PHYSICS AND RADIATION BIOLOGY

CAMIRD/III: A Revised Version of the CAMIRD/II and MIRD-S Packages for Internal Dose Calculation: Concise Communication

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We describe the characteristics of the CAMIRD/III, a software package for the calculation of radiation dose from internally distributed radionuclides. The work concerns the preparation of a revised version of both CAMIRD/II, which uses prestored data of the specific absorbed-energy fraction, and MIRD-S, which uses the precalculated "S" values. Some improvement in the dose computation has been realized, for instance in the case of organs with walls. The software, written in FORTRAN IV, runs on an IBM 370/168 computer.

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The computation of the radiation dose to a patient after the administration of radioactive tracers is becoming increasingly important because it plays a prominent role in the risk/benefit analyses when new procedures are introduced. At the same time, the correct calculation of the absorbed dose becomes more difficult, owing to the complexity and the number of factors involved.

The current method of calculation is one adopted by the MIRD (Medical Internal Radiation Dose) Committee, which uses the well-known equation of R. Loevinger et al. (*1*):

$$\bar{D}(r_k \leftarrow r_h) = \tilde{A}_h \sum_i \Delta_i \Phi_i(r_k \leftarrow r_h), \qquad (1)$$

where $\bar{D}$ (rads) is the mean dose absorbed in the target region, r_k, from the cumulated activity, $\tilde{A}_h$, (μCi-hr) in a source region, r_h; Δ_i (g-rad/μCi-hr) is the mean energy emitted by the radionuclide per unit cumulated activity for the i-th type of radiation emitted; and Φ_i (g^{-1}) is the specific absorbed-energy fraction (i.e., per unit mass) for the target region.

The MIRD Committee has further simplified the above equation, introducing the concept of the so-called "S" factor: the mean dose absorbed in the target region per unit cumulated activity, expressed in rads/μCi-hr. The values of "S" have been calculated for almost all of the emitters currently used in nuclear medicine.

In "S" are condensed all the physical parameters involved in the absorbed-dose calculation, leaving only the biological factors to be evaluated.

The equation now used thus becomes the following (*2*):

$$\bar{D}(r_k \leftarrow r_h) = \tilde{A}_h S(r_k \leftarrow r_h) \quad \text{(rads)}. \qquad (2)$$

If the value of $\tilde{A}_h$ cannot be computed mathematically on the basis of the tracer kinetics, it may be determined experimentally, by measuring at fixed time intervals the activities in those organs having a relevant tracer concentration. By extrapolating to infinity the experimental time-activity curve and integrating it, we find a value of cumulated activity whose reliability depends on the frequency and the accuracy of the measured data.

SOFTWARE IMPLEMENTATION: CAMIRD/II, MIRD-S, AND CAMIRD/III

The calculation of the total mean dose absorbed in a target organ from the cumulated activities of various source organs is a time-consuming procedure (see Appendix) and may lead to errors if it is performed manually, whereas a computer program offers the advantage of both standardization and speed of calculation. Moreover it becomes easy to change input values (i.e., biological data).

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Two series of computer programs have recently been written: CAMIRD/II and MIRD-S.

CAMIRD/II is the one designed by P. A. Feller (*3*); its main program computes the absorbed dose in a target organ by the use of Eq. 1—i.e., by the Loevinger schema in its more general form. In the computer's disk memory are stored all the physical parameters of the involved radionuclides (*4*) and the values of the specific absorbed-energy fractions, just as they were calculated and tabulated by W. S. Snyder (*5*).

The operator is asked, in conversational form, to enter the names of the desired source organs (lungs, liver, etc.), and their cumulated activities ($\tilde{A}_{lungs}$, $\tilde{A}_{liver}$, etc.), which must be computed separately. The "S" values are computed by the program separately for penetrating and nonpenetrating radiations.

The second program is the MIRD-S, by P. F. Butler et al. (*6,7*), which is based on Eq. 2. It starts with the precalculated "S" values, stored in the computer's disk memory ($\simeq$188 Kbytes are required for the 117 radionuclides of Ref. *4*), just as they were calculated by the MIRD Committee and tabulated in Pamphlet No. 11 (*2*). Unlike CAMIRD/II, this program works in batch mode rather than in conversational form, and computes the absorbed dose starting from the experimental measurements of activity in the source organs, the cumulated activity being calculated by integration of experimental curve, as described above.

Thus CAMIRD/II does not need the precalculated values of "S", and this is very important for calculating the absorbed dose from radioactive tracers not yet considered by MIRD; it is in conversational form and is therefore easy to use; yet it requires the values of cumulated activity, which must be calculated separately for the various organs.

On the other hand, MIRD-S permits the calculation of $\tilde{A}_h$, but it needs the precalculated values of "S", and can be used only in the batch mode.

Furthermore, if used under some special conditions, both programs give incorrect results.

In fact, when the target organ is not itself considered as a source organ, CAMIRD/II omits from the calculation the nonpenetrating radiations emitted inside the target organ due to the activity uniformly distributed in the remainder of the body (see Appendix). For this reason the dose is underestimated by an amount equal to:

$$\tilde{A}_{rb}\frac{m_t}{m_{rb}}S_{np}(t \leftarrow t), \qquad (3)$$

where $\tilde{A}_{rb}$ is the cumulated activity in the remainder of the body (*8*); m_t and m_{rb} are the masses of the target organ and of the remainder of the body; and $S_{np}(t \leftarrow t)$ is the "S" value for the nonpenetrating radiations from the target to itself.

On the other hand, the MIRD-S approach, using the tabulated "S" factors, automatically avoids this error (see Appendix), because the "S" values from the total body include both penetrating and nonpenetrating radiations. When the target is an organ with walls, however, the dose is always overestimated by an amount equal to:

$$\tilde{A}_{rb}\frac{\Delta_{np}}{2m_{rb}} \quad \text{(see Appendix).} \qquad (4)$$

For example, if we use CAMIRD/II to calculate the dose to the testes after administration of 1 mCi of I-131 MAA, using the activity data supplied by Kaul et al. (*9*) (source organs: liver and lungs), we obtain a value of 0.18 rads, which is 44% of the correct value of 0.41 rads, obtained either with MIRD-S or Eq. A2 of the Appendix.

A calculation of the dose to the bladder, using CAMIRD/II and MIRD-S with the same input data as in the above example, gives, respectively, 0.21 rads and 0.45 rads, which are 63.5% and 136% of the correct value of 0.33 rads, obtained by Eq. A2 in the Appendix.

Finally these two programs provide very little protection against an operator's mistake during data input, and this can sometimes lead to a faulty result or force the running of the program again.

Our laboratory has now developed a new FORTRAN IV package, to be run on the IBM 370/168 system. This package, named CAMIRD/III, is a complete revision of Feller's CAMIRD/II and includes, as a subroutine, the program TILDY, the MIRD-S subroutine that computes the cumulated activity.

CAMIRD/III consists of: (a) four programs for the user, which compute the absorbed dose, print all the physical parameters of the desired nuclides, print in tabular form the "S" values (penetrating and nonpenetrating separately), and print the specific absorbed-energy fractions for the various organs; (b) two programs to introduce permanent data (i.e., nuclear decay parameters and specific absorbed fractions) into the computer's disk memory. These programs require $\simeq$44 Kbytes for 117 radionuclides, and can easily be updated.

In these programs all the previously described shortcomings have been eliminated; moreover, important revisions of the computation schema have been added, as, for example, the replacement of the cumulated activity by the new concept, introduced by Loevinger (*10*), of "residence time", τ (hours): $\tau_h = \tilde{A}_h$/administered activity. Accordingly, the equation used is the following:

$$\bar{D}(r_k \leftarrow r_h) = \tau_h S(r_k \leftarrow r_h) \quad (\text{rads}/\mu\text{Ci}). \qquad (5)$$

Furthermore, the new SI units (gray, becquerel) (*11*) have been introduced in addition to the traditional ones (rad, curie).

The use of these programs is conversational, except for the possible input of organ and phantom counts (or

TABLE 1. FILED RADIONUCLIDES

^{3}H	^{11}C
^{15}O	^{18}F
^{43}K	^{67}Ga
^{75}Se	^{81m}Kr
^{81}Rb	^{82}Rb
^{99m}Tc	^{111}In
^{113m}In	^{123}I
^{125}I	^{131}I
^{133}Xe	^{129}Cs
^{198}Au	^{197}Hg
^{203}Hg	^{201}Tl

% injected activity) on punched cards, when the residence time is not available.

