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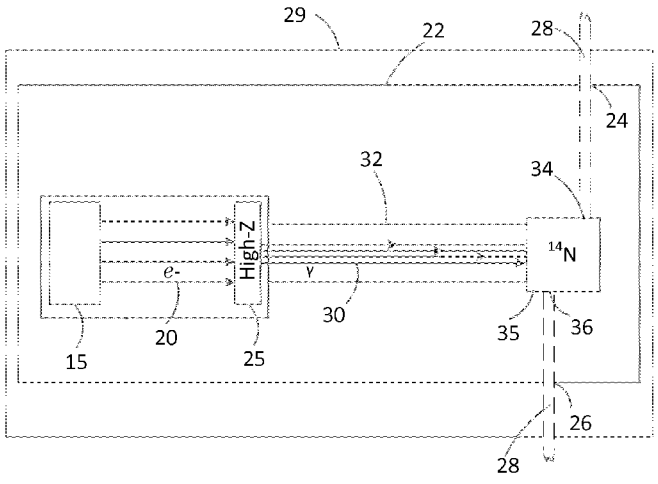
(54) Title: PRODUCTION OF N-13 AMMONIA RADIONUCLIDE

FIG. 3



(57) Abstract: A method of producing ^{13}N-ammonia for use in medical imaging is provided, which includes irradiating ^{14}N (having a natural abundance of 99.64%) with a collimated bremsstrahlung radiation (gamma-ray beam) obtained by directing high-energy electrons onto a high-Z converter. The ^{14}N to be irradiated may be in the form of liquid ammonia ($^{14}NH_3$) or ammonia gas to directly produce ^{13}N-ammonia ($^{13}NH_3$) or in the form of liquid nitrogen to indirectly produce ^{13}N-ammonia through conversion of the irradiated liquid nitrogen (N_2) via known conversion processes to ^{13}N-ammonia. The photons have an energy level above the threshold of the $^{14}N(\gamma,\eta)^{13}N$ reaction (about 10.5 MeV).

[Continued on next page]

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— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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PRODUCTION OF N-13 AMMONIA RADIONUCLIDE

INCORPORATION BY REFERENCE TO ANY PRIORITY APPLICATIONS

[0001] Any and all applications for which a foreign or domestic priority claim is identified in the Application Data Sheet as filed with the present application are hereby incorporated by reference under 37 CFR 1.57.

BACKGROUND

[0002] The present disclosure relates generally to the generation of unstable, *i.e.*, radioactive, nuclear isotopes, and more particularly to a system and method for generating the medical radionuclide nitrogen-13 (^{13}N) via the gamma-ray-induced isotopic reaction, $^{14}N(\gamma,n)^{13}N$.

[0003] Nitrogen-13 (^{13}N), used in the form of the tracer ^{13}N-ammonia (NH_3), is a valuable positron-emitting radionuclide commonly used for cardiac positron emission tomography (PET) imaging of the myocardium under rest or pharmacologic stress conditions to evaluate myocardial perfusion in patients with suspected or existing coronary artery disease or small-vessel disease. ^{13}N-ammonia can also be utilized to measure blood flow in other parts of the body, such as the liver, kidney, brain and malignant tumors.

[0004] When used for cardiac PET imaging, the ^{13}N diffuses rapidly from the blood into myocardial cells. Some of the ^{13}N-ammonia is synthesized into ^{13}N-glutamine and becomes metabolically trapped in the myocardium. Since the myocardial uptake is proportional to the blood flow, ^{13}N-ammonia is a good myocardial perfusion agent for the detection of coronary artery disease.

[0005] ^{13}N-ammonia has a short half-life (9.97 minutes) and decays by positron emission (100%) resulting in the production of two (2) 511 keV gamma-rays via the annihilation process.

[0006] One method that has been used to produce the ^{13}N used in nuclear medicine utilizes the $^{16}O(p,\alpha)^{13}N$ nuclear reaction via proton irradiation of ^{16}O. Another method involves irradiation of H_2O in the presence of 5-10 millimolar ethanol by protons from cyclotrons having energies greater than 11 MeV. The proton bombardment produces

^{13}N-ammonia as the major radionuclide, but also ^{15}O by the ^{16}O(p,pn)^{15}O nuclear reactions. The ^{13}N-ammonia is held for 10 minutes which allows the ^{15}O (half-life 2.04 minutes) to decay to less than 5% by time of delivery. Trace amounts of (^{18}F) fluoride ions are also produced from the 0.2% naturally occurring ^{18}O-water by the ^{18}O(p,n)^{18}F nuclear reactions. These traces of fluoride ions are removed by the anion exchange resin used for purification of ^{13}N-ammonia. A half-life measurement is performed for each batch of ^{13}N-ammonia, which results in a measurement between 9.5-10.5 min. Other production methods and additional details are described in Hell J Nucl Med 2009; 12(3): 248-250, which is incorporated herein by reference.

[0007] Due to the short half-life of ^{13}N, it is not possible to stock-pile the ^{13}N, so a large quantity of ^{13}N has to be produced with expensive cyclotrons using the current production methods. Several large production facilities currently are regionally dispersed to serve patients in all areas of the country. However, cyclotrons not only have huge initial setup cost, but also are expensive to maintain and operate. Accordingly, there is a need for a method for producing ^{13}N-ammonia that utilizes a very inexpensive, on-demand production system and thereby eliminates the need for large and expensive cyclotron facilities.

SUMMARY

[0008] The present disclosure is directed to a system and method for the production of ^{13}N-ammonia from nitrogen-14 (^{14}N) that includes loading a ^{14}N target into an irradiation chamber, using an incident beam of electrons impinging on a high-Z material to produce an intense collimated bremsstrahlung (photon beam) and directing the intense collimated photon beam to irradiate the ^{14}N target. ^{13}N is produced through the ^{14}N(γ,n)^{13}N nuclear reaction.

