# Krypton-79m: A New Radionuclide for Applications in Nuclear Medicine

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Krypton-79m emits 130-keV gamma rays in 27 ± 1% of its disintegrations and decays with a half-life of 50 ± 3 sec. It is generated readily by bombarding nearly saturated aqueous solutions of bromide salts, or bromoform, with 14-MeV protons. The $^{79m}$Kr is swept out continuously as it is produced by bubbling helium upward through the liquids. Up to 200 mCi per l are obtained of the resulting mixture of gases. The $^{79m}$Kr + helium is mixed with about five volumes of air and then driven continuously through a small-bore tube to an Anger scintillation camera located approximately 200 yards away. The rate of flow is adjusted so that the amounts of 13-sec $^{81m}$Kr and of 35-hr $^{79}$Kr are inconsequential at the time and point of use. When the gases are inhaled, good images of the lungs are obtained with an Anger scintillation camera. The trachea and bronchi commonly are revealed also.

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Several radionuclides of noble gases, which have widely divergent physical properties, have been used in nuclear medicine. These include: 35-hr krypton-79 ($^{79}$Kr), 13-sec $^{81m}$Kr, 4.5-hr $^{85m}$Kr, 10.7-yr $^{85}$Kr, 36-day xenon-127 ($^{127}$Xe), and 5.3-day Xe-133 (*1*). Our purpose is to describe another radionuclide, $^{79m}$Kr, together with a convenient way to generate it continuously. Some of our early experiences with it are also described.

Krypton-79m decays with a half-life of 50 ± 3 sec by emitting 130-keV gamma rays in 27 ± 1% of its disintegrations, and by internal conversion of the remainder. The metastable state decays by isomeric transition into $^{79}$Kr; this, in turn, decays with a half-life of 35.0 hr into stable bromine-79 ($^{79}$Br) (*1*). Thus, the ratio of half-lives of $^{79m}$Kr/$^{79}$Kr is only $50/35 \times 60 \times 60 = 0.00040$.

This large difference in half-lives suggests (*2,3*) that the copious amounts of $^{79m}$Kr we generate readily with a small in-hospital medical cyclotron (*4,5*) may be applied in biomedical studies before appreciable amounts of $^{79}$Kr accumulate to interfere, due to the high-energy photons that $^{79}$Kr emits. For applications, such as SPECT, the 3.8-fold longer half-life of $^{79m}$Kr over that of 13-sec $^{81m}$Kr should prove to be advantageous (*6*).

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The 130-keV gamma ray is nearly ideal for conventional imaging techniques by means of an Anger scintillation camera or similar dynamic nuclear medical imaging instrument. Since no gamma rays having higher energies are emitted during the decay of $^{79m}$Kr, use of it provides improved resolution and lower radiation exposures than commonly-used $^{133}$Xe.

An editor's consultant kindly pointed out to us that "krypton has a lower solubility in water than xenon by a factor of 2." Assuming this relationship pertains in blood also, then $^{79m}$Kr that is carried in the blood may be expected advantageously to be cleared from it by the lungs more rapidly than radioactive gases of xenon, such as $^{133}$Xe.

## MATERIALS AND METHODS

### Generation of Krypton-79m

The nuclear reaction we use was the one involved in the discovery of $^{79m}$Kr, viz., $^{79}$Br(p,n)$^{79m,79}$Kr (*7*). The Q-value is −2.40 MeV (*8*) and the threshold is 2.45 MeV (*9*).

We usually generate our $^{79m}$Kr by bombarding a nearly saturated aqueous solution of sodium bromide with protons having an incident energy of 14 MeV.* We prepare our target solutions by dissolving reagent grade sodium bromide, NaBr, in hot distilled water until no more crystals go into solution. The solution

cools to room temperature overnight. There results the formation of colorless crystals of $NaBr \cdot 2H_2O$ in the bottom of the flask. According to a standard reference, 75.0 grams of $NaBr \cdot 2H_2O$ is contained in 100 ml of a saturated solution, at 25°C. The specific gravity is 1.542. To prevent the troublesome precipitation of crystals when the fully saturated solution is poured into the target chamber, nine volumes of the supernatant above the $NaBr \cdot 2H_2O$ crystals of the saturated solution are diluted with one volume of distilled water.

