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Comparison of Isotopes for Scanning

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Although many new isotopes are now being introduced for scanning (1-6), there is no general agreement about their relative merits, and a number of different criteria have been used for evaluation (7, 8). Large tumours may be detected with any isotope, and it will be assumed in this paper that the "best" isotope is the one which will enable the smallest tumour to be detected with statistical significance when a given time is allowed for the scan, and for a given rad dose to the critical organ or whole body (9). Isotopes may then be compared quantitatively. Brain tumor localization particularly will be considered.

Various figures of merit have been used (9-12), and the use of information theory is also being investigated, but so far results do not entirely agree (8-12) and the method has not been applied with realistic levels of radioactivity. Figures of merit have been criticized (8), but the one used here can be verified experimentally (9), and appears to be a useful concept if its meaning is clearly understood.

The calculations in this paper will also indicate that the use of collimators with very large numbers of holes and hence very fine resolution is sometimes a disadvantage.

Figure of merit for tumour detection: Matthews (9) has used Dewey and Sincair's equation (10) to calculate the ratio n of the (increase in count rate over the tumour) to the (standard error of the difference in count rate over tumour and normal tissue) as a test of whether a tumour can be detected with statistical significance in a given situation. This may be compared with a "Student's t" test, and if n is greater than 3 the increase in count rate will be statistically significant.

The various factors involved are as follows: Most of these can be calculated for a new isotope, so that it can be evaluated in advance. For isotopes distributed in extracellular fluid, the tumour and nontumour concentration may be calculated, or these values may be obtained approximately from animal experiments (13,14).

1. Properties of the counting system:

(a) Collimator properties—to give the best compromise between resolution and sensitivity for a given isotope.

(b) Window width of pulse analyzer

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(c) Crystal efficiency for radiation concerned

(d) Factors affecting time in which counts accumulate—scan speed, time allowed for scan, resolution diameter (8,9)

2. Isotope properties.

(a) Physical properties—energy of radiations emitted and emission per disintegration, absorption coefficients in tissue and in collimator material.

(b) Biological properties—uptake of the isotope in the organ in question, ratio of target to non-target uptake, and number of mc which can be given to the patient to produce a given rad dose to the critical organ and/or whole body.

3. Organ properties—size and depth of organ and of lesion to be scanned.

Some of these factors are interrelated and difficult to separate.

The following equation can be derived from Dewey and Sinclair's equation (10), by expressing it in terms of the factors:

$$n = 126\sqrt{t\,r.}\qquad A.B.\sqrt{\frac{V_T^{\,2}}{V_{NT}}} \quad \text{----------} \quad (1)$$

where t = time in which counts accumulate

r = (tumour extracellular space as ml/gm of tumour)
÷ (whole body extracellular space as ml/gm of body weight)
A body weight of 70 kg is assumed.

V_T = target (tumour) volume

V_{NT} = non-target volume

$$A = \sqrt{\frac{gDp\,(f-1)^2}{f}}$$

where g = number of photons emitted per disintegration

D = radioactivity given in mc

p = ratio of (concentration of isotope in tumour)
to (concentration of isotope when uniformly distributed in e.c.f.)
For many isotopes p = 1 if scanning is carried out before much of the isotope has been excreted.

f = (concentration of isotope in target volume) ÷
(concentration of isotope in non-target volume).

$$B = \sqrt{\frac{\eta\epsilon_T^{\,2}\,\alpha_T^{\,2}}{\epsilon_{NT}\,\alpha_{NT}}},\ \text{or for coincidence counting}\ B = \sqrt{\frac{\eta^2\,\epsilon_T^{\,2}\,\alpha_T^{\,2}}{\epsilon_{NT}\,\alpha_{NT}}}$$

where η = crystal efficiency = probability of a pulse being produced per photon striking crystal for a given window width. (The effect of variation of crystal efficiency with distance of the source is neglected for distances as large as those of the target and non-target volumes)

ϵ = collimator efficiency = ratio of number of photons striking crystal to number of photons emitted from surface of body.

α = tissue attenuation factor due to absorption and scattering = number of photons emitted from surface of body ÷ number of photons emitted in the volume considered.

Subscript T refers to target volume and NT to non-target volume.