[0009] Methods for producing ^{13}N-ammonia are disclosed. In the first, the ^{14}N of the ^{14}N target may be in the form of liquid ammonia or ammonia gas, which is directly irradiated to form ^{13}N-ammonia. In the second, the ^{14}N target may be in the form of liquid nitrogen (N_2), with the ^{13}N produced then converted to ^{13}N-ammonia via a conventional synthesis process, such as the Haber process.

[0010] In contrast to the production of ^{13}N-ammonia through the ^{16}O(p,α)^{13}N nuclear reaction using a cyclotron to accelerate charged particles, the method of the instant

disclosure utilizes high energy photons to produce ^{13}N-ammonia and so does not require a cyclotron. Instead, a compact electron accelerator introduces the required energy into the system by generating an incident beam of high energy electrons impinging onto a high-Z material to produce an intense photon beam. Compact electron accelerators are much less expensive than cyclotrons to procure , -to install , and to maintain and operate.

[0011] Electrons impinging on the high-Z converter target generates photons to form the gamma-ray beam. Preferably the energy of most of the photons generated is above the threshold of the $^{14}N(\gamma,n)^{13}N$ nuclear reaction, which is about 10.5 MeV. In some embodiments, the photons generated can have an energy up to about 30 MeV. In some embodiments, the photons generated can have an energy up to about 25 MeV or up to about 20 MeV. In some embodiments, photons having an energy in the range of about 10.5 MeV to about 30 MeV, about 10.5 MeV to about 25 MeV, or about 10.5 MeV to about 20 MeV can create the isotope ^{13}N, while avoiding the production of undesirable isotopes.

[0012] The production of ^{13}N from the $^{14}N(\gamma,n)^{13}N$ reaction is shown in the graph of FIG. 1 (from the *Handbook on Photonuclear Data for Applications: Cross-Sections and Spectra, IAEA-TECDOC-1178, IAEA, 2000, page 100*). This graph shows that significant amounts of ^{13}N are produced even if the impinging gamma-ray beam has an energy of under 25 MeV.

[0013] An object of the present disclosure is to provide a system and method that produces ^{13}N-ammonia used in nuclear medicine.

[0014] An additional object of the present disclosure is to provide a ^{13}N-ammonia production system and method that produces the medical isotope ^{13}N without the usage of a cyclotron.

[0015] These and other objects, features, and advantages of the present disclosure will become more readily apparent from the attached drawings and from the detailed description of the embodiments which follow.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016] Embodiments of the disclosure will hereinafter be described in conjunction with the appended drawings, provided to illustrate and not to limit the disclosure, where like designations denote like elements.

[0017] FIG. 1 is a graph showing the cross-section of the $^{14}N(\gamma,n)^{13}N$ reaction of the current disclosure versus incident photon energy.

[0018] FIG. 2 is a graph showing the cross-section of $^{14}N(\gamma,px)$ reactions, which includes a competing reaction $^{14}N(\gamma,p)^{13}C$ having a threshold at about 7.5 MeV.

[0019] FIG. 3 is a conceptual diagram (not to scale) of the system of the present disclosure for producing ^{13}N through use of a collimated photons that irradiates a target such as liquid ammonia, ammonia gas, or liquid nitrogen to produce ^{13}N through the $^{14}N(\gamma,n)^{13}N$ reaction.

[0020] FIG. 4 is a flowchart summarizing the ^{13}N-ammonia production method in which liquid ammonia or ammonia gas is irradiated to create ^{13}N from the $^{14}N(\gamma,n)^{13}N$ reaction of the current disclosure.

[0021] FIG. 5 is a flowchart summarizing the ^{13}N-ammonia production method in which liquid nitrogen is irradiated to create ^{13}N from the $^{14}N(\gamma,n)^{13}N$ reaction of the current disclosure.

[0022] Like reference numerals refer to like parts throughout the several views of the drawings.

DETAILED DESCRIPTION

[0023] The present disclosure is directed to a system and method for the production of ^{13}N-ammonia ($^{13}NH_3$) by converting nitrogen-14 (^{14}N) to nitrogen-13 (^{13}N) utilizing the $^{14}N(\gamma,n)^{13}N$ reaction. Some embodiments are directed to a first method for producing $^{13}NH_3$ through direct irradiation of liquid ammonia or ammonia gas (FIG. 4). Some embodiments are directed to a second method for producing $^{13}NH_3$ through irradiation of liquid nitrogen and conversion of irradiated liquid nitrogen to ^{13}N-ammonia through conventional chemical processes, such as via the Haber process.

[0024] FIG. 1 shows the cross-section (in millibarns) of the photon-induced $^{14}N(\gamma,n)^{13}N$ reaction versus the photon energy (in MeV). The $^{14}N(\gamma,n)^{13}N$ reaction has a photon threshold energy at about 10.5 MeV and reaches a photon cross-section value of about 14.5 millibarns at 22 MeV.

[0025] FIG. 2 shows the reaction cross-section plot for $^{14}N(\gamma,px)$ reactions, which includes a competing reaction $^{14}N(\gamma,p)^{13}C$ having a threshold at about 7.5 MeV. This

competing reaction produces the by-product ^{13}C (step **76** in FIGS. 4-5), but since carbon is insoluble in either liquid ammonia or liquid nitrogen any traces of the ^{13}C from this competing reaction can be easily and safely removed. This ^{13}C removal may be by micro-filtration in the case of liquid ammonia or may be left behind as a residue after the nitrogen gas is evaporated before the conversion of the nitrogen gas to ammonia.