This nearly saturated solution is poured into a 40-ml target chamber made of titanium, which is equipped with a 0.0025-cm-thick tantalum-foil window. The thickness of the target solution is 1.27 cm, which is more than adequate to completely absorb the incident protons with energy of 14 MeV. We have experienced no breakage of the thin tantalum-foil window, possibly because the target solution rapidly conducts heat away from it.

The $^{79m}Kr$ is continuously sparged (stripped) from the target solution by means of helium gas, which flows at the rate of 285 ml per min from a supply tank into the bottom of the target chamber, and then bubbles upward through the sodium bromide solution, and out the top of the chamber. No gas space is present above the liquid. The helium clears the $^{79m}Kr$, as it is generated†, and then flows from the target chamber through a trap filled with sodium hydroxide pellets. Finally, the $^{79m}Kr$ + helium gases then flow through a teflon tube (0.3 cm OD × 0.1 cm ID) into a "hot" cell and into a 125-ml plastic bottle for radioassay by means of an ionization chamber into which the bottle is placed.

The decay of a highly radioactive sample of the gases was followed in the gamma-ray ionization chamber overnight and the only long-lived radioactivity found had the gamma-ray spectrum of 35-hr $^{79}Kr$, as seen in Fig. 1. These findings were confirmed several days later by means of the multichannel analyzer.

**Propulsion of Krypton-79m to a Scintillation Camera**

The mixture of gases flowing from the target are combined with about five volumes of air and driven by air tank pressure rapidly through a small-bore (0.3 cm ID) stainless steel "hot" gas tube for administration

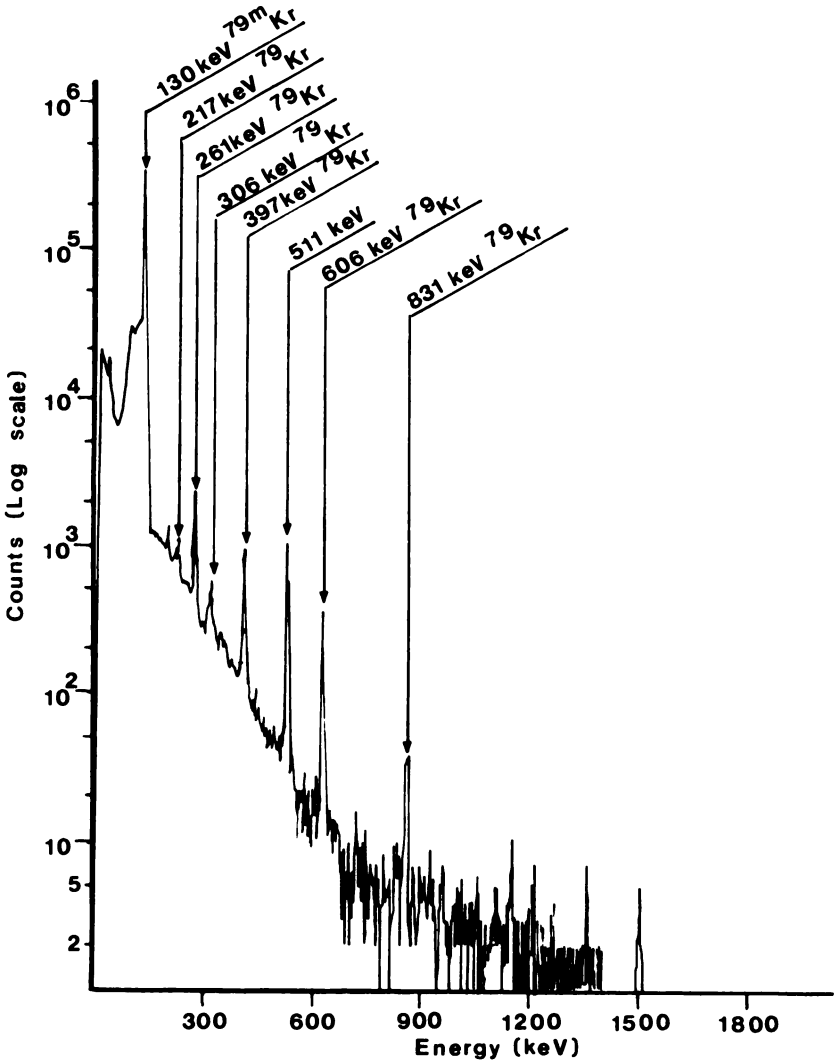


**FIGURE 1**
Semilog plot of gamma-ray spectrum of 50-sec $^{79m}Kr$ which was contaminated with small amount of 35-hr $^{79}Kr$. High-resolution 30-$cm^3$ lithium-drifted Ge(Li) detector was used, connected with 1024-channel multichannel analyzer. Counts were taken during five min live time, with sample located 25 cm above detector. Pronounced photopeak, at 130-keV, is due to $^{79m}Kr$, and other labeled peaks are due to $^{79}Kr$ (*1*). Ratio of 130-keV photopeak area of $^{79m}Kr$ to that of 261-keV peak area of $^{79}Kr$ is 137

