

AAEC/E350



AAEC/E350



AUSTRALIAN ATOMIC ENERGY COMMISSION  
RESEARCH ESTABLISHMENT  
LUCAS HEIGHTS

A NEW APPROACH TO THE ESTIMATION OF RADIOPHARMACEUTICAL  
RADIATION DOSE DISTRIBUTIONS

by

E. L. R. HETHERINGTON

N. R. WOOD

March 1975

ISBN 0 642 99680 6

AUSTRALIAN ATOMIC ENERGY COMMISSION  
RESEARCH ESTABLISHMENT  
LUCAS HEIGHTS

A NEW APPROACH TO THE ESTIMATION OF RADIOPHARMACEUTICAL  
RADIATION DOSE DISTRIBUTIONS

by

E.L.R. HETHERINGTON  
N.R. WOOD

ABSTRACT

For a photon energy of 150 keV, the Monte Carlo technique of photon history simulation was used to obtain estimates of the dose distribution in a human phantom for three activity distributions relevant to diagnostic nuclear medicine. In this preliminary work, the number of photon histories considered was insufficient to produce complete dose contours and the dose distributions are presented in the form of colour-coded diagrams.

The distributions obtained illustrate an important deficiency in the MIRD Schema for dose estimation. Although the Schema uses the same mathematical technique for calculating photon doses, the results are obtained as

(continued)

## CONTENTS

average values for the whole body and for complete organs. It is shown that the actual dose distributions, particularly those for the whole body, may differ significantly from the average value calculated using the MIRD Schema and published absorbed fractions.

National Library of Australia card number and ISBN 0 642 99680 6

The following descriptors have been selected from the INIS Thesaurus to describe the subject content of this report for information retrieval purposes. For further details please refer to IAEA-INIS-12 (INIS: Manual for Indexing) and IAEA-INIS-13 (INIS: Thesaurus) published in Vienna by the International Atomic Energy Agency.

BLOOD; DOSIMETRY; MAN; MATHEMATICAL MODELS; MONTE CARLO METHOD; ORGANS; PHOTONS; RADIATION DOSE DISTRIBUTIONS; RADIOPHARMACEUTICALS; SIMULATION; WHOLE-BODY IRRADIATION

	Page
1. INTRODUCTION	1
2. LIMITATIONS OF ABSORBED FRACTION CONCEPT	2
3. MATHEMATICAL MODELS FOR PHOTON ABSORPTION IN THE BODY	2
3.1 The Adult Human Phantom	2
3.2 Monte Carlo Simulation of Photon Interaction	3
4. PROGRAM STRUCTURE FOR DETERMINATION OF DOSE DISTRIBUTION	3
4.1 Source Routine	3
4.2 Collision Routine	4
4.3 Evaluation Routines	4
5. DOSE DISTRIBUTION IN THE HUMAN PHANTOM	5
5.1 Dose Distribution for a Uniform Photon Source Distribution	5
5.2 Dose Distribution for a Photon Source Distributed Approximately as the Blood	5
5.3 Dose Distribution for a Simple Organ Distribution of Photon Sources	6
6. DISCUSSION	6
7. ACKNOWLEDGEMENT	7
8. REFERENCES	7

Figure 1	The adult human phantom
Figure 2	Simplified Monte Carlo photon history generation
Figure 3	Dose distribution from homogeneous source
Figure 4	Dose distribution from approximate blood source
Figure 5	Dose distribution from arbitrary organ distribution of activity

## 1. INTRODUCTION

The historical development of methods for the dosimetry of radionuclides distributed in the body has been outlined by several authors [Loevinger 1969, Quimby 1970]. The most recent development has been a generalised procedure applicable to all radiations from all radionuclides [Loevinger & Berman 1968, Brownell, Ellet & Reddy 1968]. This procedure, known as the Medical Internal Radiation Dose (MIRD) Committee Schema, provides a single equation for all organ dose calculations. This equation may be written:

$$D_{(v \leftarrow r)} = \frac{\tilde{A}_r}{M_v} \sum \Delta_i \phi_{i(v \leftarrow r)} \text{ rad}$$

where  $D_{(v \leftarrow r)}$  = average absorbed dose to a volume  $v$  from a source  $r$ ;

$\tilde{A}_r$  = cumulated activity in a region,  $r$ , in microcurie-hours;

$M_v$  = mass of target volume,  $v$ , in grams;

$\Delta_i$  = absorbed dose constant for the  $i$ -th emission from the source  $r$  in g-rad/ $\mu$ Ci-h;

$\phi_{i(v \leftarrow r)}$  = absorbed fraction for the  $i$ -th emission with the source in region  $r$  and  $v$  the target volume.