[0026] FIG. 3 depicts an embodiment of the system for the production of ^{13}N-ammonia ($^{13}NH_3$). An electron accelerator **15** produces an electron beam **20** that is directed onto a high-Z converter **25**. In some embodiments, the electron accelerator **15** and high-Z converter **25** may be disposed within a vacuum system. The impinging electrons produce an intense collimated bremsstrahlung (gamma-ray) radiation **30** that is emitted from the high-Z converter **25** into a ^{14}N target in the sample holder **35**. In some embodiments, the ^{14}N target may be liquid ammonia or ammonia gas. In other embodiments, the ^{14}N target may be liquid nitrogen.

[0027] The electron accelerator **15** is a compact, high-power electron accelerator that generates an electron beam **20** with electrons having an energy above about 10.5 MeV, which is the photon energy threshold of the $^{14}N(\gamma,n)^{13}N$ reaction. In some embodiments, the electrons may have an energy up to about 30 MeV. The intensities of the bremsstrahlung spectra produced by this type of relativistic electron beam are all forward-peaking and sometimes referred to as a "radiation cone," which is the collimated photon (gamma-ray) beam **30** in FIG. 3. In the production methods of the current disclosure, the radiation cone of the bremsstrahlung spectrum (i.e., collimated gamma-ray beam **30**) is directed toward and irradiates the sample holder **35** containing the ammonia or nitrogen target to activate the ^{13}N within the liquid ammonia, ammonia gas, or liquid nitrogen.

[0028] The appropriate electron accelerator **15** is chosen based on considerations of economics and technical requirements for successful process implementation. For example, a suitable electron accelerator is the Varian CLINAC 2100C high energy electron linear accelerator, having an energy of about 30 MeV, which can deliver about 125 Gray of radiation per minute while delivering an electron current >1 milliamp.

[0029] The high-Z converter **25** is placed in the path of the incident electron beam **20** to convert the relativistic electrons via the (e-,γ) reaction with the photon maximum energy roughly equal to the maximum incident electron energy. Although any of a number of

high-Z materials may be used, exemplary high-Z materials are uranium (U), tantalum (Ta), and tungsten (W). The high-Z converter **25** may be in a solid form (such as a plate or sheet), may be multiple solid pieces (such as multiple sheets), or may be in the form of a mesh or matrix array of material. The conversion (production) efficiency of bremsstrahlung for electrons with a thin high-Z converter and energy of about 30 MeV is about 70%. About 30% of the produced high energy photons (or hard x-rays, or gamma-rays) are contained within a narrow solid angle of about 5 steradians.

[0030] The target sample holder **35** may be configured to receive a predetermined volume of the liquid ammonia or ammonia gas to be irradiated. In some embodiments, the liquid ammonia may be anhydrous liquid ammonia. The sample holder **35** preferably is positioned within the narrow solid angle of about 5 steradians of the forward-peaking bremsstrahlung cone of photons. In some embodiments, a 3 cc vial may be used to hold the target, but vials of other sizes can also be used. Optionally, in some embodiments, input/output piping **28** may be included to allow introduction and extraction of the target material into and out of the sample holder **35**.

[0031] With reference to FIG. 3, the electron accelerator components **15**, the high-Z converter material **25**, and the target sample holder **35** are disposed in the irradiation chamber **22.** In some embodiments, the electron accelerator components **15** and the high-Z converter material **25** may optionally be disposed within a vacuum system inside of the irradiation chamber **22**. Optionally, input/output piping **28** may be installed by routing it from an irradiation chamber inlet **24** to an inlet **34** into the sample holder **35** and by routing it from an outlet **36** of the sample holder **35** to an outlet **26** in the irradiation chamber. Optionally, one or more internal reflectors **32** may be installed within the irradiation chamber **22**, such as to enhance the collimation of the gamma-rays. In some embodiments, a biological shield **29** may also be installed outside the irradiation chamber **22**.

[0032] In some embodiments, the cross-sectional area of the sample holder **35** is 1 cm^2; the length is 3 cm; and the volume is 3 cc. Using this configuration and the output from the electron accelerator of 1 milliampere of current, the output of the system would be 6.24×10^{15} electrons/second. The photon flux (the number of photons above 10 MeV/cm^2/second) produced from a 25 MeV electron beam using a converter imparting onto a sample with a cross sectional area of 1 cm^2 that is placed at a distance of 1 meter from

the converter is equal to $(0.7)\times(0.3)\times(0.1)\times(6.24\times10^{15})$ photons/cm^2/second, which is 1.3×10^{14} photons/cm^2/second. Since the $^{14}N(\gamma,n)^{13}N$ nuclear reaction cross-section has an average of about 10 millibarns between 10 MeV and 25 MeV, the total number of ^{13}N nuclei that could be produced in one second within the liquid ammonia sample is equal to [(photon flux)×(density)×(Avogadro number)×(reaction cross-sections)×(thickness of sample)×(atomic weight)], which equals to about 1×10^{11} ^{13}N nuclei produced per sec. Therefore, 7.2×10^{10} ^{13}N nuclei can be produced in 1 second with a 1 mA, 25 MeV electron beam through a thin high-Z converter (such as 4 mm Tungsten) with a sample holder **35** that is 3 cm long with a cross-sectional area of 1 cm^2, placed at 1 meter away from the converter.

[0033] FIG. 4 is a flowchart showing steps involved in the first method of production of the ^{13}N-ammonia radionuclide using an ammonia target. The ammonia target may be liquid ammonia or ammonia gas. In some embodiments, the liquid ammonia may include anhydrous liquid ammonia. In some embodiments, the ammonia target contains >99% of $^{14}NH_3$. The ammonia target may be made or purchased. In some embodiments, the ammonia gas target may be made by reaction Devarda's alloy as a reducing agent with nitrate solution under alkaline conditions. The produced ammonia gas can be irradiated directly or can be condensed (and optionally compressed) into a liquid form for use in direct irradiation.

