Contamination from ^{131}I, ^{103}Ru, and ^{239}Np in the Eluate of ^{99}Mo–^{99m}Tc Generators Loaded with (n, γ)-Produced ^{99}Mo

M. W. Billinghurst and F. W. Hreczuch

Health Sciences Centre, Winnipeg, Manitoba, Canada

Iodine-131, ruthenium-103, and neptunium-239 are present as contaminants in the eluate of ^{99}Mo–^{99m}Tc generators loaded with ^{99}Mo prepared by thermal-neutron irradiation of enriched ^{98}Mo. The elution pattern of each of these contaminants is determined, together with the amounts found in the eluate of all generators tested over a 7-month period.

J Nucl Med 17: 840–843, 1976

The literature contains a number of reports on the radioactive contaminants found in ^{99m}Tc-pertechnetate. Some are concerned with the ^{99m}Tc obtained by liquid–liquid extraction from the parent ^{99}Mo (*1–3*), one paper deals with the ^{99m}Tc obtained from commercial suppliers as "instant" pertechnetate (*4*), and still others with the ^{99m}Tc obtained from commercially available ^{99}Mo–^{99m}Tc generators (*3,5–8*). These reports may also be classified by noting whether the parent ^{99}Mo was obtained from fission-product material (*4,8*) or from thermal-neutron irradiation of enriched ^{98}Mo (*1,3,5–7*).

Iodine-131, ruthenium-103, and molybdenum-99 are fission products that are difficult to eliminate completely. For this reason, ^{131}I and ^{103}Ru frequently contaminate the ^{99m}Tc produced from fission-product ^{99}Mo. In recognition of this fact, the atomic energy control agencies have specified maximum permissible levels of these two contaminants in ^{99m}Tc at the time of injection. However, such contamination has not been reported previously for the ^{99m}Tc obtained from (n,γ)-produced ^{99}Mo. In this paper we report the consistent appearance of ^{131}I, ^{103}Ru, and ^{239}Np in the eluate of commercially available generators loaded with (n,γ) ^{99}Mo between the end of February and the end of September 1975.

MATERIALS AND METHODS

As part of our routine quality-control program, all ^{99}Mo–^{99m}Tc generators are eluted a final time on the day the new generators arrive, i.e., on a Monday after a week of use. This eluate is stored for 1 week and then analyzed with a Ge(Li) detector coupled to a 512-channel analyzer. In this way we obtain, after the fact, data on any gamma-emitting impurities present in nanocurie amounts after the ^{99m}Tc has decayed to about 0.1 μCi.

All the ^{99}Mo–^{99m}Tc generators used in this study were New England Nuclear 400- or 500-mCi generators. The ^{99}Mo used in these generators was supplied to New England Nuclear by General Electric and is produced by the (n,γ) reaction. Since the liquid–liquid extraction system that supplied part of our ^{99m}Tc requirements was also loaded with (n,γ) ^{99}Mo supplied by General Electric, we investigated the contamination found in this ^{99m}Tc. The ^{99}Mo used in the generators and the liquid–liquid extraction system was prepared from the same batch of enriched ^{98}Mo (personal communication from General Electric Co.).

The elution patterns of the identified contaminants were determined by taking 1 ml of each eluate and setting it aside for 1 week before counting on the Ge(Li) system. These evaluations were carried out on generators eluted either once or twice daily, the second elution being 3 hr after the first. Half-lives

Received Dec. 3, 1975; revision accepted April 18, 1976.

For reprints contact: M. W. Billinghurst, Health Sciences Centre, 700 William Ave., Winnipeg, Manitoba, Canada R3E 0Z3.

were determined by repeated countings over a period of approximately one half-life for each contaminant identified, using a fixed geometry between the counted vial and the detector.

The quantity of ^{131}I present in the tested samples was estimated from the Ge(Li) spectrum of a sample of $Na^{131}I$ that was assayed in our calibrator and then serially diluted to approximately 0.1 μCi/ml. All other activity calculations were based on the estimated gamma response curve of the Ge(Li) detector. This estimated response curve was based on spectra of serial dilutions of assayed samples of ^{99m}Tc and ^{131}I and calibrated samples of ^{60}Co and ^{134}Cs together with their relative gamma-photon abundances (9).