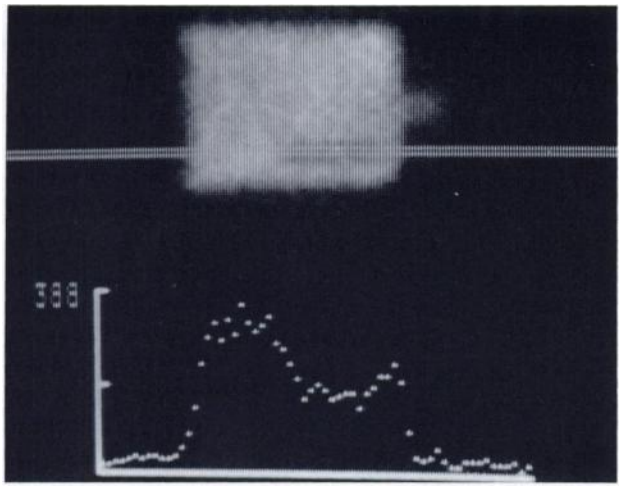

**FIGURE 2**
One hundred twenty milliliter small lung/heart plastic bottle phantom 2.6 × 5.5 × 7.5 cm was filled with $^{79m}$Kr, admixed with helium and air. A stirring bar, 1.0 × 3.3 cm, was placed within it to simulate embolus, abscess, cancer, or infarct. Sharpness of image of decreased $^{79m}$Kr occupied by this bar indicated high resolution that is attainable. "Slice" profile of relative radioactivity below it confirms high resolution

near a scintillation camera located about 200 yards from the cyclotron.

Approximately half of the $^{79m}$Kr decays during transit. The continuous "on-line" equilibrium concentrations of the $^{79m}$Kr, admixed with helium and air, are 3–10 mCi per l upon arrival near the Anger scintillation camera.

**Administration of Krypton-79m at the Anger Camera**

The Anger scintillation camera is equipped with (a) a large field-of-view NaI(Tl) crystal plate which is 1.3-cm thick; and (b) a high-resolution lead collimator which is commonly used for imaging the 141-keV gamma rays emitted by 6-hr technetium-99m ($^{99m}$Tc). The face of the camera is oriented vertically to the floor, and the subject sits upright with his/her back against the camera face. The subject then breathes the $^{79m}$Kr + helium + air mixture in either of two ways (a) simply by repeatedly inhaling the gases from the delivery tube to tidal volume and exhaling them until the appropriate number of counts accumulate; or (b) by deeply inhaling the gases and holding his/her breath about 20–30 sec.

## RESULTS

Figure 1 is a semilog plot of the gamma-ray spectrum of the 50-sec $^{79m}$Kr, which was contaminated with a small amount of 35-hr $^{79}$Kr. The $^{79}$Kr results from the isomeric transition of $^{79m}$Kr during assay and from $^{79}$Kr formed directly in the nuclear reaction of protons on $^{79}$Br. The two radioactive gases were mixed with helium, as used in these studies. The spectrum sample was made by counting a 125-ml volume of the gases as they flowed, at the rate of 285 ml/min, from the target chamber to the Anger scintillation camera.

Assay was by means of a high-resolution 30-cm$^3$ lithium-drifted Ge(Li) detector, which was connected with a 1024-channel multichannel analyzer. The counts were taken during five min of live time. The sample was located at an average distance of 25 cm above the detector.

The pronounced photopeak, at 130-keV in Fig. 1, is due to the 50-sec $^{79m}$Kr. The other labeled photopeaks are due to the $^{79}$Kr (*1*). The ratio of the 130-keV photopeak area to that of the 261-keV peak area is 137. Thus, the $^{79}$K contaminant did not exceed a few percent of the $^{79m}$Kr present. These minuscule amounts of $^{79}$Kr did not interfere significantly with imaging and they were inconsequential for our purposes.

