ICRU REPORT 32

Methods of Assessment of Absorbed Dose in Clinical Use of Radionuclides

INTERNATIONAL COMMISSION
ON RADIATION UNITS
AND MEASUREMENTS

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INTERNATIONAL COMMISSION ON RADIATION UNITS AND MEASUREMENTS
7910 WOODMONT AVENUE
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U.S.A.

Preface

Scope of ICRU Activities

The International Commission on Radiation Units and Measurements (ICRU), since its inception in 1925, has had as its principal objective the development of internationally acceptable recommendations regarding:

(1) Quantities and units of radiation and radioactivity,

(2) Procedures suitable for the measurement and application of these quantities in clinical radiology and radiobiology,

(3) Physical data needed in the application of these procedures, the use of which tends to assure uniformity in reporting.

The Commission also considers and makes similar types of recommendations for the radiation protection field. In this connection, its work is carried out in close cooperation with the International Commission on Radiological Protection (ICRP).

Policy

The ICRU endeavors to collect and evaluate the latest data and information pertinent to the problems of radiation measurement and dosimetry and to recommend the most acceptable values and techniques for current use.

The Commission's recommendations are kept under continual review in order to keep abreast of the rapidly expanding uses of radiation.

The ICRU feels it is the responsibility of national organizations to introduce their own detailed technical procedures for the development and maintenance of standards. However, it urges that all countries adhere as closely as possible to the internationally recommended basic concepts of radiation quantities and units.

The Commission feels that its responsibility lies in developing a system of quantities and units having the widest possible range of applicability. Situations may arise from time to time when an expedient solution of a current problem may seem advisable. Generally speaking, however, the Commission feels that action based on expediency is inadvisable from a long-term viewpoint; it endeavors to base its decisions on the long-range advantages to be expected.

The ICRU invites and welcomes constructive comments and suggestions regarding its recommendations and reports. These may be transmitted to the Chairman.

Current Program

The Commission has divided its field of interest into twelve technical areas and has assigned one or more members of the Commission the responsibility for identification of potential topics for new ICRU activities in each area. A body of consultants has been constituted for each technical area to advise the Commission on the need for ICRU recommendations relating to the technical area and on the means for meeting an identified need. Each area is reviewed periodically by its sponsors and consultants. Recommendations of such groups for new reports are then reviewed by the Commission and a priority assigned. The Technical areas are:

Radiation Therapy
Radiation Diagnosis
Nuclear Medicine
Radiobiology
Radioactivity
Radiation Physics—X Rays, Gamma Rays and Electrons
Radiation Physics—Neutrons and Heavy Particles
Radiation Protection
Radiation Chemistry
Values of Factors—*W*, *S*, etc.
Theoretical Aspects
Quantities and Units

The actual preparation of ICRU reports is carried out by ICRU report committees. One or more Commission members serve as sponsors to each committee and provide close liaison with the Commission. The

currently active report committees are:

C_λ and C_E
Computer Uses in Radiotherapy
Definitions and Terminology for Computed Tomography
Dose Specification for Reporting Intracavitary and Interstitial Therapy
Dosimetry of Pulsed Radiation
Fundamental Quantities and Units
High-Energy Electron-Beam Dosimetry
Measurement of Low-Level Radioactivity in Humans
Microdosimetry
Photographic Dosimetry in External Beam Therapy
Scanning
Stopping Power

ICRU Reports

In 1962 the ICRU, in recognition of the fact that its triennial reports were becoming too extensive and in some cases too specialized to justify single-volume publication, initiated the publication of a series of reports, each dealing with a limited range of topics. This series was initiated with the publication of six reports:

ICRU Report 10a, *Radiation Quantities and Units*
ICRU Report 10b, *Physical Aspects of Irradiation*
ICRU Report 10c, *Radioactivity*
ICRU Report 10d, *Clinical Dosimetry*
ICRU Report 10e, *Radiobiological Dosimetry*
ICRU Report 10f, *Methods of Evaluating Radiological Equipment and Materials*

These reports were published, as had been many of the previous reports of the Commission, by the United States Government Printing Office as Handbooks of the National Bureau of Standards.

In 1967 the Commission determined that in the future the recommendations formulated by the ICRU would be published by the Commission itself. This report is published by the ICRU pursuant to this policy. With the exception of ICRU Reports 10a and 10e, the other reports of the "10" series have continuing validity and, since none of the reports now in preparation is designed specifically to supersede them, they will remain available until the material is essentially obsolete. All future reports of the Commission, however, will be published under the ICRU's own auspices. Information about the availability of ICRU Reports is given on page 59.

ICRU's Relationships With Other Organizations

In addition to its close relationship with the International Commission on Radiological Protection, the ICRU has developed relationships with other organizations interested in the problems of radiation quantities, units and measurements. Since 1955, the ICRU has had an official relationship with the World Health Organization (WHO) whereby the ICRU is looked to for primary guidance in matters of radiation units and measurements and, in turn, the WHO assists in the world-wide dissemination of the Commission's recommendations. In 1960 the ICRU entered into consultative status with the International Atomic Energy Agency. The Commission has a formal relationship with the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), whereby ICRU observers are invited to attend UNSCEAR meetings. The Commission and the International Organization for Standardization (ISO) informally exchange notifications of meetings and the ICRU is formally designated for liaison with two of the ISO Technical Committees. The ICRU also corresponds and exchanges final reports with the following organizations:

Bureau International des Poids et Mesures
Commission of the European Communities
Council for International Organizations of Medical Sciences
Food and Agriculture Organization
International Council of Scientific Unions
International Electrotechnical Commission
International Labor Office
International Radiation Protection Association
International Union of Pure and Applied Physics
United Nations Educational, Scientific and Cultural Organization

The Commission has found its relationship with all of these organizations fruitful and of substantial benefit to the ICRU program. Relations with these other international bodies do not affect the basic affiliation of the ICRU with the International Society of Radiology.