RESULTS

Since the end of February 1975 we have been concerned by the appearance of peaks at roughly 105, 225, 280, 365, and 495 keV (to the nearest 5 keV) in the Ge(Li) spectra of quality-control samples taken from the ^{99}Mo–^{99m}Tc generators. Half-life determinations gave values of 8.1 ± 0.1 days for the peak at 365 keV and 39 ± 1 days for the peak at 495 keV, identifying them as due to ^{131}I and ^{103}Ru, respectively. The peaks at 105, 225, and 280 keV all had a half-life of 2.35 ± 0.10 days. This, together with the fact that these three peaks always appeared with the same relative magnitudes (10:1.1:1.1), led us to postulate that all three gamma photons could be attributed to the same emitter. If these relative magnitudes are corrected for the relative gamma-energy detector efficiencies (5.6:1.19:1), obtained from the Ge(Li) response curve, we obtain the relative gamma abundances of 1:0.52:0.62. On this basis, we concluded that the contaminant was ^{239}Np, which has a half-life of 2.35 days, a 22.8%-abundant 106-keV gamma photon, an 11.8%-abundant 228-keV gamma photon, and a 14.1%-abundant 277-keV gamma photon. These abundances are in the required ratio of 1:0.52:0.62. Neptunium-239 also has a 3.4%-abundant 209-keV gamma photon, which was observed on retrospective examination of the spectra. The next most abundant gamma photon, 2.1% at 334 keV, could not be distinguished from background.

Table 1 shows the contaminant levels detected in the final elutions of all the generators tested during the period from the end of February until the end of September 1975. Iodine-131 was detected in the ^{99m}Tc obtained by liquid–liquid extraction, but the amounts of ^{131}I were too low to make quantitation possible. Ruthenium-103 and neptunium-239 were not detected in the product from the liquid–liquid extraction system.

Analysis of samples taken from each elution of five generators, eluted once daily, showed that the elution pattern of each radionuclide was reproducible, with only the quantity being eluted varying from generator to generator. These patterns are shown in Fig. 1 (the vertical axis is in arbitrary units and does not indicate the relative proportions of the different nuclides).

Analysis of samples taken from each elution of five generators, eluted twice daily (3 hr apart), showed that:

1. The amount of ^{131}I in the first elution each day corresponded well with the amount of ^{131}I in the eluate of the generators eluted only once daily. The amount of ^{131}I in each second elution was approximately two-thirds that in the first elution that day. (*N.B.*: The ^{99m}Tc in the second elution was only one-third of the amount obtained in the first elution since only 3 hr had been allowed for regeneration.)
2. The amount of ^{103}Ru increased steadily in each elution, with the same rate of increase from elution to elution as was observed with the generators eluted once daily. The final elution contained twice as much ^{103}Ru as the final elution of the generator eluted once daily.
3. The quantity of ^{239}Np in the first and second elution each day was approximately the same. The quantity each day decreased in the same manner as was observed with the generator eluted only once a day.

DISCUSSION

Iodine-131. The level of ^{131}I in the ^{99m}Tc product of these generators was as high as 0.4 μCi in the final elution. Since the elution profile suggests that approximately three times this amount could be expected in the first elution, and since these were either 400- or 500-mCi generators calibrated for the Friday following delivery, the iodine figure represents a maximum of approximately 1.5 μCi per curie of

TABLE 1. CONTAMINANTS IN GENERATOR PRODUCT

Generator calibration date	^{131}I (μCi)	^{103}Ru (μCi)	^{239}Np (μCi)
February 28 to March 28	0.2 –0.4	0.04 –0.07	0.02–0.2
April 4 to May 2	0.02–0.04	0.002–0.01	0.03–0.1
May 9 to September 19	0.08–0.1	0.02 –0.04	0.02–0.2