N.B. For large values of f, the above expression for n should be multiplied by $\frac{2}{2 + Sf}$, where

$$S = \frac{\epsilon_T}{\epsilon_{NT}} \cdot \frac{\alpha_T}{\alpha_{NT}} \cdot \frac{V_T}{V_{NT}}$$

The quantity $\frac{\epsilon_T^2}{\epsilon_{NT}}$ may be used as a "collimator figure of merit." This seems more convenient than Dewey and Sinclair's collimator figure of merit (9, 10), which depends on a number of factors which are not all determined by collimator design. Using the same notation, Dewey and Sinclair's figure of merit is equal to:

$$g\ \eta_T \frac{\epsilon^2_T}{\epsilon_{NT}} \cdot \frac{\alpha^2_T}{\alpha_{NT}} \cdot \frac{V_T^2}{V_{NT}} \times 2.22 \times 10^6$$

As Kuhl (15) points out, comparison between isotopes should always be made using the optimum collimator for each isotope. The design of the optimum collimator for a given γ energy has been worked out theoretically by Beck (11, 12). In practice it may be difficult to separate collimator efficiency from the absorption and scattering factor, so that it may be necessary to take $\frac{\epsilon^2_T\ \alpha^2_T}{\epsilon_{NT}\ \alpha_{NT}}$ as the figure of merit. This quantity is easily obtained for given target and non-target volumes from an experimental measurement in a phantom of target and non-target overall efficiencies, when crystal efficiency and gamma emission are known.

For comparison of different isotopes, the tumour factor r, the time factor t and the volumes V_T and V_{NT} can be considered constant. Thus, AB may be regarded as a "figure of merit" for isotopes. A depends on the physical and biological properties of the isotope, and B depends on the physical properties of the isotope and the properties of the counting system.

$$B^2 = \frac{\textit{pulses counted from target per unit time}}{\textit{photons emitted from target per unit time}} \times \frac{\textit{count rate for } \times \mu c \textit{ in target volume}}{\textit{count rate for } \times \mu c \textit{ in nontarget volume}} \quad . \ . \ . \quad (7)$$

and is easily obtained experimentally with a phantom. A depends on g, D, p and f. D can usually be calculated if the distribution and excretion of the isotope is known. p and f can probably be obtained from animal experiments when values in patients are not available (13, 14), and for many isotopes p will be equal to one g is usually known.

Brain tumour localization: Considering now brain tumour localization in particular, only two classes of isotopes are likely to give the best results, (a) isotopes emitting only low energy γ rays, and (b) positron emitters. Since brain tumour localization depends on the exclusion of radioactivity from the brain, rather than on selective concentration of isotope by the tumour, the amount of radioactivity in the rest of the body will always be much greater than the

amount in the head. It is therefore very important to reduce as far as possible the effect of the radioactivity in the rest of the body, otherwise the effective background will be greatly increased and the effective target/non-target ratio reduced. This can be achieved with lead shielding for low energy γ rays and with coincidence counting for positron emitters.

To reduce the radiation dose, it is preferable that the half life should be as short as possible; the limitations here are the time required for the scan and the inconvenience of a very short half life, unless the isotope can be milked off a "cow", or produced continuously. One of the main advantages of the positron and γ cameras is the shorter time required for the picture compared with conventional scanning, and this should open up a new range of isotopes. Since each element of the picture is observed continuously with a camera, it will not matter if there is appreciable decay of the isotope during the counting period. If the counting period is about five times longer than the half life, practically all disintegrations contribute to the effect produced and the efficiency for a given rad dose is as high as possible. Efficiencies approaching the optimum might be achieved by using, for example, cyclotron-produced ^{11}C (half-life 20 minutes) or even ^{15}O (half-life 2 minutes). These isotopes would have to be used in chemical forms which equilibrate with the extracellular space, for example, ^{15}O might be used as sulphate.

Positron emitters: For different positron emitters, B will be constant, and so these isotopes may be compared by considering A only. Values of A for different positron emitters are given in Table I, and it can be seen that a considerable gain may be expected compared with ^{72}As or ^{74}As, the positron emitters which have been most used (16, 17). With these high levels of radioactivity, it would be essential to use a fast coincidence unit to reduce random coincidences.