Operating Funds

In the early days of its existence, the ICRU operated essentially on a voluntary basis, with the travel and operating costs being borne by the parent organizations of the participants. (Only token assistance was originally available from the International Society of Radiology.) Recognizing the impracticability of continuing this mode of operation on an indefinite basis, operating funds were sought from various sources.

Financial support has been received from the following organizations:

B.A.T. Cigaretten-Fabriken GMBH
Commission of the European Communities
Council for International Organizations of Medical Sciences
Eastman Kodak Company
E. I. duPont de Nemours and Company
Ford Foundation
General Electric Company

International Atomic Energy Agency
International Radiation Protection Association
International Society of Radiology
Japan Industries Association of Radiation Apparatus
John och Augusta Perssons stiftelse
National Cancer Institute of the U.S. Department of Health, Education and Welfare
N. V. Philips Gloeilampenfabrieken
Picker Corporation
Radiological Society of North America
Rockefeller Foundation
Siemens Corporation
Society of Nuclear Medicine
Statens laegevidenskabelige Forskningsrad
U.S. Bureau of Radiological Health of the Food and Drug Administration

In recognition of the fact that its work is made possible by the generous support provided by these organizations, the Commission expresses its deep appreciation.

HAROLD O. WYCKOFF,
Chairman, ICRU

Washington, D.C.
1 March 1979

List of Symbols

A activity
A_0 administered activity
$A(t)$ activity at time t in tissue of interest
$\tilde{A}$ time integral of activity
$B_{en}(\mu x)$ energy absorption buildup factor at distance x
C activity per unit mass
$\tilde{C}$ time integral of activity per unit mass
D absorbed dose
$\overline{D}$ mean absorbed dose
D_{eq} absorbed dose under equilibrium conditions
$\dot{D}$ absorbed dose rate
E_i mean energy per particle of the i th type
F_m fraction of administered activity in the tissue of interest obtained by extrapolation of the decaying activity to zero time
$F(t)$ fraction of administered activity present in tissue of interest at time t
g geometric factor
k conversion factor for units
l number of half lives
m mass
n_i mean number of particles of i^{th} type per nuclear transformation of the parent nuclide
p point
q_j activity of j^{th} component corrected for decay to zero time
r region
r_1 target region
r_2 source region
s used as subscript to indicate summation (see p. 10)
R_{90} 90% absorption radius in water
t time
T physical half life
T_{eff} effective half life
$\overline{T}$ mean physical life
$\overline{T}_{eff}$ effective mean life
v volume
x distance
Z atomic number
Δ_i mean energy of radiation of i^{th} type per nuclear transformation of the parent nuclide
Γ exposure-rate constant
μ attenuation coefficient
λ physical decay constant
λ_j biological disappearance constant* of j^{th} component
μ_{en} energy-absorption coefficient
ρ mass density
γ life span of red cells
ϕ absorbed fraction
Φ specific absorbed fraction
$\Phi(x)$ point isotropic specific absorbed fraction at distance x

* The Medical Internal Radiation Dose (MIRD) Committee of the Society of Nuclear Medicine (USA) uses "biological disappearance constant" for this quantity but it is used both for "disappearance" and "accretion."

Contents

Methods of Assessment of Absorbed Dose in Clinical Use of Radionuclides

1. Introduction

This report is concerned with the methods of evaluating the absorbed dose received by the tissues of persons to whom radiopharmaceuticals are administered. Even though only one site in the body is the primary object of the investigation or treatment with a radiopharmaceutical, generally many tissues in the body are irradiated.

In diagnostic work, estimation of the absorbed dose delivered to particular organs and tissues for different possible techniques is needed to determine the presumed risk for each technique, in choosing between techniques, and, so far as practicable, in comparing risks attributable to the radiation with the possible benefits of the investigation. The procedures described in this report are now probably adequate for this purpose. The same procedures can be applied in estimating the absorbed dose in therapeutic applications, but in the present state of the art, one must be cautious in interpreting the results obtained; the techniques of therapy with radionuclides have often evolved empirically, guided only by approximate assessments of the dose delivered.

1.1 Need for Recommendations

Hitherto, reports of the International Commission on Radiation Units and Measurements (ICRU) have included detailed considerations of the dosimetry of x and γ-ray, neutron and electron beams, but not of radionuclides used systemically for medical purposes; the publication of a comprehensive report and recommendations on this topic now appears both necessary and timely. Factors which influenced both the decision to prepare such a report, and the form it has finally taken can be briefly summarized as follows:

(a) *Imaging procedures.* Radiopharmaceuticals are widely and increasingly used in routine medical diagnosis. In certain techniques, particularly in producing images of distributions of radioactivity by various types of equipment, it is necessary to accumulate as much data as possible in a comparatively short time during which the patient must remain immobile; in such procedures successful diagnosis is closely linked with the level of activity regarded as clinically acceptable and thus with the availability of satisfactory methods for carrying out calculations of the absorbed dose resulting from these procedures.