All programs check errors of internal compatibility of both input names and numerical values (e.g., wrong names, number of source organs exceeding maximum, repetition of the same source organ, introducing the total body in a list of source organs, etc.). Such errors are immediately detected and the operator is asked to type again.

The whole package is available through the Biomedical Computing Technology Information Center (BCTIC) of Oak Ridge, and contains data for calculating the absorbed dose from 22 radionuclides of medical interest (Table 1). The physical data for other radionuclides (*4*) can easily be added, via item (b), mentioned above.

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APPENDIX

Considering the "source organs" as those organs for which the tracer behavior has been mathematically described (*9*) or for which a certain number of activity-versus-time values have been measured, the total mean dose to an organ (the "target") results from the sum of three components (*8*): (a) dose due to nonpenetrating radiations emitted by the target itself; (b) dose due to penetrating radiations emitted by the target and by the source organs; and (c) dose due to penetrating radiation emitted by the rest of the body (whose cumulated activity is taken as the total-body value minus that for the source organs). The dose is therefore defined by the following equation:

$$\bar{D}_t = \tilde{A}_t S_{np}(t \leftarrow t) + \sum_{s=s_1}^{t} \tilde{A}_s S_p(t \leftarrow s) + \tilde{A}_{rb} S_p(t \leftarrow rb), \quad (A1)$$

where t is the target organ, s is the source organ, rb is the remainder of the body, S_p and S_{np} are the "S" values for penetrating and nonpenetrating radiations.

In order to use this equation, one must consider the target organ itself as a source organ. But it happens very often that the exact value of the target's cumulated activity ($\tilde{A}_t$) is unknown—e.g., when targets are gonads or bone marrow. In such a case the target is not included among the source organs, but is part of the remainder of the body. It follows that if the foregoing equation is, nevertheless, used without the first term (e.g., setting $\tilde{A}_t = 0$, as in CAMIRD/II), the nonpenetrating radiations will not be included in the calculation. This produces an underestimate of the dose, because a fraction of the activity considered as uniformly distributed in the remainder of the body is contained in the target organ, proportionate to its mass. This activity causes absorption of nonpenetrating radiation, from the target itself, whose contribution to the total dose depends on the kind of tracer.

The contribution from the penetrating radiations emitted by the target, which otherwise is usually very low, remains always included in Eq. A1, because it passes automatically from the second to the third term.

Thus, when the target is not specifically considered as a source, Eq. A1 needs to be transformed as follows:

$$\bar{D}_t = \tilde{A}_{rb} \frac{m_t}{m_{rb}} S_{np}(t \leftarrow t) + \sum_{s=s_1}^{s_n} \tilde{A}_s S_p(t \leftarrow s) + \tilde{A}_{rb} S_p(t \leftarrow rb), \quad (A2)$$

where m_t and m_{rb} are the masses of the target organ and of the remainder of the body.

Equations A1 and A2 can be used only when "S" values are available separately for penetrating and nonpenetrating radiations (i.e., S_p and S_{np} as in CAMIRD/III).

On the other hand, when the "S" values tabulated by the MIRD Committee are used (as for instance in MIRD-S), we must consider that $S = S_p + S_{np}$, in which case the total mean dose to the target must be calculated only by the following equation (*6*):

$$\bar{D}_t = \sum_{s} \tilde{A}_s S(t \leftarrow s) + \tilde{A}_{rb} S(t \leftarrow rb) \quad (A3)$$

where the "S" values are now total "S" values.

We can demonstrate that even the use of Eq. A3 leads to the same results as are obtained by Eq. A1 or Eq. A2; but this, as we will explain, is true only if the target is not an organ with walls.

