Smith's Publication on Internal Dose Calculation for ^{99m}Tc: An Excellent Paper with Approximate Methods

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The internal dosimetry of β- and γ-emitters has been established by several authors. Smith [1] cites the work of Loevinger et al. [2] and Ellett et al. [3], pioneers in the field. Somehow, internal dosimetry manages to intimidate many, when, as shown by Smith, it is just energy per unit mass, as is external dosimetry. The difficulty arises from the calculation of the absorbed fraction of energy from a source region to itself or to a different target. For particulate radiation, the energy per emission and its abundance are sufficient, as we assume that all energy emitted in a source is absorbed there (a generally good assumption), but for photons, more work is needed. Smith, like Marinelli, Quimby, and others [4,5], used reasonable approximations. In 1965, we did not have the elaborate Monte Carlo methods that were developed later by Cristy

and Eckerman [6], among others. These approximations were wonderful at the time and were shown by more exact computer methods to be quite reasonable. All of the unit conversions were, of course, absolute. The "remainder of the body" method developed by Cloutier et al. [7] was not available, but notice the agreement between Smith's final answers and those of the latest methods, using highly sophisticated anthropomorphic phantoms and the best kinetic data (Table 1).

TABLE 1
^{99m}TcO$_4$ Injection (rad/mCi)

Site	Smith [1]	RADAR [8]
Male gonads	0.012	0.00925
Female gonads	0.015	0.028
Stomach	0.059	0.072
Upper large intestine	0.096	0.17
Thyroid	0.009	0.0925
Whole body	0.012	0.014

Internal Dose Calculation for ^{99m}Tc

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New York

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The method of producing technetium bound serum albumin is given by McAfee, Stern et al [5]. The method of producing the technetium-sulfur colloid is given by Richards [6].

CALCULATION OF $\bar{E}_\beta$, Γ AND Σγ FOR ^{99m}Tc

Figure 1 gives the decay scheme for ^{99m}Tc. Additional data needed to calculate the total local energy deposited per disintegration, $\bar{E}_\beta$, is found in the Nuclear Data Sheets [7]. The K/L/MN ratios for the relative occurrence of conversion electrons from the 0.140 MeV photon is 790/100/30, the ratio of K conversion electrons for the 0.140 MeV photon to the K conversion of the 0.142 MeV photon is 0.097 and the K/L$_{III}$ ratio for the relative occurrence of conversion electrons from the 0.142 MeV is 2.5. From these data and the internal conversion coefficient, α_t = 0.095, the number of conversion electrons resulting from internal conversion of the 0.140 MeV and 0.142 MeV photon can be calculated. Using the equation presented by Smith et al [8], which is an extension of the treatment by

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The major discrepancy is in the thyroid dose; Smith assumed some thyroid blocking. Smith was using a preliminary model that showed that the ''male gonadal dose is identical to the total body absorbed dose'' but that ''the female gonadal absorbed dose is the same as the male gonadal absorbed dose except that a backscatter factor is introduced in calculating the gamma component of the absorbed dose.'' He also did not consider the 0.5 factor for stomach wall dose to stomach contents dose (9). Nonetheless, this was an excellent paper using the available models and factors of the time.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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CALCULATION OF $\bar{E}_\beta$, Γ AND Σ_γ FOR ^{99m}TC

Figure 1 gives the decay scheme for ^{99m}Tc. Additional data needed to calculate the total local energy deposited per disintegration, $\bar{E}_\beta$, is found in the Nuclear Data Sheets (7). The K/L/MN ratios for the relative occurrence of conversion electrons from the 0.140 MeV photon is 790/100/30, the ratio of K conversion electrons for the 0.140 MeV photon to the K conversion of the 0.142 MeV photon is 0.097 and the K/L_{III} ratio for the relative occurrence of conversion electrons from the 0.142 MeV is 2.5. From these data and the internal conversion coefficient, $\alpha_t = 0.095$, the number of conversion electrons resulting from internal conversion of the 0.140 MeV and 0.142 MeV photon can be calculated. Using the equation presented by Smith *et al* (8), which is an extension of the treatment by Loevinger (1), the energy associated with internal conversion, E_e, which is to be included in $\bar{E}_\beta$ can be calculated.

$$E_e = fN_{e_K}\left\{E_\gamma - \omega_K E_K + \omega_K\left[\left(\frac{K_\alpha}{K_\alpha + K_\beta}\right)E_{L_{II\text{-}III}}\right.\right.$$
$$\left.\left. + \left(\frac{K_\beta}{K_\alpha + K_\beta}\right)E_{M_{II\text{-}III}}\right]\right\} +$$
$$+ fN_{e_L}\ldots E_\gamma \qquad \text{MeV/dis} \qquad \qquad 1.$$

where E_e = energy associated with internal conversion per disintegration (MeV/dis)

f = fraction of disintegrations that give rise to a photon of energy E_γ

N_{e_t} = total number of conversion electrons,

$N_{e_t} = N_{e_K} + N_{e_L\ldots}$

N_{e_K} = number of K conversion electrons arising from a photon of energy E_γ per disintegration

$N_{e_L\ldots}$ = number of L,M,N . . . conversion electrons arising from a photon of energy $E\gamma$ per disintegration

ω_K = K − fluorescent yield

$\frac{K_\alpha}{K_\alpha + K_\beta}$ = relative intensity of K_α x-rays emitted per disintegraticn due to K internal conversion

$\frac{K_\beta}{K_\alpha + K_\beta}$ = relative intensity of K_β x-rays emitted per disintegration due to K internal conversion

E_K = bonding energy of the K electron

$E_{L_{II\text{-}III}}$ = average binding energy of the L_{II} and L_{III} electrons

$E_{M_{II\text{-}III}}$ = average binding energy of the M_{II} and M_{III} electrons

The relative intensities of the K_α and K_β x-rays may be calculated from Table VIII-17 of Compton and Allison (9) by setting up simultaneous equations for the ratios of $K_{\alpha_1}/K_{\alpha_3}$, x-rays, K_{β_1}/K_{β_2} x-rays and $K_{\alpha_2}/K_{\alpha_1}$ x-rays and solving. For ^{99}Tc, $\frac{K_\alpha}{K_\alpha + K_\beta} = 0.815$ and $\frac{K_\beta}{K_\alpha + K_\beta} = 0.185$.