Low energy γ emitters: Similarly, low energy γ emitters with the same γ energy may be compared on the basis of factor A only, and this comparison is shown in Table II. In this case B cannot be considered exactly constant, since the γ energies for the isotopes in the table are not all exactly the same; however, the variation of B is likely to be much less than that of A. The factors affecting B are discussed below. If B does not vary rapidly with energy, again a considerable gain can be expected when ^{123}I HSA or ^{99m}Tc are used compared with ^{131}I HSA or ^{203}Hg neohydrin. For ^{99m}Tc the amount of radioactivity which will give 14 rads to the critical organ (the stomach) is 44 mc, and the value of A was calculated using this figure. However, a value for A is also given for 10 mc, since it may be difficult to obtain as much as 44 mc of ^{99m}Tc per patient. Also the calculation of dose in rads depends on the conversion coefficient; the entire β dose is due to conversion electrons. Only one measurement of the conversion coefficient is listed (18), with a possible error of $\pm$ 20 per cent. Until more data on this factor is obtained, it does not seem advisable to give such a large dose as 44 mc.

Comparison between low energy γ emitters and positrons: In order to relate the values for A at least approximately to the ratio n for a given V_T and V_{NT}, and hence to the minimum size of tumour which can be detected, and also to obtain an approximate comparison between positron and low energy γ emitters,

the factors which affect B will now be considered. This quantity can be calculated from experimental measurements of Dewey and Sinclair's figure of merit (10), which have already been published for several different isotopes for a particular counting system (9). The results of this calculation are given in Table III, for spherical target volumes (glass bulbs) at the geometrical focus of the collimator in a tank containing 5 liters of water as the non-target volume (9). The collimator had seven holes and was made of heavy alloy (density 16.8 gm/cc). It was 4 inches long and the focus was 4 inches from the end. As mentioned in the original publication, the values for ^{125}I are inaccurate, since owing to the high photoelectric absorption in water the count rate changed very rapidly with the position of the spherical glass bulb representing the tumour. However, the ^{125}I results have been included to give some idea of the effect of reducing the γ energy below that of ^{203}Hg γ rays. The ^{125}I values are considerably

TABLE I

POSITRON EMITTERS

	$t_{\frac{1}{2}}$ hrs	g	f	$\frac{(f-1)^2}{f}$	p	D	$A=\sqrt{gDp\frac{(f-1)^2}{f}}$
$KB^{18}F_4$	1.83	1.94	[1]11	9.1	1	[6]10.0	13.3
^{68}Ga	1.10	1.72	[2]10	8.1	1	[6]10.2	11.9
^{11}Co	0.33	2.00	~[3]10	8.1	[3]1	[6,8]8.2–54	11.6–29.6
$C^{15}o$	0.033	2.00	~[3]10	8.1	[3]1	[6,8]32.7–94	23.0–39.1
^{90}Nb	14.6	0.50 (.511 mev)	[4]30	28	[4]4	[6]0.44	5.0
^{72}As	26	1.55 (.511 mev)	[5]15	13.1	1	[7]1.5	5.5
^{74}As	17.5 days	0.56 (.511 mev)	[5]15	13.1	1	[7]2.5	4.3

g = photons emitted per disintegration.
f = tumour/brain concentration ratio.
p = tumour concentration ÷ tumour concentration for a substance uniformly distributed in extracellular fluid.
D = radioactivity given in mc (see notes)

Notes

1. See references (4) and (23).
2. See reference (3), approximate mean value taken.
3. Assuming that these isotopes can be used in a form which equilibrates rapidly with tumour extracellular space.
4. See references (14) and (24).
5. See reference (16), approximate mean value for different tumours taken.
6. To give 0.57 rads to whole body, *i.e.* equivalent to 300 μc of ^{131}I HSA.
7. To give 14 rads to kidney, *i.e.* equivalent to 2.5 mc of ^{74}As.
8. Lower limit taking volume of distribution equal to blood volume for positron dose. Upper limit taking whole body volume (25).

TABLE II

LOW ENERGY γ EMITTERS

	$t_{\frac{1}{2}}$ hrs	g	f	$\frac{(f-1)^2}{f}$	p	D mc	$A=\sqrt{gDp\frac{(f-1)^2}{f}}$
^{123}I HSA	13	0.84	[2]15	13.1	1	[6]12	[10]7.5
^{99m}Tc	6 (parent 67)	0.99	[4]2–11	1–9.1	1	[7]10–44	3.15–9.50 for 10 mC 6.60–19.9 for 44 mC
^{197}Hg neohydrin[1]	65	0.98	[2,3]11	9.1	[5]1	[8,9]2.16	4.40
^{203}Hg neohydrin[1]	47 days	0.81	[2,3]11	9.1	[5]1	[9]0.36	1.63
^{131}I HSA	8 days	1.00	[2]15	13.1	1	[6]0.30	1.98

g = photons emitted per disintegration.
f = tumour/brain concentration ratio.
p = tumour concentration ÷ tumour concentration for a substance uniformly distributed in extracellular fluid.
D = radioactivity in mc (see notes).

