.

16. An apparatus for producing a radionuclide using a particle accelerator, comprising:

a target container;
means for introducing a target material into the target container, the target material being dissolved or mixed in liquid;
drying means for drying an inside of the target container to reduce liquid component; and

means for irradiating the target container with a beam from the particle accelerator.

17. The apparatus for producing the radionuclide using the particle accelerator according to claim 16, wherein the drying means dries the target material inside of the target container to deposit solid component, the target material being dissolved or mixed in the liquid, the target material being introduced into the target container.

18. The apparatus for producing the radionuclide using the particle accelerator according to claim 16 or 17, wherein the drying means includes at least one of heating means, gas supplying means, and exhausting means.

19. The apparatus for producing the radionuclide using the particle accelerator according to claim 16, wherein the target container includes a metal thin film, the metal thin film sealing the target container, the metal thin film allowing the beam to pass through, and
the metal thin film is cooled.

20. The apparatus for producing the radionuclide using the particle accelerator according to any one of claims 16 to 19, further comprising:

means for introducing liquid into the target container after irradiation of the beam terminates; and
means for dissolving or mixing the target material in the liquid again and extracting the target material from the target container.

21. The apparatus for producing the radionuclide using the particle accelerator according to claim 20, further comprising means for recovering liquid extracted from the target container without disposal.

22. The apparatus for producing the radionuclide using the particle accelerator according to claim 20, wherein the means for recovering includes a filter disposed in a middle of a pipe.

23. An apparatus for producing a radionuclide by extracting a target material from a target container after the target material is irradiated with a beam from a particle accelerator, the apparatus comprising
means for introducing liquid into the target container, dissolving or mixing the target material in the liquid, and extracting the target material from the target container.

