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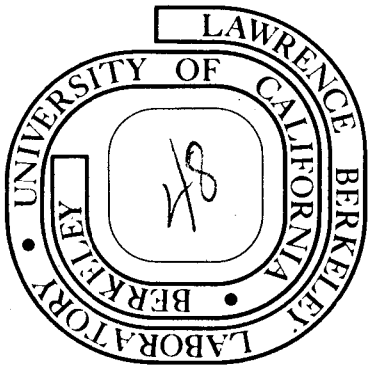

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Radionuclide Generators: Current and Future Applications in Nuclear Medicine

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Abstract

The rapid development of diagnostic nuclear medicine has been stimulated by the advances in instrumentation and in radionuclide generator systems. Generator produced radionuclides provide a high flux of useful photons from short-lived radionuclides which are conveniently and economically obtained from their long-lived parent isotopes. A number of radionuclide generators are possible, however only a limited number are useful for scintigraphy.

Developments in the ^{99m}Tc generator, either solvent extraction or alumina column, are presented together with some results of radiopharmaceutical preparations using $^{99m}TcO_4^-$ from various sources.

Developments in the ^{113m}In and ^{87m}Sr generators as well as other less used generators are presented. Ultra-short-lived radionuclides such as ^{137m}Ba, ^{128}Cs, ^{82}Rb and ^{191m}Ir are discussed and their applicability to blood flow studies are presented.

The use of high energy proton beams at the BLIP and LAMPF facilities to produce curie amounts of parent radionuclides, which are now difficult to obtain, could aid in the development of ultra-short-lived radionuclide generator systems.

Introduction

Nuclear medicine has experienced a rather phenomenal growth rate in a period of less than 15 years since the development of scanners and scintillation cameras (1,2). They brought with them a need for radionuclides that are readily available and yet provide a high photon flux while delivering a low radiation dose to the patient. The usefulness of a radionuclide generator to accomplish this task can be seen from Table I, which relates the radiation dose of various radionuclides to their half lives. The relative radiation dose factor (D.F.) is shown to be primarily half life dependent and a comparison is made to relate the D.F. of various medically useful radionuclides to the D.F. of ^{99m}Tc. The D.F. calculated as:

$$D.F. = [f(\bar{E}) + f(e^-) \times \gamma(mev)] \times T_{1/2}(sec)$$

f = Fraction/dis, $\bar{E}$ = avg $\beta^{\pm}$mev

$f(e)$ = Fraction internal conversion

$\gamma(mev)$ = gamma energy MeV

$T_{1/2}(sec)$ = half life of radionuclide,

will be referred to later in the paper.

Fortunately progress was being made in the field of radioisotope generators by Stang, Greene, Tucker, Richards and others at Brookhaven National Laboratories (BNL) in the early 1950's (3-8). From their work and that of others it became apparent that radioisotope generators would provide the radionuclides needed for diagnostic imaging with the newly developed instruments for scintigraphy.

A number of highly informative reviews and symposium proceedings (7-11,15) have been published which describe the function, purpose and application of generator produced radionuclides in Nuclear Medicine.

This paper will deal briefly with the historical development of

radionuclide generators. It will cover recent progress in the more readily utilized generator systems and it will look at some future applications of ultra-short-lived isotope generators.

Some of the radionuclide generators that have been developed or proposed for use in nuclear medicine are listed in Table II. It is readily apparent that from a list of twenty-seven potentially useful generator systems only a limited number have been used in nuclear medicine, and of these only two, ^{99m}Tc and ^{113m}In have found widespread applications. Of these two generators only ^{99m}Tc is uniquely suited for its predominant role in scintigraphy.

Technetium-99m

Technetium-99m ($T_{1/2}$ 6 hr) is the daughter of ^{99}Mo ($T_{1/2}$ 57 hr). The half lives of daughter and parent isotopes permit milkings every few hours while providing a useful generator life of at least one week for ^{99}Mo. The 140 keV photon emission of ^{99m}Tc is readily collimated and efficiently detected (about 90%) with the scintillation camera (12).

The introduction of the ^{99m}Tc-^{99}Mo generator to nuclear medicine by Richards (13,14) and the use of $^{99m}TcO_4^-$ and $^{99m}Tc_2S_7$ for in vivo imaging by Harper (15,16) provided the nearly ideal radionuclide for scintigraphy with respect to the physical characteristics, such as energy, half life, etc. The high flux of useful photons from ^{99m}Tc was a significant factor in the rapid development of nuclear medicine.