Case 1. Let us take the case in which we would use Eq. A1—i.e., when the target is itself considered as a source. Equation A3 may then be written as:

$$\bar{D}_t = \sum_{s=s_1}^{t} \tilde{A}_s S(t \leftarrow s) + \tilde{A}_{rb} S(t \leftarrow rb) \quad (A3a)$$

Since (*12*) $S = S_p + S_{np}$ when $r_h = r_k = t$, or when $r_h = tb$(total body), or when $r_k = tb$; and since $S = S_p$ when $r_h = s$ (S_{np} being 0); Eq. A3a is equivalent to the following:

$$\bar{D}_t = \sum_{s=s_1}^{t} \tilde{A}_s S_p(t \leftarrow s) + \tilde{A}_t S_{np}(t \leftarrow t) + \tilde{A}_{rb} S(t \leftarrow rb) \quad (A3b)$$

Comparing Eq. A3b with Eq. A1, we can see that both give the same result only if we can demonstrate that:

$$\tilde{A}_{rb} S(t \leftarrow rb) = \tilde{A}_{rb} S_p(t \leftarrow rb)$$

$$\text{i.e., if } S(t \leftarrow rb) = S_p(t \leftarrow rb)$$

According to Ref. (*8*):

$$S_p(t \leftarrow rb) = \frac{m_{tb}}{m_{rb}} S_p(t \leftarrow tb) - \sum_{s=s_1}^{t} \frac{m_s}{m_{rb}} S_p(t \leftarrow s) \quad (A4)$$

and considering that $S = S_p + S_{np}$, or $S = S_p$ as described above:

$$S(t \leftarrow rb) = \frac{m_{tb}}{m_{rb}} S_p(t \leftarrow tb) + \frac{m_{tb}}{m_{rb}} S_{np}(t \leftarrow tb) - \sum_{s=s_1}^{t} \frac{m_s}{m_{rb}} S_p(t \leftarrow s) - \frac{m_t}{m_{rb}} S_{np}(t \leftarrow t) \quad (A5)$$

Since (2) $S_{np}(r_k \leftarrow r_h) = \Delta_{np}\Phi_{np}(r_k \leftarrow r_h)$, and $\Phi_{np}(r_k \leftarrow tb) = 1/m_{tb}$, the second term of Eq. A5 is equal to:

$$\frac{m_{tb}}{m_{rb}} S_{np}(t \leftarrow tb) = \frac{m_{tb}}{m_{rb}} \frac{\Delta_{np}}{m_{tb}} = \frac{\Delta_{np}}{m_{rb}} \quad \text{(A6)}$$

At this point we must distinguish two cases.

(a) When the target *is not* an organ with walls. (If $r_h = r_k = t$ (2): $\Phi_{np}(t \leftarrow t) = 1/m_t$.) The 4th term of Eq. A5 then becomes:

$$\frac{m_t}{m_{rb}} S_{np}(t \leftarrow t) = \frac{m_t}{m_{rb}} \frac{\Delta_{np}}{m_t} = \frac{\Delta_{np}}{m_{rb}} \quad \text{(A7a)}$$

In this case the second and fourth terms of Eq. A5 (as revalued in Eqs. A6 and A7a) vanish, since:

$$\frac{m_{tb}}{m_{rb}} S_{np}(t \leftarrow tb) - \frac{m_t}{m_{rb}} S_{np}(t \leftarrow t) = \frac{\Delta_{np}}{m_{rb}} - \frac{\Delta_{np}}{m_{rb}} = 0$$

For this reason Eqs. A4 and A5 are equivalent, and therefore Eqs. A3 and A1 yield the same result.

(b) When the target *is* an organ with walls. (Even if r_h and r_k are in the same organ (2): r_h = contents, r_k = walls, and $\Phi_{np}(r_k \leftarrow r_h) = 1/2m_h$). The fourth term of Eq. A5 then becomes:

$$\frac{m_t}{m_{rb}} S_{np}(t \leftarrow t) = \frac{m_h}{m_{rb}} \frac{\Delta_{np}}{2m_h} = \frac{\Delta_{np}}{2m_{rb}} \quad \text{(A7b)}$$

In this case the second and fourth terms of Eq. A5 (as revalued in Eqs. A6 and A7b) do not vanish, in which case:

$$\frac{m_{tb}}{m_{rb}} S_{np}(t \leftarrow tb) - \frac{m_t}{m_{rb}} S_{np}(t \leftarrow t) = \frac{\Delta_{np}}{m_{rb}} - \frac{\Delta_{np}}{2m_{rb}} = \frac{\Delta_{np}}{2m_{rb}}.$$

