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Properties, Uses, Radiochemical Purity and Calibration of Tc^{99m}

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In the first part of this two-part article, the characteristics, potential uses, radiochemical purity and method of evaluating the activity of Tc^{99m} will be discussed. In the second part of the article, the dosimetry of this radionuclide will be presented for various routes of administration as well as for various chemical configurations, such as the pertechnetate ion, the colloid and the protein-bound state.

Tc^{99m}, first investigated by Richards and Harper in 1960, appears to have potential widespread uses in nuclear medicine. The radionuclide allows the physician to visualize and study many organ systems with better definition and speed than are presently attainable with other radionuclides while the patient receives a low radiation exposure. This is possible because of the nuclear and chemical properties of technetium. The monoenergetic gamma-ray of 140 kev emitted by Tc^{99m} is readily collimated, yet of sufficient energy to be useful for deep organ scanning. The absorbed radiation dose is low because of the short physical half-life of six hours, the low specific gamma-ray constant of 0.56 R-cm^2/mc-hr^2 at 1 cm and an $\bar{E}_\beta$ of 14 kev per disintegration. In the oxidized state, as the pertechnetate ion (TcO_4^-) it behaves in a manner similar to iodide in that it is concentrated by the thyroid gland, salivary glands and gastric mucosa. It is apparently not organified by the thyroid gland. However, in the reduced state, technetium may be readily tagged to various compounds. The chemistry of technetium is discussed in another publication (1).

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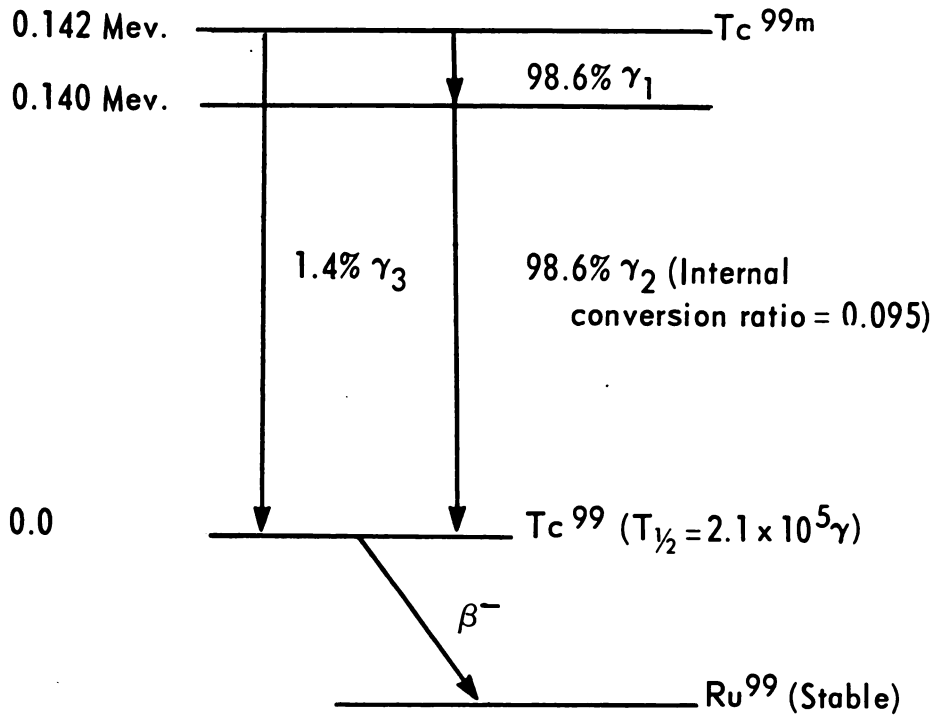
[2]The specific gamma-ray constant is 0.70 R-cm^2/mc-hr at 1 cm if the K_α and K_β rays are included. The energies of these x-rays are 18.3 and 20.6 Kev respectively.

The method of evaluating x-rays of these energies in internal dosimetry is quite difficult and will be discussed in detail in the second part of this paper.

CHARACTERISTICS

Tc^{99m} is obtained as the daughter product of Mo^{99} which in turn is recovered as a fission product or produced by neutron bombardment of Mo^{98}. Figure 1 gives the decay scheme and nuclear properties (2).

The parent radionuclide, Mo^{99}, is adsorbed on an alumina column after the other radionuclides are separated (3). Tc^{99m} may then be eluted as the pertechnetate ion from the alumina column (radionuclide generator) with approximately 15 ml of 0.1 N HCl. Since Tc^{99m} is produced by the radioactive decay of Mo^{99}, the generator may be re-eluted as soon as a sufficient activity of Tc^{99m} has grown-in. The Mo^{99} obtained via the fission process is approximately carrier-free, and



Specific Gamma-ray Constant

$\Gamma = 0.56$ R · cm^2/mC · hr. at 1 cm.