[0034] Electrons are generated (step **71**) by the electron accelerator components **15** as shown in FIG. 3. This high energy electron beam **20** impinges the high-Z converter target **25** to generate photons (step **72**) that form an intense collimated gamma-ray beam **30**. This gamma-ray radiation cone irradiates the ammonia target contained within the sample holder **35** (step **70**). The nitrogen isotope in the ammonia target is substantially all ^{14}N, as ^{14}N has a natural abundance of 99.64%. Some of the nitrogen atoms within the ammonia target are activated, with ^{14}N converted to ^{13}N (step 77), which results in irradiated ammonia that has both ^{14}N and ^{13}N atoms (i.e., $^{13}NH_3$ and $^{14}NH_3$) (step **75**).

[0035] The irradiated ammonia (having a portion of the nitrogen being ^{14}N and a portion being ^{13}N) is removed from the nitrogen target sample holder **35**. In embodiments where ammonia gas is used as ammonia target, the irradiated ammonia gas can be converted to irradiate liquid ammonia by further passing through a condenser. In some embodiments, the irradiated ammonia gas can also pass through a condenser and a compressor.

[0036] In some embodiments, the irradiated liquid ammonia can undergo a purification process (step **79**), where it is filtered, purified and prepared (step **79**) for use. The purified ammonia is packaged and transported to the location of use, which is usually within the same facility, due to the short half-life of ^{13}N. In some embodiments, before or after transporting, the liquid ammonia is diluted to an appropriate volume with a sodium solution. Once the dose rate is checked, the dose of ^{13}N-ammonia can be administered to the patient.

[0037] By-products are formed by the competing reaction $^{14}N(\gamma,p)^{13}C$ **78** and from neutrons generated from deuterium (step **76**). Though deuterium has only a 0.01% natural abundance, its low photoneutron threshold of 2.22 MeV makes it an important potential neutron source when liquid ammonia is used to produce ^{13}N-ammonia. The photoneutrons produced through the $^{2}H(\gamma,n)^{1}H$ nuclear reaction **74** will interact with the ^{14}N atoms via the following nuclear reactions: $^{14}N(n,\alpha)^{11}B$; $^{14}N(n,p)^{14}C$; $^{14}N(n,\gamma)^{15}N$; and $^{14}N(n,2n)^{13}N$. The $^{14}N(n,\alpha)^{11}B$ has a threshold at about 1 MeV and produces ^{11}B. The $^{14}N(n,p)^{14}C$ nuclear reaction also has a low threshold and has a cross-section equivalent to the cross-section of the $^{14}N(n,\alpha)^{11}B$ reaction at 1 MeV. However, both ^{11}B and ^{14}C are insoluble in liquid ammonia, so these impurities can be removed by micro-filtration in the purify and prepare operation of step **79**. The $^{14}N(n,\gamma)^{15}N$ nuclear reaction produces ^{15}N, which is a stable isotope of nitrogen that does not affect the chemical and physical properties of ^{13}N-ammonia, so removal of ^{15}N is unnecessary. The $^{14}N(n,2n)^{13}N$ nuclear reaction produces ^{13}N, which is the desired isotope, and thus it will merely aid in producing a higher concentration of the desirable ^{13}N-ammonia product.

[0038] FIG. 5 is a flowchart showing the steps involved in the second method of production of the ^{13}N-ammonia radionuclide using liquid nitrogen. As in the first method, high energy electrons are generated by the electron accelerator components **15** (step **71**) as shown in FIG. 3, which impinge the high-Z target **25** to generate photons (step **72**) that form an intense collimated gamma-ray beam **30**. This gamma-ray radiation cone irradiates the liquid nitrogen contained within the sample holder **35** (step **90**). A substantial portion of the ^{14}N of the liquid nitrogen is converted to ^{13}N within the ^{14}N liquid nitrogen (step 77), which results in irradiated liquid nitrogen (step **95**) that has both ^{14}N and ^{13}N atoms.

[0039] The irradiated liquid nitrogen (step **95**) (including ^{14}N and ^{13}N) is removed from the sample holder **35**, and then converted to liquid ammonia (step **99**). In some

embodiments, conversion of liquid nitrogen to liquid ammonia in step **99** may be accomplished using the Haber process. The liquid nitrogen (from step **95**) is converted to nitrogen gas, and then combined with hydrogen gas in 1:3 ratio by volume. The gas mixture is compressed and introduced into a reaction chamber, where the reaction takes place at a temperature of about 400 to about 450 ^{o}C, a pressure of about 200 to about 250 atm, and in the presence of a catalyst. The catalyst may be osmium, platinum, iron (such as prepared by reducing magnetite (Fe_3O_4)), or ruthenium-based catalyst or other known Haber catalyst. After the reaction, the resultant gas is cooled and condensed into liquid ammonia. In some embodiments, the resultant ammonia gas may also be compressed during the process of conversion to liquid ammonia.

[0040] In some embodiments, the resultant liquid ammonia can undergo a purification process (step **79**), where it is filtered, purified and prepared for use. The purified ammonia is packaged and transported to the location of use, which is usually within the same facility, due to the short half-life of ^{13}N. In some embodiments, before or after transporting, the liquid ammonia is diluted to an appropriate volume with a sodium solution. Once the dose rate is checked, the dose of ^{13}N-ammonia can be administered to the patient.

[0041] In this second production method depicted in FIG. 5, a lesser amount of by-products are formed (step **76**) than in the first method, because no hydrogen atoms are present when the nitrogen target is irradiated.

[0042] Since many modifications, variations, and changes in detail can be made to the described preferred embodiments of the disclosure, it is intended that all matters in the foregoing description and shown in the accompanying drawings be interpreted as illustrative and not in a limiting sense. Thus, the scope of the disclosure should be determined by the appended claims and their legal equivalents.