(b) *Types of radionuclide.* Many of the radionuclides now in diagnostic use decay by electron capture, or by isomeric transition from a metastable state and frequently the energy of the x and γ radiation emitted lies in the range 5–500 keV. Until a few years ago, comparatively little detailed consideration was given to the most appropriate methods of calculating absorbed dose from such radionuclides. The absorbed dose may be seriously underestimated if no allowance is made for the contributions from x rays and Auger and internal conversion electrons.

(c) *Biological data and clinical measurements.* The necessary calculations of absorbed dose can only be carried out if adequate data are available on the metabolism of the particular radiopharmaceutical used. Methods of securing such data from measurements on human subjects or in other ways present a number of difficult problems in radiation measurement; furthermore, recommendations are needed on the form in which such data are presented and the supporting evidence that should be made available.

(d) *Procedure in calculations of absorbed dose.* Several different methods of calculating absorbed dose, given the necessary biological data on the pattern of distribution of the radionuclide in the body, have been proposed and used. However, efforts have been made for some years to achieve unification of these methods; there is now a considerable literature based on a particular system which has proved both straightforward and flexible in use. This unified system has provided the basis for this report.

1.2 Structure of the Report

In the report, basic concepts and formulae are first set out in Section 2. This is followed in Section 3 by a critical account of the methods used in obtaining the biological data needed for calculations of dose. Section 4 summarizes the actual procedures recommended for the calculations. Although these procedures make it possible to carry out many of the calculations required, there are, nevertheless, limitations and difficulties which are noted in the concluding section of the report (Section 5). There are five appendices. These give: details of sources of information on the characteristics of radionuclides in medical use, together with convenient tables of data (Appendix A); a survey of the published work on absorbed fractions for γ rays, including appropriate graphical presentation of data (Appendix B); a series of examples of calculations of dose based upon the methods set out (Appendix C). It is not the function of this report to survey the results of calculations of radiation dose for particular radiopharmaceuticals, but each of the examples in Appendix C is intended to illustrate a specific type of problem. Comments on some of the problems raised in the dosimetry of radionuclides emitting Auger electrons and other low energy radiations appear in Appendix D, and sources of biological data in Appendix E.

1.3 Formalism and Physical Data

The methods recommended here for calculating absorbed dose from radionuclides distributed in the body are based on a formalism now widely adopted, in which all types of radiation are dealt with in a simple and consistent way, in contrast to some of the methods previously developed and still sometimes used, in which different procedures were applied to radiation of different types such as β-particles and photons. The most important general principles involved in this formalism are reviewed in Section 2. The practical use of the formalism is associated with extensive new data on the absorption of electromagnetic radiation and β-particles; these data cover point and distributed sources, a wide range of energies, and absorbing regions of varied dimensions under differing conditions of scattering from the surroundings. This work (Loevinger and Berman, 1968 a and b, 1976; Fisher and Snyder, 1968; Brownell *et al.*, 1968; Snyder, 1970; Snyder *et al.*, 1969; Reddy *et al.*, 1969) provides a basis for the calculation of absorbed dose for the radiation emitted by numerous radionuclides now used in medical diagnosis and therapy, free from some of the limitations and approximations involved in earlier methods. This work is still under development but extensive new data have already been published in tabular and graphical form which can be applied directly to the solution of many types of dose problems arising in the medical use of radionuclides. Section 2.5 relates the new methods to the pioneering work of Marinelli *et al.* (1948 a and b), Mayneord (1950) and others. The Medical Internal Radiation Dose (MIRD) Committee of the Society of Nuclear Medicine (USA) has been very active in this field over the past decade, and has published a number of reports. The general procedures for absorbed-dose calculation recommended in this ICRU report are based on principles similar to those followed by the MIRD Committee, which have already proved their value to workers in this field (see for example Husak, 1972).

1.4 Limitations in Scope of Report

(a) *Accuracy of biological data.* Although the mathematical procedures for calculating the absorbed dose from the physical and biological data available may be very refined, there are inherent limitations on the accuracy of the biological data. In consequence, notwithstanding refinement of the physical methods, there may be considerable uncertainty in the actual estimate of absorbed dose received.

(b) *Therapeutic applications.* This report is primarily concerned with the diagnostic applications of radionuclides. Although, in principle, the physical methods considered here apply generally to internally distributed radionuclides, one must note that in therapeutic applications (a) changes in kinetics may result from the effects of radiation; (b) one is concerned not with potential risks but with demonstrable effects on the individual patient; the comparison of average absorbed dose to body organs resulting from internally distributed radionuclides and external x radiation provides a partial basis for recommendations on maximum activities to be used in diagnostic procedures but may not be relevant in therapy; and (c) in setting up models it will generally be necessary to allow for the heterogeneity of tissues and of activity distributions. Clinically, success has been achieved, for example, in the treatment of thyroid disease with radioactive iodine, or of polycythemia vera with ^{32}P (Krauss and Wasserman, 1970), and valuable studies of dosimetry at these and other sites have been made (Gillespie *et al.*, 1970; Spiers *et al.*, 1976) but many problems of dosimetry are still unresolved. Some of the topics were considered in ICRP Publications 8 (1966a), 9 (1966b), and 14 (1969a).

1.5 Applications of the Report

The procedures, physical data and examples included in this report are intended to provide workers with radiopharmaceuticals with a convenient handbook for use

in carrying out absorbed-dose calculations. Such calculations can, of course, only be made if the biological data are available; it is hoped that many more users than at present will be encouraged to try to acquire such data by applying the methods discussed in Section 3 and will publish their findings.