Since it is difficult to obtain specific information on organ shape and size for individual patients, dose calculations are usually made for appropriate mathematical models, although patient studies are used to determine the fate of radionuclides in the body and hence values of cumulated activities.

Where the source organ is also the target organ, the absorbed fractions for non-penetrating emissions (beta particles, conversion electrons, etc.), are usually taken as unity since most organs are large compared with the range of these emissions. It is assumed that these emissions do not contribute to the dose to regions outside the source organ, and that the dose distribution in the organ corresponds to the source distribution. The most widely used model for photon-absorbed fraction data is the adult human phantom (Figure 1) described by Fisher & Snyder [1967].

The MIRD approach to dose estimation has been used with appropriate biological data for several AAEC-produced radiopharmaceuticals [Boyd, Hetherington & Wood 1971, Boyd et al. 1973, Hetherington 1973]. The experience gained from these studies has indicated a need for further developments in internal dosimetry.

## 2. LIMITATIONS OF ABSORBED FRACTION CONCEPT

The use of absorbed fractions calculated for a given model assumes that

- (a) there is no variation with time in the size of any organ containing radioactivity; and
- (b) a uniform distribution of a photon source in an organ produces a meaningful average dose in the organ itself and a different, but still only average, dose to each of several target organs.

For assumption (a) it has been shown that, because of large changes in organ size, the simple absorbed fraction concept cannot be used to estimate the bladder dose [Snyder, Ford & Warner 1970, Unnikrishnan 1973]. These authors have developed an alternative concept of volume-dependent dose rate constants.

For assumption (b) it will be shown that, with available mathematical and computing techniques, it is possible to ignore the average dose concept and substitute a complete dose distribution for any cumulated activity distribution of a photon emitter in an appropriate human phantom. To illustrate this approach, only one photon energy (150 keV) is considered. This is regarded as the optimum photon energy for organ imaging using a gamma camera and is close to the principal photon emissions of the nuclides  $^{99m}\text{Tc}$ ,  $^{123}\text{I}$ ,  $^{134m}\text{Cs}$  and  $^{67}\text{Ga}$  used in nuclear medicine.

## 3. MATHEMATICAL MODELS FOR PHOTON ABSORPTION IN THE BODY

### 3.1 The Adult Human Phantom

The general form of the adult human phantom (Figure 1) described by Fisher & Snyder [1967] was chosen as an appropriate mathematical model of the human body for the calculation of absorbed dose distribution. The phantom comprises three sections:

- . an elliptical cylinder representing the arms and torso;
- . a truncated elliptical cone representing the legs and feet; and
- . an elliptical cylinder representing the head and neck.

Individual organs have not been included, and all parts of the phantom have the same density and composition. The tissue composition used is given in Table 1 [Brownell, Ellet & Reddy 1968]. The calculations were made for a phantom density of unity.

The effect on dose distributions from different organ densities is generally small compared with the large effect of the abrupt change from an absorbing to a non-absorbing medium at the boundary of the phantom.

TABLE 1  
COMPOSITION OF HUMAN PHANTOM TISSUE

Element	Mass per cent
Hydrogen	10.00
Oxygen	71.39
Carbon	14.89
Nitrogen	3.47
Chlorine	0.10
Sodium	0.15

### 3.2 Monte Carlo Simulation of Photon Interaction

Since 1964, the Monte Carlo technique has been used to estimate radiation doses from internally deposited photon emitters [Ellet, Callahan & Brownell 1964]. This method estimates the radiation dose by tracing mathematically the history of the photons from their emission within the phantom until they are absorbed or escape after several energy depositing collisions.

For the most part, the technique has been used to calculate absorbed fractions for organs in the human phantom. As mentioned previously, the use of these absorbed fractions leads to average organ dose estimates which may not be meaningful. The Monte Carlo technique may also be used to determine actual dose distributions in any region of interest of the phantom for a given activity distribution.