WHAT IS CLAIMED IS:

1. A method of producing ^{13}N-ammonia via an isotopic conversion reaction comprising:

providing a target having nitrogen atoms that are substantially ^{14}N, wherein the target is ammonia or nitrogen;

directing high-energy electrons onto a high-Z converter to produce a collimated gamma-ray beam; and

directing said collimated gamma-ray beam to irradiate said ammonia target or nitrogen target to convert at least a portion of the ^{14}N to ^{13}N isotope, thereby forming an irradiated ammonia or irradiated nitrogen.

2. The method of claim 1, wherein said high-energy electrons have an energy level above the threshold of a $^{14}N(\gamma,n)^{13}N$ reaction.

3. The method of claim 1 or 2, wherein said high-energy electrons have an energy level up to about 30 MeV.

4. The method of any one of claims 1-3, wherein said high-Z converter is uranium, tantalum, or tungsten.

5. The method of any one of claims 1-4, further comprises purifying irradiated ammonia.

6. The method of any one of claims 1-5, wherein the target is liquid ammonia or ammonia gas.

7. The method of claim 6, wherein the target is anhydrous liquid ammonia.

8. The method of any one of claims 1-7, wherein the target is liquid nitrogen.

9. The method of claim 8, wherein further comprising converting said irradiated nitrogen to irradiated ammonia.

10. The method of claim 9, further comprises purifying irradiated ammonia.

11. A method of producing ^{13}N-ammonia via an isotopic conversion reaction comprising:

providing a liquid nitrogen target comprising ^{14}N atoms;

directing high-energy electrons onto a high-Z target to produce a collimated gamma-ray beam;

directing said collimated gamma-ray beam to irradiate said liquid nitrogen target to isotopically convert the liquid nitrogen target to an irradiated liquid nitrogen having at least a portion of said ^{14}N atoms converted to a ^{13}N isotope; and

converting said resulting irradiated liquid nitrogen to ^{13}N-ammonia ($^{13}NH_3$).

12. The method of claim 11, wherein said high-energy electrons have an energy level above the threshold of said $^{14}N(\gamma,n)^{13}N$ reaction.

13. The method of claim 11 or 12, wherein said high-energy electrons have an energy level below about 30 MeV.

14. The method of claim 11-13, wherein said high-Z converter target is one of uranium, tantalum, or tungsten.

15. The method of claim 11-14, wherein said converting said irradiated liquid nitrogen to said ^{13}N-ammonia comprises utilizing the Haber process.

16. The method of claim 15, wherein said Haber process comprises a Haber reaction combining said irradiated liquid nitrogen in the form of nitrogen gas (N_2) with hydrogen gas (H_2) in the presence of a catalyst at a temperature of about 400 to about 500 °C and at a pressure of about 175 to about 250 atmospheres.

17. The method of claim 16, wherein said catalyst is selected from the group consisting of osmium catalyst, platinum catalyst, ruthenium catalyst, and iron catalyst.

FIG. 1

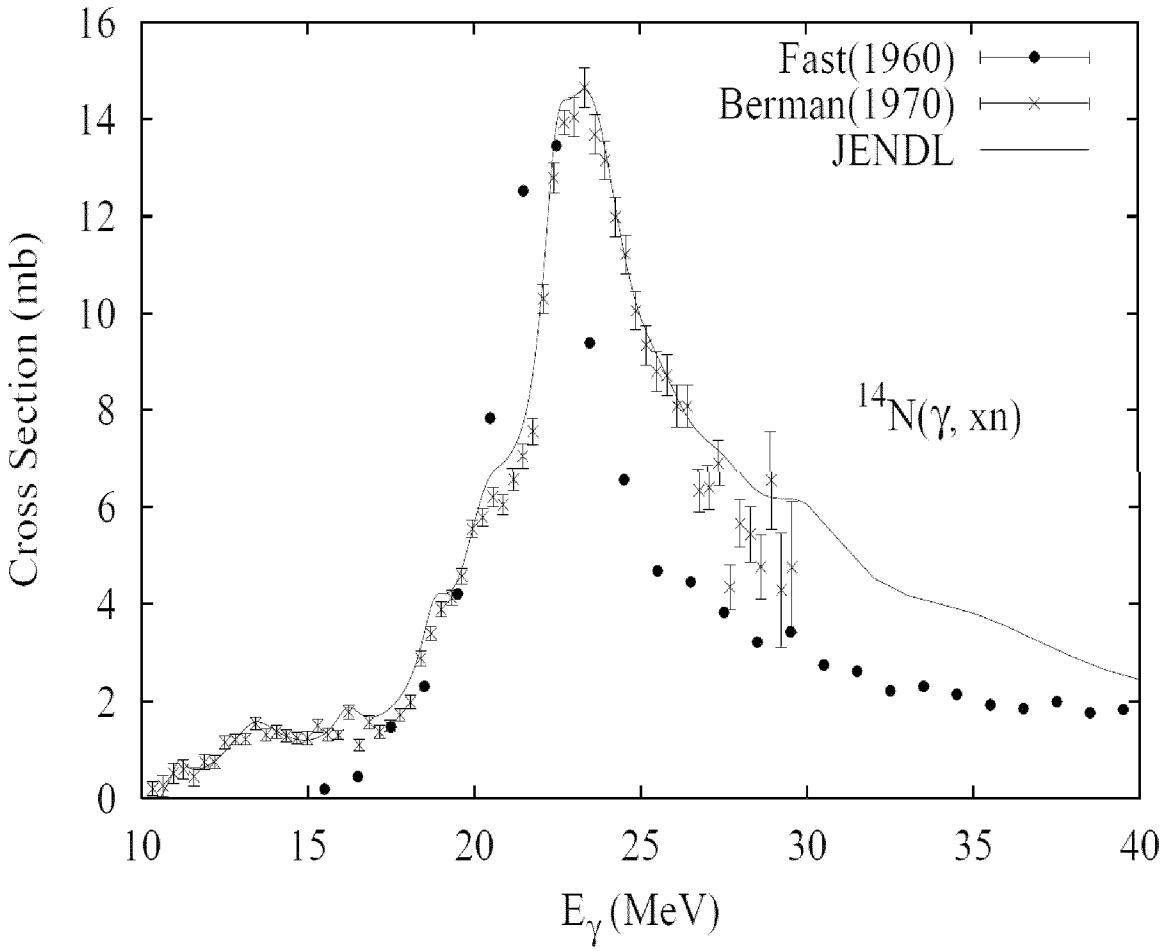
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FIG. 2