Figure 2 is an image of $^{79m}$Kr confined within a 120-ml small lung/heart plastic bottle phantom, with dimensions of 2.6 × 5.5 × 7.5 cm. A stirring bar, 1.0 × 3.3 cm, was placed within the bottle to simulate an embolus, abscess, cancer, infarct, or other space-occupying lesion. The location of this obstruction is seen clearly, and the "slice" profile of relative radioactivity shown below the bottle indicates the sharpness of the outline of decreased $^{79m}$Kr activity in the part of the bottle occupied by the bar, as well as the high resolution attainable with 50-sec $^{79m}$Kr. The neck of the bottle was 1.4 cm in diameter and it is discernible also.

One sees in Fig. 3A an image of the lungs of a volunteer after he inhaled and exhaled the $^{79m}$Kr + helium + air mixture repeatedly until 285 kilocounts accumulated. Not only are the lungs seen well, but the heart silhouette indentation of the left lung is visible, as expected. The trachea and bronchi distinctly are visible also; and, by appropriately thresholding the digital images, these structures readily became enhanced and even more discernible (not shown).

Figure 3B shows images of the lungs of the same subject when he held his breath about 30 sec, after inhaling the gas mixture, until 1200 kilocounts accumulated. Figure 3C shows images of the lungs of another volunteer who held his breath after inhaling the gas mixture until 727 kilocounts were recorded.

## DISCUSSION

The calculated narrow-beam half-thicknesses, in centimeters, of the 130-keV gamma rays of $^{79m}$Kr, based on graphical interpolations of the values of Hubbell (*10*), are: water, 4.5; sodium iodide, 0.22; and lead, 0.022.

The 4.4-cm half-thickness in water provides adequate penetration of overlying tissues; it compares favorably