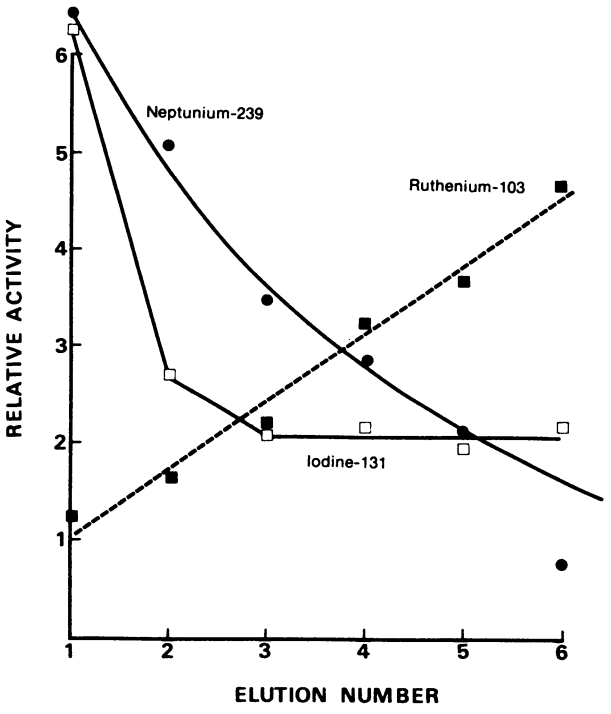

FIG. 1. Typical contamination levels of ^{131}I, ^{103}Ru, and ^{239}Np in technetium generators using (n,γ) ^{99}Mo on successive daily elutions. *Note:* Elution 6 is 3 days after elution 5. If ^{239}Np value for elution 6 is adjusted for extra 2 days of decay, it fits exponential curve.

^{99m}Tc at the time of the first elution. The maximum permissible ^{131}I in ^{99m}Tc at the time of injection is 6 μCi per curie (*10*); thus, our material would exceed maximum permissible levels if administered 12 hr after elution.

The presence of ^{131}I in the parent ^{99}Mo was confirmed from the manufacturer's radioisotopic analysis (*11*). The ^{131}I concentration reported in this analysis was $3 \times 10^{-4}\%$ of the ^{99}Mo on the calibration date. Atomic Energy of Canada (*12*) and Union Carbide (*13*), the major North American suppliers of fission-produced ^{99}Mo, specify a maximum ^{131}I contamination of $5 \times 10^{-3}\%$ on the calibration date. Thus, the maximum ^{131}I that might be expected in fission-produced ^{99}Mo is an order of magnitude larger than that reported for the (n,γ) ^{99}Mo used in our generators. Furthermore, since the alumina column used in most fission-product generators is smaller than that used in a (n,γ) ^{99}Mo generator, more contaminant breakthrough into the eluate might be expected. We have examined the pertechnetate from fission ^{99}Mo generators marketed by three radiopharmaceutical companies (New England Nuclear, Charles E. Frosst, and Mallinckrodt/Nuclear) and have not found ^{131}I contamination at the levels observed with the (n,γ) ^{99}Mo generators. However, an examination of the Ge(Li) spectra of the decayed alumina columns of the fission-product generators indicated that the ^{131}I levels were at least an order of magnitude below the specified maximum. Thus, if the fission-produced ^{99}Mo used in the generators were barely to meet specifications, the product from the generator might be unacceptable.

Ruthenium-103. In one case where the generator was eluted twice daily, the steady increase in ^{103}Ru with each elution resulted in a maximum level (in the second elution on Friday) of 0.1 μCi of ^{103}Ru in about 100 mCi of ^{99m}Tc. Thus, the ^{103}Ru contamination level never approaches the maximum permissible level of $5 \times 10^{-3}\%$ of the ^{99m}Tc. Ruthenium-103 was also observed on the decayed columns of the generators, indicating that only a small percentage of the total amount was ever eluted off the alumina column.

The manufacturer's contamination analysis (*11*) lists a ^{103}Ru level of $2 \times 10^{-4}\%$ of the ^{99}Mo on calibration date. This is more than an order of magnitude below the limit for fission-product ^{99}Mo (*12,13*). However, as with ^{131}I, the fission generators examined showed very little ^{103}Ru in the eluate, and the Ge(Li) spectra of the alumina columns showed much lower levels of ^{103}Ru than the maximum permissible.

Neptunium-239. The presence of ^{239}Np is not supported by the manufacturer's radioisotopic analysis of the parent ^{99}Mo (*11*). However, the neptunium peaks would be obscured by those of ^{91m}Nb (104.5 keV, half-life 62 days), ^{132}Te (228 keV, half-life 78 hr), and ^{131}I (364 and 284 keV, half-life 8 days), which are all present in the parent ^{99}Mo. Iodine-131 is, of course, present in the eluate as already discussed; however, its contribution to the peak at 280 keV is small at the time of the intial Ge(Li) spectra. Continued observations of the 280-keV peak past the first half-life showed an apparent increase in half-life due to an increasing proportion of ^{131}I.

The typical elution profile for ^{239}Np shows that the quantity of ^{239}Np in each elution decreases at a rate approximately equivalent to its rate of decay. Thus, up to 1.6 μCi of ^{239}Np may be found in the first elution. The maximum permissible level of gamma-emitting impurities in ^{99m}Tc (other than ^{99}Mo, ^{103}Ru, ^{131}I, ^{132}I, and ^{134}Cs) is 0.01 μCi total per millicurie of ^{99m}Tc (*10*). This is approximately six times what might be observed in normal daily elutions but only twice what might be observed in a second elution on any given day if it were performed 3 hr after the first elution.