2. Physical Concepts and Basic Formulae

2.1 Introduction

When considering the radiological protection of persons who may be exposed to radiation, it has been the practice to identify the organs or tissues which are likely to be most at risk in showing late biological effects. These organs or tissues have been called the critical organs. However, in this report we are concerned primarily with *methods* of estimating absorbed dose and we shall refer to particular *regions of interest* for which the dose is determined. In carrying out calculations of absorbed dose, such a region of interest is identified as a *target region*, while the radiation to which it is exposed will be said to originate from a particular *source region*. Target and source regions may overlap, or may coincide. These source and target regions will ordinarily be identified with particular tissues or organs.

In this report the term *particle* is used in the sense defined by ICRU (1971) for directly and indirectly ionizing particles.

The absorbed dose in a particular target region is determined by both the *physical* and the *biological* parameters; to carry out a calculation of the absorbed dose, the following data are required.

(a) the activity administered;
(b) the physical half-life of the radionuclide;
(c) the decay data for the radionuclide;
(d) the identity (and hence location), mass and shape of the target regions;
(e) the temporal and spatial distribution of activity in the source regions; and
(f) the fraction of the radiation energy emitted in the source region which is absorbed in the target region.

Data of types (a) to (c) involve only physical information relating to the radionuclide used, while (d) to (f) involve biological information.

Calculations of absorbed dose are broadly of two types, namely, those in which the biological information either (i) represents an average for some class or group of individuals, or (ii) has been derived from an administration of activity to a single individual. The former type of calculation may be based, for example, on biological data derived from investigations on many individuals and/or on work with experimental animals and will be used in predicting the absorbed dose to be expected in a clinical application. Calculations of the second type will apply to a particular individual or class of individuals and can only be made retrospectively. Regardless of which type of calculation is made, a *model* must first be adopted which incorporates data of types (d) and (e) above in a form simple enough to allow calculation but detailed enough to have biological significance. Using such a model, together with data of types (a), (b), (c), and (f), suitable tabulations may be made of data for dose calculation. The interpretation of the final result thus depends largely on a judgement of the validity of the model used for the calculation.

2.2 Basic Concepts

In order to illustrate the basic concepts, we consider first a radionuclide that decays with the emission of one type of particle only. The activity is assumed to be distributed in a source region, the size and shape of which need not be specified until an actual model calculation is undertaken. We seek an expression, valid for all types of radiation, for the absorbed dose in a target region which may or may not coincide with part or all of the source region. In the time interval of interest, the average energy absorbed per unit mass in the target region (assumed for the moment to be a volume), i.e., the mean absorbed dose, $\overline{D}$, is equal to the product of five terms:

(a) the number of nuclear transformations in the source region during the time interval of interest, $\tilde{A}$;
(b) the mean number of ionizing particles per nuclear transformation, n;
(c) the mean energy per particle, E;
(d) the fraction of the particle energy emitted by the source region and imparted to the target region, called the *absorbed fraction*, ϕ; and
(e) the reciprocal of the mass of the target region, m^{-1}.

The mean absorbed dose, $\overline{D}$, to the target region produced by the nuclear transformations in the source region during a particular time interval of interest may thus be expressed in the form:

$$\overline{D} = \tilde{A} n E \phi m^{-1} \qquad (2.2\text{-}1)$$

although, in general, absorbed dose varies from point to point within the target region. The product of n by E is simply the *mean energy emitted per nuclear transformation*, and is here represented by $\Delta = nE$. Likewise, the quotient of the absorbed fraction ϕ and the mass m is a useful quantity, given here the name *specific absorbed fraction* and represented by $\Phi = \phi/m$. Making these substitutions, the mean absorbed dose to the target region can be expressed in the form:

$$\overline{D} = \tilde{A} \Delta \Phi. \qquad (2.2\text{-}2)$$

It may be noted that, while Eq. (2.2-1) is limited to target regions that are finite volumes, Eq. (2.2-2) is more general, and applies to any target region. Neither equation contains any assumption about the size or shape of source or target regions, nor about the uniformity or extent of the source activity or the absorbing medium. In practice, however, it is almost always necessary to place limitations on the model to which the equations are applied, in order to obtain numerical values for the quantities.

The number of nuclear transformations during the relevant time interval is calculated using the model which must be set up to represent the anatomical and physiological conditions. A certain time course of variation of activity $A(t)$ in the source region will have been assumed in this model and the integral of this activity over the period of interest gives the total number of nuclear transformations $\tilde{A}$.

The mean energy emitted per nuclear transformation, Δ, is calculated from the decay data.

Values of the absorbed fraction, ϕ, and the specific absorbed fraction, Φ, have been calculated for various source and target regions, and are available in the form of tables and charts, some of which are included in this report (Appendix B). From these the appropriate values may be selected for the various radiations occurring in the decay scheme, and for the geometrical shapes and relationships specified in the model adopted. If absorbed fractions for the shapes chosen are not directly available, tables of specific absorbed fractions for point sources may be used. Presently available calculated values of absorbed fractions or specific absorbed fractions generally assume either a uniform distribution of the activity or a point source in a homogeneous absorbing medium and sometimes assume that there are no boundary effects.

The mass m of the target region is assumed as part of the model.