For $Z = 43$; $\omega_K = 0.76$ (10); $E_K = 0.0211$ MeV, $E_{L_{II\text{-}III}} = 0.0027$ MeV and $E_{M_{II\text{-}III}} = 0.0004$ MeV (11).

For the 0.140 MeV photon

$$N_{e_t} = \frac{\bar{\alpha}_t}{1 + \alpha_t} = \frac{0.095}{1 + 0.095} = 0.0868$$

then

$$N_{e_K} = \left(\frac{790}{790 + 100 + 30}\right)N_{e_t} = 0.0746$$

and

$$N_{e_L\ldots} = N_{e_t} - N_{e_K} = 0.0122$$

Substituting in equation 1

$$E_e = 0.0109 \text{ MeV/dis}$$

For the 0.142 MeV photon

$$N_{e_{K_{0.142}}} = 0.097 N_{e_{K_{0.140}}} = 0.00724$$

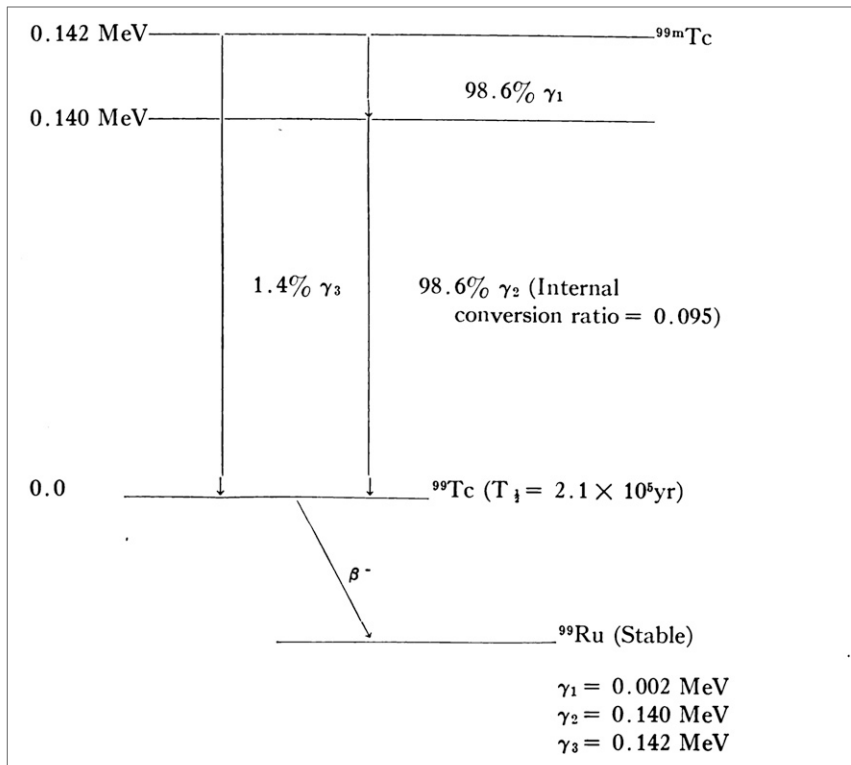$$N_{e_{L_{III}}} = N_{e_K}/2.5 = 0.02290$$

0.142 MeV————————————————— ⁹⁹ᵐTc

98.6% γ_1

0.140 MeV———————————————

1.4% γ_3 98.6% γ_2 (Internal
                       conversion ratio = 0.095)

0.0 —————————————   ⁹⁹Tc (T₁ = 2.1 × 10⁵yr)

β^-

⁹⁹Ru (Stable)

$\gamma_1 = 0.002$ MeV
$\gamma_2 = 0.140$ MeV
$\gamma_3 = 0.142$ MeV

FIGURE 1. Decay scheme of ⁹⁹ᵐTc.

Substituting into equation 1

$$E_e = 0.0013 \, \text{MeV/dis}$$

The 0.002 mev photon emitted 98.6 per cent of the time is included in $\overline{E}_\beta$, since the photon energy is less than 11.3 kev, and by definition included in beta particle component of the absorbed dose (1).

The $\overline{E}_\beta$ for ⁹⁹ᵐTc is

$$\overline{E}_\beta = 0.0109 + 0.0013 + 0.0020$$

$$\overline{E}_\beta = 0.014 \, \text{MeV/dis}$$

The specific gamma-ray constant, Γ, may be calculated from the equation (12):

$$\Gamma = 1.50 \times 10^5 \sum_i n_i \mu_{air_i} E_i$$

$$\text{R-cm}^2/\text{mc-hr}.$$

2.

Where n_i is the number of photons of energy E_i per disintegration with a linear absorption coefficient in air of μ_{air_i}. Table I presents

the calculated value of Γ for each of the component photons of ⁹⁹ᵐTc. The additional 0.16 R-cm²/mc-hr added to Γ due to the K_α and K_β x-rays presents a perplexing problem which will be considered shortly.

The integral gamma-ray dose-rate constant, E_γ, (2,3,12) represents complete energy absorption in an infinite water medium, and can be calculated by the following equation:

$$\sum_\gamma = 2.13 \sum_i n_i E_i \quad \frac{\text{rads-gm}}{\mu\text{C-hr}}$$

3.

Where n_i is the fraction of the disintegrations occurring with the emission of a gamma-ray having an energy E_i (MeV) and 2.13 is the conversion constant from MeV/disintegration to rads-gm/μc-hr. Table II presents the calculated value of $\sum_\gamma$ for each of the component photons of ⁹⁹ᵐTc.

From Table I, the K x-rays from ⁹⁹ᵐTc make up 29 per cent of Γ and from Table II, the K x-rays make up only 1.2 per cent of $\sum_\gamma$, the total photon energy emitted. The value of Γ is inflated because the linear air absorption coefficient increases rapidly in the very low photon energy region. The use of the larger value of Γ would result in increasing the average gamma-ray exposure-rate, $\overline{R}_\gamma$, by 29 per cent whereas the total energy associated with the K x-rays is only 1.2 per cent of the total photon energy emitted by ⁹⁹ᵐTc.

EVALUATION OF THE GAMMA-RAY ABSORBED DOSE-RATE

Loevinger et al (1) give the classical equations for calculating the average gamma-ray exposure-rate, $\overline{R}_\gamma(t)$.

$$\overline{R}_\gamma(t) = 10^{-3} C(t) \Gamma_\rho \, \overline{g} \, \text{R/hr}$$

4.