Notes

1. With blocking dose of inactive mercurhydrin.
2. See reference (14).
3. See reference (26).
4. See references (27) and (28).
5. Although ^{203}Hg neohydrin does penetrate into cells, the tumour concentration was approximately the same as for extracellular substances (14).
6. To give 0.57 rads to whole body, *i.e.* equivalent to 300 μc of ^{131}I HSA. The thyroid is assumed to be effectively blocked.
7. To give 14 rads to stomach (29), *i.e.* same dose as 2.5 mc of ^{74}As to kidney.
8. See references (2) and (30).
9. Taking kidney uptake when blocked as 0.033% dose/gm. Cf. (31, 32, 33).
10. Corrected for decay, assuming scan carried out 16 hrs after injection.

TABLE III

	Bulb diameter (approx) cm	V_T *ml*	η *or* η^2 *(for 1" thick crystal)*[1]	$\epsilon_T\alpha_T$	$\frac{\epsilon_T\alpha_T}{\epsilon_{NT}\alpha_{NT}}$	$\epsilon_{NT}\alpha_{NT}$	$B=\sqrt{\frac{\eta\epsilon_T^2\alpha_T^2}{\epsilon_{NT}\alpha_{NT}}}$ or $\sqrt{\frac{\eta^2\epsilon_T\alpha_T^2}{\epsilon_{NT}\alpha_{NT}}}$
^{18}F coincidence	1.1	0.42	[2]0.260	2.17×10^{-3}	15.6	$140\times10-6$	0.0934
	2.1	4.09		2.04×10^{-3}	14.6		0.0880
	3.1	13.7		1.92×10^{-3}	13.7		0.0828
	4.2	32.6		1.72×10^{-3}	11.9		0.0730
	5.0	55.1		1.51×10^{-3}	10.8		0.0650
^{18}F focusing collimator	1.1	0.42	0.209	3.44×10^{-3}	34.4	$100\times10-6$	0.158
	2.1	4.09		3.25×10^{-3}	32.8		0.149
	3.1	13.7		3.08×10^{-3}	30.6		0.140
	4.2	32.6		2.91×10^{-3}	28.9		0.133
	5.0	55.1		2.54×10^{-3}	25.4		0.116
^{131}I	1.1	0.55	0.403	2.06×10^{-3}	27.8	$73.8\times10-6$	0.152
	2.1	4.00		1.94×10^{-3}	26.2		0.144
	3.1	13.0		1.59×10^{-3}	21.5		0.117
	4.2	29.5		1.27×10^{-3}	17.4		0.0942
	5.0	54.3		1.05×10^{-3}	14.2		0.0805

TABLE III (contd)

	Bulb diameter (approx) cm	V_T *ml*	η *or* η^2 *(for 1" thick crystal)*[1]	$\epsilon_T\alpha_T$	$\frac{\epsilon_T\alpha_T}{\epsilon_{NT}\alpha_{NT}}$	$\epsilon_{NT}\alpha_{NT}$	$B=\sqrt{\frac{\eta\epsilon_T^2\alpha_T^2}{\epsilon_{NT}\alpha_{NT}}}$ or $\sqrt{\frac{\eta^2\epsilon_T\alpha_T^2}{\epsilon_{NT}\alpha_{NT}}}$
^{203}Hg	1.1	0.335	0.620	1.36×10^{-3}	20.6	$66.4\times10-6$	0.132
	2.2	4.11		0.92×10^{-3}	14.1		0.0897
	3.0	10.0		1.08×10^{-3}	16.2		0.104
	4.2	31.4		0.80×10^{-3}	12.0		0.0770
	5.0	55.7		0.56×10^{-3}	8.4		0.0540
^{125}I	1.1	0.44	1.00	0.091×10^{-3}	13.6	$6.66\times10-6$	0.0351
	2.1	4.15		0.079×10^{-3}	11.8		0.0306
	2.9	12.0		0.062×10^{-3}	9.3		0.0240
	4.1	32.0		0.057×10^{-3}	8.4		0.0218
	5.0	55.6		0.044×10^{-3}	6.6		0.0171

Notes

1. The crystal efficiency was taken from values for total efficiency for a 1½ x 1 inch crystal at 20 cm, and for peak/total efficiency ratio for a 1½ x 1 inch crystal at 2.5 cm (34). The actual crystal used was 3 inch diameter by 1 inch thick, and the source was at 20 cm.
2. For coincidence the whole spectrum was used, otherwise the photoelectric peak only was used.

lower than for the other isotopes, mainly due to the increased photoelectric absorption (see below). For coincidence counting the whole spectrum was used, and not just the photoelectric peak.

Apart from ^{125}I, it can be seen that for a given tumour size B varies much less than A for different isotopes. Although B for coincidence counting is definitely lower than for a focussing collimator with the same isotope, it is only about 25 per cent lower than B for ^{203}Hg. Since B falls with decreasing γ energy, there is probably not very much difference between B for coincidence and for low energy γ emitters such as ^{99m}Tc and ^{123}I. The sharp fall off for ^{125}I is not likely to be observed above about 80 kev, since it is below this energy that the photoelectric absorption coefficient in water rises steeply. Therefore the values in Tables I and II can probably be compared with each other very approximately. However, a proper comparison could only be made if the optimum collimator was used for each isotope. Also the values of B for the positron emitters could be increased by using a thicker crystal.

Factors affecting B: It is of interest to analyze the values of B further to find out why there is an increase with increasing γ energy. This problem is more complex than the consideration of factors affecting A, and will only be treated very approximately. Much work has been done on calculation of the theoretical efficiency of collimators, but it is difficult to allow adequately for the effect of scattered radiation, although Beck does discuss this problem (19). The following considerations indicate that the effect of scatter may not be negligible and should be allowed for, either by making experimental measurements of B or by theoretical treatment if this is possible.

If there were no septa penetration or scatter, and if the target volume was a point source, the value for ϵ_T would be equal to the solid angle Ω, subtended by the crystal at the source, multiplied by the fraction of the crystal area not covered by lead. The value of a_T must lie between $e^{-\mu_0 x}$ and $e^{-\mu_A x}$ where μ = linear total absorption coefficient, μ_A = linear true absorption coefficient for water, and x = distance from target to surface of tank, or for coincidence thickness of tank. These estimates of $\epsilon_T a_T$ are shown in Table IV for the different isotopes, and may be compared with the experimental values given in Table III. Considering the ratio of experimental results to calculated values using the total absorption coefficient, this ratio is less than one for ^{125}I, but rises with increasing γ energy to greater than one for ^{18}F. The ratio might be expected to be less than one due to the finite source volume. Other factors which may lead to a difference in the values found in Tables III and IV are septa penetration, scatter in collimator, and scatter in tissue. These other factors will all tend to increase the ratio of experimental to theoretical values when the total absorption coefficient is used for the calculation. An approximate calculation of the effect of finite source volume was made by considering theoretical (8) and experimental isocount curves, and this indicated that the efficiency should not be reduced by more than about 20 per cent for a 1 cm diameter bulb and about 80 per cent for a 5 cm diameter bulb. The ^{125}I values appear to be reduced by more than this, but these are inaccurate as already stated. For ^{203}Hg the reduction factors appear to be about 25 and 73 per

cent for the 1 cm and 5 cm bulbs respectively and this agreement is satisfactory considering the approximations used. It appears then that there is little effect of penetration or scatter for ^{203}Hg γ rays. However, there is some effect for ^{131}I, and more for ^{18}F.

The effect of septa penetration was estimated approximately using Myhill's equation (20), and it was found that this could not increase the efficiency for ^{18}F by more than about 10 per cent for the 1 cm diameter bulb and about 20 per cent for the 5 cm diameter bulb. For ^{131}I these increases cannot be greater than about 3 and 8 per cent, respectively.