The Eq. (2.2-1) and (2.2-2) have been simplified in order to make clear the basic concepts behind the method of dose calculation being described. In order to cover the various situations which arise in practice, a

TABLE 2-1—*Principal quantities*[a] *with their symbols and SI units*[b]

Quantity	Symbol	SI Unit[c]
Quantities Involving Type of Radiation		
Mean energy per particle of the i^{th} type	E_i	kg Gy≡J
Mean number of particles of the i^{th} type per nuclear transformation of the parent nuclide	n_i	$Bq^{-1}s^{-1}\equiv 1$
Mean energy of radiation of the i^{th} type per nuclear transformation of the parent nuclide	Δ_i	kg Gy $Bq^{-1}s^{-1}$ ≡J $Bq^{-1}s^{-1}\equiv$J
Physical decay constant	λ	s^{-1}
Half-life	T	s
Mean life	$\overline{T}$	s
Quantities Involving Type of Radiation and Absorbing Material		
Point isotropic specific absorbed fraction at distance x	$\Phi(x)$	kg^{-1}
Point isotropic energy-absorption buildup factor	$B_{en}(\mu x)$	1
Linear energy-absorption coefficient	μ_{en}	m^{-1}
Linear attenuation coefficient	μ	m^{-1}
90% absorption radius in water	R_{90}	m
Quantities Involving Type of Radiation and Absorbing Material and Source and Target Regions		
Absorbed dose	D	Gy≡J kg^{-1}
Absorbed-dose rate	$\dot{D}$	Gy s^{-1}
Absorbed fraction	ϕ	1
Specific absorbed fraction	Φ	kg^{-1}
Quantities Characterizing Source and Target Regions		
Activity	A	Bq≡s^{-1}
Time integral of the activity	$\tilde{A}$	Bq s≡1
Biological disappearance constant of jth component	λ_j	s^{-1}
Activity of jth component corrected for decay to zero time.	q_j	Bq
Activity per unit mass	C	Bq kg^{-1}
Time integral of the activity per unit mass	$\tilde{C}$	Bq s $kg^{-1}\equiv kg^{-1}$
Mass	m	kg
Volume	v	m^3
Other Quantities		
Distance	x	m
Mass density	ρ	kg m^{-3}
Time	t	s

[a] See subsection 2.4 for definitions of quantities.

[b] The term *particle* is used to include photons, as recommended in ICRU Report 19 (ICRU, 1971). The subscript s is used to indicate a group of radiation types with similar absorption properties and for which the mean energy per nuclear transformation has been summed.

[c] The SI derived units with special names used in this table are the unit of energy, joule (J); the unit of absorbed dose, gray (Gy = J kg^{-1}); and the unit of activity, becquerel (Bq = s^{-1}).

somewhat more formal and elaborate approach is necessary, and is given in the following paragraphs.

2.3 Assumptions and Notation

The notation is explained in the text as it occurs, and so far as possible is consistent with current practice and recommendations of the ICRU. However, attention is called here to certain special features of the assumptions and notation.

In this report we are concerned particularly with the non-stochastic quantity absorbed dose, D, defined by ICRU (1971) and its mean value, $\overline{D}$. The word *model* is used to designate the total set of assumed conditions, spatial, structural and kinetic, for which an absorbed-dose calculation is to be made. An *infinite absorbing medium* is one so large that boundary effects can be neglected. The symbol r represents a *region,* which is a point, line, surface or volume. When the region considered is a *point* or *volume,* the symbols p and v are used. A *mean value* is indicated by a line over the symbol unless the symbol is defined as a *mean value* in the list of symbols, a dot denotes a *time derivative,* and a tilde a *time integral.*

In order to avoid ambiguity, a notation that specifies both source and target is convenient in the general formulae which follow. However, in actual calculations, notation can be simplified as appropriate. If both source and target are specified, the target should be written first, but if only one is specified it should be the target. Thus, in referring to specific absorbed fractions one would write $\Phi(r_1 \leftarrow r_2)$, where r_1 is the target and r_2 the source region, which can be read "the specific absorbed fraction in target region r_1 from source region r_2". If a quantity such as Φ depends symmetrically on the two regions, it is written in the form $\Phi(r_1 \leftrightarrow r_2)$ which can be read "the specific absorbed fraction in r_1 from r_2 or in r_2 from r_1". If the source and target are identical, the arrow is omitted, as for example $\Phi(v,v)$.

The symbols and units for the quantities used in this report are summarized in Table 2-1.

In the mathematical formalism for absorbed-dose computation presented here, the absorbed doses due to nuclear radiations are expressed in a common unit and added. When this is done, it is tacitly assumed that the radiation effects associated with the various nuclear radiations are additive and the total effect depends only on the total absorbed dose. For radiations not considered to be additive in this manner, or where there are significant differences in dose rates, the formalism can still be used, but the absorbed doses should be tabulated separately.

Under certain circumstances, attempts to calculate absorbed dose to a point, line or surface could lead to a divergent mathematical expression. While this would seldom if ever occur with models of interest in the medical use of radionuclides, two formal restrictions on the models are necessary to remove this mathematical complication: a target region that is a point, line or surface must be entirely contained within a volume inside which the mass density is everywhere finite and not zero; and there can be no point in common between a source and its target region unless either the source region, or the target region (or both) is a volume.

2.4 Formulae

2.4.1 Absorbed Dose under Equilibrium Conditions

Consider a radionuclide that gives rise to particles of types i = 1, 2, 3 . . . . . , the mean energy per particle being E_i and the mean number of particles per nuclear transformation n_i. The mean energy emitted per nuclear transformation as particles of type i is then

$$\Delta_i = k n_i E_i \qquad (2.4\text{-}1)$$

where the numerical factor k depends on the choice of units (see Section 2.4.7).