$\gamma_1 = 0.002$ Mev.

$\gamma_2 = 0.140$ Mev.

$\gamma_3 = 0.142$ Mev.

Average Local Energy Deposition

$\bar{E}_\beta = 0.014$ Mev. per Disintegration

Fig. 1. Decay scheme and nuclear properties of Tc^{99m}.

therefore a large activity may be adsorbed on a relatively small alumina column. When Mo^{99} is produced by neutron bombardment, the specific activity of Mo^{99} is limited to approximately 10 mc/g of Mo, therefore a much larger alumina column must be used to obtain an equivalent activity of Mo^{99}.

At present Brookhaven National Laboratory[3] supplies the Tc^{99m} generators with activities between 100 to 250 mc on a regularly scheduled basis. Figure 2 illustrates two of these generators. The radiation fields surrounding these generators are quite high. At the surface of the shipping can of a 150 mc generator the exposure-rate is approximately 250 mR/hr, and at 5 cm from the unshielded generator 1.5 R/hr. Although the first eluate from the generator has associated with it a radiation field of approximately 1 R/hr at contact with the containing flask, elaborate remote handling facilities are not necessary to manipulate this radionuclide. Well planned procedures which minimize personnel exposure time and adequate shadow shielding to reduce whole-body irradiation are sufficient.

Generators, if desired, may be supplied with a Dowex 50 × 8 resin column (Fig. 2—generator on left side) to remove the aluminum from the eluate. Currently, the Dowex column is not used by this laboratory to remove the aluminum from the eluate, instead it is delivered to the radiopharmacy service where the aluminum is precipitated out when the pH is adjusted. The precipitate is removed by passage through a sintered glass filter.

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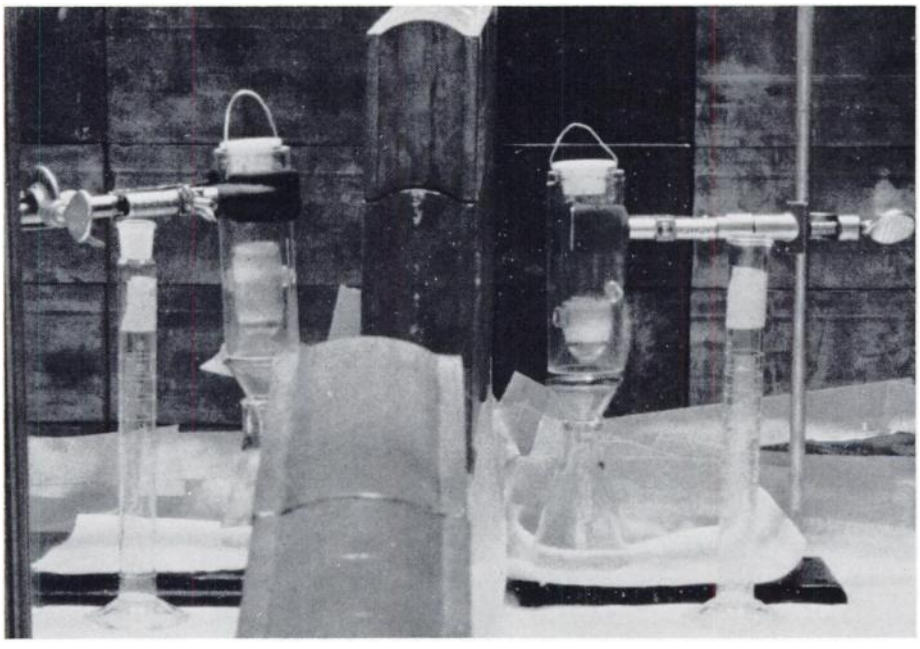

Fig. 2. Tc^{99m} generators in shielded enclosure. Generator on left has the Dowex 50 × 8 resin column added.

The elution efficiency of the generator is initially about 75 per cent and gradually improves to around 85. The elution efficiency is calculated on the basis of the Tc^{99m} assay supplied by BNL and our laboratory's method of calibrating Tc^{99m}.

The initial concentration of Tc^{99m} in the column eluate from a 100 mc generator is approximately 5 mc/ml. To increase the concentration of Tc^{99m} in the eluate, as the generator decays with the 66 hour half-life of Mo^{99}, one may elute the generator with 5 ml of eluent and then with 10 ml, collecting the latter fraction for use. This procedure will almost double the Tc^{99m} concentration. The elution curve is shown in Fig. 3.