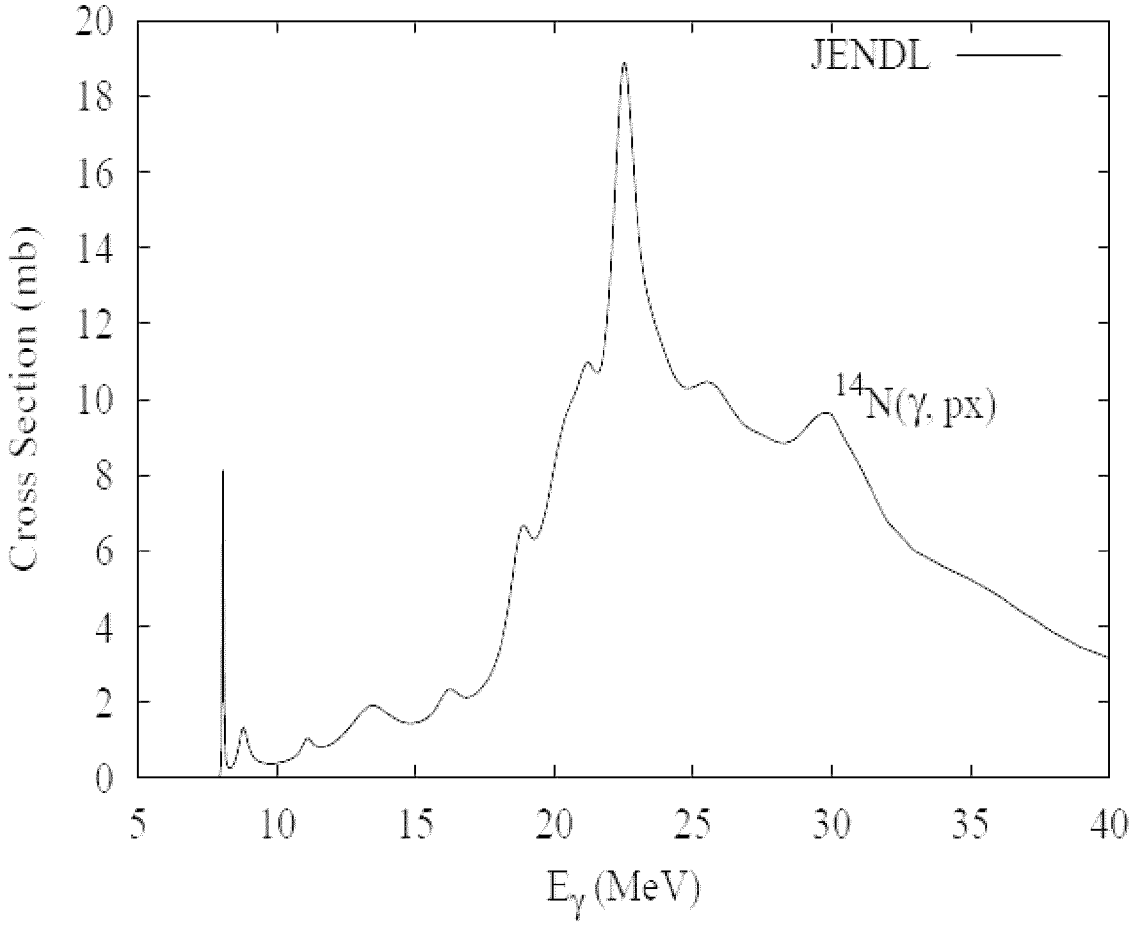
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FIG. 3