Figure 2 outlines the mathematical process required to produce a simple photon history by the Monte Carlo method. The history is generated by a sequence of random events. In a mathematical simulation, the event that occurs at any stage must be determined using probability distributions followed by the real behaviour.

## 4. PROGRAM STRUCTURE FOR DETERMINATION OF DOSE DISTRIBUTION

The Monte Carlo simulation of photon transport (in situations of practical interest) is so large a problem that a realistic model can only be implemented by using a fast digital computer. Programs for this simulation comprise three distinct parts: these are the source routine, collision routine and evaluation routine(s). A detailed example of a photon transport simulation for radiation dose estimates has been given by Wood [1975].

### 4.1 Source Routine

The source routine produces the original random locations of photon

source points within the phantom, together with an original random direction. To approximate a given spatial distribution of a mono-energetic photon emitter, two procedures are possible.

- (i) A point can be chosen at random in the phantom and a source weight assigned on the basis of source point location, i.e. high weights are assigned in regions of high photon source density.
- (ii) The routine generating the source point location can be biased to generate more source points in regions of high photon source density. In this case the photons are all source-weighted equally.

The routine used to determine the dose distribution for a radiopharmaceutical is of the first type since activity is usually present, to some degree, in all parts of the body. The latter form would be used if all the activity had a definite location, as would be the case for a nuclear cardiac pacemaker implant.

#### 4.2 Collision Routine

For photons supplied by the source routine, the collision routine generates random photon paths through the phantom. The path is influenced in a statistical fashion by the medium properties and its geometry. For photon energies less than 1.0 MeV, the only important interactions are the photoelectric effect and Compton scattering. The mathematical routine uses collision weights to account for the variance reducing technique of only allowing the photon to undergo Compton scattering. There is no absorption, and the photon history terminates only when the photon escapes the phantom, or its collision weight becomes negligible.

Each photon interaction which deposits energy is examined to see whether the interaction occurred in a predetermined region of interest in the phantom. If the interaction is so located, it is termed an interesting event. If such an event occurs, the routine stores its location and the amount of energy deposited. The routine continues to generate photon histories until approximately 1,000 interesting events have occurred. It then stops temporarily and an evaluation routine sorts these interesting events into suitably small spatial subdivisions, giving an indication of the absorbed energy distribution in the region of interest. The procedure is repeated until a sufficient number of interesting events have occurred to give a meaningful absorbed energy (i.e. dose) distribution. The batch nature of the routine minimises computer storage requirements.

#### 4.3 Evaluation Routines

There are three simple routines which sort the interesting events and

produce a raw absorbed energy distribution, correct the result for energy deposited in incomplete subdivisions of the region of interest at the edge of the phantom, and normalise the energy distribution for display.

### 5. DOSE DISTRIBUTION IN THE HUMAN PHANTOM

The mathematical procedure outlined above can be used to obtain the dose distribution in selected 'regions of interest' of the human phantom for any arbitrary photon source distribution in the phantom. Three photon source distributions relevant to nuclear medicine are considered.

In this initial investigation, the region of interest chosen was the phantom volume between the  $Y = 1$  and  $Y = -1$  planes (see Figure 1 for the coordinate system). This is a 2 cm thick region in the phantom parallel to the X-Z plane. The X-Z plane was divided into a 2 cm x 2 cm mesh containing approximately 1,200 mesh squares. For each source distribution, an estimate of the dose was made for each 2 cm x 2 cm x 2 cm volume element by running the collision routine until ~ 100,000 'interesting events' had occurred, and the overall distribution presented as a colour-coded diagram (Figures 3 to 5). In each case the relation between the MIRDO average whole body dose and the colour code is given.

#### 5.1 Dose Distribution for a Uniform Photon Source Distribution

An estimate of the whole body dose distribution for a uniformly distributed photon source was obtained by programming the source routine to weight equally all the source photons produced. The resultant dose distribution and the average dose obtained using the Snyder et al. [1969] absorbed fraction data are shown in Figure 3. It can be seen that the average dose does not give a completely adequate description of the dose to a considerable portion of the region of interest.