The increase in efficiency with γ energy when compared with calculated values must therefore be due to scatter. Since for ^{18}F the effect is less with coincidence counting, it seems likely to be mainly due to scatter in the collimator rather than in the water. For ^{18}F with the focussing collimator, the ratio of photopeak to total counts was about 0.80 for the bulbs instead of about 0.41 as expected if there was no scatter. For the tank with the focussing collimator this ratio was about 0.42, and for coincidence it was 0.38 and 0.54 for bulbs and tank respectively. For ^{131}I the ratio was also slightly higher than expected for the

TABLE IV

	^{18}F *Coincidence*	^{18}F *Focusing collimator*	^{131}I	^{203}Hg	^{125}I
γ energy (mev)	0.511	0.511	0.364	0.280	0.030
(a) $e^{-\mu_0 x}$	0.237	0.485	0.433	0.372	0.087
(b) $e^{-\mu_a x}$	0.605	0.778	0.784	0.790	0.295
Correctional factor[1]	0.884	0.940	0.930	0.924	0.564
(a) $\epsilon_T \alpha_T$	1.84×10^{-3}	2.72×10^{-3}	2.40×10^{-3}	2.04×10^{-3}	0.292×10^{-3}
(b) $\epsilon_T \alpha_T$	4.70×10^{-3}	4.35×10^{-3}	4.39×10^{-3}	4.34×10^{-3}	0.985×10^{-3}

μ_0 = total linear absorption coefficient.
μ_a = true linear absorption coefficient.
x = depth of tumour = 7.6 cm. or thickness of head for coincidence = 15.2 cm.
ϵ_T = collimator efficiency for target volume.
α_T = attenuation factor due to absorption and scattering in tissue.

Note

Solid angle = 0.0088. Fraction of crystal not covered by lead = 0.676, or 1.0 for coincidence. Crystal 3 inch diameter by 1 inch thick. 7-hole heavy alloy collimator.

1. Correction for absorption in aluminum cap of collimator and in glass, and for window width too small for ^{125}I peak.

smaller bulbs. It seems likely, therefore, that the increase in efficiency for higher energy γ rays is due mainly to small angle scattering in the collimator material. The setting of the bias used for ^{18}F would allow γ rays scattered through an angle of about 50° to be recorded. This scatter is helpful rather than unwanted as the ratio of target to non-target efficiency is increased also (see Table III).

Minimum tumour size detectable

Having found B for a given collimator, it is interesting to calculate approximately the minimum tumour size which can be detected by that collimator. For the seven-hole heavy alloy collimator used to obtain the results shown in Table 3, the value of B for a given tumour volume did not vary much for different isotopes. Let us assume a maximum value of B of about 0.10 for coincidence and 0.15 for focusing collimators for tumours of 1–2 cm diameter. The following values are assumed for the other parameters:

V_{NT} = 5000 ccs (This represents volume of head approximately)
r = 3 (see (14))
t = 4 secs = 0.0667 mins = d/v where v is speed of scan.

If t is made much greater than this for normal scanning speeds, maximum count rate over the tumour will be reduced; the scanning speed is fixed by the time for the whole scan, which is limited by factors such as the time for which the patient can be kept still (9).

Then $n = 0.08\, A\, V_T$ for coincidence
and $n = 0.12\, A\, V_T$ for focusing collimators.

Hence for coincidence:

$$A = \frac{37.5}{V_T} \text{ for } n = 3$$

$$\text{and } A = \frac{25}{V_T} \text{ for } n = 2.$$

Also for focusing collimators:

$$A = \frac{25}{V_T} \text{ for } n = 3$$

$$\text{and } A = \frac{16.7}{V_T} \text{ for } n = 2.$$

These equations give the minimum value of A required to detect a tumour of volume V_T with a given statistical probability under the conditions given. Values of A required can now be calculated and compared with values in Tables 1 and 2.

For 1 cm and 2 cm diameter tumours, the values of V_T are 0.524 and 4.19 cc respectively.

Hence for *coincidence:*

A = 72 for a 1 cm diameter tumour and n = 3
A = 48 for a 1 cm diameter tumour and n = 2
A = 9.0 for a 2 cm diameter tumour and n = 3

Thus a 2 cm diameter tumour would be detected with $KB^{18}F_4$ and ^{68}Ga, but a 1 cm tumour would not be detected with any of the isotopes in Table 1. (Values of A could be reduced to about two thirds of these values by using a crystal 3″ thick instead of 1″ thick)

For *focusing collimators:*

$A = 48$ for a 1 cm diameter tumour and $n = 3$
$A = 32$ for a 1 cm diameter tumour and $n = 2$
$A = 6.0$ for a 2 cm diameter tumour and $n = 3$

In this case a 2 cm diameter tumour would be detected with ^{99m}Tc or ^{123}I HSA, but again a 1 cm tumour would not be detected with any of the isotopes in Table 2.