Where $C(t)$ is the concentration of the radionuclide in μc/gm at some moment of time in an organ whose density is ρ and has an average geometrical factor of $\overline{g}$. The average geometrical factor is a complex parameter and relates attenuation of the radiation field by tissue and diminution of the radiation field by the inverse square law. The magnitude of $\overline{g}$ depends on phantom shape, phantom mass and photon energy. The equation for $\overline{g}$ is given by

TABLE I
Evaluation of Γ for ⁹⁹ᵐTc

Photon Energy (E_i) (MeV)	n_i (Corrected for Conversion electrons)	$\mu_{air_t(11)}(cm^{-1})$	$\Gamma(R\text{-}cm^2/mc\text{-}hr$	% 0f Total Γ
0.140 + 0.142	0.904	2.94×10^{-5}	0.56	78
0.0183	0.067	8.0×10^{-4}	0.14	19
0.0206	0.014	5.6×10^{-4}	0.02	3
		TOTAL	0.72	100

Table II
Evaluation of Σ_γ for ^{99m}Tc

Photon Energy (E_i) (MeV)	n_i (Corrected for Conversion Electrons)	$\Sigma_\gamma \left(\frac{rads-gm}{\mu c-hr}\right)$	% of Total $\Sigma\gamma$
0.140 + 0.142	0.904	0.2697	98.83
0.0183	0.067	0.0026	0.95
0.0206	0.014	0.0006	0.22
	TOTAL	0.2729	100.00

$$\bar{g} = \frac{1}{V}\int_V g_P \, dV \quad cm \qquad 5.$$

and

$$g_P = \int_V \frac{e^{-\mu_e ff^r}}{r_2} \, dV \quad cm \qquad 6.$$

In the calculation of $\bar{g}$ (12), the value used for the effective tissue absorption coefficient, μ_{eff}, is 0.028 cm^{-1} which is assumed to be constant. The value used for μ_{eff} and the assumption that it is constant is a good approximation for the photon energies emitted by radium, over a limited range of distance upon which the values of $\bar{g}$ and g_P appearing in the literature are based. For radionuclides which emit low energy photons such as ^{197}Hg, ^{99m}Tc and ^{199}Au, as well as the x-rays emitted resulting from internal conversion and electron capture processes, μ_{eff} should not be assumed constant. This is true for low energy photons because the Compton effect becomes less important as a mechanism for energy deposition in tissue with decreasing photon energy, and the photoelectric effect becomes increasingly more important as the energy of the photon is degraded. The probability of a photoelectric effect occurring is highly dependent upon photon energy as is the Compton process below 0.1 MeV.

The other factors which are important in evaluating $\bar{g}$ are the shape of the phantom and mass of the phantom. These two factors will determine the average distance a photon traverses in a phantom, which is a measure of the number of interactions a photon will experience. Each interaction decreases the photon energy and changes the probability for the next interaction, i.e., μ_{eff}. As will be seen in Table III, the standard method may underestimate the absorbed dose resulting from low energy photons by as much as 30 per cent due to the assumption of a constant μ_{eff}.

Recently, Ellett, Callahan and Brownell (2, 3) have presented a technique for calculating the gamma-ray absorbed dose using Monte Carlo type calculations. In this technique, the actual energy absorbed in the phantom per photon interaction, and the probability of the next interaction is considered, thereby eliminating the difficulties encountered by the standard technique with low energy photons. The fraction of Σ_γ, Eq. 3, absorbed in phantoms of various geometrical shapes and of various masses for different photon energies is determined. The average absorbed dose rate may then be calculated by the equation

$$\bar{R}_\gamma(t) = C(t)\sum_i \Sigma_{\gamma_i}(A.F.)_{E_iM}$$

and evaluating $\Sigma_{\gamma i}$ from Eq. 3

$$R_\gamma(t) = 2.13 \, C(t)\sum_i n_i E_i (A.F.)_{E_iM} \quad rads \, hr \qquad 7.$$

The absorbed fraction, A.F., is that fraction of the emitted photon energy absorbed by a phantom of specified mass and geometry. The A.F. is dependent upon the geometrical shape of the phantom,

TABLE III
Comparison of the Values for $\bar{R}_\gamma$ for ^{99m}Tc as Calculated by the Standard Method and the Absorbed Fraction Method

Geometry	Mass kg	$\bar{g}$ (1) cm	$\bar{R}_\gamma = 10^{-3}C(\dagger)\rho\Gamma\,\bar{g}$ (mrad/hr)* $\Gamma = 0.56$	$\Gamma = 0.72$	Equation 7† (mrads/hr)	Ratio of eq. 4. to eq. 7. for $\Gamma = 0.56$
Sphere	0.3	39	21	27	25	0.84
Sphere	0.5	26	25	32	30	0.83
Sphere	1.0	58	31	40	37	0.84
Sphere	2.0	74	39	51	47	0.83
Std. Man‡	70.0	125	67	86	97	0.69
Liver§	1.7	46	25	32	38	0.66

* Phantoms are of equal height (185 cm) and an ellipsoid is used for Eq. 7.
** For Eq. 4 the liver is considered to be a cylinder 15 cm long with a radius of 6 cm, and for Eq. 7 a flat ellipsoid is used. The length of the ellipsoid is twice the thick diameter and 4 times the thin diameter.
†The exposure-rate is converted to the absorbed-dose-rate by multiplying the exposure- rate by 0.96 (NBS-85, Table IA1 and Eq. IA6.)
‡The A.F. are obtained from (3) for the 140 kev and the 20 kev photons.

the mass of the phantom, photon energy and distribution of the radionuclide in the phantom.

$$\text{A.F.} = \frac{\text{absorbed energy from a photon of energy, } E_i}{\text{emitted energy from a photon of energy, } E_i}$$

and $\sum_{\gamma i}$ is the parameter describing the total energy emitted. Tables of A. F. for various photon energies, geometrical shapes, phantom masses and radionuclide distributions are given by Ellett, *et al* (*2, 3*).