Fig. 1

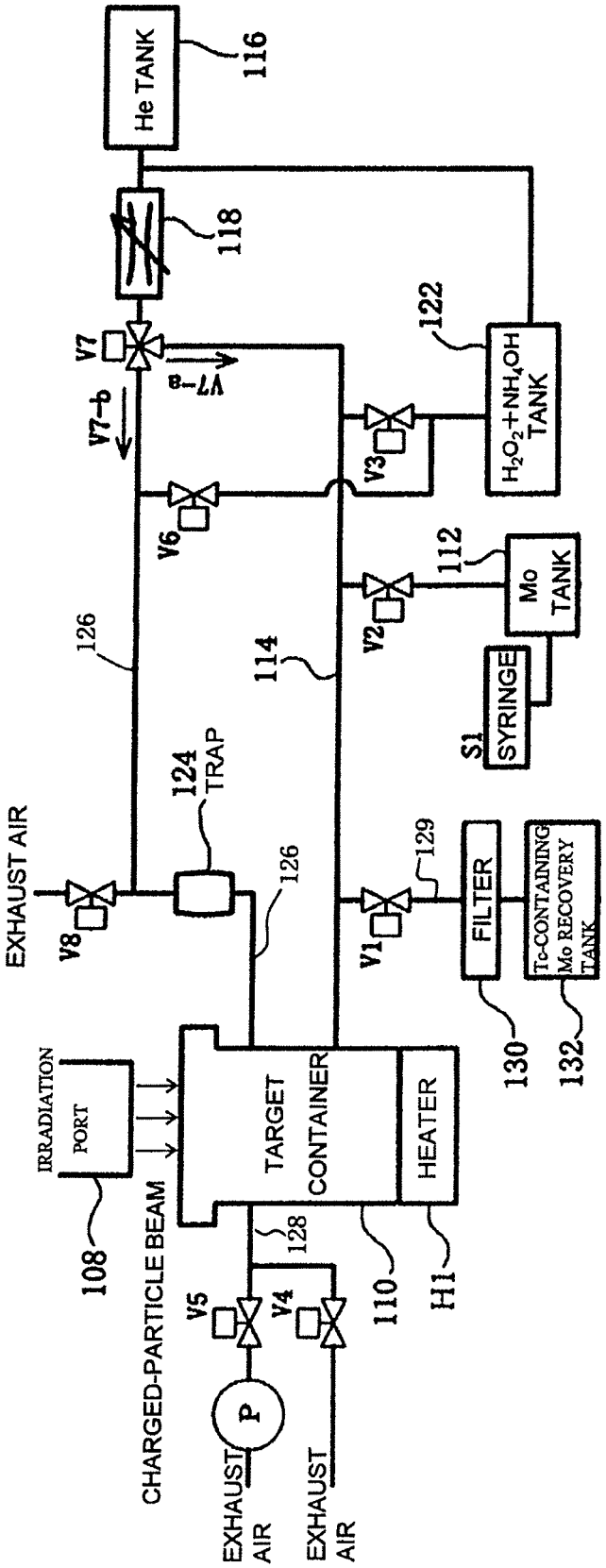

He TANK
116
118
122
V7
V7-a
V7-b
$H_2O_2+NH_4OH$ TANK
V3
V6
112
Mo TANK
V2
126
114
S1
SYRINGE
124
TRAP
EXHAUST AIR
V8
126
129
V1
FILTER
Tc-CONTAINING Mo RECOVERY TANK
130
132
IRRADIATION PORT
108
CHARGED-PARTICLE BEAM
TARGET CONTAINER
HEATER
128
110
H1
V5
V4
P
EXHAUST AIR
EXHAUST AIR

Fig. 2

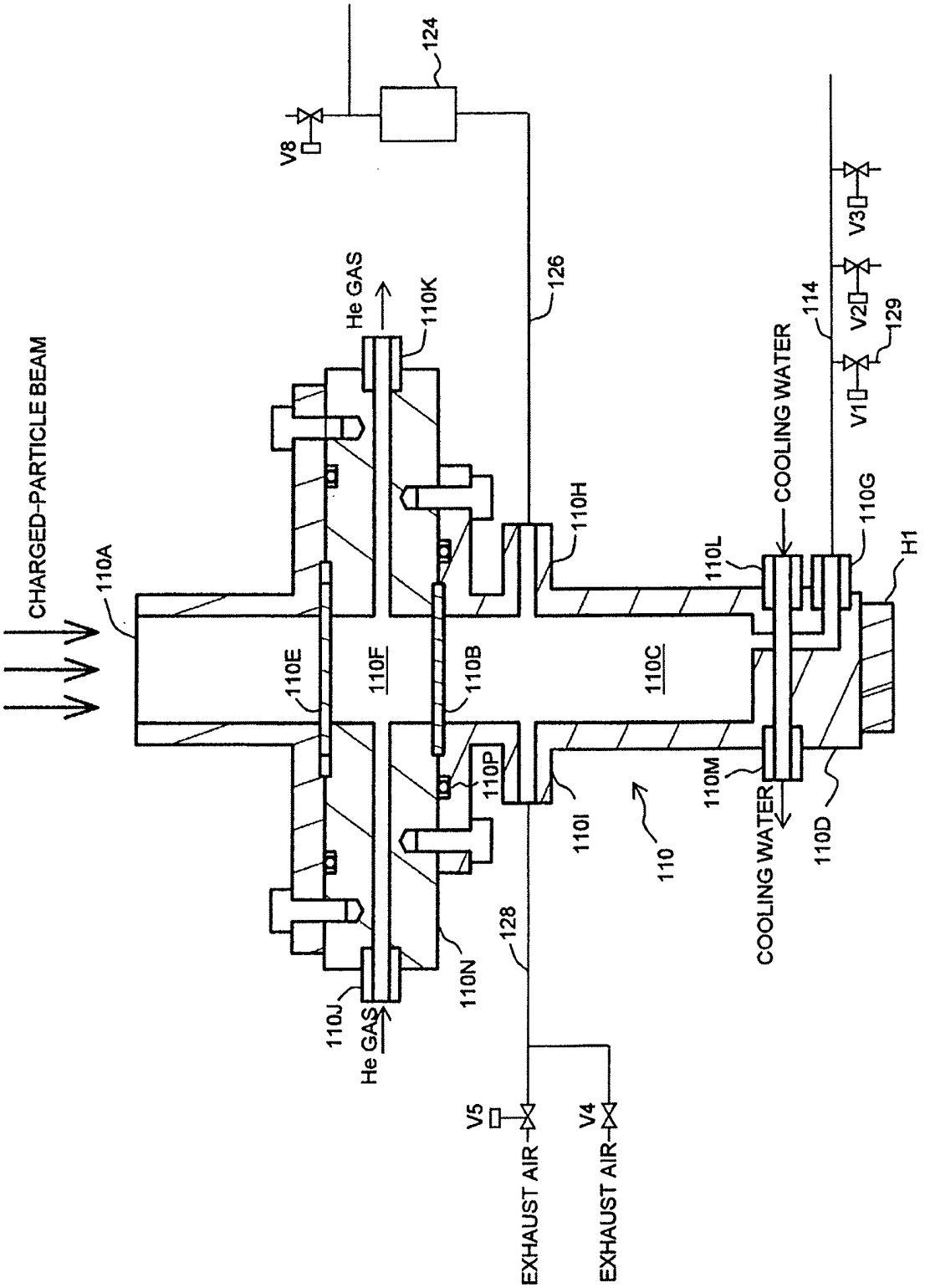

CHARGED-PARTICLE BEAM
110A
110E
110F
110B
110C
110H
110K
He GAS
126
124
V8
V3
V2
V1
129
114
COOLING WATER
110G
H1
110L
110M
110P
110I
110
110D
COOLING WATER
128
110N
110J
He GAS
V5
V4
EXHAUST AIR
EXHAUST AIR