#### 5.2 Dose Distribution for a Photon Source Distributed Approximately as the Blood

A logical rationalisation of the uniform activity distribution approach is to assume a photon source in the body having the same distribution as its means of transport. Thus, it is often assumed that the activity has the same distribution as the blood. This procedure has been used by Cloutier & Watson [1970] who made dose estimates for a number of organs based on the blood volume of those organs.

A pseudo-blood distribution for the source routine was produced by weighting photon emission from various parts of the phantom according to the approximate blood contents of those parts. The blood was assumed to occupy three main regions with different concentrations. These regions were the

head, the viscera and the extremities. The viscera was assumed to be an elliptic cylinder resting on the X-Y plane with a height of 90 per cent of the trunk height. The major and minor axes of the elliptic cross section were 80 per cent of the respective trunk axes. The weights assumed for source location in the viscera, extremities and head were 3.0, 1.0 and 0.2 respectively.

The resultant dose distribution and average dose calculated using the absorbed fraction concept are shown in Figure 4. The 'absorbed fractions' for this source target geometry were calculated by Wood [1975]. It is obvious that the absorbed fraction approach gives a far from satisfactory indication of the dose distribution in the region of interest.

### 5.3 Dose Distribution for a Simple Organ Distribution of Photon Sources

A third example of the limitation of the absorbed fraction approach and the resulting average dose estimates can be seen from a simple organ distribution of activity. It was assumed that activity was concentrated in one lung, the bladder and, to a lesser extent, the remainder of the body. Source weights of 15, 5 and 0.1 were assigned arbitrarily to these three regions. These source weights correspond in MIRD terms to cumulated activities in the approximate ratio 15 : 2 : 7. (The cumulated activity is proportional to the product of the source weight and the organ volume. In an actual dose determination, the procedure would first be to determine the organ cumulated activities by a combination of physical and biological techniques as outlined by Smith [1970]. The ratio of the source weights for computing purposes would be obtained by dividing the cumulated activity by the organ volume.) The resultant dose distribution is shown in Figure 5. The doses in the lung and bladder regions are similar to those calculated using absorbed fractions and the MIRD Schema. The dose to the region immediately surrounding the lung is marginally underestimated because no allowance was made for the lower density of the lung relative to the rest of the body. There are significant variations from the MIRD average in most other parts of the phantom.

### 6. DISCUSSION

It has been shown that the limitations of the MIRD Schema and its use of organ-absorbed fractions to describe dose distributions can be overcome. The Monte Carlo technique of photon transport simulation remains the basis of the determination. In this preliminary work, dose distributions are indicated by colour-coded diagrams. A more complete determination, involving a considerably greater number of photon histories and an improvement in the efficiency of the Monte Carlo simulation, would provide data of sufficient

quality for true contour plots of the dose distribution. The technique can be extended to produce full three dimensional dose distributions for a given photon source distribution.

These distributions are not restricted to those which result from administration of radiopharmaceuticals and would include any *in vivo* photon source distribution, e.g. as a result of the implantation of a nuclear cardiac pacemaker.

It is unlikely that the approach to radiopharmaceutical dosimetry outlined in this report would be used for routine patient dose assessments in a hospital nuclear medicine department. It could be used to advantage by the developer/manufacture of radiopharmaceuticals in providing definitive dosimetry data on a product.

### 7. ACKNOWLEDGEMENT

The authors acknowledge the assistance of Mr. J. Bellinger in the preparation of the colour-coded dose distribution diagrams.