In Table III, $\overline{R}_\gamma$ has been calculated for ^{99m}Tc with a C(t) equal to 1 $\mu c/gm$ uniformly distributed in phantoms of various geometrical shapes and masses using equations 4 and 7. In all cases the standard method underestimates the absorbed dose by 16 to 34 per cent, depending upon phantom mass and geometrical shape.

In the author's opinion, the gamma-ray absorbed dose for ^{99m}Tc should be evaluated using the technique of Ellett, Callahan and Brownell rather than the standard method, and in fact, all gamma-ray absorbed dose calculations should be evaluated in this manner. Ellett's technique will be used in this paper. This technique eliminates the error introduced by assuming a constant μ_{eff} and also eliminates the perplexing problem of how to handle Γ when the value of it has been inflated by very low energy photons.

METHOD OF CALCULATING THE ABSORBED DOSE

The absorbed dose will be calculated for the complete disintegration of the radionuclide in question using the appropriate effective half-life. The radiopharmaceutical will be assumed to be administered intravenously into a 70 kg standard man as defined by the I.C.R.P. Report II (*13*). The model for the gastrointestinal tract as defined by the I.C.R.P. will be used except for a stomach emptying time of one-half hour rather than one hour. This model has been questioned with regard to the transit times (*14*) and effective radii (*15*) of the various segments of the gastrointestinal tract, but in consideration of the short physical half-life of ^{99m}Tc, the variability of the fecal data and the manner in which the absorbed dose calculations will be performed, the I.C.R.P. model is adequate. The nuclear properties of the radionuclides under consideration are given in Table IV.

The average absorbed dose resulting from beta type radiations will be treated by standard techniques (*1*). For dose calculation purposes, the sum of exponentials will be used to describe the concentration of the radiopharmaceutical as a function of time.

$$\overline{D}_{\beta(\infty)} = 73.8 \ \overline{E}_\beta \sum_j Co_j T_{eff_j} \qquad 8.$$

Where Co_j is the initial concentration of the radiopharmaceutical associated with the jth component of the uptake or disappearance curve for a given organ n $\mu c/gm$. The effective half-life of the jth component is T_{eff_j} in days. It should be remembered that, in many instances, the effective half-life used in dose calculations has no physiological significance. Also, Co_j should not be indiscriminately used to calculate pool size.

The average absorbed dose resulting from gamma type radiations will be treated, as discussed previously, by the techniques of Ellett *et al* (*2,3*).

$$\overline{D}_{\gamma(\infty)} = 73.8 \left[\sum_i n_i E_i (\text{A.F.})_{EiM} \right] \sum_j Co_j T_{effj} \quad \text{rads} \qquad 9.$$

Where $\sum_i n_i E_i (\text{A.F.})_{EiM}$ retains the definition of equation 7, but is evaluated for the organ under consideration. The term $\sum_i n_i E_i (\text{A.F.})_{EiM}$ can be evaluated for the case where the radiopharmaceutical is

TABLE IV
Nuclear Properties of Radionuclides Under Consideration

Radionuclide*	Physical Half-life (days)	$\overline{E}_\beta{}^\dagger (MeV/dis)$	$\Sigma_\gamma \left(\frac{rads/gm}{\mu c-hr} \right)^\ddagger$
Tc-99m	0.25	0.014	0.273
1-131	8.05	0.188§	0.828
Hg-203	47.0	0.009	0.502
Hg-197	2.71	0.080	0.151
Au-198	2.70	0.338	0.848
Au-199	3.15	0.158	0.200

•Decay schemes used in calculation of $\overline{E}_\beta$ and Σ_γ are from the Nuclear Data Sheets, National Research Council, National Academy of Science.
••Calculated using equations from reference 8 and $\overline{E}_\beta$ – calculated using equation from reference 13, and reference 16.
†Calculated for an infinite tissue-like medium, *i.e.,* A. F. = 1.
‡From Slack and Way, reference 10.

uniformly distributed in the organ or concentrated and treated as a central point source in the organ. The former gives the average gamma-ray absorbed dose and the latter the maximum.

The absorbed fraction, A.F., does not include photons scattered back from the surrounding medium (*2*), therefore the absorbed dose that might result from backscattered photons is not included. This component must be included in the absorbed dose calculation for organs centrally located in the body. For 40 kev photons this amounts to an increase in the absorbed dose of 14 per cent, for 80 kev photons 28 per cent, for 160 kev photons 17 per cent, for 364 kev photons 5 per cent and for 662 kev photons 4 per cent (*3*).

The total body absorbed dose calculations are based on excretion data, and the traditional assumption that the radiopharmaceutical is uniformly distributed in the TOTAL body mass. This calculation is usually made and required when a radiopharmaceutical is being evaluated from a dosimetry point of view, however, the significance of this calculation from a biological standpoint is questionable. A radiopharmaceutical is rarely, if ever, distributed uniformly throughout the TOTAL body mass, and therefore a low value for the total body absorbed dose is not indicative that one or more essential organs will not receive ten or one hundred or even more times the total body absorbed dose. In fact, this is usually the case. For example, the kidney absorbed dose for ^{203}Hg Neohydrin is approximately 85 times greater than the total body absorbed dose, Table VII.

The beta contribution to the gonadal absorbed dose is assumed to be equal to the total body beta absorbed dose unless the actual concentration of the radiopharmaceutical is known in the gonads. In calculating the gamma contribution to the absorbed dose to the female gonads the backscatter correction factor is used. The gamma contribution to the gonadal absorbed dose is based on a uniform distribution of the radiopharmaceutical unless an organ in the vicinity of the gonads concentrates the radiopharmaceutical. Then, the fraction of the activity concentrated in that organ is treated as a central point source in calculating this component of the gonadal absorbed dose. It is realized that this approach is an approximation, but it is probably as accurate as attempting to fix the coordinates of two organs that may vary their positions with respect to one another,

and then to calculate the absorbed dose that one organ receives from the other. The contribution to the female gonadal absorbed dose from urine activity in the bladder and fecal activity in the gastrointestinal tract is adequately handled by treating this activity as a central point source in consideration of the discussion on urinary irradiation of the ovaries by Comas, *et al* (*17*) and the discussion on fecal irradiation of the ovaries by MacIntyre, *et al* (*18*).