Fig. 3

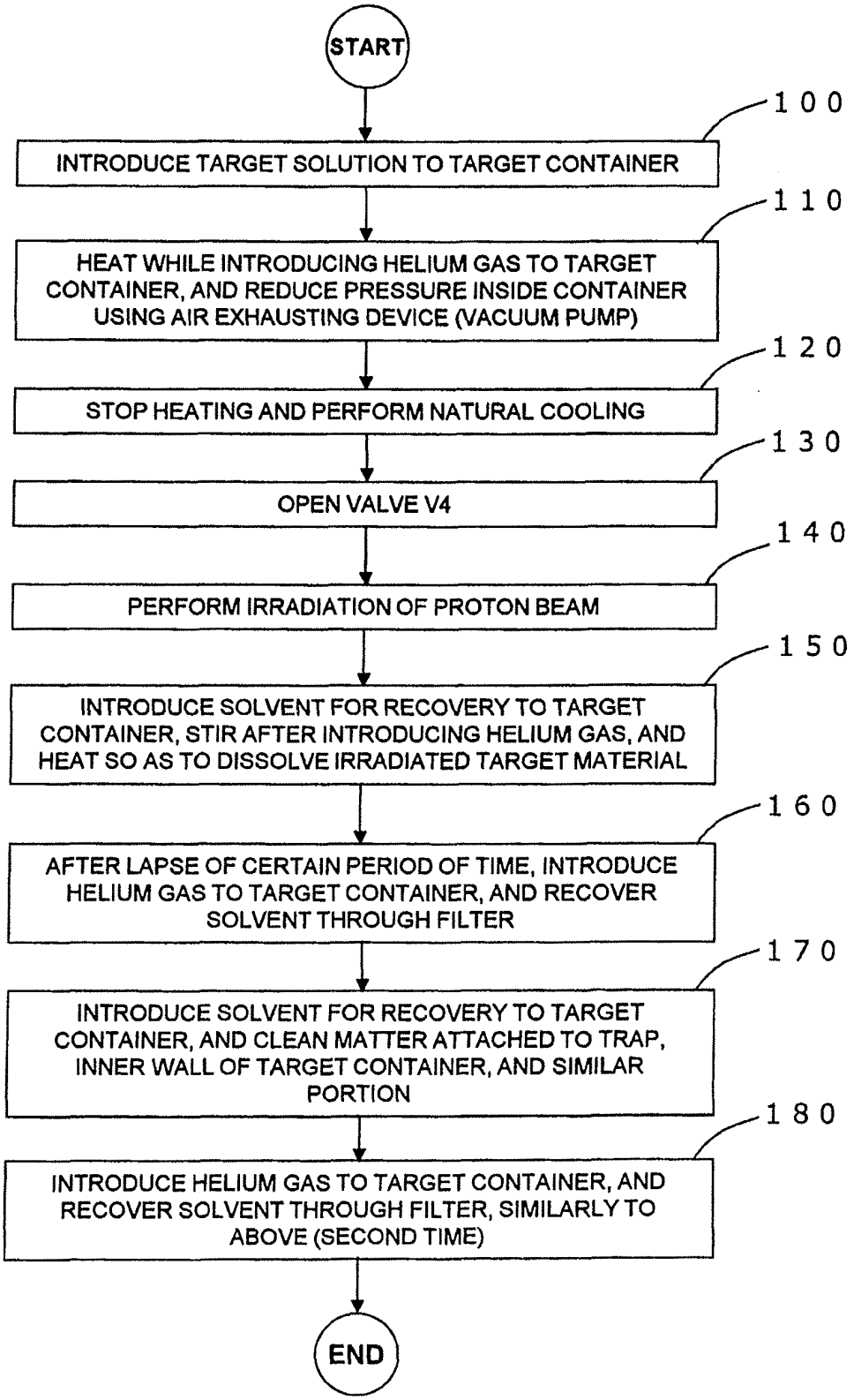

START
100
INTRODUCE TARGET SOLUTION TO TARGET CONTAINER
110
HEAT WHILE INTRODUCING HELIUM GAS TO TARGET CONTAINER, AND REDUCE PRESSURE INSIDE CONTAINER USING AIR EXHAUSTING DEVICE (VACUUM PUMP)
120
STOP HEATING AND PERFORM NATURAL COOLING
130
OPEN VALVE V4
140
PERFORM IRRADIATION OF PROTON BEAM
150
INTRODUCE SOLVENT FOR RECOVERY TO TARGET CONTAINER, STIR AFTER INTRODUCING HELIUM GAS, AND HEAT SO AS TO DISSOLVE IRRADIATED TARGET MATERIAL
160
AFTER LAPSE OF CERTAIN PERIOD OF TIME, INTRODUCE HELIUM GAS TO TARGET CONTAINER, AND RECOVER SOLVENT THROUGH FILTER
170
INTRODUCE SOLVENT FOR RECOVERY TO TARGET CONTAINER, AND CLEAN MATTER ATTACHED TO TRAP, INNER WALL OF TARGET CONTAINER, AND SIMILAR PORTION
180
INTRODUCE HELIUM GAS TO TARGET CONTAINER, AND RECOVER SOLVENT THROUGH FILTER, SIMILARLY TO ABOVE (SECOND TIME)
END