USES

One of the primary advantages of Tc^{99m} is that large activities may be administered without the patient receiving a large absorbed dose. For example, 10 mc of Tc^{99m} administered intravenously as pertechnetate will result in a whole-body adsorbed dose of approximately 100 mrads. The use of large activities

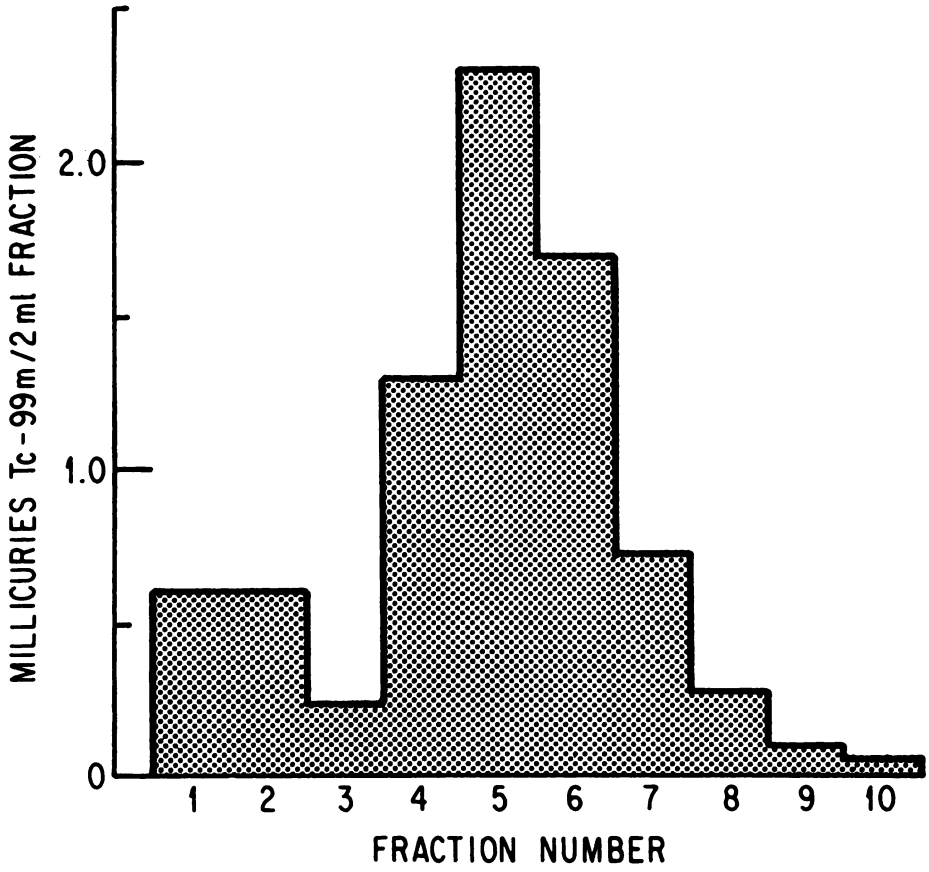

Fig. 3. Elution curve for a representative Tc^{99m} generator without the Dowex 50 × 8 resin column.

enables one to use high resolution collimators thereby improving the spatial resolution of the scintillation scans or increasing the scanning speed so that a brain scan may be completed in thirty minutes rather than two hours. Harper, Beck *et al* (4) have discussed some of the uses for Tc^{99m}, and have developed a collimator which takes advantage of the low energy monoenergetic gamma-ray. In addition to brain and thyroid scanning, using the pertechnetate ion they have successfully formed a stable sulfur colloid of technetium which localizes in the reticuloendothelial system enabling liver and bone marrow scans. (5) From the available data to date, it appears that if one to ten millicuries of Tc^{99m} are administered to a patient, sufficient Tc^{99m} activity is present in the blood to perform a brain scan whether the pertechnetate ion is administered orally or intravenously. When the pertechnetate ion is administered orally, the patient must be in the fasting state and the column eluate must be free of aluminum oxide to permit rapid absorption from the gut. McAfee, Fueger *et al,* (6), discuss the relative clinical merits of using the oral and intravenous routes for administering the pertechnetate ion for brain scanning. McAfee, Stern *et al,* (7), have tagged albumin, for placental and cardiovascular scans. These investigators and others are currently studying additional compounds which may be tagged with Tc^{99m} which may allow them to visualize other organs such as the pancreas, kidneys and spleen.