Calculations for the absorbed dose to specific organs are based on the concentration of the radionuclide in that organ, the geometrical shape and the mass of that organ. Also included in the absorbed dose is the contribution from photons associated with the activity distributed in the total body. The same criteria that applied to the gonadal absorbed dose calculations apply to other organs, namely consideration of backscatter and concentration of the radionuclide in nearby organs.

99mTC AS THE PERTECHNETATE ION

^{99m}Technetium as the pertechnetate ion, TcO_4^- , was first used by Harper *et al* (*19*) for thyroid and brain scintillation scanning. McAfee *et al* (*20*) have discussed in detail the technique of brain scanning using TcO_4^- and the distribution of TcO_4^- in man. In their paper, they considered the effect that preadministering perchlorate and/or iodide had on the distribution of TcO_4^- in man as well as the method of administering the radiopharmaceutical. Like iodide, TcO_4^- is concentrated by the thyroid, salivary glands and gastric mucosa (*21*). Pretreating with iodide will block the thyroid, while pretreating with perchlorate will block the thyroid and also decrease the concentration of TcO_4^- in the gastric mucosa (*21*). Fifteen to twenty-five percent of the intravenously administered ^{99m}Tc activity is recovered in the first three days in the feces, whereas little if any ^{131}I as the iodide ion is excreted in the feces. In this respect, TcO_4^- may differ from iodide in that it is not completely absorbed in the intestines; however, there is the possibility that a fraction of the ^{99m}Tc found in the feces may be the result of some metabolic process involving the liver. This inference is based on McAfee's data (*20*) indicating a longer disappearance time for ^{99m}Tc in the liver and the high ^{99m}Tc levels in the liver of mice.

Harper (*21*) has performed studies in man and various animal species to evaluate the factors which control the rate at which TcO_4^- equilibrates with various body spaces. The blood disappearance curve for an intravenously administered dose of TcO_4^- is made up of at least two resolvable components. Harper postulates that the fast component (biological half-time of approximately 10 minutes) is due to equilibrium with interstitial fluid, and the slow component (biological half-time of approximately 6 hours) is associated with intracellular penetration.

The data from human excretion studies carried out by McAfee and Harper are summarized in Table V. Excreta were collected for three days and a laxative was given at the beginning of the second or third day. Pretreating the volunteers with iodide had no effect on the rate that ^{99m}Tc was excreted. Pretreatment with perchlorate had no apparent effect on the excretory pattern of ^{99m}Tc when it was orally administered; however, there was a 10 percent reduction in fecal excretion when ^{99m}Tc was administered intravenously with perchlorate pretreatment. Approximately 90 percent of the fraction of ^{99m}Tc that is excreted in the urine is excreted in the first 24 hours, and approximately 90 percent or more of the fraction of ^{99m}Tc that is excreted in the feces is excreted in the second and third day.

External counting studies were performed by Atkins (*22*) and McAfee (*20*) on volunteers who had received TcO_4^- to evaluate the disappearance curve of ^{99m}Tc from various organs of the body. All of the organs evaluated, except the liver and stomach, followed the blood disappearance curve. The sustained ^{99m}Tc level in the stomach is due to the high concentration of ^{99m}Tc in the gastric mucosal cells, gastric secretions and swallowed saliva.

ASSUMPTIONS AND CONSIDERATIONS

The total body absorbed dose is based on the excretion data in Table V. Since the urinary excretion curve follows the blood disappearance curve (*22*), the activity eliminated in the urine was assigned a biological half-life of 0.25 days. Since ^{99m}Tc has a very short physical half-life, the remaining activity was assigned an effective half-life equal to the physical half-life. The activity in the body is assumed to be uniformly distributed unless otherwise noted.

The male gonadal absorbed dose is identical to the total body absorbed dose except that the beta component of the activity in the feces is not included in the absorbed dose calculation. The female gonadal absorbed dose is the same as the male gonadal absorbed dose except that a backscatter factor is introduced in calculating the gamma component of the absorbed dose. Also, the activity contained in the feces was treated as a central point source in calculating the gamma component of the absorbed dose to the female gonads from the activity contained in the feces. The backscatter factor increases the gamma component of the absorbed dose by approximately 20 percent, and the central point source assumption increases the gamma component of the absorbed dose from the activity in the feces by approximately 50 percent.

The author, while in the process of attempting to make an estimate of the absorbed dose to the female gonads and the various segments of the gastro-intestinal tract was impressed by the multiplicity of assumptions that had to be made. Procedures should be developed which will allow investigators to calculate an absorbed dose range in these cases.

In calculating the stomach (gastric mucosa) absorbed dose, it was assumed that 10 percent of the ^{99m}Tc was taken up by the stomach wall when the TcO_4^- was intravenously administered (*20*) and 7.5 percent of the ^{99m}Tc was taken up when orally administered. In animal studies, Harper *et al* (*21*) found that the stomach uptake for an intravenously administered dose of ^{99m}Tc as TcO_4^- may be as high as 25 percent. It was further assumed that pretreatment with perchlorate will reduce the stomach uptake by 50 percent. The maximum activity in the stomach occurred between two and three hours after the ^{99m}Tc was injected (*20*). Within 30 minutes after injection, the activity in the stomach was within 50 percent of the maximum level, therefore for purposes of absorbed dose calculations, instantaneous uptake was assumed. The stomach, itself, was assumed to weigh 150 gm. The activity concentrated in the stomach wall was assumed to have a biological half-life of 6 hours. The gamma component of the stomach absorbed dose from the activity in the stomach wall along with the activity in the feces was treated as a central point source with backscatter. The remaining activity in the body was assumed to be uniformly distributed, and the gamma component of the stomach absorbed dose from this activity was calculated using the backscatter factor and the appropriate effective half-life.

For the case when the TcO_4^- is orally administered a 30 minute residence time in the stomach was used, and the activity was

TABLE V
Fractional Distribution of TcO_1^- for Intravenous and Oral Administration With and Without Pretreatment With Perchlorate Ion

Route of Administration	Distribution of TcO_4^-	Treatment	
		None	Perchlorate
Intravenous	Urine	0.35 (6)*	0.45 (5)
	Feces	0.25	0.15
	Difference	0.40	0.40
Oral	Urine	0.20 (4)	0.25 (3)
	Feces	0.50	0.50
	Difference	0.30	0.25

*Number of subjects in study.

assumed to be uniformly distributed in the stomach contents which has a mass of 250 gm (13). The gastric mucosa is irradiated by the stomach contents under 50 percent geometry (2π). The effective radius of the stomach is 5 cm which will yield a sphere weighing 524 gm from which the absorbed fraction was calculated to determine the gamma component of the absorbed dose.