Fig. 4

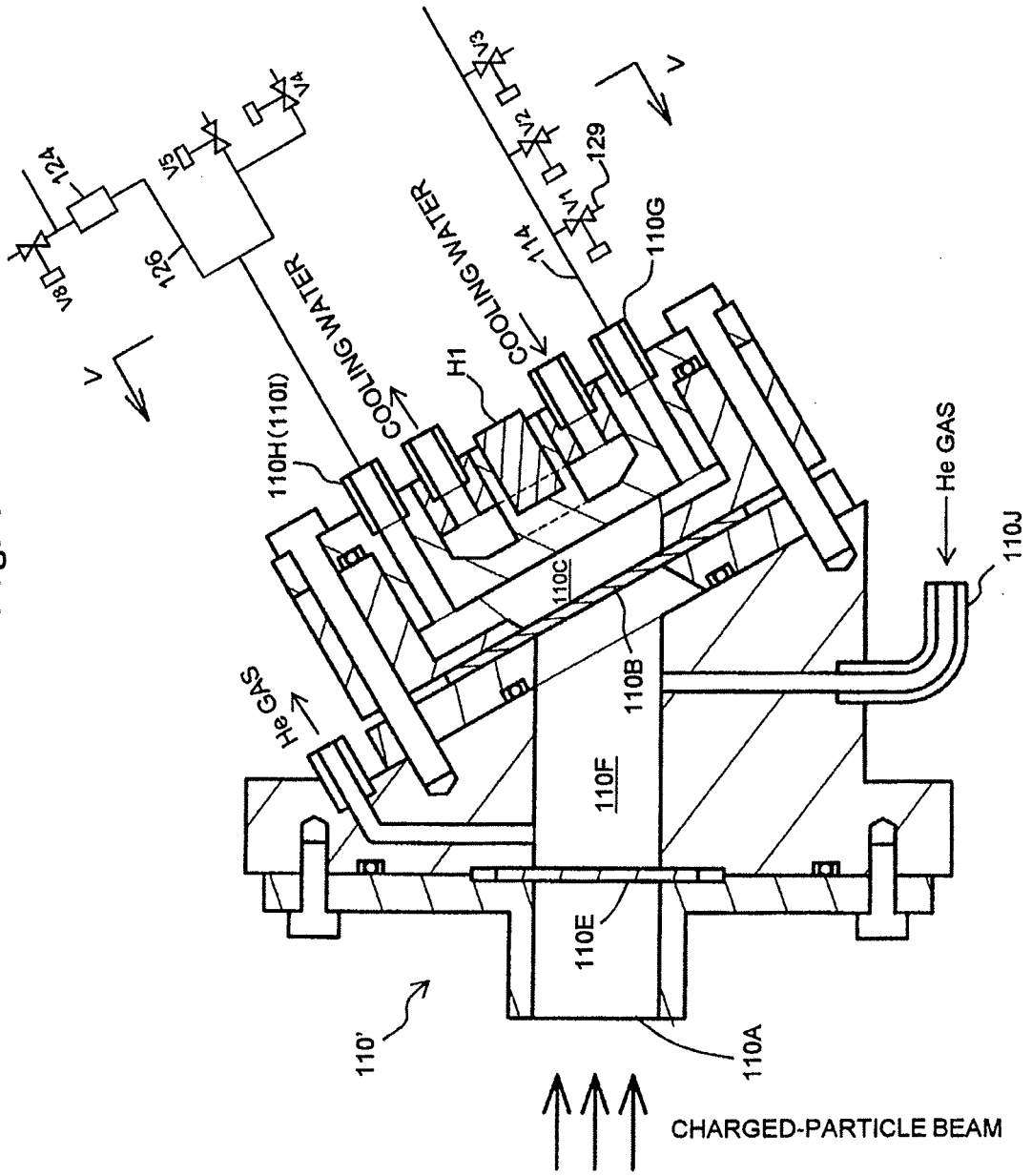
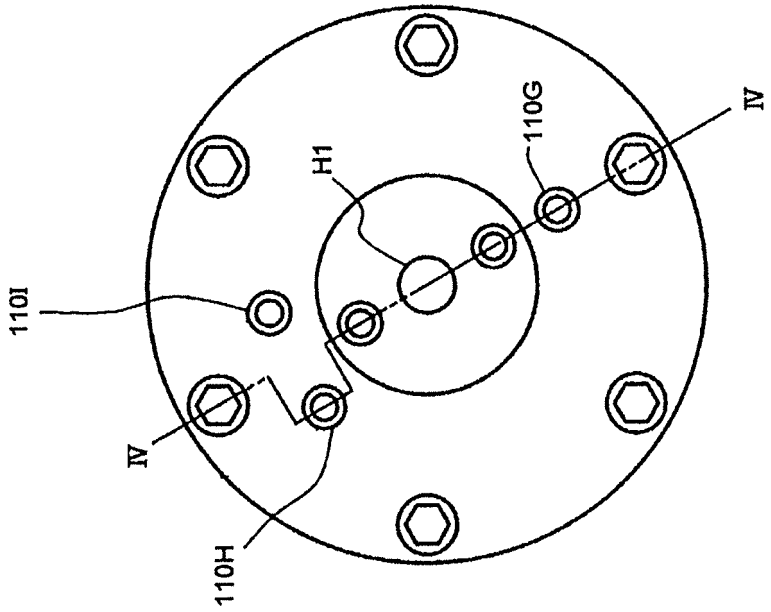

V3
V2
V1
129
V
114
110G
COOLING WATER
H1
COOLING WATER
V
V4
V5
124
126
V6
110H(110I)
He GAS
110J
110C
110B
110F
110E
110'
110A
CHARGED-PARTICLE BEAM

Fig. 5



INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2010/066433

A. CLASSIFICATION OF SUBJECT MATTER
G21G1/10(2006.01)i, *H05H6/00*(2006.01)i

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)
G21G1/10, H05H6/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Jitsuyo Shinan Koho 1922-1996 Jitsuyo Shinan Toroku Koho 1996-2010
Kokai Jitsuyo Shinan Koho 1971-2010 Toroku Jitsuyo Shinan Koho 1994-2010

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	JP 2007-536533 A (Actinium Pharmaceuticals, Inc.), 13 December 2007 (13.12.2007), paragraphs [0047], [0058] to [0075] & US 2007/153954 A1 & EP 1742670 A1 & WO 2005/105160 A1	1-5,16-18 6-15,20-23
A	JP 2008-102078 A (Japan Atomic Energy Agency, Kaken Co., Ltd.), 01 May 2008 (01.05.2008), entire text; all drawings & EP 2104113 A1 & WO 2008/47946 A1	1-18,20-23
A	WO 01/15176 A1 (Hitachi, Ltd.), 01 March 2001 (01.03.2001), page 28 (Family: none)	1-18,20-23

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
07 December, 2010 (07.12.10)	21 December, 2010 (21.12.10)
Name and mailing address of the ISA/ Japanese Patent Office Facsimile No.	Authorized officer Telephone No.