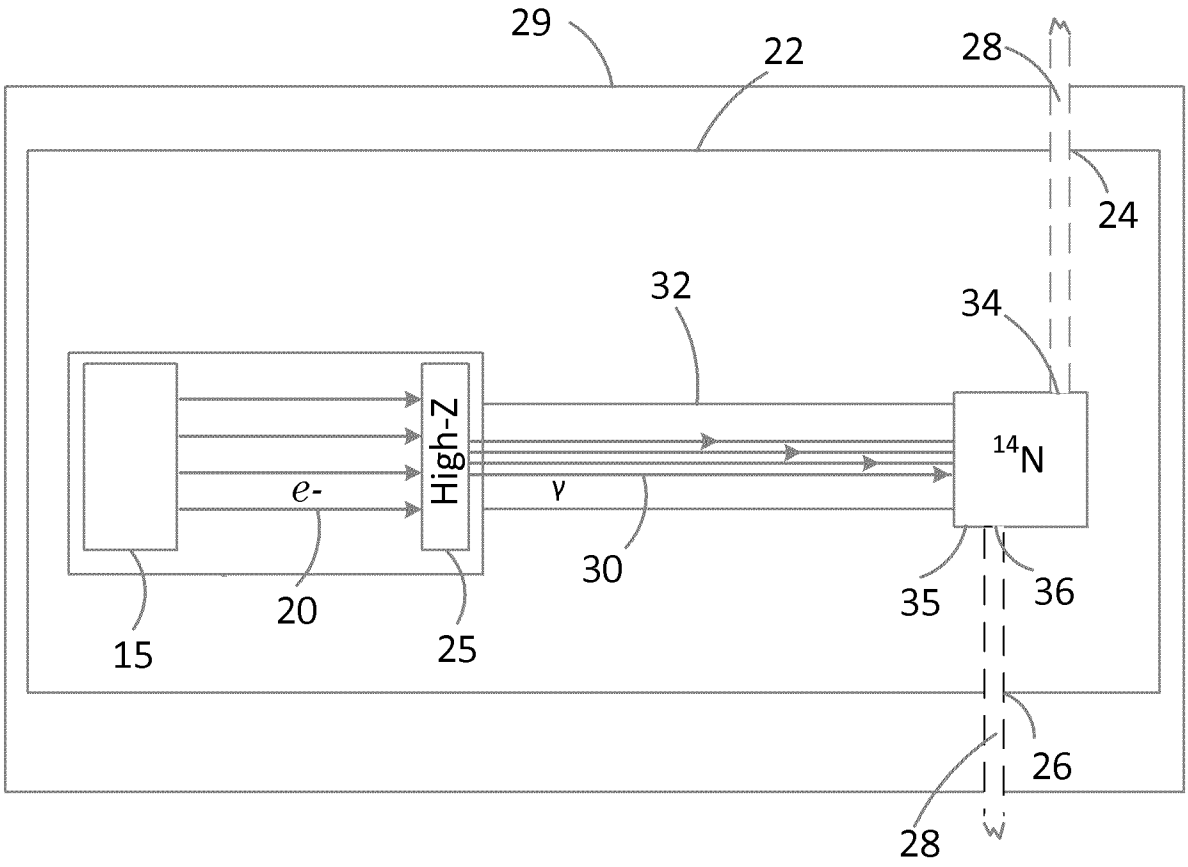


FIG. 4

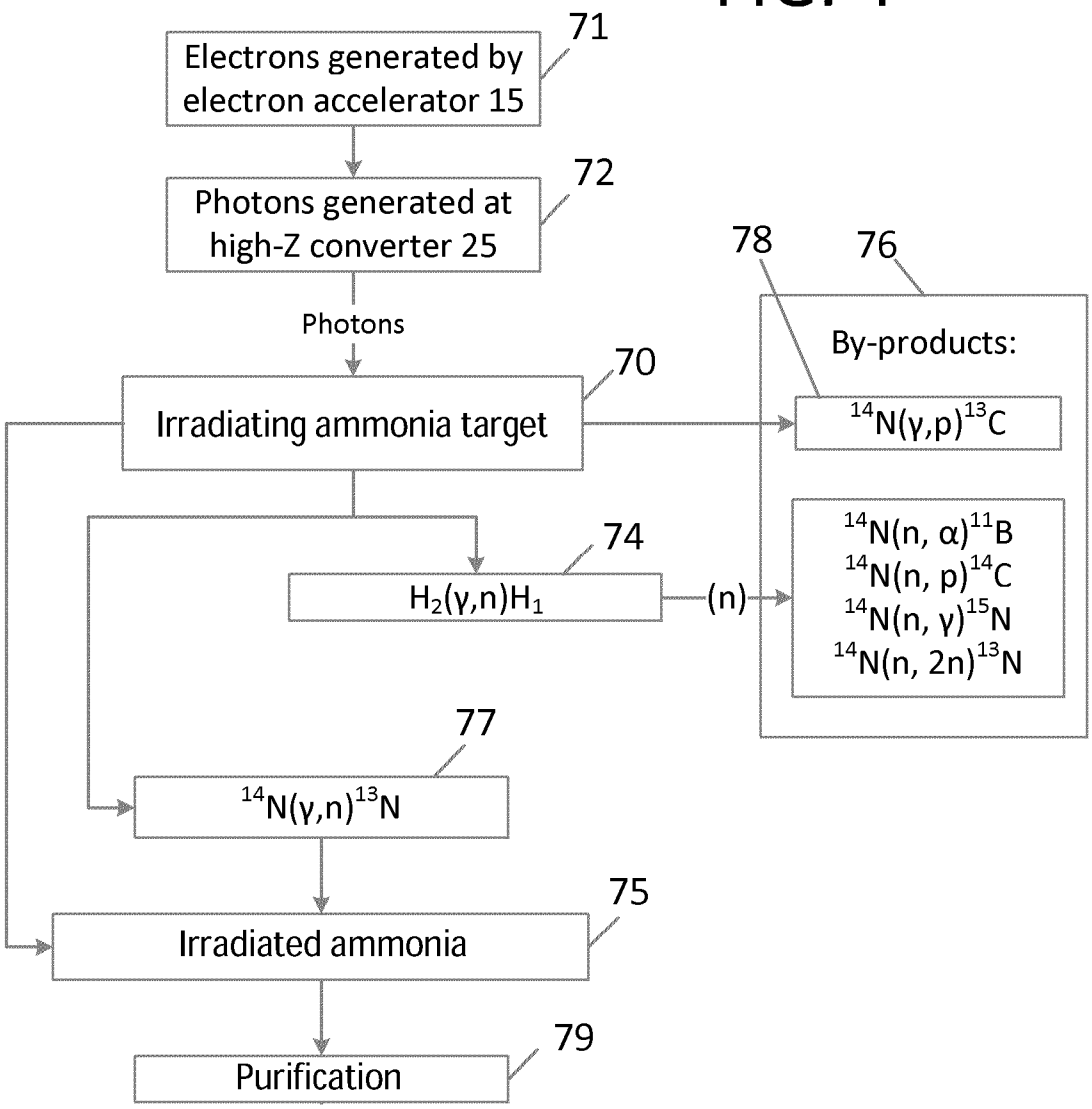
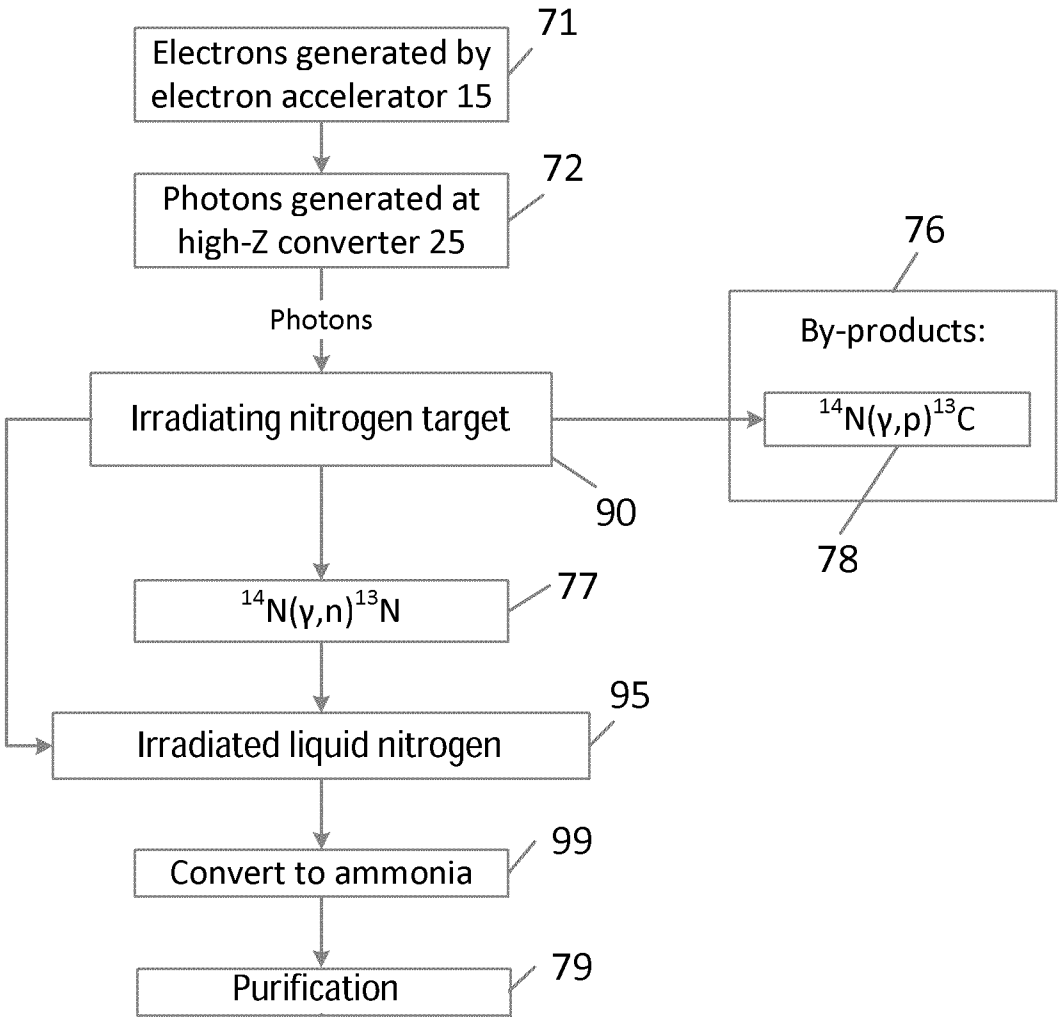