The calculation of the absorbed dose to the upper large intestines (intestinal mucosa) from the activity in the feces was based on the fecal excretion data, Table V, and the model for the gastrointestinal tract as given by the I.C.R.P. Report II (13). The absorbed dose to the intestinal mucosa from the activity in the feces was calculated in the same way as the absorbed dose to the gastric mucosa was calculated for the ^{99m}Tc residing in the stomach for 30 minutes. The gamma component of the absorbed dose to the intestinal mucosa was calculated in the same manner as was the gamma component for the stomach absorbed dose except the backscatter factor was not used.

The absorbed dose to the thyroid was calculated for a 20 gm gland. Based on Atkin's and Schiffer's data (22), a 3 percent uptake was assumed when TcO_4^- was intravenously administered, 2.3 percent uptake when orally administered and no uptake when the patient was pretreated with perchlorate. The biological disappearance half-time from the thyroid was taken as 12 hours (22), and instantaneous uptake by the gland was assumed. The gamma component of the absorbed dose to the thyroid from the activity uniformly distributed in the body was calculated as previously discussed.

DISCUSSION

In Table VI, the absorbed dose to various organs from 10 mc of ^{99m}Tc as TcO_4^- is compared for both oral and intravenous administration, with and without pretreatment with perchlorate. In Table VII, the absorbed dose received from ^{99m}Tc is compared to other brain scanning agents such as ^{131}I labeled serum albumin (23,24), ^{197}Hg and ^{203}Hg labeled Neohydrin (25,26). The gamma component of the absorbed dose for these radiopharmaceuticals was calculated as previously described. The term "critical organ" implies that organ which receives the highest absorbed dose, and does not consider the radiosensitivity or essentialness of the organ. From an absorbed dose standpoint, ^{99m}Tc is definitely superior to the other agents evaluated. At present 10 mc of ^{99m}Tc are administered for a brain scan, this activity may be reduced by as much as a

factor of two as soon as more sensitive collimators are used which take advantage of the nuclear properties of ^{99m}Tc. Harris *et al* (27), recently described such a collimator.

The absorbed dose to the blood from ^{131}I labeled serum albumin was calculated using the levels of activity in plasma and a volume of distribution equivalent to the blood volume for calculating the beta component of the absorbed dose. It is realized that using the blood volume as the volume of distribution may lead to overestimating the beta component of the absorbed dose by as much as a factor of two, since in many regions of the vascular system the particulate radiations will not be completely absorbed in the blood, but will be absorbed in adjacent soft tissue. Use of the above criterion is better than possibly underestimating the beta component of the absorbed dose to blood by a factor of thirteen, *i.e.* using the total body as the volume of distribution. This is especially true if one uses the blood absorbed dose to reflect the absorbed dose to the hemapoietic system. Ideally one would like to divide the vascular system into two or three sub-systems, assign an effective diameter to each and then calculate an effective blood volume for various electron energies.

Absorbed dose estimates should be made at the suborgan level when it is known that a radiopharmaceutical concentrates in an anatomically separate portion of an organ, and the anatomical separation is greater than the range of particles taken into account by $\overline{E}_\beta$. A well-known example of this is the increase in concentration of Neohydrin in the cortex of the kidney as compared to the medulla (28,29). The increased concentration of Neohydrin in the cortex of the kidney could double the absorbed dose estimate given in Table VII. The range in the kidney absorbed dose estimate given in Table VII is due to the lack of adequate kinetic data for this radiopharmaceutical.

^{99m}Tc LABELED SERUM ALBUMIN

McAfee *et al* (5) has used ^{99m}Tc labeled serum albumin for scintillation scanning of the placenta and other vascular structures. For placental scans, 1 mc of ^{99m}Tc labeled serum albumin is used in comparison to 5 μc of ^{131}I labeled serum albumin (30,31,32), for placental localization studies. Placenta scans give the clinician detailed information on the exact location of the placenta, whereas with placental localization studies the clinician must evaluate the location of the placenta from measurements made at ten to twenty arbitrary locations on the abdomen of the mother.

Studies carried out by McAfee *et al* (5), in pregnant rabbits near term indicated that the tissue distribution of ^{99m}Tc labeled serum albumin was similar to ^{131}I serum labeled albumin. In three normal volunteers, less than 0.5 percent of the injected radioactivity was recovered in either the urine or feces within the first 24 hours after injection. In these volunteers, the initial biological half-time in the bloodstream is about six hours and a similar initial biological half-time was found in pregnant women who were administered ^{99m}Tc labeled serum albumin for placental scans. There is no concentration of ^{99m}Tc when administered as labeled serum albumin in the thyroid, salivary glands or gastric mucosa, when the patient is given 200 mgms of potassium perchlorate one to two hours prior to injection of the radiopharmaceutical.

The bodies of two infants (delivered approximately one and four hours following the injection of 1 mc of ^{99m}Tc albumin to the mother) contained 0.4 percent of the administered dose as determined by external counting and comparison with a phantom. The ^{99m}Tc

TABLE VI
Absorbed Dose to Various Organs from 10 mc of $^{99m}TcO_4^-$ for Oral and Intravenous Administration With and Without Pretreatment With ClO_4^-

| | Type of Administration and Pretreatment | | |
| | Intravenous None | Intravenous ClO_4^- | Oral None |
Organs	Absorbed Dose Estimate (rads)		
Total Body	0.13	0.12	0.14
Male Gonads	0.12	0.12	0.12
Female Gonads	0.16	0.15	0.18
Stomach (Gastric Mucosa)	1.0	0.59	1.4
Upper Large Intestines (Intestinal Mucosa)	1.5	0.96	2.9
Thyroid	2.7	0.09	2.1

concentration of cord blood was two percent of the maternal blood concentration (5), which is very similar to the values reported for ^{131}I labeled serum albumin, (30,33). The ratio of ^{131}I activity in cord blood to maternal blood is relatively constant for at least 78 hours after the injection of the radiopharmaceutical (33).