For collimators with smaller 50% resolution diameters, the value of B will be affected in two ways. The factor $\sqrt{\eta\epsilon_T\alpha_T}$ (or $\sqrt{\eta^2\epsilon_T\alpha_T}$ for coincidence), that is, pulses produced ÷ photons emitted from target, will tend to fall as efficiency is reduced when resolution diameter is reduced. However, the factor $\sqrt{\frac{\epsilon_T\alpha_T}{\epsilon_{NT}\alpha_{NT}}}$, that is, counts for x$\mu$C in target volume ÷ counts for xμC in non-target volume, will tend to increase. The overall value of a figure of merit which is proportional to B for a given crystal efficiency and gamma emission was found to vary little for several different collimators (Matthews, 1964). A more detailed study of how B varies with resolution is required in order to decide on the optimum resolution for brain scanning, but it does not appear likely that tumours of much less than 2 cm diameter can be detected with conventional scanning and isotopes. Hence, unless much higher values of B can be obtained, resolution should not be better than about 2 cm or the sensitivity will be reduced unnecessarily.

However, with cameras the situation will be much improved, since t can now be increased considerably, so that probably a 1 cm tumour will be detectable and resolution will become an important factor. Gottschalk and Anger (22) report that a 1.3 cm balloon containing 0.03 μc ^{68}Ga/ml can be detected in a tank containing 3 μc in 1500 ml. On the basis of the calculations given in this paper for tumour uptake, this would correspond to 7 mc of ^{68}Ga given to the patient.

As pointed out by Gottschalk and Anger, calculations based on tumour/brain concentration ratios do not allow for radioactivity in muscle, skin, and bone of the head, and so these calculations give optimum results and in practice the tumour size which can be detected is likely to be larger than the calculated values.

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SUMMARY

A method of calculating the minimum tumour size detectable with a given isotope and counting system is presented. An experimental measurement with a phantom is required and also the tumour and normal tissue concentrations of

isotope must be known. These concentrations may often be found in terms of extracellular spaces. In this way, different isotopes, collimators and counting systems may be compared quantitatively. This may be a useful method of evaluating the many new isotopes which are being used. In this paper brain tumour localization is considered in detail, and it is found that a considerable gain may be obtained by using certain short lived isotopes. Owing to interference from radiation from the rest of the body, only positron emitters and low energy γ emitters can be used for brain scanning. The minimum tumour size detectable and the optimum collimator resolution for brain scanning is discussed.

REFERENCES

1. HARPER, P. V., BECK, R., CHARLESTON, D. and LATHROP, K. A.: Optimisation of a scanning method using ^{99m}Tc, *Nucleonics* **22**:50, 1964.

2. SODEE, D. B.: Renal uptakes and renal scanning with radioactive ^{197}Hg neohydrin and ^{203}Hg neohydrin *J. Nucl. Med.* **4**:190, 1963.

3. SHEALY, C. N., ARONOW, S. and BROWNELL, G. L.: Ga-68 as a scanning agent for intracranial lesions, *J. Nucl. Med.* **5**:161, 1964.

4. ENTZIAN, W., ARONOW, S., SOLOWAY, A. H. and SWEET, W. H.: A preliminary evaluation of fluorine-18 labelled tetrafluoroborate as a scanning agent for intracranial tumours, *J. Nucl. Med.* **5**:542, 1964.

5. SORENSEN, L. B.: Liver Scanning with radio-molybdenum, I.A.E.A. symposium on Medical Radioisotope Scanning, 1964. In press.

6. MYERS, W. G. and ANGER, H. O.: Radioiodine-123, *J. Nucl. Med.* **3**:183, 1962.

7. DI CHIRO, G.: Anatomy of the brain and basic principles of brain scanning, Progress in Medical Radioisotope Scanning, U.S. Atomic Energy Commission, 1962. Eds. R. M. Kniseley, G. A. Andrews, C. C. Harris and E. B. Anderson, p. 347.

8. BROWNELL, G. L.: Theory of radioisotope scanning, I.A.E.A. symposium on Medical Radioisotope Scanning, 1964. In Press.

9. MATTHEWS, C. M. E.: Comparison of coincidence counting and focusing collimators with various isotopes in brain tumour detection, *Brit. J. Radiol.* **37**:531, 1964.