RADIOCHEMICAL PURITY

Figure 4 is the gamma-ray spectrum of a respresentative eluate from a Tc^{99m} generator illustrating photopeaks which can be identified as arising from radioactive contaminants. The peak occurring between 0.92 and 0.96 mev is a sum coincidence peak arising from the 0.18, 0.74 and 0.78 mev photopeaks of Mo^{99}. The Tc^{99m} photopeak in the gamma-ray spectrum is due to the presence of Mo^{99}, its parent radionuclide from which the Tc^{99m} was generated. In the evaluation of more than fifteen generators the following are typical levels of the radiocontaminants in the column eluate: 0.05 μc Mo^{99}, 0.003 μc Ru^{103} and 0.0002 μc I^{131}. These radiocontaminants are calculated on the basis of microcuries of radiocontaminant per millicurie of Tc^{99m} at the time of elution. In general, the levels of the radiocontaminants decrease as the generator is used. Beta-ray spectroscopy on the eluates from the generators has not been performed. There are, however, no radionuclides that decay by pure beta emission or electron capture resulting from the fission process that are ± 4 atomic numbers of technetium.

In the area where the Tc^{99m} generator is used, the only chemical reagent that should be present is the one used to elute the generator. If the generator is eluted with the wrong reagent, Mo^{99} may also be eluted from the generator.

Figure 5 shows the gamma-ray spectra of two dilutions of the same eluate. The dilution factor is twenty. These spectra demonstrate the phenomenon of the accidental sum coincidence peak. An accidental sum coincidence event occurs when two gamma-rays, not in cascade, both interact with the NaI(Tl) crystal within a time span shorter than the resolving time of the scintillation spec-