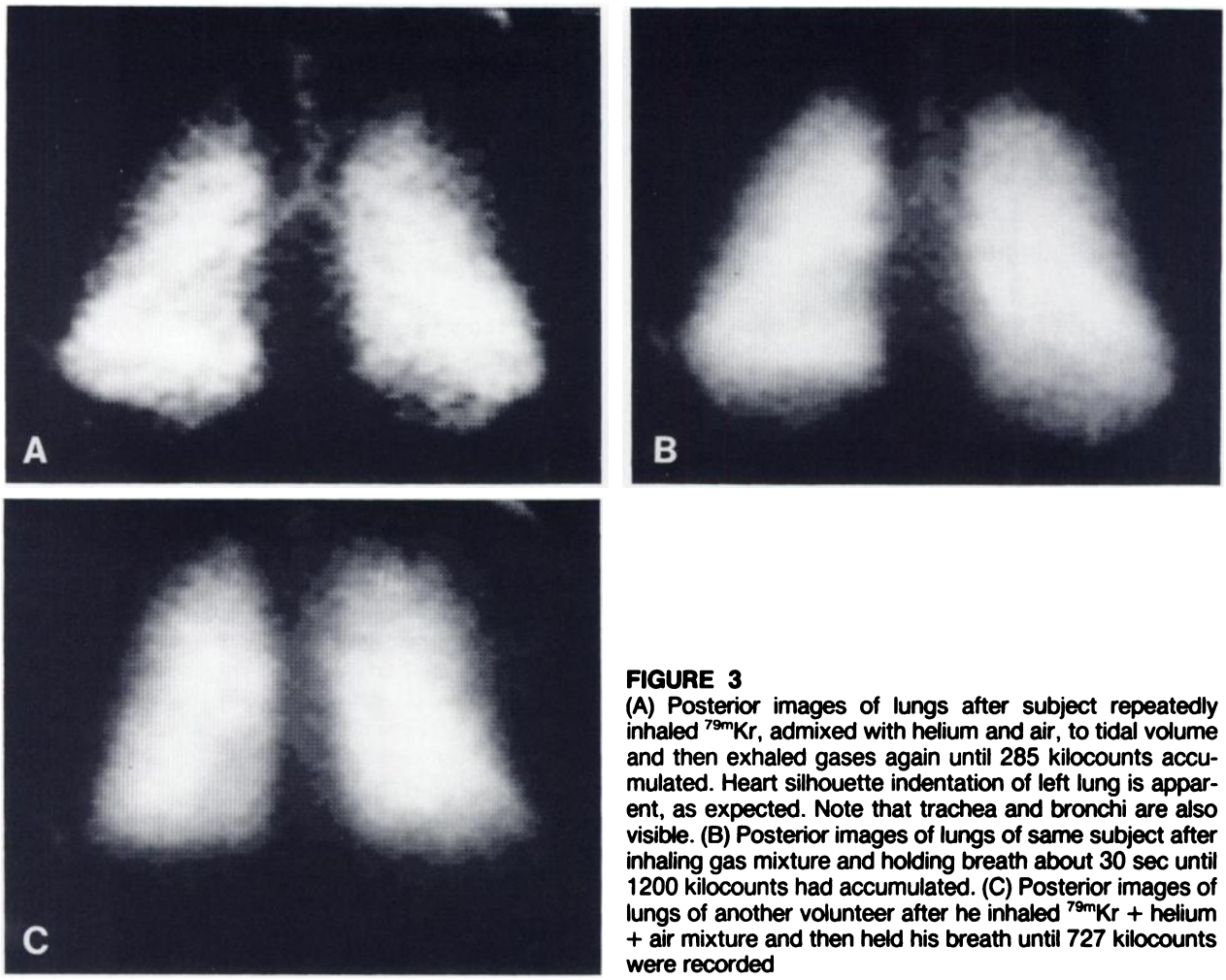


**FIGURE 3**
(A) Posterior images of lungs after subject repeatedly inhaled $^{79m}$Kr, admixed with helium and air, to tidal volume and then exhaled gases again until 285 kilocounts accumulated. Heart silhouette indentation of left lung is apparent, as expected. Note that trachea and bronchi are also visible. (B) Posterior images of lungs of same subject after inhaling gas mixture and holding breath about 30 sec until 1200 kilocounts had accumulated. (C) Posterior images of lungs of another volunteer after he inhaled $^{79m}$Kr + helium + air mixture and then held his breath until 727 kilocounts were recorded

with the 4.5-cm half-thickness in water of the 141-keV photons of commonly-imaged 6-hr $^{99m}$Tc.

The 0.22-cm half-thickness in sodium iodide assures efficient interactions of the 130-keV gamma rays with the 1.3-cm-thick sodium iodide detector plate in the Anger scintillation camera. High resolution results from the 95% photopeak detection efficiency in such a crystal (*11*). By contrast, 76% photopeak detection occurs for the 190-keV photons of $^{81m}$Kr in this detector. This 1.25-fold increase in photopeak interactions of the 130-keV gamma rays of $^{79m}$Kr compared with the 190-keV gamma rays emitted by $^{81m}$Kr is advantageous.

The 0.022-cm half-thickness in lead facilitates highly efficient collimation, and shielding protection. By comparison, the 141-keV gamma rays emitted by $^{99m}$Tc have only a slightly greater half-thickness in lead of 0.026 cm. Thus, imaging of the 130-keV gamma rays of $^{79m}$Kr by means of a high-resolution collimator, which is commonly used with $^{99m}$Tc, is appropriate.

The ease of collimation is a distinct advantage of 50-sec $^{79m}$Kr over 13-sec $^{81m}$Kr. The latter emits 190-keV gamma rays in 67% of its disintegrations (*1*). The 60-keV greater energy of the $^{81m}$Kr gamma rays necessitates the use of relatively coarse collimators because of septal penetration with a high-resolution collimator. Relatively, then, resolution is enhanced *inherently* when $^{79m}$Kr is used instead of $^{81m}$Kr.

We were unable to find excitation functions in the literature for the $^{79}$Br(p,n)$^{79m,79}$Kr nuclear reactions; we found only those for the $^{79}$Br(p,n)$^{79}$Kr reaction (*9*). Collé and Kishore found for the latter the large maximum cross-section of 725 millibarns at 10.98 MeV. Calculations, based on their data, indicate the average cross-section to be 464 millibarns for 3–14 MeV protons.

Our results shown in Fig. 1 indicate that little $^{79}$Kr is generated directly when the protons bombard $^{79}$Br; it seems to arise principally from isomeric transition of $^{79m}$Kr into $^{79}$Kr. If it is assumed that the average cross-sections are approximately the same for the formation of the two isomers by way of the (p,n) nuclear reactions on $^{79}$Br at proton energies <14 MeV, and that the radioisomers are swept out continuously by the helium from the target solution as rapidly as they are formed, then the small $^{79}$Kr contamination of the $^{79m}$Kr will be consistent with the results shown in Fig. 1.