The commercially available ^{99m}Tc generators have not changed significantly from the early BNL generators. However, commercial suppliers have improved the quality of the elution product (i.e. lower alumina leakage), simplified and automated the elution procedure

to provide a sterile product and increased the shielding for radiation protection. Fission ^{99}Mo was used in the early ^{99m}Tc generators produced at BNL. However, as commercial suppliers entered the generator field and as the demand for ^{99}Mo increased there was a change to ^{99}Mo obtained by the $^{98}Mo\ (n,\gamma)^{99}Mo$ reaction.

Recently there has been a renewed interest in fission produced ^{99}Mo to obtain high specific activity ^{99m}Tc. Carrier-free fission ^{99}Mo can be retained on smaller columns of alumina than can the ^{98}Mo neutron activated ^{99}Mo which requires larger volumes of alumina to prevent ^{99}Mo breakthrough. Thus smaller elution volumes are required for fission ^{99}Mo generators and the specific activity of the ^{99m}Tc can be increased by a factor of 3 or 4. However, the possibilities of radionuclidic contamination by other than ^{99}Mo breakthrough are increased because other fission produced radionuclides such as ^{103}Ru, ^{131}I, and ^{132}Te are present (17).

In recent years there has also been a resurgence of interest in the methyl-ethyl-ketone (MEK) extraction of ^{99m}Tc from basic ^{99}Mo-molybdate solution. Several of the larger medical and research centers (18,19) and a commercially available automated extractor (20) are providing MEK extracted $^{99m}TcO_4^-$ in the dry form. Most of the "instant" ^{99m}Tc supplied by radiopharmaceutical companies are obtained by MEK extraction and some are obtained by sublimation.

Methyl-ethyl-ketone extraction of ^{99m}Tc offers the advantages of economy (i.e. buying only the ^{99}Mo-molybdate solution), controlled specific activity by adding the desired volume of saline to the dry $^{99m}TcO_4$, lower alumina contamination by a factor of 4 or 5 and lower ^{99}Mo breakthrough by a factor of 100 (21). Low specific activity ^{99}Mo, which can not be used for the alumina column generator, can be

used for the MEK extraction procedures.

The availability of $^{99m}TcO_4$ from a variety of sources requires that some evaluation be made of the labeling efficiency and in vivo distribution of radiopharmaceutical preparations made with $^{99m}TcO_4$ obtained from alumina column generators, commercial suppliers of "instant" ^{99m}Tc and from "in-house" MEK extraction. Bardfield (22) has shown significant variations in the ^{99}Mo content of "instant" ^{99m}Tc from commercial sources.

Technetium colloid and human serum albumin labeled with ^{99m}Tc from various sources of $^{99m}TcO_4^-$

Technetium-99m sulfur colloid and ^{99}Tc-tin colloid were prepared by using three commercially available colloid kits (NEN, SQB and MPI) and $^{99m}TcO_4$ obtained from alumina generator with 0.9% saline (NEN, MKDT), "instant" ^{99m}Tc (MPI, MEK extracted) and automated MEK-TEK extractor. The labeling efficiency was determined by ascending paper chromatography using Whatman #1 paper and 80% methanol. These results are shown in Table III. The labeling efficiency ranged from 83.6% for NEN-I kit and NEN $^{99m}TcO_4$ to 99.7% for MPI kit with MPI $^{99m}TcO_4$ or with MEK-TEK $^{99m}TcO_4$.

Technetium colloid obtained from these preparations were injected in rats and the per cent uptake of the injected activity in various organs was determined 20 minutes post i.v. administration. The results of these studies which include the liver to lung uptake ratio are shown in Table IV. It shows that the liver uptake ranged from 67.8 per cent to 91.6 per cent and that the liver to lung ratio ranged from 32.1 to 183. There was considerable variation within an individual supplier's colloid kit $^{99m}TcO_4$ preparation as well as sim-

ilar variations among the different "kits" and $^{99m}TcO_4^-$ combinations of preparation. Variations in the quality of $^{99m}Tc_2S_7$ from "kit" preparations were reported earlier by Tubis (23).