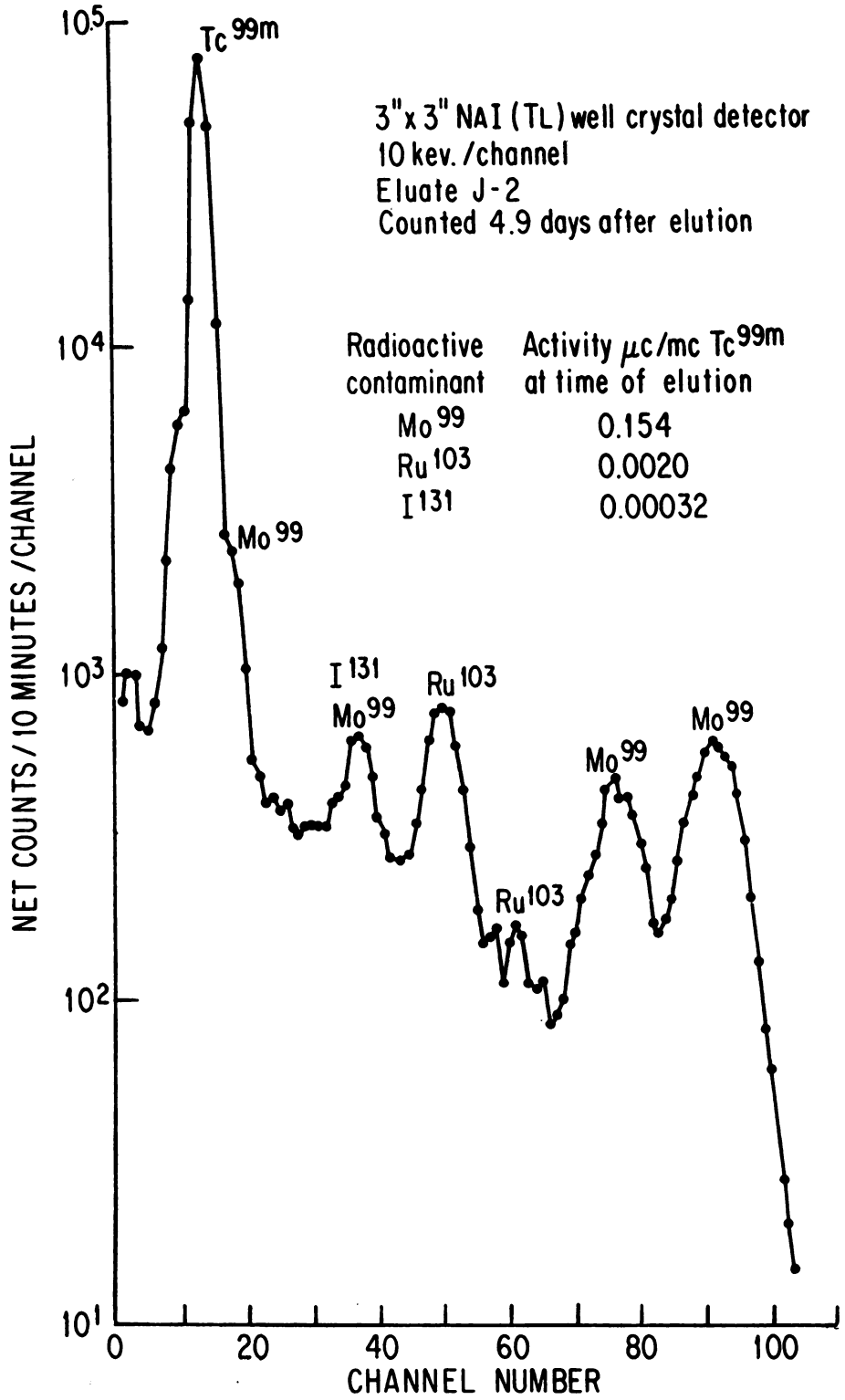

Fig. 4. Gamma-ray spectrum of an eluate from a Tc^{99m} generator illustrating photopeaks which can be identified as arising from radioactive contaminants.

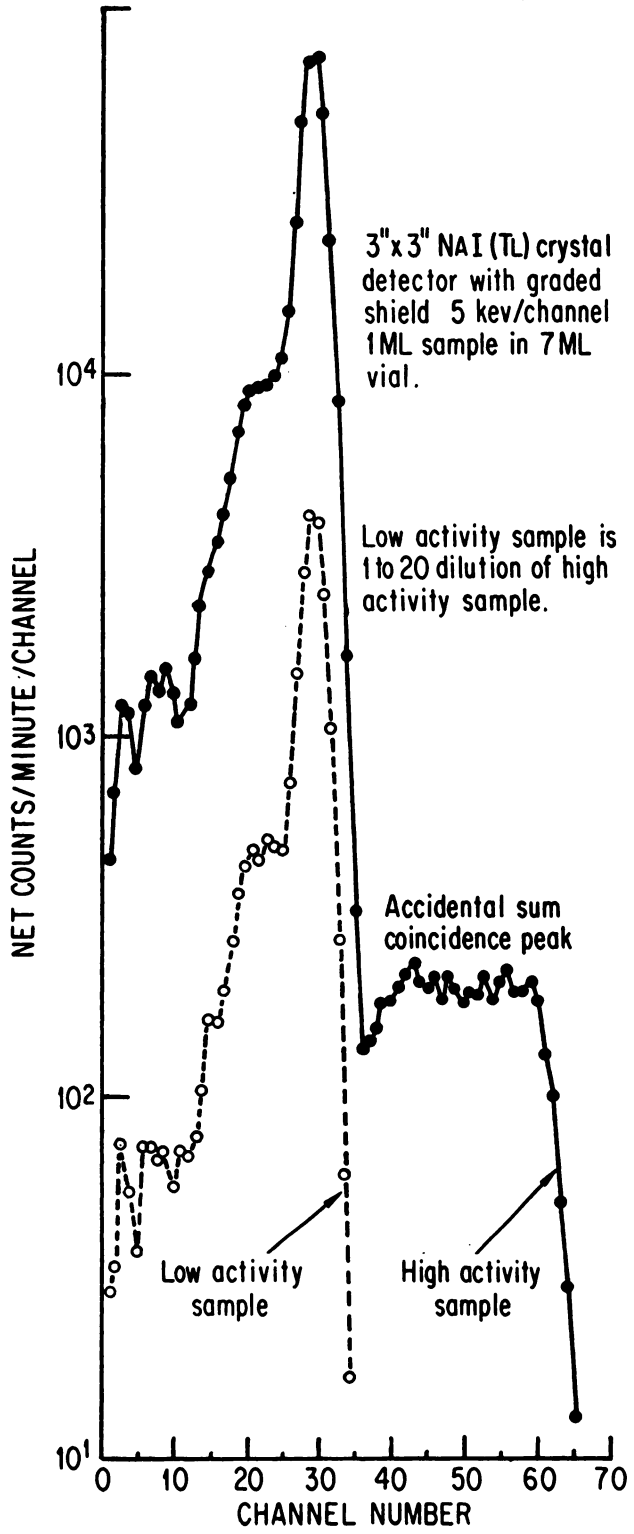

Fig. 5. Comparison of the gamma-ray spectra of high and low activty Tc^{99m} samples measured at 200 cm.

trometer. This produces a spurious signal indicative of a photon with an energy greater than the photon energy corresponding to the photopeak of either gamma-ray. This phenomenon may lead one to believe that a radiocontaminant is present or may in fact mask an actual radiocontaminant. The solution to this problem is to reduce the count-rate of the Tc^{99m} sample by diluting the sample before counting.