### 8. REFERENCES

- Boyd, R.E., Hetherington, E.L.R. & Wood, N.R. [1971] - Technetium-99m Generators Prepared from Fission Produced Molybdenum 99 - Quality Control and Performance Aspects. AAEC/E224.
- Boyd, R.E., Robson, J., Hunt, F.C., Sorby, P.J., Murray, I.P.C. & McKay, W.J. [1973] - <sup>99m</sup>Tc Gluconate Complexes for Renal Scintigraphy. *Brit. J. Radiol.* **46** : 604.
- Brownell, G.L., Ellet, W.H. & Reddy, A.R. [1968] - Absorbed Fractions for Photon Dosimetry. *J. Nucl. Med.* Supplement 1, Pamphlet No.3.
- Cloutier, R.J. & Watson, E.E. [1970] - Radiation Dose from Radioisotopes in the Blood. Proc. Symp. on Medical Radionuclides: Radiation Dose and Effects, Oak Ridge Associated Universities, December 8-11, 1969. CONF. 691212, p.325.
- Ellet, W.H., Callahan, A.B. & Brownell, G.L. [1964] - Gamma-ray Dosimetry of Internal Emitters, Monte Carlo Calculation of Absorbed Dose from Point Sources. *Brit. J. Radiol.*, **37** : 45.
- Fisher, H.L. & Snyder, W.S. [1967] - Distribution of Dose in the Body from a Source of Gamma Rays Distributed Uniformly in an Organ. ORNL-4168, p.245.
- Hetherington, E.L.R. [1973] - The Radiation Dose Incurred from the Administration of Skeltec. AAEC/E247.
- Loevinger, R. & Berman, M. [1968] - A Schema for Absorbed Dose Calculations for Biologically Distributed Radionuclides. *J. Nucl. Med.*

Supplement 1, Pamphlet No.1.

Loevinger, R. [1969] - Distributed Radionuclide Sources. Radiation Dosimetry. Vol.3. Academic Press, New York, p.51.

Quimby, E.H. [1970] - The Development of Radiation Dosimetry in Nuclear Medicine. Proc. Symp. on Medical Radionuclides: Radiation Dose and Effects, Oak Ridge Associated Universities, December 8-11, 1969. CONF. 691212, p.7.

Smith, E.M. [1970] - General Considerations in Calculation of the Absorbed Dose of Radiopharmaceuticals used in Nuclear Medicine. Proc. Symp. on Medical Radionuclides: Radiation Dose and Effects, Oak Ridge Associated Universities, December 8-11, 1969. CONF. 691212, p.17.

Snyder, W.S., Fisher, H.L., Ford, M.R. & Warner, G.G. [1969] - Estimates of Absorbed Fractions for Monoenergetic Photon Sources Uniformly Distributed in Various Organs of a Heterogeneous Phantom. *J. Nucl. Med.* Supplement 3, Pamphlet No.5.

Snyder, W.S., Ford, M.R. & Warner, G.G. [1970] - Estimation of Dose and Dose Commitment to Bladder Wall from a Radionuclide Present in Urine. ORNL-4584, p.206.

Unnikrishnan, K. [1973] - Dose to the Urinary Bladder from Radionuclides in Urine. *Phys. Med. Biol.* 19 (3) 329.

Wood, N.R. [1975] - Monte Carlo Studies of Absorbed Dose from Radiopharmaceuticals. M. Eng. Sci. Project Report. University of New South Wales.