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2010/066433

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JP 2002-214395 A (Hitachi, Ltd.), 31 July 2002 (31.07.2002), paragraph [0004] (Family: none)	1-18,20-23
A	JP 55-22102 A (Japan Atomic Energy Research Institute), 16 February 1980 (16.02.1980), page 2, upper right column (Family: none)	1-18,20-23
A	JP 10-206597 A (The Institute of Physical and Chemical Research), 07 August 1998 (07.08.1998), paragraph [0022] (Family: none)	1-18,20-23
A	JP 1-254900 A (Daiichi Radioisotope Laboratories, Ltd.), 11 October 1989 (11.10.1989), entire text; all drawings (Family: none)	1-18,20-23
A	JP 63-2199 U (The Japan Steel Works, Ltd.), 08 January 1988 (08.01.1988), entire text; all drawings (Family: none)	1-18,20-23

Form PCT/ISA/210 (continuation of second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2010/066433

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

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

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Document 1 (JP 2007-536533 A (Actinium Pharmaceuticals, Inc.), 13 December, 2007 (13.12.2007), paragraphs [0047], [0058]-[0075]) discloses a method for producing a radioactive nuclei by an accelerator, by introducing a target substance (a radium-containing aqueous-organic solution or a suspension) dissolved in or mixed with a liquid, into a target container (or a cylinder-shaped hollow container), by drying the same in said target container to reduce the liquid component thereof, and by irradiating the target substance with a beam (or a proton beam) from an accelerator. Moreover, the invention of document 1 precipitates a solid component by heating the same at a temperature of 100 °C.
(continued to extra sheet)

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

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

3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
Claims 1-18 and 20-23.

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 and, where applicable, the payment of a protest fee.

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

☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (2)) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2010/066433

Continuation of Box No.III of continuation of first sheet(2)

Thus, the inventions of claims 1, 2, 4, 5 and 16-18 are not admitted to involve any novelty to and any special technical feature over the invention disclosed in document 1. Therefore, it is admitted that the dependent claims of claim 1 contain the five inventions which are related in the individual special technical features, as indicated in the following, if the special technical features are determined thereon.

Incidentally, the inventions of claims 1, 2, 4, 5 and 16-18 but having no special technical feature are grouped into invention 1.

(Invention 1) Invention of claims 1-5, 8, 9, 14, 16-18 and 20-22, and invention of claims 10-13, and having the following special technical features

A method for producing a radioactive nuclei by an accelerator, "by introducing a liquid into the inside of said target container after the end of the irradiation of a beam, by dissolving said target substance again into said liquid or mixing the same with said liquid, and by extracting the same to the outside of said target container".

Here, the invention of claim 3 is grouped into invention 1, since the same is only the conversion of the well-known technique to the invention of claim 2 but does not take any new effect.

(Invention 2) Invention of claims 6 and 7, and invention of claims 8-14 and having the following special technical features

A method for producing a radioactive nuclei by an accelerator "using a gas for drying".

(Invention 3) Invention of claims 10-13

A method for producing a radioactive nuclei by an accelerator, "wherein a target substance is molybdenum 100, wherein a beam is a proton beam of 40-9 MeV, and wherein the radioactive nuclei to be produced is technetium 99m and/or molybdenum 99".

(Invention 4) Invention of claims 15 and 23

A method for producing a radioactive nuclei by an accelerator, "by introducing a liquid into the inside of said target container when a target substance after the end of the irradiation of a beam in the accelerator is extracted to the outside of said target container, by dissolving said target substance into said liquid or mixing the same with said liquid, and by extracting the substance to the outside of said target container".

(Invention 5) Invention of claim 19, and invention of claims 20-22 and having the following special technical features

A method for producing a radioactive nuclei by an accelerator, wherein said target container includes a metal thin film for closing said target container and for passing said beam, and wherein said metal thin film is cooled".

Form PCT/ISA/210 (extra sheet) (July 2009)

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Non-patent literature cited in the description

- **LAGUNAS-SOLAR, M.C. et al.** Cyclotron production of NCA 99mTc and 99Mo. An alternative non-reactor supply source of instant 99mTc and 99Mo----99mTc generators. *Appl. Radiat. Isot.,* 1991, vol. 42 (7), 643-657 **[0006]**
- **BEAVER, J.E. ; HUPF, H.B.** Production of 99mTc on a medical cyclotron: A feasibility study. *J. Nucl. Med.,* 1971, vol. 12 (11), 739-741 **[0006]**