CALIBRATION

Ionization chamber (quartz fiber electroscope) and scintillation spectrometry techniques for calibrating Tc^{99m} have been compared. Table 1 shows the results of this study. On the basis of this study and theoretical considerations, scintillation spectrometry is the method of choice to calibrate Tc^{99m}.

The primary difficulty in using ionization chamber techniques is the evaluation of the appropriate specific gamma-ray constant (Γ) to be used. The cumulative value for Γ is shown in Table II for the inclusion of various photon energies of Tc^{99m} and Co^{57}. Once a Γ is chosen, an attempt must then be made to modify Γ for the relative attenuation of the various low energy photons by the source container, the intervening air and the wall of the ion chamber. The specific gamma-ray constant must also be corrected for the energy of the photon that actually interacts with the sensitive volume of the ion chamber, since the linear energy absorption coefficient is a very strong function of photon energy below 80 kev. To make the above corrections, the decay schemes for the radionuclides must be known, especially the electron shells in which internal conversion and electron capture occur. The accuracy to which these values are known for many radionuclides is only 10 to 20 percent.

The use of scintillation spectrometry for calibration purposes requires the knowledge of the fractional occurrence and internal conversion ratio for the photon upon which the calibration is based. These values for most radionuclides are accurately known, especially for higher energy photons. Another reason for using scintillation spectrometry and Co^{57} to calibrate Tc^{99m} is that the intrinsic efficiency and photofraction of NaI(Tl) crystals for photons in the gamma-ray emitted by Co^{57} and Tc^{99m} are essentially identical.

A simulated Tc^{99m} calibration source set is shown in Fig. 6. The purpose of the calibrated source set is to provide a simple and accurate method of assaying the Tc^{99m} activity as well as permitting users of Tc^{99m} to refer the activities of Tc^{99m} used to a common reference point. These sources are calibrated against NBS Co^{57} standards as well as standards from commercial laboratories. The Co^{57} activity is then converted to an equivalent activity of Tc^{99m} using the fact that there are 98 usable photons per 100 disintegrations of Co^{57} and 90.4 usable photons per 100 disintegrations of Tc^{99m}. Figure 7 compares the gamma-ray spectrum of the simulated Tc^{99m} source to an actual Tc^{99m} sample in the sample holder.

TABLE I.

COMPARISON OF THE CALIBRATION OF Tc^{99m} UTILIZING GAMMA-RAY SPECTROMETRY AND IONIZATION CHAMBER TECHNIQUES USING Co^{57} AND RADIUM AS STANDARDS

	Tc^{99m} Activity by Ion Chamber (Ra Std.)	*Tc^{99m} Activity by Ion Chamber (Co^{57} Std.)*
	Tc^{99m} Activity by γ-Spectrometry (Co^{57} Std.)	*Tc^{99m} Activity by γ-Spectrometry (Co^{57} Std.)*
Ratio $\pm$ 1σ	1.67 ± 0.04	0.90 ± 0.03
Range of Values	1.62 to 1.72	0.85 to 0.94
No. of Determination	10	10

1. All Ion Chamber determinations made at 50 cm.
2. All standards and samples contained in 7 ml. vials.
3. Γ (Ra) $= 8.25$ R-cm²/mc-hr.
4. $\Gamma(Co^{57}) = 0.53$ R-cm²/mc-hr.
5. Γ (Tc^{99m}) $= 0.56$ R-cm²/mc-hr.

TABLE II.

CUMMULATIVE SPECIFIC GAMMA-RAY CONSTANTS FOR Co^{57} AND Tc^{99m}

Photon Contribution to Γ	*Cummulative Γ for Various Photon Groups (R-cm²/mc-hr)*
Co^{57}	
123 and 137 kev photons	0.53
14.4 kev photon	0.91
6.4 Kα x-rays from electron capture	7.4
Internal conversion of the 14.4 kev photon	12.5
Tc^{99m}	
140 and 142 Kev photons	0.56
18.3 Kα x-rays from internal conversion	0.58
20.6 Kβ x-rays from internal conversion	0.70

Values of Γ for Co^{57} from NBS Handbook 80

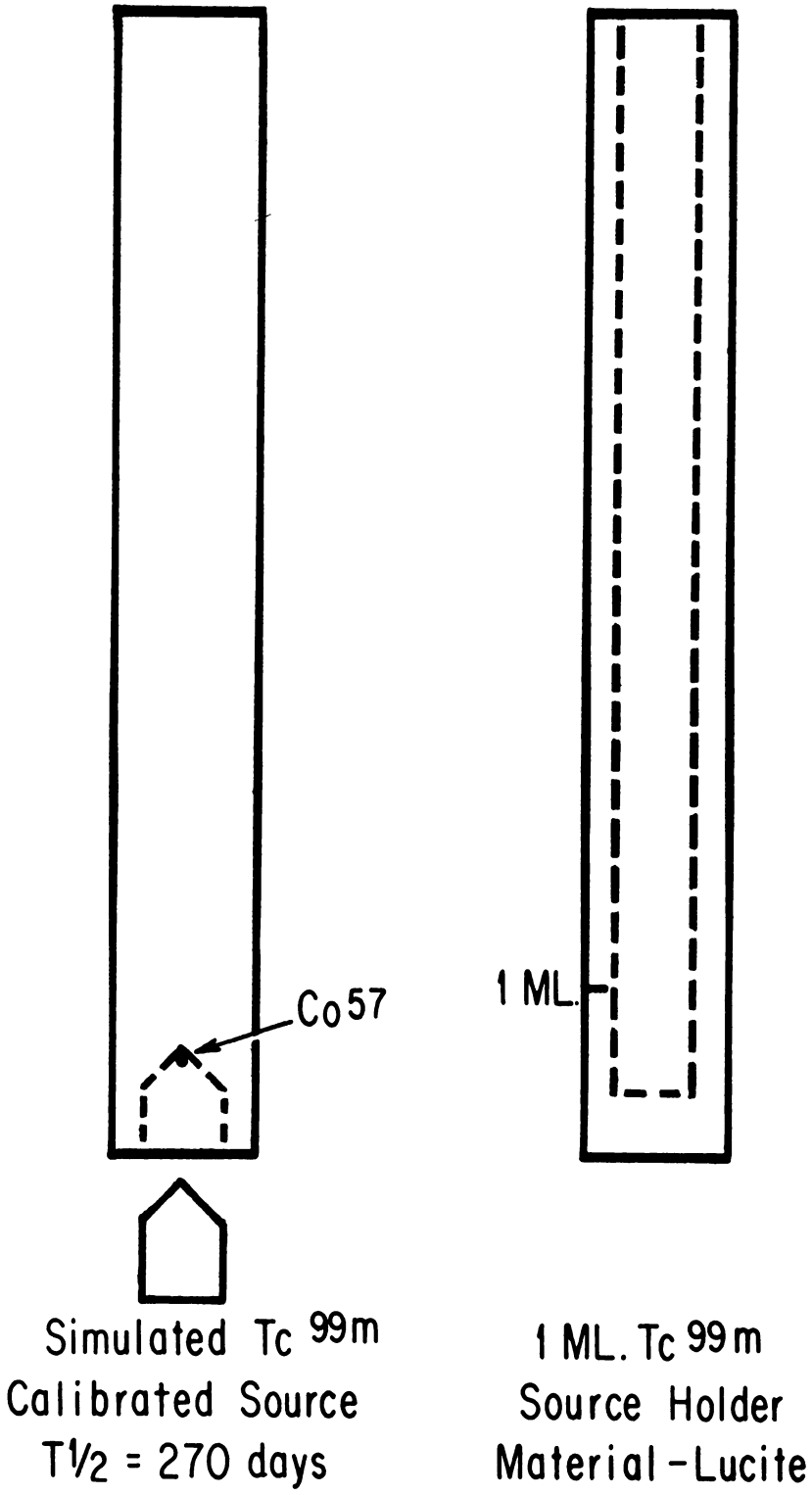

Fig. 6. Simulated Tc^{99m} calibration source set.

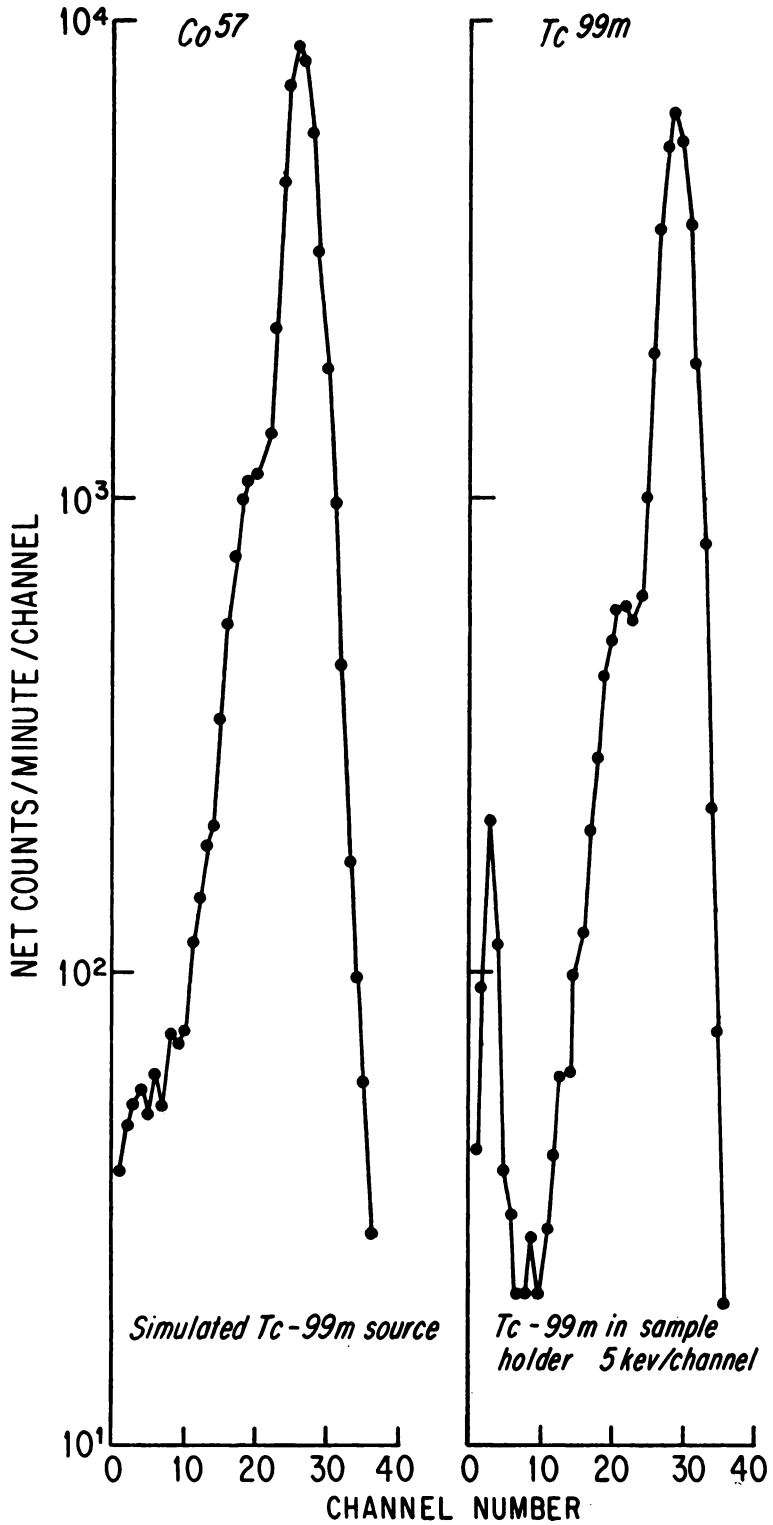

Fig. 7. Comparison of Co^{57} and Tc^{99m} gamma-ray spectrum in a NaI(Tl) well-crystal using the simulated Tc^{99m} calibration source set.

DISPENSING OF Tc^{99m} FOR HUMAN USE

The following protocol is followed at the NIH in dispensing Tc^{99m} for human use:

1. As soon as possible after a Tc^{99m} generator arrives it is eluted with 25 ml of 0.1 N HCl. This eluate will be quite cloudy and have a relatively high level of radiocontaminants. The Tc^{99m} activity is determined and the elution efficiency of the generator is calculated.
2. The generator is eluted four hours later, and the radiochemical purity and the pyrogenicity of the eluate is determined. As soon as the determinations are completed and the results are satisfactory, the eluates from the generator are released for human use.
3. An aliquot of each Tc^{99m} sample to be administered to humans is retained by the Radiation Safety Department to be calibrated and the radiochemical purity assured. The eluate is delivered to the radiopharmacy for processing and sterilization if necessary. After the fact, pyrogen tests are run on each eluate if the material will be administered intravenously or intrathecally.
4. After the radiopharmacy processing is completed, but before autoclaving the final product, an aliquot is returned to the Radiation Safety Department for final assay. There is no loss of Tc^{99m} during the autoclaving procedure.

CONCLUSIONS

From the experience to date, the radiochemical purity of Tc^{99m} from the Tc^{99m} generator is comparable with other radiopharmaceuticals currently available. Scintillation spectrometry should be used initially to calibrate Tc^{99m}. Ionization chamber calibration techniques may be used once the ionization chamber has been cross-calibrated against the scintillation spectrometry technique.

At present only four to six institutions are using Tc^{99m}. This number will increase rapidly, especially as this element's chemical characteristics are taken advantage of to direct its uptake and movement throughout the body.

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