Bromine is comprised of two stable nuclides: $^{79}$Br = 50.59% and $^{81}$Br = 49.31% (*1*). Thus, 13-sec $^{81m}$Kr,

**TABLE 1**
Absorbed Doses from Continuous Inhalation of 10 mCi of Krypton-79m*

| Target organ | Dose mrad/mCi | Total dose mrad |
|---|---|---|
| Total body | 0.37 | 3.7 |
| Lungs | 2.05 | 20.5 |
| Ovaries | 0.22 | 2.2 |
| Testes | 0.22 | 2.2 |

* These doses are comparable to, and in most cases lower than, those from routine diagnostic x-ray or nuclear medicine procedures. For example, the estimated dose to the lungs from $^{81m}$Kr is 75 mrad.

which was generated simultaneously in the $^{81}$Br(p,n)$^{81m}$Kr reaction, was discovered along with the $^{79m}$Kr (*7*). Since we bombarded aqueous solutions of reagent-grade sodium bromide, which had not been enriched in $^{79}$Br, we did find significant amounts of $^{81m}$Kr to be present initially. Its concentration was minimized by selecting the flow rate of the delivery system so that 90 to 150 sec elapsed between the departure of a differential volume of gas from the target chamber until its arrival at the site of use. Thus, because of the 3.8-fold shorter half-life of 13-sec $^{81m}$Kr, it had decayed almost completely in the "hot" gas line en route to the Anger scintillation camera; consequently, it did not interfere with imaging of the 50-sec $^{79m}$Kr. The concentration of $^{79}$Kr is minimized by continuously sweeping it out of the target solution with the helium.

The effective collimation of the 130-keV gamma rays of 50-sec $^{79m}$Kr with a high-resolution collimator facilitates its use just before a [$^{99m}$Tc]MAA perfusion lung scan without interfering with the latter study. Hence, at the numerous modern nuclear medicine facilities equipped with medical cyclotrons (*4,5,12*) capable of putting about 40 $\mu$A of 10–14 MeV protons into target solutions, the use of $^{79m}$Kr will extend the utility of the cyclotron and exclude or reduce dependence on generators of 13-sec $^{81m}$Kr.

Radiation dosimetry estimates appear in Table 1. The $^{79m}$Kr dosimetry was calculated according to the standard absorbed fraction methodology outlined in MIRD phamphlets 1–3. The nuclear data were those of Lederer (*1*). The source organs are the lungs (which are the primary sources), and the total body. The target organs are the lungs, total body, testes, and ovaries. It was assumed that $^{79m}$Kr decays to $^{79}$Kr which then decays in situ. It was assumed also that there was 1% of $^{79}$Kr present initially.

## FOOTNOTES

* Copious amounts of 9.96-min nitrogen-13 ($^{13}$N) (*1*) are generated simultaneously in the $^{16}$O(p,$\alpha$)$^{13}$N nuclear reaction when we bombard our aqueous solutions with 14-MeV protons. No $^{13}$N appears in the gas phase, but all of it remains in the solution, presumably due to rapid oxidation of it to [$^{13}$N]-$NO_3$. (Tilbury RS, Dahl JR: Nitrogen-13 species formed by the proton irradiation of water. *Radiation Research* 79: 22–33, 1979.) The likelihood of conversion of $^{13}$N to [$^{13}$N]-$N_2$ is very small because it has been shown to be necessary to add carrier, in the form of $NH_3$, to the target solution to do this.

Appropriate precautions are, of course, required to avoid approaching the solutions soon after bombardment because of the presence of large amounts of highly-penetrating 511-keV photons, which are emitted incidental to the decay of the positron-emitter, $^{13}$N.

† Our method of bombarding nearly saturated aqueous solutions of salts with protons, and continuously sweeping out the desired short-lived product gases by means of helium, is proving to be a generally advantageous and convenient one. Thus, our early experiences indicate that 69-sec $^{127m}$Xe is generated in copious amounts by bombarding nearly saturated aqueous solutions of sodium iodide with protons and sweeping out the $^{127m}$Xe with helium. Similarly, bombarding nearly saturated aqueous solutions of sodium fluoride readily generates large amounts of the 17.1-sec 99+% positron emitter, neon-19, which we continuously sweep out of the solution with helium. Papers in which these findings are described in detail now are in preparation and will be submitted for publication subsequently.

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