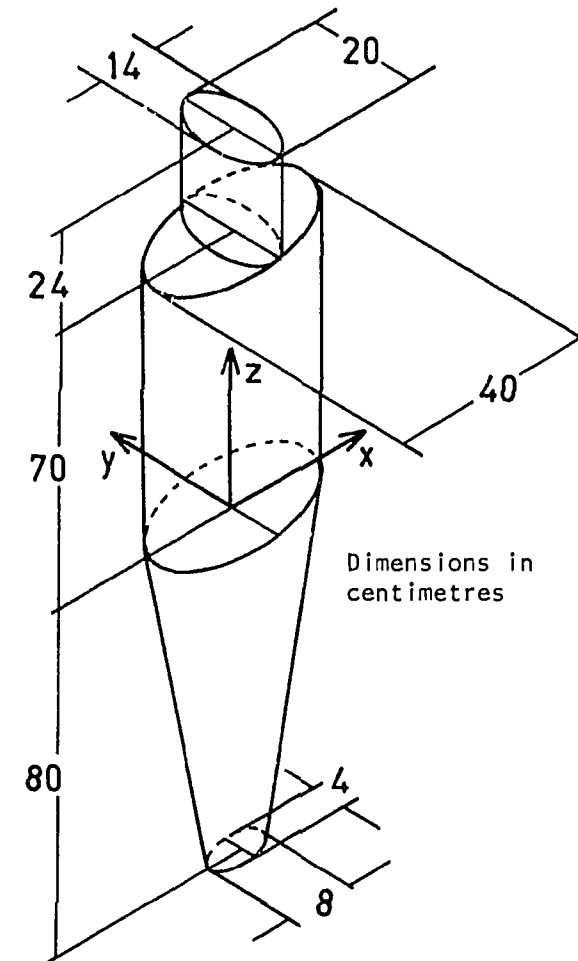


FIGURE 1. ADULT HUMAN PHANTOM



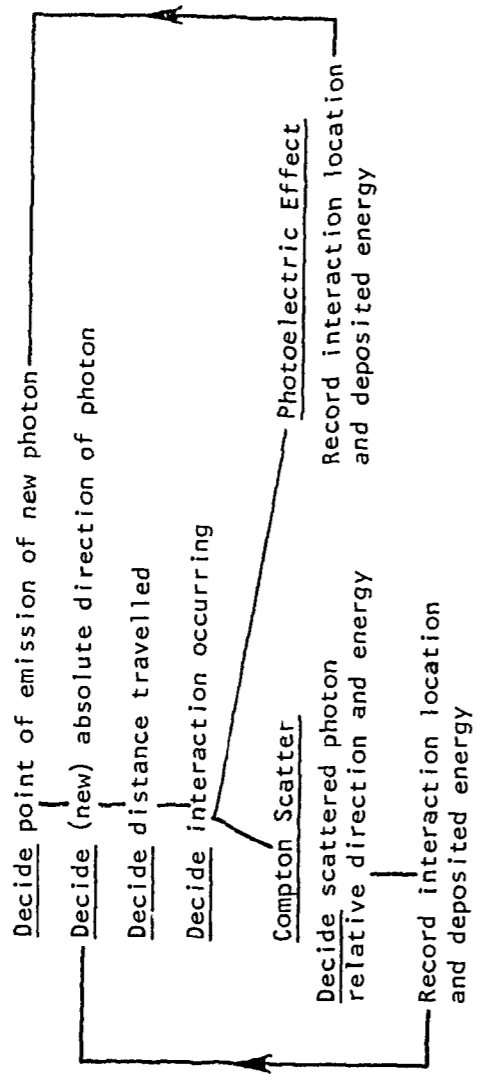


FIGURE 2. SIMPLIFIED MONTE CARLO PHOTON HISTORY GENERATION

Dose Scale

> 2.0	
1.6-2.0	
1.2-1.6	
0.8-1.2	
0.4-0.8	
< 0.4	

Where 1 = whole body 'average dose'