ASSUMPTIONS AND CONSIDERATIONS

The absorbed dose to the maternal blood and total body was calculated based on a 65 kg mother with a blood volume of 60 ml/kg of body weight. It was assumed that the blood disappearance curve followed a six hour biological half-life. The total body absorbed dose was calculated using the physical decay of ^{99m}Tc, since there was no significantly detectable amount of ^{99m}Tc activity in the urine or feces during the first twenty-four hours after administering the ^{99m}Tc. The gamma component of the absorbed dose was based on a uniform distribution of ^{99m}Tc.

The beta component of the absorbed dose to the fetal blood was calculated based on the assumption that the ^{99m}Tc concentration in fetal blood was 2 percent of the concentration in maternal blood.

In consideration of the location of the fetus in the mother and the surrounding tissues, the gamma component of the absorbed dose to the fetal blood was assumed equal to the gamma component of the maternal total body absorbed dose. The ^{99m}Tc activity in the placenta and uterine wall were not given special consideration in the calculation of the gamma component of the absorbed dose. It was assumed that the mother was pretreated with potassium perchlorate so that there would be no significant uptake of the ^{99m}Tc by the fetal or maternal thyroids.

DISCUSSIONS

The absorbed dose from 1 mc of ^{99m}Tc as the labeled serum albumin is compared, Table VIII, to the absorbed dose received from 5 μc of ^{131}I labeled serum albumin. The absorbed dose calculations for the ^{131}I labeled serum albumin are based on the kinetic data of Weinberg et al (30). The fetal blood absorbed dose is approximately three times greater from ^{99m}Tc than from ^{131}I; however, when more efficient collimators for the 140 kev photon of ^{99m}Tc are employed, the ^{99m}Tc activity may be reduced by a

TABLE VII
Comparison of the Absorbed Dose from Various Radiopharmaceuticals Used for Brain Scanning

| | | | Absorbed Dose to "Critical Organ" | |
Radio-pharm	Activity admin	Total Body Absorbed Dose Estimate (rads)	Organ	Absorbed Dose Estimate (rads)
$Tc^{99m}O_4^-$*	10 mc	0.12	U.L.I.[†]	0.96
I^{151} Albumin[‡]	375 μc	0.72	Blood	2.5
Hg^{203} Neohydrin[§]	750 μc	0.46	Kidney	38–115
Hg^{197} Neohydrin[§]	750 μc	0.09	Kidney	4.0

•Intravenous injection with potassium perchlorate pretreatment.
••Absorbed dose to intestinal mucosa of upper large intestines.
[†]Pretreatment with Lugol's solution, and the absorbed dose calculated on basis of kinetic data from reference 23 and 24.
[‡]Absorbed dose calculated on basis of kinetic data from reference 25 and 26.

TABLE VIII

Comparison of the Absorbed Dose from [99mTc] Labelled Serum Albumin for Placental Scanning and [131I] Labeled Serum Albumin for Placental Localization

Radiopharm. and Activity Admin	Organ	Absorbed Dose Estimate (mrads)		
		From β Type Radiation	From γ Type Radiation	Total
Tc-99m Albumin*	Maternal Total Body	4.0	0.8	5
1 mc	Maternal Blood	34	13	47
	Fetal Blood†	0.7	13	14
1-131 Albumin‡	Maternal Total Body	5.0	0.2	5
5 μc	Maternal Blood	83	3.6	87
	Fetal Blood†	1.3	3.6	5

*Mother pretreated with potassium perchlorate.
†Calculation based on fetus remaining in utero indefinitely.
‡Mother pretreated with Lugol's solution.

factor of as much as two. The fetus received a substantially smaller absorbed dose from either of these procedures when compared to radiographic procedures used for placental localization. Clayton *et al* (*34*), estimates from a single AP abdominal radiograph that the fetal gonads receive 0.32 R, and the exposure to the center of the fetus is 0.21 R.

Hibbard *et al* (*33*), estimates that if, for some reason, the fetal thyroid is not blocked before [131I] labeled serum albumin is administered to the mother, the absorbed dose to the fetal thyroid from 5 μc of the radiopharmaceutical may be as high as 2 rads. This hazard does not exist when [99mTc] is used because [99mTc] has a short physical half-life and the thyroid has a lower uptake for TcO_4^- than for I^-. Using Hibbards approximations and modifying them for [99mTc], the estimated absorbed dose to an unblocked fetal thyroid from 1 mc of [99mTc] labeled serum albumin would be approximately 50 mrads.

The fetal blood dose will be 4 mrads if the fetus is delivered two hours after the [99mTc] labeled serum albumin is administered to the mother, 9 mrads for eight hours in utero and 13 mrads for one day in utero.

[99mTc] SULFUR COLLOID

The [99mTc] sulfur colloid has been used by Harper *et al* (*35*), and Atkins *et al* (*36*), to obtain liver and bone marrow scans. There are many radiopharmaceuticals which permit scintillation scanning of the liver, such as colloidal [198Au], colloidal [199Au], [131I] aggregated serum albumin (*37*), and Rose Bengal. The first three of these agents are concentrated by the reticuloendothelial cells of the liver, spleen and red bone marrow, as is the [99mTc] sulfur colloid. Edwards *et al* (*38*), performed a series of 32 bone marrow scans using both isotopes of colloidal gold as well as heat-treated human serum albumin tagged with [131I]. The disadvantages of the latter radiopharmaceutical are that the metabolized [131I] produces a high background for the bone marrow scan and the [131I] that accumulates in the bladder obscures some of the marrow areas. Only the isotopes of colloidal gold yielded satisfactory scans. However, Edwards concluded that the possibility of harmful effects from the radiation absorbed dose from the radioactive colloidal gold years after administration, limits the method to selected patients. The absorbed dose from [99mTc] is not a limiting factor in bone marrow scanning using the [99mTc] sulfur colloid.

The distribution of the [99m·Tc] sulfur colloid in man when administered intravenously appears to be very similar to the distribution of colloidal gold. Root *et al* (*39*), studied the distribution of colloidal [198Au] in six terminal cancer patients and roughly estimated that normal liver tissue contains between 60 to 94 per cent of the administered dose, and the spleen and red bone marrow contains approximately 5 to 16 per cent each.