71
Electrons generated by electron accelerator 15
72
Photons generated at high-Z converter 25
Photons
70
Irradiating ammonia target
78
76
By-products:
$^{14}N(\gamma,p)^{13}C$
74
$H_2(\gamma,n)H_1$
(n)
$^{14}N(n, \alpha)^{11}B$
$^{14}N(n, p)^{14}C$
$^{14}N(n, \gamma)^{15}N$
$^{14}N(n, 2n)^{13}N$
77
$^{14}N(\gamma,n)^{13}N$
75
Irradiated ammonia
79
Purification

FIG. 5


Electrons generated by electron accelerator 15
71
Photons generated at high-Z converter 25
72
Photons
Irradiating nitrogen target
90
76
By-products:
$^{14}N(\gamma,p)^{13}C$
78
$^{14}N(\gamma,n)^{13}N$
77
Irradiated liquid nitrogen
95
Convert to ammonia
99
Purification
79

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 17/41786

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - B01D 61/44, C01C 1/02 (2017.01)
CPC - Y02P 20/52, B01D 61/54, B01D 2311/18

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)

See Search History Document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See Search History Document

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

See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2013/0163707 A1 (LUDWIG-MAXIMILIANS-UNIVERSITAT MUNCHEN) 27 June 2013 (27.06.2013); Fig. 1, Fig. 3, para [0006-0008] [0043] [0060] [0104] [0106] [0112]	1-3, 11-13
A	US 5,598,449 A (YAMAZAKI et al.) 28 January 1997 (28.01.1997); entire document	1-3, 11-13
A	US 5,468,355 A (SHEFER et al.) 21 November 1995 (21.11.1995); entire document	1-3, 11-13
A	US 4,752,432 A (BIDA et al.) 21 June 1988 (21.06.1988); entire document	1-3, 11-13
A	US 5,425,063 A (FERRIERI et al.) 13 June 1995 (13.06.1995); entire document	1-3, 11-13

☐ 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
12 September 2017	28 SEP 2017
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 17/41786

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.: 4-10, 14-17
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:

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.:

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.