The results in Table IV are not intended as an evaluation of the superiority of any particular kit or $^{99m}TcO_4$ supplier to any other, but merely to point to the problems inherent in maintaining a consistent preparation within the laboratory. Similar results and conclusions can be obtained from Table V showing the labeling efficiency for ^{99m}Tc-human serum albumin using the electrolytic method of Benjamin (24). This method appears to be sensitive to the quality of $^{99m}TcO_4^-$ and it shows a wide variability of labeling efficiency with $^{99m}TcO_4$ obtained from (1) Al_2O_3 column, (2) "instant" ^{99m}Tc and (3) MEK-TEK extractor. These results indicate a mean labeling efficiency of 63.4% from alumina generator $^{99m}TcO_4$, 28.6 to 44.6% from commercial "instant" ^{99m}Tc and 80.7% from MEK-TEK extracted $^{99m}TcO_4$.

It is evident that careful consideration should be given in selecting the source of the $^{99m}TcO_4^-$ if meaningful results are to be obtained from labeling experiments.

Other radionuclide generators that have been or are being used in nuclear medicine include ^{113m}In-^{113}Sn, ^{87m}Sr-^{87}Y and ^{68}Ga-^{68}Ge. Of these generator systems the ^{113}In generator has been the most useful.

Indium-113m generator

The indium-113m-tin 113 generator was introduced in 1966 by Stern (25). Tin 113 ($T_{1/2}$ 115 d) is retained on hydrous zirconium oxide and the 1.7 h half life ^{113m}In is milked from the generator with 0.05 M HCl. Because of the long half life of the parent, ^{113}Sn,

this generator system is useful in terms of supplying radionuclides to areas that are remotely located from a radionuclide production facility. Although the 393 keV photon of ^{113m}In is somewhat high for use with the scintillation camera, the long half-life parent makes this generator economical and convenient for underdeveloped areas (26). The chemistry of ^{113m}In is adaptable to the preparation of radiopharmaceuticals for imaging lungs, liver, brain tumors and kidneys (27). Indium-113m also readily labels transferrin to provide a useful agent for blood pool, cardiac and CSF studies (25,28). In the case of CSF studies, however, the relatively short 1.7 h half life of ^{113m}In could be a factor limiting its usefulness. The immediate and strong binding of ^{113m}In to transferrin when it is administered intravenously in an acid medium makes ^{113m}In useful as a blood pool label for monitoring cardiac and pulmonary blood flow with detector probes for evaluating heart function by the method developed by Steele and Van Dyke (29).

Since the introduction of the ^{113m}In-^{113}Sn generator to nuclear medicine some seven years ago, ^{113m}In has not attained the stature of ^{99m}Tc for scintigraphy, however with advances in instrumentation which will provide improved collimation and more efficient detectors for the 393 keV photon, ^{113m}In can have a promising future in nuclear medicine.

Other Radionuclide Generators

The ^{87m}Sr-^{87}Y generator introduced by Myers (30) for bone scanning has been developed (31-33) and proved to be useful for the detection of bone tumors (34-35). However the relatively slow clearance of ^{87m}Sr from the blood and soft tissues combined with its 2.8 h half life limits the bone to blood uptake ratio below that of other bone scanning agents such as ^{18}F (36). The rapid development of ^{99m}Tc

labeled bone scanning agents such as polyphosphates, diphosphonates and pyrophosphates would indicate that ^{87m}Sr will not be a predominant factor in bone scanning. There is however, some indication that ^{87m}Sr might be useful in certain types of nonosseous tumor localization (37-38) and in the diagnosis of pulmonary aspergillosis (39).

The ^{68}Ga-^{68}Ge generator introduced by Gleason (40) and developed into an alumina column generator by Green and Tucker (41) was used by Anger and Gottschalk (42) for localization of brain tumors with ^{68}Ga-EDTA and the Anger positron scintillation camera. Although Hayes and Edwards (43-44) used ^{68}Ga for bone scanning, ^{68}Ga has not been utilized to any great extent in nuclear medicine since the introduction of ^{99m}Tc. Because the ^{68}Ga generator is nearly ideal in so far as the half-lives of the daughter (^{68}Ga $T_{1/2}$ 68 min) and parent ^{68}Ge (275 days) are concerned and because of the high radionuclidic purity of ^{68}Ga which contains less than 10^{-3} per cent ^{68}Ge contamination, ^{68}Ga could be a useful radionuclide depending upon the progress made in the capability of imaging with the 511 keV annihilation photons and the development of useful radiopharmaceutical agents labeled with ^{68}Ga (45).