Urinary excretion and blood disappearance studies were performed by Atkins *et al* (*36*), in six patients who had received the [99mTc] sulfur colloid. These studies indicated that the blood disappearance half-time averaged 2.5 min with a range of 1.5 min to 4.4 min while the 24 hr urinary excretion averaged 3.0 per cent with a range of 2.4 per cent to 3.7 per cent of the administered dose. The results of these studies are very similar to those of Harper's *et al* (*35*), performed in mice and dogs. Studies in rabbits, mice and dogs indicate that the body distribution of the colloid is similar to colloidal gold. The particle size of the [99mTc] sulfur colloid in these studies were 500 millimicrons or less. The distribution of the colloid in man may be somewhat dependent on particle size, and therefore would effect the absorbed dose calculations. There is less than 3 μg of sulfur per ml of the sulfur colloid (*6*), and the [99mTc] activity per μg of sulfur colloid is in the mc/μg of colloid range. Therefore, a minuscule mass of the sulfur colloid is administered to the patient.

ASSUMPTIONS AND CONSIDERATIONS

The absorbed dose to the liver, spleen and red bone marrow was calculated for a distribution of 90 per cent of the colloid in the liver, 5 per cent each in the spleen and red bone marrow with an alternative distribution of 70 per cent in the liver and 15 per cent in the spleen and red bone marrow (*39*). The colloid was assumed to be instantaneously taken up by these organs, and the effective half-life for the elimination of the colloid from these organs was taken to be equal to the physical half-life. The liver was assumed to be a 1700 gm flat ellipsoid, the spleen a 150 gm flat ellipsoid, and the red bone marrow mass was assumed to be 1500 gm and distributed throughout the body (A.F. calculated for a 70 kg

TABLE IX
Comparison of the Absorbed Dose from Various Radiopharmaceuticals Used for Liver Scanning

Radio-pharm	Activity admin	Absorbed Dose Estimate (rads)					
		Total Body	Male Gonads	Female Gonads	Liver	Spleen	Red Bone Marrow
99mTcS Colloid	3 mc	0.05	0.04	0.07	0.99–0.72	0.48–1.3	007–0.10
198Au Colloid	150 μc	0.35	0.06	0.09	3.9–6.4	3.7–11.0	0.4–1.1
131I Agg.Alb.	150 μc	0.02	–	–	0.09	–	–

Absorbed dose for 198Au calculated on basis of kinetic data from reference 39.
Absorbed dose for 131I aggregated albumin calculated on basis of kinetic data from reference 37.

ellipsoid). The length of a flat ellipsoid is four times the thin diameter, and the thick diameter is twice the thin diameter. The method of calculating the absorbed dose to these organs has already been discussed.

Only physical decay was considered in calculating the total body, male and female gonadal absorbed dose. The method of calculating these values using the backscatter factor and the central point source consideration where appropriate has already been discussed.

DISCUSSION

The absorbed dose of ^{099m}Tc as the ^{99m}Tc sulfur colloid is compared to the absorbed dose received from colloidal ^{198}Au and ^{131}I aggregated albumin for liver scanning, Table IX, and is compared to the absorbed dose received from colloidal ^{198}Au and colloidal ^{199}Au for bone marrow scanning, Table X. The absorbed dose for these radiopharmaceuticals was calculated as previously described. The approximate absorbed dose estimates to the liver and total body for ^{131}I aggregated albumin were based on the kinetic data of Taplin *et al* (*37*).

The two alternative distributions of the radioactive colloids produce significant changes in the absorbed dose received by the spleen and red bone marrow. The distribution in which only 70 per cent of the colloid was in the liver, and the remaining colloid equally distributed between the spleen and red bone marrow results in a colloid concentration which is higher in the spleen than in the liver. This could be indicative of a diseased liver. Since nuclear medical procedures are performed to determine whether an organ or an organ system is pathological or normal, due consideration should be given to the absorbed

dose for the pathological state. As can be seen from Tables IX and X the absorbed dose to an organ normally not considered to receive a large absorbed dose may in fact be the organ receiving the highest absorbed dose when a possible pathological state exists in the patient. An illustrative example would be an uremic patient who is to have a renal scan with ^{203}Hg Neohydrin. The hepatic uptake of the radiopharmaceutical in this case is greatly increased (40), resulting in an unexpectedly high absorbed dose to the liver, as compared to the absorbed dose calculated based on the kinetics of Neohydrin for normal individuals.

SUMMARY

The total local energy deposited per distintegration, $\overline{E}_\beta$ for ^{99m}Tc is 14 kev per disintegration. The specific gamma-ray constant, Γ, for ^{99m}Tc is 0.72 R-cm^2/mc-hr; however, 29 per cent of this value is due to K_α and k_β x-rays which make up only 1.2 per cent of the total photon energy emitted by ^{99m}Tc. Standard methods of calculating the gamma component of the absorbed dose for ^{99m}Tc using the geometrical factor and Γ yield results which underestimate the absorbed dose by 16 to 30 per cent compared to calculations based on Monte Carlo techniques which take into account the energy dependence of μ_{air} and the inflated value of Γ. The Monte Carlo technique was used in making the absorbed dose estimates in this paper.

Absorbed dose estimates were made for ^{99m}Tc as (a) TcO_4^- for brain scanning, as compared to ^{131}I labeled serum albumin and ^{203}Hg and ^{97}Hg labeled Neohydrin; (b) ^{99m}Tc labeled serum albumin for placental scanning, as compared to ^{131}I labeled serum albumin; and (c) the ^{99m}Tc sulfur colloid for liver and bone marrow

TABLE X
Comparison of the Absorbed Dose from Various Radiopharmaceuticals Used for Bone Marrow Scanning

Radio-pharm	Activity admin	Absorbed Dose Estimate (rads)					
		Total Body	Male Gonads	Female Gonads	Liver	Spleen	Red Bone Marrow
99mTcS Colloid	5.0 mc	0.08	0.06	0.11	6.2-1.1	0.8-2.2	0.13-0.17
198Au Colloid	2.5 mc	5.8	0.98	1.5	51-108	62-183	7.0-18
Au199 Colloid	2.5 mc	1.7	0.28	0.49	31-54	32-96	3.5-9.4

Absorbed dose for 198Au and 199Au calculated on basis of kinetic data from reference 39.

scanning as compared to colloidal ^{198}Au, colloidal ^{199}Au and ^{131}I aggregated albumin. Some of the biological problems encountered in calculating the absorbed dose are discussed.

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