If the radionuclide is uniformly distributed in an infinite homogeneous absorbing material, the energy emitted per unit mass must be in equilibrium with the energy absorbed per unit mass. We can therefore define *absorbed dose under equilibrium conditions*

$$D_{eq} = \tilde{C} \sum_i \Delta_i \qquad (2.4\text{-}2)$$

where $\tilde{C} = \int C dt$ is the time integral of the activity per unit mass, integrated over the relevant time interval (which may extend to infinity) and $\sum_i \Delta_i$ is the total mean energy of ionizing radiation emitted per nuclear transformation. It should be noted that radioactive daughter products must be considered separately as their lifetime in the source region may differ from that of the parent.

2.4.2 Absorbed Fraction and Specific Absorbed Fraction

If a target region v has absorbed energy from activity in a source region r, *the absorbed fraction in v from r* is defined as the quotient of the absorbed energy imparted to target region v from source region r, and the energy, exclusive of rest energy, emitted in the source region. Annihilation radiation is included as gamma radiation emitted in the source. For i-type radiation this is written $\phi_i(v \leftarrow r)$. While this definition is general, applying to all types of nuclear radiations, the target region is by definition limited to a volume. (If the target region were a point, line or surface, the absorbed fraction would be zero.)

The *specific absorbed fraction* is defined as the absorbed fraction per unit mass of target, i.e.,

$$\Phi_i(v \leftarrow r) = \frac{\phi_i(v \leftarrow r)}{m_v}. \qquad (2.4\text{-}3)$$

It can be shown that Eq. (2.4-3) holds even for a vanishingly small target region v. As a result the specific absorbed fraction is not limited to volume targets, and may be written $\Phi_i(r_1 \leftarrow r_2)$, where r_1 is the target region and r_2 is the source region. These may be any two regions, subject only to the restrictions given at the end of Section 2.3.

If a target region is divided into a number of sub-regions, the absorbed fraction in that region is simply the sum of the absorbed fractions of the sub-regions, i.e.,

$$\phi_i = (\phi_1 + \phi_2 + \ldots\ldots\ldots)_i. \qquad (2.4\text{-}4)$$

The specific absorbed fraction of the target region is the weighted mean of the values for the sub-regions where the weighting factor is the mass of each sub-region, i.e.,

$$\Phi_i\left(=\frac{\phi_i}{m}\right) = \frac{(m_1\Phi_1 + m_2\Phi_2 + \ldots.)_i}{m_1 + m_2 + \ldots.} \qquad (2.4\text{-}5)$$

since $\Phi_1 = \phi_1/m_1$, etc. Equations (2.4-4) and (2.4-5) are useful when the region of interest can be represented by sub-regions of simple shape for which absorbed fractions or specific absorbed fractions are already tabulated.

The definitions of absorbed fraction and specific absorbed fraction, as well as equations (2.4-4) and (2.4-5) are quite general, in that they apply to all types of nuclear radiation, to any distribution of activity, and to any absorbing medium however distributed.

For a point source in an infinite, homogeneous medium, the specific absorbed fraction is a function of the distance x from the source point to the target point. It is then given the name *point isotropic specific absorbed fraction*, and is written $\Phi(x)$. The specific absorbed fraction between any target region and a point source is simply the mean of the values of $\Phi(x)$ (the point isotropic specific absorbed fraction from the point) in that region

$$\Phi(r \leftarrow p) = \overline{\Phi(x)}. \qquad (2.4\text{-}6)$$

Even more generally, the specific absorbed fraction in any region from a source in another region is simply the mean of the values of the point isotropic specific absorbed fraction for all pairs of points in the two regions, i.e.,

$$\Phi(r_1 \leftrightarrow r_2) = \overline{\Phi(x)}. \qquad (2.4\text{-}7)$$

Equations (2.4-6) and (2.4-7) are useful because the point isotropic specific absorbed fraction has been tabulated for various types and energies of radiation (Berger, 1968). As a result, it is often possible to estimate the specific absorbed fraction for an arbitrary region by carrying out the averaging process indicated in these equations, provided both source and target can be adequately represented as falling within an infinite, homogeneous medium. Sometimes only an approximate value is needed, and the average specific absorbed fraction is then readily evaluated by an elementary calculation, or simply by inspection (see Example 2, Appendix C).

When the target region is a volume, it is immaterial whether the absorbed fraction, ϕ, or the specific absorbed fraction, Φ, is used, because either can be converted to the other by means of Eq. (2.4-3). As tabulated values of these quantities are necessarily limited, it is almost always necessary to interpolate or extrapolate in order to get values for a particular model, and the choice between ϕ and Φ should be made to facilitate that step. The absorbed fraction, ϕ, will be more convenient under circumstances where $\phi \approx 1$, since it will not then be sensitive to changes in target size or shape. The specific absorbed fraction, Φ, will usually be more convenient under circumstances where $\phi \ll 1$, because the target is distant from the source and Φ will not then be sensitive to changes in target size or shape.

2.4.3 Reciprocity Theorem

A general reciprocity theorem is valid if the radionuclide is uniformly distributed in regions of an absorbing material that either (a) is infinite and homogeneous, or (b) absorbs the radiation without scatter. This theorem states that *for any pair of regions, the specific absorbed fraction is independent of which region is designated source and which is designated target.* In equation form this becomes

$$\Phi_i(r_1 \leftrightarrow r_2) = \Phi_i(r_1 \leftarrow r_2) = \Phi_i(r_2 \leftarrow r_1) \qquad (2.4\text{-}8)$$

where the double-ended arrow indicates that either region can be target or source. For two volumes, the reciprocity theorem can be expressed in the form:

$$\frac{\phi_i(v_1 \leftarrow v_2)}{m_1} = \frac{\phi_i(v_2 \leftarrow v_1)}{m_2}. \qquad (2.4\text{-}9)$$

For a volume and any other region, the reciprocity theorem can be given in the form:

$$\Phi_i(r \leftrightarrow v) = \frac{\phi_i(v \leftarrow r)}{m_v}. \qquad (2.4\text{-}10)$$

The reciprocity theorem, as expressed in equations (2.4-8) to (2.4-10) is independent of activity and absorbed dose, since the basis of the theorem is simply a symmetrical relationship between two regions, as regards radiation attenuation.