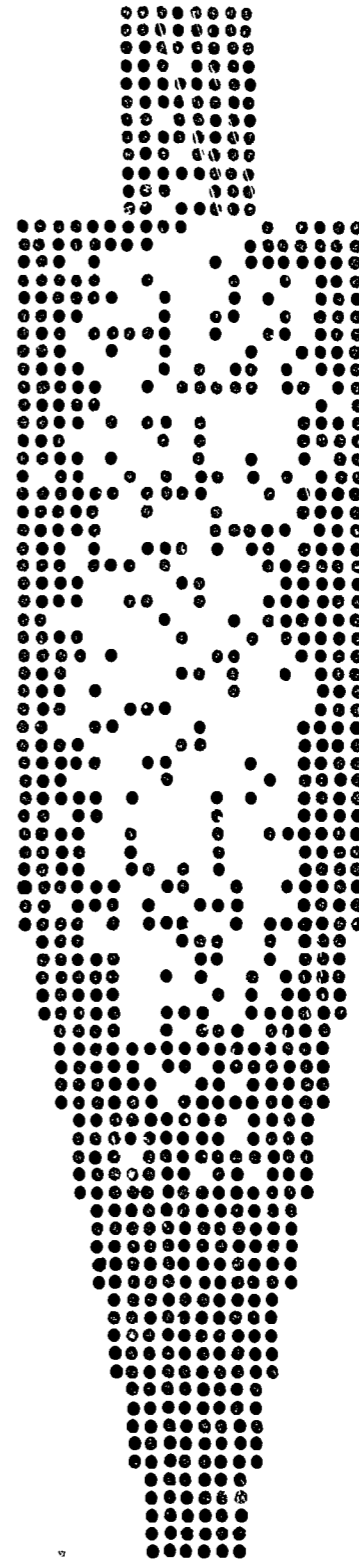


FIGURE 3. DOSE DISTRIBUTION FROM HOMOGENEOUS SOURCE

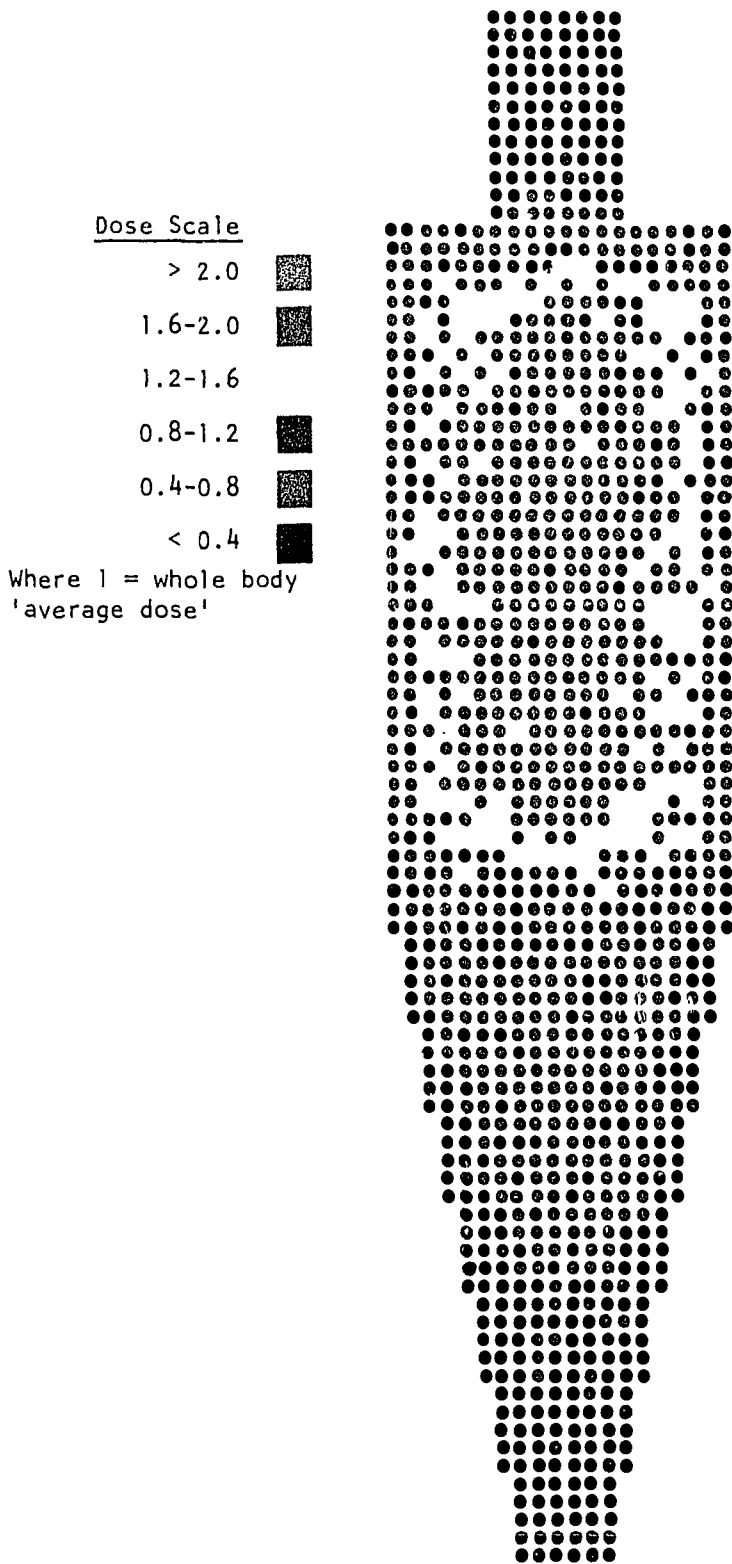


FIGURE 4. DOSE DISTRIBUTION FROM APPROXIMATE BLOOD SOURCE



FIGURE 5. DOSE DISTRIBUTION FROM ARBITRARY ORGAN DISTRIBUTION OF ACTIVITY