For this reason Eqs. A4 and A5 are not equivalent and:

$$S(t \leftarrow rb) = S_p(t \leftarrow rb) + \frac{\Delta_{np}}{2m_{rb}},$$

$$\text{i.e., } \tilde{A}_{rb} S(t \leftarrow rb) = \tilde{A}_{rb} S_p(t \leftarrow rb) + \tilde{A}_{rb} \frac{\Delta_{np}}{2m_{rb}}$$

Therefore Eq. A3, compared with Eq. A1, overestimates the dose by an amount equal to:

$$\tilde{A}_{rb} \frac{\Delta_{np}}{2m_{rb}}$$

Case 2. On the other hand let us take the case in which we would use Eq. A2—i.e., when the target organ is part of the remainder of the body. Eq. A3 may be written as:

$$\bar{D}_t = \sum_{s=s_1}^{s_n} \tilde{A}_s S_p(t \leftarrow s) + \tilde{A}_{rb} S(t \leftarrow rb) \quad \text{(A3c)}$$

Comparing Eq. A3c with Eq. A2, we can see that Eqs. A3 and A2 yield the same result only if we can demonstrate that:

$$\tilde{A}_{rb} S(t \leftarrow rb) = \tilde{A}_{rb} S_p(t \leftarrow rb) + \tilde{A}_{rb} \frac{m_t}{m_{rb}} S_{np}(t \leftarrow t)$$

$$\text{i.e., if } S(t \leftarrow rb) = S_p(t \leftarrow rb) + \frac{m_t}{m_{rb}} S_{np}(t \leftarrow t)$$

Then:

(a) when the target *is not* an organ with walls, according to Eq. A7a, we should have:

$$S(t \leftarrow rb) = S_p(t \leftarrow rb) + \frac{\Delta_{np}}{m_{rb}}; \text{ or}$$

(b) when the target *is* an organ with walls, according to Eq. A7b, we should have:

$$S(t \leftarrow rb) = S_p(t \leftarrow rb) + \frac{\Delta_{np}}{2m_{rb}}.$$

But in both cases:

$$S(t \leftarrow rb) = \frac{m_{tb}}{m_{rb}} S_p(t \leftarrow tb) + \frac{m_{tb}}{m_{rb}} S_{np}(t \leftarrow tb) - \sum_{s=s_1}^{s_n} \frac{m_s}{m_{rb}} S_p(t \leftarrow s) \quad \text{(A8)}$$

which, according to Eq. A6, may be written as

$$S(t \leftarrow rb) = \frac{m_{tb}}{m_{rb}} S_p(t \leftarrow tb) + \frac{\Delta_{np}}{m_{rb}} - \sum_{s=s_1}^{s_n} \frac{m_s}{m_{rb}} S_p(t \leftarrow s) \quad \text{(A8a)}$$

and

$$S_p(t \leftarrow rb) = \frac{m_{tb}}{m_{rb}} S_p(t \leftarrow tb) - \sum_{s=s_1}^{s_n} \frac{m_s}{m_{rb}} S_p(t \leftarrow s) \quad \text{(A9)}$$

Comparing Eq. A8a with Eq. A9, we can see that either in case (a) or in case (b) we have:

$$S(t \leftarrow rb) = S_p(t \leftarrow rb) + \frac{\Delta_{np}}{m_{rb}}$$

Therefore Eqs. A3 and A2 yield the same result only when the target is not an organ with walls; otherwise Eq. A3 will overestimate the dose by an amount equal to:

$$\tilde{A}_{rb}\left(\frac{\Delta_{np}}{m_{rb}} - \frac{\Delta_{np}}{2m_{rb}}\right) = \tilde{A}_{rb} \frac{\Delta_{np}}{2m_{rb}}$$

In conclusion, in the computation of an absorbed dose with the CAMIRD/II, we must always consider the target organ as a source organ, even when the exact value of its cumulated activity is not known. This value must then be estimated as:

$$\tilde{A}_t = \tilde{A}_{rb} \frac{m_t}{m_{rb}}$$

On the other hand, if the target organ is one with walls, and one is using either MIRD-S or doing a manual calculation with the "S" values tabulated by MIRD, the result for total dose must always be reduced by an amount:

$$\tilde{A}_{rb} \frac{\Delta_{np}}{2m_{rb}}.$$

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