Since condition (b) above, the absorption of nuclear radiation without scatter, has little practical significance, application of the reciprocity theorem is generally based on condition (a), the assumption that both source

and target regions lie within and form part of an infinite homogeneous absorbing material. This means that, in principle, all boundary effects are excluded, but in practice it is generally not necessary to be highly rigorous in meeting this requirement for an "infinite" medium.

The reciprocity theorem has long been known (King, 1912; Mayneord, 1945) and has been stated in a variety of forms (Loevinger *et al.*, 1956a). The original derivations were in terms of a more limited model in which monoenergetic photons showed exponential attenuation, i.e., were absorbed without scatter.

2.4.4 Absorbed-Dose Equations

To obtain a general absorbed-dose equation, it is only necessary to write Eq. (2.2-2) in the general notation that has been developed here, and sum the result over the various radiations emitted by a radionuclide. The basic equation for the mean absorbed dose so obtained is:

$$\overline{D}(r_1 \leftarrow r_2) = \tilde{A}_2 \sum_i \Delta_i \Phi_i(r_1 \leftarrow r_2). \qquad (2.4\text{-}11)$$

If the reciprocity theorem is applicable (Loevinger and Berman, 1968a, 1968b and 1976; Loevinger, 1969), Eq. (2.4-8) may be applied. Equation (2.4-11) applies to all radionuclides, covering both charged particles and electromagnetic nuclear radiations, places no limitations on the size or shape of source or target regions, and does not imply any restrictions on the uniformity of the activity or the absorbing medium.

A very common and important practical case occurs if the target region, r_1 and the source region, r_2, are the same volume, v. Then the basic absorbed-dose equation takes on a simplified form, giving the mean "self-dose" to the volume, v:

$$\overline{D}(v,v) = \tilde{C}_v \sum_i \Delta_i \phi_i(v,v) \qquad (2.4\text{-}12)$$

since $\tilde{C}_v = \tilde{A}_v/m_v$ and $\phi_i = m_v \Phi_i$. The arrows are omitted from Eq. (2.4-12) since there is identity of source and target.

For another important case, the mean absorbed dose to a volume from a point, Eq. (2.4-11) may be expressed in the form:

$$\overline{D}(v \leftarrow p) = \frac{\tilde{A}_p}{m_v} \sum_i \Delta_i \phi_i(v,p). \qquad (2.4\text{-}13)$$

If the reciprocity theorem is assumed to be valid, the absorbed dose to a point from a volume is given by the equation

$$D(p \leftarrow v) = \tilde{C}_v \sum_i \Delta_i \phi_i(v,p). \qquad (2.4\text{-}14)$$

The arrows can be omitted from the right side of Eq. (2.4-13) and (2.4-14) since the absorbed fraction can only be defined for a target region that is a volume, but the arrows are still useful in the left side of these equations, to distinguish the two cases.

2.4.5 Conversion from Absorbed-Dose to Absorbed-Dose-Rate Equations

In the models used in calculations it is often assumed that the distribution of the activity in any region is constant except for a factor that is a function of time. Then ϕ_i and Φ are independent of time, and the Eq. (2.2-1), (2.2-2), (2.4-2), and (2.4-11) to (2.4-14) have only one quantity on each side of the equality sign which is a function of time. As a result, the equations can be converted from dose to dose-rate equations by substituting the symbols $\dot{D}$, A, and C for symbols D, $\tilde{A}$, and $\tilde{C}$.

2.4.6 Time Dependence of Source Activity

To simplify the discussion of time dependence, only the activity $A(t)$ is used in this paragraph, but an exactly analogous description can be given for the activity per unit mass $C(t)$.

If the activity $A(t)$ is known as a function of time, it must be integrated over the relevant time interval to give $\tilde{A}$. This integration may be performed graphically, numerically or analytically. Without implying any special functional form for $A(t)$, it is often convenient and sufficiently accurate for purposes of dosimetry, to represent the function $A(t)$ as a sum of exponentials, in the form:

$$A(t) = \exp(-\lambda t) \sum_j q_j \exp(-\lambda_j t) \qquad (2.4\text{-}15)$$

where q_j is the value of the j^{th} component of $A(0)$, λ is the physical decay constant of the radionuclide, and λ_j is the biological disappearance constant of the j^{th} component. Many variations can, of course, arise in the formulation of the appropriate equation, as, for example, if the period of uptake is significant in comparison with the period of clearance or physical half-life; reference can be made to texts on compartment analysis for further details, e.g., Sheppard (1962); AEC (1967).