The question is: "Where did the neptunium-239 come from?" The manufacturer stated that the target material used over this period was unfortunately contaminated with two parts per million of spent

uranium before they received it (personal communication, 1975). On this basis, we suggest that the following nuclear reactions are responsible for the ^{239}Np:

$$^{238}U + {}^{1}n \rightarrow {}^{239}U$$

(thermal-neutron cross section = 2.7 barns)

$$^{239}U \rightarrow {}^{239}Np + \beta$$

($T_{1/2}$ = 23 min).

Molybdenum-98 has a thermal-neutron cross section of 0.14 barns. If we ignore the difference between the half-lives of ^{99}Mo (66.6 hr) and ^{239}Np (56.5 hr), we calculate that a contamination level of approximately 40 μCi of ^{239}Np per curie of ^{99}Mo would be expected from the 2 ppm of uranium contamination in the ^{98}Mo. This is about 25 times the maximum amount estimated for the first elution.

CONCLUSIONS

Iodine-131, ruthenium-103, and neptunium-239 were found in the eluates of ^{99}Mo–^{99m}Tc generators loaded with ^{99}Mo manufactured by thermal-neutron irradiation of ^{98}Mo. The level of contamination did not exceed maximum permissible levels (*10*) at any time, although on several occasions the contamination would have approached the maximum permissible levels less than 12 hr after elution.

Unfortunately, ^{131}I and ^{239}Np are not detected with adequate sensitivity in routine ^{99}Mo breakthrough tests. Detecting 6 nCi of ^{131}I per millicurie of ^{99m}Tc is difficult with equipment normally available in a nuclear medicine laboratory, and detecting 10 nCi of ^{239}Np per millicurie of ^{99m}Tc is completely impossible. Therefore, the control of these impurities must rest with the manufacturer. The manufacturer should ensure that the parent ^{99}Mo does not contain enough impurities to yield a product that is unacceptable. On the other hand, "after the fact" testing is possible for any nuclear medicine laboratory and should be carried out as a routine procedure so that the quality of the product is well established on a continuing basis.

REFERENCES

1. ROBINSON GD: Impurities in ^{99m}Tc sodium pertechnetate produced by methyl–ethyl–ketone extraction. *J Nucl Med* 13: 318–320, 1972

2. AMWAR M, LATHROP K, ROSSKELLY D, et al.: Pertechnetate production from ^{99}Mo by liquid–liquid extraction. *J Nucl Med* 9: 298–299, 1968

3. BILLINGHURST MW, GROOTHEDDE M, PALSER R: Radiochemical purity of ^{99m}Tc pertechnetate. *J Nucl Med* 15: 266–269, 1974

4. CROSBY EH: Radiochemical purity of short lived technetium-99m from commercial suppliers. *Radiology* 93: 435–439, 1969

5. WOOD DE, BOWEN BM: ^{95}Zr and ^{124}Sb in ^{99}Mo–^{99m}Tc generators. *J Nucl Med* 12: 307–309, 1971

6. BARRALL RC: Reduction of radioactive impurities in radiopharmaceuticals. *J Nucl Med* 13: 570, 1972

7. PODOLAK EM: ^{131}Cs, ^{86}Rb and ^{60}Co in ^{99}Mo–^{99m}Tc generator eluate. *J Nucl Med* 13: 388–390, 1972

8. SMITH EM: Properties, uses, radiochemical purity and calibration of Tc^{99m}. *J Nucl Med* 5: 871–882, 1964

9. HEATH RK: Table of isotopes. In *Handbook of Chemistry and Physics*, 4th ed. Cleveland, Ohio, CRC Press, 1973–1974, pp B250–B544

10. Information Letter No. 417: Health Protection Branch, Department of National Health and Welfare, Canada

11. General Electric Co.: Radiopurity analysis of General Electric lot No. 17

12. Atomic Energy of Canada: ^{99}Molybdenum specifications. February 12, 1974

13. Union Carbide: Fission product generator specifications

ERRATUM

In the article "Thallium-201 for Myocardial Imaging: Appearance of the Normal Heart" (*J Nucl Med* 17: 583–589, 1976), it was incorrectly stated that Dr. David J. Cook had been supported by a Clinical Research Fellowship from the Post-Graduate Committee in Medicine of the University of Sydney. Actually, it was Dr. Ian Bailey who had received this Fellowship. Also, the unit of measurement (cm) was omitted from Table 2.