10. DEWEY, W. C. and SINCLAIR, W. K.: Criteria for evaluating collimators used in In Vivo distribution studies with radioisotopes, *Int. J. Appl. Radiat. and Isotopes* **10**:1, 1961.

11. BECK, R. N.: A theoretical evaluation of brain scanning systems, *J. Nucl. Med.* **2**:314, 1961.

12. BECK, R. N.: Collimators for radioisotope scanning systems, I.A.E.A. symposium on Medical Radioisotope Scanning, 1964. In press.

13. LOCKSLEY, H. B., SWEET, W. H., POWSNER, H. J. and DOW, E.: Suitability of tumour-bearing mice for predicting relative usefulness of isotopes in brain tumours, *Arch. Neurol. Psychiat.* **71**:684, 1954.

14. MATTHEWS, C. M. E. and MOLINARO, G.: A study of the relative value of radioactive substances used for brain tumour localisation and of the mechanism of tumour:brain concentration, *Brit. J. Exp. Pathol.* **44**:260, 1963.

15. KUHL, D. E.: Influence of collimator design, photon energy, and radiation dose on detection effectiveness in liver scanning, *Phys. Med. Biol.* In press.

16. SWEET, W. H., MEALEY, J., BROWNELL, G. L. and ARONOW, S. Coincidence scanning with positron emitting arsenic or copper in the diagnosis of focal intracranial disease, Medical Radioisotope Scanning I.A.E.A. Vienna, p. 163, 1959.

17. MALLARD, J. R., FOWLER, J. F. and SUTTON, M.: Brain Tumour detection using radioactive arsenic, *Brit. J. Radiol.* **34**:562, 1961.

18. Nuclear Data Sheets. Sheet No. 61-1-56. National Academy of Sciences, National Research Council, Washington, D.C.

19. BECK, R. N.: A theory of radioisotope scanning systems, I.A.E.A. symposium on Medical Radioisotope Scanning, 1964. In press.

20. MYHILL, J.: Theory of multichannel collimated scintillation detectors, *Int. J. appl. Radiat. and Isotopes* **12**:10, 1961.

21. JENSEN, P. G.: Medical Radioisotope Scanning, I.A.E.A. Vienna, p. 29, 1959.

22. GOTTSCHALK, A. and ANGER, H. O.: The sensitivity of the positron scintillation camera for detecting simulated brain tumours with Gallium-68-EDTA, *Amer. J. Rotentgenol.* **92**:174, 1964.

23. MATTHEWS, C. M. E. and SILVESTER, D. J.: Unpublished results, 1964.

24. MATTHEWS, *C. M. E.* and GARTSIDE, J.: *Brit. J. Ca.*, in press.

25. DOLLERY, C. T., FOWLER, J. F., HUGH-JONES, P. MATTHEWS, C. M. E. and WEST, J. B.: The preparation and use of radioactive oxygen, carbon monoxide, and carbon dioxide for investigation of regional lung function, and their comparison with ^{133}Xe, *Strahlentherapie, Supplement* **53**:88, 1963.

26. MATTHEWS, C. M. E.: Unpublished results, 1963.

27. HARPER, P. V.: Discussion, I.A.E.A. symposium on Medical Radioisotope Scanning, 1964. In press, and personal communication.

28. MATTHEWS, C. M. E. and MALLARD, J.: To be published.

29. SMITH, E. M.: Radiochemical purity, internal dosimetry and calibration of ^{99m}Tc, *J. Nucl. Med.* **5**:382, 1964.

30. HARRIS, C. C. and ROHRER, R. H.: Letter to the Editor, *J. Nucl. Med.* **5**:317, 1964.

31. MILLER, H. C., GREEN, J. T. and LEVINE, J.: Metabolism of chormerodrin-Hg^{203}, *J. Nucl. Med.* **3**:208, 1962.

32. GREENLAW, R. H. and QUAIFE, M.: Retention of neohydrin-Hg^{203} as determined with a total body scintillation counter, *Radiology*, **78**:970, 1962.

33. MILLER, H. C., GREEN, J. P. and LEVINE, J.: Metabolism of chlormerodrin-Hg^{203}, *Invest. Urol.* **1**:112, 1963.

34. SIEGBAHN, K. (Ed.) Beta and Gamma Ray Spectroscopy, North Holland Publishing Co., Amsterdam. pp. 138 and 154, 1955.