Ultra-short-Lived Radionuclide Generators

The concept of maximum photon yield with a minimum radiation exposure can best be met by the use of radionuclides with half lives that fall into the ideal range proposed by Wagner (46-47), namely the effective half life of the radionuclide is 0.693 times the time at which the study is completed.

In the case of many dynamic studies a radionuclide with a half life of a minute or less would be useful. From Table I, which relates

the radiation dose to the half life of the radionuclide, it can be seen that the photon yield for radiation dose delivered is primarily half life dependent. Furthermore ultra-short-lived radionuclides will permit dynamic studies to be repeated within a few minutes as the injected activity rapidly decays away (48). With these considerations in mind it is conceivable that some of the ultra-short-lived radionuclide generators in Table II such as ^{81m}Kr (49), ^{82}Rb (50), ^{128}Cs, ^{137m}Ba (51,52), and ^{191m}Ir (48) will find useful applications in nuclear medicine. Two problems which confront the development of ultra-short-lived radionuclide generators are (1) difficulty in producing adequate amounts of the parent radionuclide and (2) the need for automated systems for elution and direct infusion of the daughter radionuclide with built in monitoring controls which would insure the integrity of the eluate. Castronovo (53) has described a monitoring control for maintaining a constant pH of ^{137m}Ba-EDTA for continuous infusion. Other monitoring controls need to be developed for the infusion of ultra-short-lived radionuclides.

In the case of positron emitting radionuclides the development of instrumentation for imaging the 511 keV annihilation gammas will determine the future usefulness of radionuclides such as ^{82}Rb and ^{128}Cs. A similar problem exists for the 2.6 min ^{137m}Ba whose 666 keV gamma emission are difficult to collimate. A further problem for ^{137m}Ba is the long half life of the ^{137}Cs parent ($T_{1/2}$ 30.0 y) which would pose a radiation hazard in the event of ^{137}Cs leakage from the generator.

Two other radionuclide generators listed in Table II, the 24 sec ^{90m}Nb and the 30.6 sec ^{195m}Au, are being investigated. The parent radionuclides ^{90}Mo ($T_{1/2}$ 5.7 h) and ^{195m}Hg ($T_{1/2}$ 1.7 d) respec-

tively are produced by proton irradiation at the LBL 88-inch cyclotron. The separations of the daughter radionuclides by ion exchange column chromatography are being studied.

Future Developments

In view of the desirability of obtaining the highest photon yield with a minimum radiation exposure, it appears reasonable to pursue the development of ultra-short-lived radionuclide generators as a means of achieving this goal. Recent developments in the use of high energy proton beams at BLIP (Brookhaven Linac Isotope Producer) (54) and at LAMPF (Los Alamos Meson Production Facility) (55) open the possibility of obtaining curie amounts of parent radionuclides such as ^{82}Sr and ^{128}Ba from high energy proton or spallation reactions.

Summary

The progress of nuclear medicine has been marked by the developments in instrumentation and in radiopharmaceuticals, including radionuclide generator systems which provide short-lived daughters without the expense of frequent shipments.

It does not appear likely that there will be any significant change in the predominant role of ^{99m}Tc in the immediate future. The most fruitful area of research may well be in the development of new radiopharmaceuticals labeled with ^{99m}Tc. A promising area of development is new radioisotope generators to provide ultra-short-lived nuclides for dynamic studies of blood flow through the brain, heart and other organs.

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Table I. Relative Radiation Dose Factor (D.F.)*

Radionuclide	$F(\bar{E})$	$(f)e^-$	γ(Mev)	$T_{1/2}$(sec)	D.F./sec	D.F.x $T_{1/2}$	$\frac{\text{D.F. nuclide}}{\text{D.F. } ^{99m}Tc}$
Carbon-11	0.39			1.22×10^3	0.39	4.76×10^2	1.5
Nitrogen-13	0.30			6.00×10^2	0.30	1.80×10^2	0.6
Fluorine-18	0.25			6.60×10^3	0.25	1.65×10^3	5.3
Potassium-43	0.32			8.06×10^4	0.32	2.58×10^4	83
Iron-52 (+ Mn-52m)	0.83			2.95×10^4	0.83	2.44×10^4	79
Copper-64	0.14			4.61×10^4	0.14	6.45×10^3	21
Gallium-67	0.017			2.81×10^5	0.017	4.78×10^3	15
→ Gallium-68	0.67			4.08×10^3	0.67	2.73×10^3	8.8
Arsenic-71	0.10	0.1	0.175	2.20×10^5	0.12	2.64×10^4	85
Arsenic-74	0.29			1.55×10^6	0.29	4.50×10^5	1450
Selenium-75	0.020			1.04×10^7	0.02	2.08×10^5	671
→ Krypton-81m		0.34	0.190	13.0	0.065	0.85	.003
Rubidium-81	0.05	0.34	0.190	1.69×10^4	0.12	2.03×10^3	6.6
→ Rubidium-82	1.26			75	1.26	94.5	0.3
→ Strontium-87m		0.15	0.389	1.02×10^4	0.058	5.92×10^2	1.9
→ Technetium-99m		0.1	0.140	2.20×10^4	0.014	3.10×10^2	1
Indium-111		0.1 0.05	0.173 0.247	1.91×10^5	0.029	5.54×10^3	17.9

Table I. (Continued)

Radionuclide	$F(\bar{E})$	$(f)e^-$	γ(Mev)	$T_{1/2}$(sec)	D.F./sec	D.F.x $T_{1/2}$	$\frac{\text{D.F. nuclide}}{\text{D.F. } ^{99m}Tc}$
→ Indium-113m		0.30	0.393	6.0×10^3	0.12	7.2×10^2	2.3
Iodine-123		0.14	0.159	4.79×10^4	0.022	1.05×10^3	3.4
Iodine-125		0.93	0.035	5.18×10^6	0.033	1.71×10^5	552
Iodine-131	0.19	0.016	0.326	6.95×10^5	0.195	1.36×10^5	437
Xenon-133	0.138	0.60	0.081	4.55×10^5	0.187	8.51×10^4	274
→ Cesium-128	0.592			2.28×10^2	0.592	1.35×10^2	0.4
Cesium-129	0.017			1.15×10^5	0.017	1.96×10^3	6.3
→ Barium-137m		0.084	0.662	1.53×10^2	0.056	8.57	0.03
→ Iridium-191m		0.66	0.129	4.9	0.085	0.42	0.001
Mercury-197		0.80	0.077	2.34×10^5	0.062	1.45×10^4	46
Mercury-203	0.086	0.14	0.279	4.05×10^6	0.125	5.06×10^5	1630

→ Generator produced

* D.F. = $[f(\bar{E}) + f(e^-)(\gamma\text{mev})] \times T_{1/2}\text{sec}$

Table II. Generator Produced Short-lived Radionuclides for Use in Nuclear Medicine

	Daughter					Parent				
	Isotope	$T_{1/2}$	Decay(%)	Photon Mev(%)	*Status	Isotope	$T_{1/2}$	Decay(%)	Photon Mev(%)	Production
1	^{28}Al	2.3 m	β^-(100)	1.78(100)		^{28}Mg	21.2 h	β^-(100)	.031(96) .40(30) .95(30) 1.35(70)	$^{26}Mg\left(\begin{matrix}t,p\\ ^4He,2p\end{matrix}\right)$
2	^{38}Cl	37.3 m	β^-(100)	1.60(38) 2.17(47)		^{38}S	2.9 h	β^-(100)	1.88(95)	$^{37}Cl(^4He,3p)$
3	^{47}Sc	3.4 d	β^-(100)	0.160(73)	C	^{47}Ca	4.5 d	β^-(100)	.49(5) .815(5) 1.31(74)	$^{46}Ca(n,\gamma)$
4	^{52m}Mn	21.1 m	β^+(98) IT(2)	0.511(196) 1.43(100)		^{52}Fe	8.2 h	β^+(56) EC(44)	.165(100) 0.511(112)	$^{50}Cr(^4He,2n)$
5	^{62}Cu	9.8 m	β^+(97)	0.511(194)		^{62}Zn	9.1 h	β^+(18) EC(82)	.042(20) .51(47) .59(22)	$^{63}Cu(p,2n)$
6	^{68}Ga	68.3 m	β^+(88) EC(12)	0.511(176) 1.08(3.5)	C	^{68}Ge	275 d	EC(100)	---	$^{66}Zn(^4He,2n)$
7	^{72}As	1.1 d	β^+(75) EC	0.511(150) 0.63(8) 0.835(78)		^{72}Se	8.4 d	EC(100)	0.046(59)	$^{75}As(d,5n)$ $^{70}Ge(^4He,2n)$
8	^{81m}Kr	13 sec	IT(100)	0.190(65)	C	^{81}Rb	4.7 h	β^+(13) EC(87)	0.253 0.450 0.511(26)	$^{79}Br(^4He,2n)$
9	^{82}Rb	1.3 m	β^+(96) EC(4)	0.511(192) 0.777(9)	C	^{82}Sr	25 d	EC(100)	---	$^{85}Rb(p,4n)$

Table II. (Continued)

	Daughter					Parent				
	Isotope	$T_{1/2}$	Decay(%)	Photon Mev(%)	Status	Isotope	$T_{1/2}$	Decay(%)	Photon Mev(%)	Production
10	^{83}Kr	1.86 h	IT(100)	0.009(9)	B	^{83}Rb	83 d	EC	0.53(93) 0.79(0.9)	$^{81}Br(^{4}He,2n)$
11	^{87m}Sr	2.83 h	IT(99+)	0.388(80)	D	^{87}Y	3.3 d	$\beta^+(<1)$ EC(99)	0.483	$^{86}Sr(d,n)$ $^{87}Sr(p,n)$ $^{88}Sr(p,2n)$
12	^{89m}Y	16.1 sec	IT(100)	0.91(99)		^{89}Zr	3.3 d	$\beta^+(22)$ EC(78)	0.511(44)	$^{89}Y(p,n)$
13	^{90m}Nb	24 sec	IT(100)	0.122(71)	A	^{90}Mo	5.7 h	$\beta^+(25)$ EC(75)	0.257(85) .445(9) .511(50)	$^{93}Nb(p,4n)$
14	^{99m}Tc	6.0 h	IT(100)	0.140(90)	D	^{99}Mo	2.78 d	$\beta^-(100)$	0.181(7) 0.740(12) 0.780(4)	F.P. $^{98}Mo(n,\gamma)$
15	^{109m}Ag	39.2 sec	IT(100)	0.088(5)	B	^{109}Cd	1.24 y	EC(100)	---	$^{108}Cd(n,\gamma)$ $^{109}Ag(d,2n)$
16	^{113m}In	1.66 h	IT(100)	0.393(64)	D	^{113}Sn	115 d	EC(100)	0.225(1.8)	$^{112}Sn(n,\gamma)$
17	^{118}Sb	3.5 m	$\beta^+(75)$ EC(25)	0.511(150) 1.23(3)		^{118}Te	6.0 d	EC(100)	---	$^{121}Sb(d,5n)$
18	^{122}I	3.5 m	$\beta^+(65)$ EC	0.511(130) 0.564		^{122}Xe	20.1 h	EC(100)	0.060 0.090 0.110	$^{127}I(p,6n)$
19	^{132}I	2.26 h	$\beta^-(100)$	0.52(20) 0.67(144) 0.73(89) 0.95(22)	C	^{132}Te	3.24 d	$\beta^-(100)$	0.053(17) 0.230(90)	F.P.

Table II. (Continued)

	Daughter					Parent				
	Isotope	$T_{1/2}$	Decay(%)	Photon Mev(%)	Status	Isotope	$T_{1/2}$	Decay(%)	Photon Mev(%)	Production
20	^{128}Cs	3.8 m	β^+(51) EC(49)	0.441(27) 0.511(102) 0.528	B	^{128}Ba	2.43 d	EC(100)	0.134 0.278	$^{133}Cs(p,6n)$
21	^{137m}Ba	2.55 m	IT(100)	0.662(89)	C	^{137}Cs	30.0 y	β^-(100)	----	F.P.
22	^{134}La	6.8 m	β^+(62) EC(38)	0.511(124) 0.605(61)		^{134}Ce	3.0 d	EC(100)	----	$^{139}La(p,6n)$
23	^{140}Pr	3.4 m	β^+(50) EC(50)	0.511(100) 1.60(0.3)	A	^{140}Nd	3.3 d	EC	----	$^{141}Pr(^4He,2n)$
24	^{178}Ta	9.4 m	β^+(1) EC(99)	0.093 0.511		^{178}W	21.5 d	EC	----	$^{181}Ta(p,4n)$
25	^{183}W	5.3 sec	IT(100)	0.108(19)		^{183}Ta	5.0 d	β^-(100)	.246(33)	$^{181}Ta(nn,\gamma)$
26	^{191m}Ir	4.9 sec	IT(100)	0.129(25)	C	^{191}Os	15.0 d	β^-	----	$^{190}Os(n,\gamma)$
27	^{195m}Au	30.6 sec	IT(100)	0.261(77)	A	^{195m}Hg	1.67 d	IT(50) EC(50)	0.200(35) 0.261(20) 0.560(20)	$^{197}Au(p,3n)$

* A = Preliminary investigation
B = Separation of daughter, animal studies
C = Preliminary human studies
D = Clinical applications

Table III. Labeling Efficiency of ^{99m}Tc-Colloid for Liver Uptake Prepared from Various "Kits" and Sources of TcO_4

Source of $^{99m}TcO_4$	Kits		
	NEN	Squibb	MPI (SnII)
	Per cent Activity at Rf 0 - 0.2 ± aver. deviation		
NEN	Lot I - (9) 83.6 ± 5.84		
	Lot II - (10) 90.1 ± 3.05	(6) 89.5 ± 2.06	(5) 99.3 ± 0.68
MKDT	(1) 89.0	(1) 89.0	----
MPI	(7) 95.6 ± 1.35	(21) 95.4 ± 3.21	(2) 99.7 ± 0.1
MEK-TEC	(12) 91.2 ± 3.39	(2) 95.7 ± 0.3	(2) 99.7 ± 0.1

( ) = number of preparations

Table IV. Per cent Uptake of ^{99m}Tc-Colloid in Rats, 20 minutes after I.V. Injection

TcO_4	Kit	mean of	Blood	Liver	Spleen	Lungs	Kidneys	Gut	Carcass	% Recovery	Liver-Lung Ratio
NEN	MPI	2	1.97* 0.16+	85.2	4.36	1.29	0.48	0.47	5.7	99.6	66.0
NEN	I-Lot NEN	6	1.79* 0.12+	79.4	1.81	0.79	0.61	0.24	5.5	90.1	101
NEN	II-Lot NEN	4	1.91* 0.26+	67.8	3.59	1.54	0.58	1.17	7.2	83.8	44
NEN	SQB	2	1.91* 0.13+	79.2	5.10	2.78	0.76	0.62	6.1	90.4	28.5
MEK-TEC	MPI	2	4.68* 0.277+	81.5	3.86	1.65	0.94	0.87	10.0	99.7	49.4
MEK-TEC	NEN	2	1.46* 0.093+	84.4	3.06	0.46	0.29	0.30	2.5	91.2	183
MEK-TEC	SQB	2	0.613* 0.045+	83.6	3.79	2.51	0.46	0.64	6.2	97.9	33.3
MPI	MPI	2	2.44* 0.160+	75.0	2.25	2.31	0.40	1.09	8.24	89.6	32.5
MPI	NEN	2	2.78* 0.181+	91.6	3.30	.741	0.32	3.26	3.44	103	124
MPI	SQB	2	0.960* 0.062+	85.3	2.71	2.66	0.45	2.25	14.9	108	32.1

* total blood -- assuming 6.38% total body weight is blood

+ blood/ml

Table V. Labeling Efficiency for ^{99m}Tc-HSA by Electrolytic Method Using $^{99m}TcO_4$ from Various Sources

Labeling Method	$^{99m}TcO_4$ Source	$^{99m}TcO_4$ Volume	Number of Preparations	% Binding[a]	Ave.Dev.	% free[b] $^{99m}TcO_4$	Ave.Dev.
Zr Crucible	MPI	5	7	28.6	± 11.0	14.0	± 3.5
" "	NEN	5	8	63.4	± 5.0	6.3	± 0.9
Zr Crucible	MPI	2.5	3	44.6	± 12.2	14.4	± 2.3
" "	MEK-TEC	2.5	5	80.7	± 11.4	12.1	± 5.7
Zr Wire	MPI	2.5	2	20.6	± 0.05	24.6	± 2.1
" "	MEK-TEC	2.5	7	83.4	± 12.0	10.1	± 7.1

[a]Per cent ^{99m}Tc recovered from resin column AG 1x8 pH 1.3

[b]Determined by paper chromatography after resin column AG 1x8 pH 1.3

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