The value of $\tilde{A}$ for the time interval t is given by:

$$\tilde{A}(t) = \sum_j \frac{q_j}{\lambda + \lambda_j} (1 - \exp(-(\lambda + \lambda_j)t)) \qquad (2.4\text{-}16)$$

and for complete decay

$$\tilde{A} = \sum_j \frac{q_j}{\lambda + \lambda_j}. \qquad (2.4\text{-}17)$$

For convenience in calculation, Eq. (2.4-15), (2.4-16), and (2.4-17) are often written in terms of mean lives or half-lives, instead of decay constants. This is readily done by using the following substitutions. The physical mean life $\overline{T}$ and the physical half-life T are:

$$\overline{T} = 1/\lambda \text{ and } T = (\ln 2)/\lambda. \qquad (2.4\text{-}18)$$

The biological mean life and biological half-life for the j^{th} component are:

$$\overline{T}_j = 1/\lambda_j \text{ and } T_j = (\ln 2)/\lambda_j. \qquad (2.4\text{-}19)$$

The effective mean life and effective half-life of the j^{th} component are:

$$\overline{T}_{j,eff} = 1/(\lambda + \lambda_j) \text{ and } T_{j,eff} = (\ln 2)/(\lambda + \lambda_j) \quad (2.4\text{-}20)$$

where $\ln 2 \approx 0.693 \approx 1/1.443$.

From Eq. (2.4-18), (2.4-19), and (2.4-20) there follow at once the well-known relationships between the mean lives and between the half-lives:

$$\overline{T}_{j,eff}^{-1} = \overline{T}^{-1} + \overline{T}_j^{-1} \text{ and } T_{j,eff}^{-1} = T^{-1} + T_j^{-1}. \quad (2.4\text{-}21)$$

It is often convenient to write Eq. (2.4-15) and (2.4-16) in terms of exponential functions to the base 2, using the relationship:

$$\exp(-\lambda t) = 2^{l} \quad (2.4\text{-}22)$$

where the number of half-lives that have elapsed is $l = t/T$. The elapsed time and the half-lives may be expressed in any units provided that numerator and denominator are in the same unit for ratios of the form t/T, etc.

If $A(t)$ can be adequately represented by a single exponential, then it can be characterized by a single effective mean life, $\overline{T}_{eff}$, calculated from Eq. (2.4-20) or (2.4-21).

2.4.7 Conversion of Units

All of the equations used in this report are valid for any self-consistent set of units, and only the numerical factor k in Eq. (2.4-1) depends on the choice of units.

The units of the modernized metric system known as Le Système International d'Unites (SI) (see, e.g., ICRU, 1971) form a coherent set, and the numerical factor k in Eq. (2.4-1) has the value unity. Thus, the mean energy of the i^{th} type per nuclear transformation is

$$\Delta_i = n_i E_i \quad (2.4\text{-}23)$$

when all quantities are expressed in SI units, as given in Table 2-1. The simplicity of this relationship illustrates an important advantage of SI units, which are recommended for use unless a strong reason exists for making another choice.

It is common practice to tabulate the energies of nuclear particles in some multiple of the electron volt, and that unit has been accepted for use with SI units (see, NPL, 1977; NBS, 1977). Then the mean energy of the i^{th} type per nuclear transformation becomes

$$\Delta_i = 1.602 \times 10^{-13} n_i E_i. \quad (2.4\text{-}24)$$

In Eq. (2.4-24) Δ_i is in joules and E_i in MeV. This is the appropriate value of Δ_i when all quantities are given in SI units except for the mean energy per particle E_i.

Another system of units, still commonly found in laboratory practice, but scheduled for replacement by SI makes use of

absorbed dose D in	rad
activity A in	μCi
mean energy per particle E_i in	MeV
time t in	h
mass m in	g.

For this system of units, the mean energy of the i^{th} type per nuclear transformation now becomes the mean energy of the i^{th} type per unit time integral of activity and

$$\Delta_i = 2.13 n_i E_i. \quad (2.4\text{-}25)$$

where Δ_i is in g rad μCi^{-1} h^{-1} and E_i is in MeV. This is the appropriate value of Δ_i when all quantities are given in the units enumerated above.

For Eq. (2.4-24) and (2.4-25) the numerical values of k [Eq. (2.4-1)] are calculated from the following relationships:

$1 \text{ MeV} = 1.602 \times 10^{-13} \text{ J}$
$1 \text{ kg rad} = 10^{-2} \text{ J}$
$1 \text{ g} = 10^{-3} \text{ kg}$
$1 \mu\text{Ci} = 3.7 \times 10^{4} \text{ s}^{-1} = 3.7 \times 10^{4} \text{ Bq}$
$1 \text{ h} = 3.6 \times 10^{3} \text{ s}.$

In Appendix C one of the examples is given both in SI and traditional units.

2.4.8 Penetrating and Nonpenetrating Radiations

In general, a radionuclide gives rise to a number of types and energies of nuclear radiations, that are designated by the subscript i = 1, 2, 3 . . . in the equations of this report. For many of these radiations the calculation of absorbed dose requires information on the spatial distribution of energy transport from the source region. The energy of other nuclear radiations, however, is absorbed within distances so short that it is sometimes appropriate to consider such energy as absorbed within the source, and as a result it is unneccessary to obtain information on the spatial distribution of the imparted energy. As a result, it is frequently convenient to classify nuclear radiations as either *penetrating* or *nonpenetrating*, depending on the penetrating properties of that particular radiation relative to the dimensions of the source region. The classification is not made by the type of particle alone, but by the size and shape of the source as well as the type and energy of the particles and the use to which the dose calculation will be put.

The term *nonpenetrating* is applied to those radiations which impart outside a source volume such a small fraction of their energy that it can be neglected in calculating the mean absorbed dose to the volume. For such radiations the mean self-dose to a source volume is calculated from the total energy emitted within the source. For all nonpenetrating radiations: