

# Concepts of Microdosimetry\*

## I. Quantities

A. M. Kellerer and D. Chmelevsky\*\*

Department of Radiology, Radiological Research Laboratory,  
College of Physicians and Surgeons, Columbia University, New York

Received February 28, 1975

*Summary.* This is the first part of an investigation of microdosimetric concepts relevant to numerical calculations. The definitions of the microdosimetric quantities are reviewed and formalized, and some additional conventions are adopted. The common interpretation of the quantities in terms of energy imparted to spherical sites is contrasted with their interpretation as the result of a diffusion process applied to the initial spatial pattern of energy transfers in the irradiated medium.

### Introduction

Fluctuations of energy deposition on a microdosimetric scale have long been one of the major topics of radiation biology. These fluctuations have been dealt with in crude form in the early target and hit theories and in more sophisticated manner in Lea's classic treatise [5]. A systematic treatment has become possible after Rossi and his co-workers introduced and developed the concepts of microdosimetry [1, 4, 9—15]. In recent years the application of microdosimetry to radiation biology has grown and the quantities specific energy,  $z$ , and lineal energy,  $y$ , *i.e.* the statistical variables which correspond to absorbed dose and to LET, are now included in the list of basic radiation quantities defined by ICRU [3].

Microdosimetric techniques are well established for tissue regions with diameters of the order of  $1\ \mu\text{m}$ , and the experimental data are in good agreement with calculations. With existing microdosimetric equipment it is, however, not possible to obtain results for regions much smaller than  $1\ \mu\text{m}$ . For this reason we have begun to derive such results theoretically. The method adopted for this purpose is the calculation of microdosimetric data from charged particle tracks generated by Monte Carlo methods [6—8]. Calculations of this type require not only numerical procedures, they give rise also to questions concerning the definition and interpretation of microdosimetric quantities. Such questions will be dealt with in the following.

The first problem one encounters is that it is not always obvious whether the amount of energy deposited or the number of ions produced in very small regions

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\* This investigation was supported by Contract AT (11-1) 3243 from the United States Atomic Energy Commission and Public Health Service Research Grants No. CA 12536 and CA 15307 from the National Cancer Institute.

\*\* Present address: Centre d'Études Nucléaires, DPr/Sps, Fontenay-aux-Roses, France

are meaningful quantities. For larger regions the situation is less complicated because the energies imparted to such regions are usually large in the sense that the number of ionizations produced multiplied by the  $W$ -value is a good approximation to the energy imparted. In fact, most microdosimetric experiments are based on the collection of ionizations, but the results are commonly given in terms of imparted energy. It is doubtful whether such simplified treatment is appropriate for very small regions which may contain only one or a few electronic alterations after being traversed by a charged particle. Therefore, a conceptual framework is desirable which discriminates between the various quantities which may be measured or computed.

A rigorous theoretical treatment is required not only for conceptual reasons but also for the computational procedures. In the experimental approach one obtains certain quantities by direct measurement, and one may disregard the complex intermediary factors which determine these quantities. The computational approach necessitates a more complete description; the present inquiry is concerned with such a description. The treatment is not conceived as an introduction to microdosimetry or to its radiobiological applications. Familiarity with the original publications [1, 9—12, 15] or with review articles which lead from the concrete to the more abstract notions [2, 13, 14,] will therefore be helpful.

The present investigation deals not with numerical data for various types of radiation but with the mathematical background relevant to the derivation of such data. In the analysis one can adopt two different, although essentially equivalent, points of view. One may either consider the distribution of energy increments in one repeatedly exposed microscopic region, or one may analyse the spatial profile of energy density in an extended medium. The latter possibility, which is implied in some of Lea's methods [5], has been discussed by Rossi [13] but is not usually invoked in the definition of microdosimetric quantities. However, it has proved valuable in numerical calculations, and has led to some notable relations between the microdosimetric distributions and their mean values. These findings will be presented in the following survey of the microdosimetric quantities, their distributions, and their mean values. This first part of the inquiry deals with the definition and interpretation of the quantities.

### The Established Definitions

The basic microdosimetric quantities are the energy imparted,  $\epsilon$ , the specific energy,  $z$ , and the lineal energy,  $y$ . In this section the existing definitions will be reviewed and a few additional conventions will be adopted. In the following section the quantities will be reconsidered from a somewhat different point of view.

Since the quantities are closely linked, it is merely a matter of convenience whether in a given situation one uses  $\epsilon$ ,  $z$ , or  $y$ . An additional quantity is the number,  $n$ , of ionizations produced in the region of interest. This quantity must be considered because it is the one commonly measured. Moreover it is an open question whether cellular effects are more closely related to the energy imparted or to the number of ionizations produced.

ICRU [3] gives the following definition of the random variable  $\epsilon$ :

The stochastic quantity energy imparted,  $\epsilon$ , by ionizing radiation to the matter in a volume is:

$$\epsilon = \sum \epsilon_{\text{in}} - \sum \epsilon_{\text{ex}} + \sum Q, \quad (1)$$

where

$\sum \epsilon_{\text{in}}$  = the sum of the energies (excluding rest energies) of all those directly and indirectly ionizing particles which have entered the volume,

$\sum \epsilon_{\text{ex}}$  = the sum of the energies (excluding rest energies) of all those directly and indirectly ionizing particles which have left the volume, and

$\sum Q$  = the sum of all the energies released, minus the sum of all the energies expended, in any transformations of nuclei and elementary particles which have occurred within the volume.

The related quantity specific energy,  $z$ , is defined in the same document as the ratio of  $\epsilon$  to the mass,  $m$ , in the volume of reference. The lineal energy,  $y$ , is defined as the ratio of  $\epsilon$  to the mean chord length,  $\bar{l}$ , in the volume of interest. The quantity  $y$  is restricted to individual events, *i.e.* to energy deposition in the volume due to a primary particle and/or its secondaries.

The definition of  $\epsilon$  may appear incomplete insofar as it does not explicitly state the energy levels below which charged or uncharged particles are no longer considered as ionizing. However, the numerical values of these levels do not affect the meaning of the quantity. Another possible objection against the definition is that it may not, even in principle, be possible to localize the energy transfers in the exposed medium with absolute precision. The volumes which will be considered in this and the following articles are, however, always sufficiently large so that such difficulties, which may be connected with quantum mechanical uncertainty, can be disregarded. It will be assumed that the imparted energy is localized in the exposed medium in such a way that a value of  $\epsilon$  can be assigned to any specified volume.

A similar assumption will be made regarding the number of ionizations,  $n$ , in a region. It will be postulated that the concept of ionization is clearly defined even in a condensed medium and that the ionizations have, at least in principle, precise coordinates. Even if one disregards the characteristic differences between gases and condensed media, there will always be inaccuracies in experimental determinations of  $n$  due to the diffusion of ions away from their points of formation; however one can at least reduce this error by considering positive instead of negative ions whenever one deals with regions sufficiently small that diffusion becomes important.

The quantities  $\epsilon$ ,  $z$ ,  $y$ , or  $n$  refer to regions of specified shape and size. In the following, spherical regions will be considered if not otherwise stated. Furthermore it will be assumed that one deals with uniform and isotropic radiation fields in a uniform medium. This means that one is concerned only with those microscopic fluctuations which are due to the discrete nature of the radiation field and its interaction with matter. Moreover, the temporal distribution of energy deposition will be disregarded; it will be assumed that a specified absorbed dose is delivered instantaneously.

The microdosimetric quantities and their distributions will in the following be examined from a somewhat more general standpoint than usually adopted. This requires some additional conventions.

The quantities are defined on extended regions rather than on points. It will however be more convenient to consider them as functions defined on points throughout the irradiated medium. This presents no difficulties if the reference regions are spheres. For a specified sphere radius,  $r$ , one assigns those values  $\epsilon$ ,  $z$ ,  $y$ , and  $n$  to a point which apply to the sphere of radius  $r$  centered around the point. Although this is merely a convention, it will simplify the formalism and clarify terminology.

The quantities depend on the parameter  $r$  and are functions of the position  $\mathbf{x}$  in the exposed medium<sup>1</sup>. Accordingly an explicit notation such as  $\epsilon_r(\mathbf{x})$  or  $z_r(\mathbf{x})$  may be employed whenever this is necessary in the interest of clarity; otherwise the index  $r$  or the argument  $\mathbf{x}$  can be omitted. The random variables depend also on absorbed dose  $D$ , and  $D$  may therefore be inserted as an additional argument. Many theoretical considerations in microdosimetry deal however with energy deposition in individual events. In this case the absorbed dose need not be considered.

### Alternative Interpretation of the Microdosimetric Quantities

The variables  $\epsilon$  and  $z$  are defined in terms of the energy imparted to a specific region in the exposed medium; consequently  $z$  is an average concentration of energy over such a volume. One can, however, take a different view [13] and consider  $z$  as an actual concentration at individual points throughout the medium which results from a dissipation process applied to the original spatial distribution of imparted energy<sup>2</sup>. Assume that energy is imparted to the irradiated medium at discrete points,  $T_i$ . These points will be called *transfer* points. Let  $\epsilon_i$  be the energy increments<sup>3</sup> which have been imparted at the transfer points  $T_i$ . If each of these *energy transfers*,  $\epsilon_i$ , is dissipated uniformly over a sphere of radius  $r$  centered at the corresponding transfer point, then the resulting concentration at *any* point,  $P$ , throughout the medium is numerically equal to the function  $z_r$  defined in terms of the energy content of spherical sites of radius  $r$  around the point  $P$ .

This double interpretation of  $z$  suggests that the microdosimetric quantities can not only be invoked when one deals with geometrically defined sensitive sites in the irradiated material, but that they equally apply to situations where radiation products diffuse in a homogeneous medium before they interact. In the following the expression local concentration will somewhat loosely be used to refer to  $z$

<sup>1</sup> For brevity  $\mathbf{x}$  is written for the co-ordinates  $(x_1, x_2, x_3)$ . In the context of numerical calculations where this could lead to confusion the co-ordinates will be given explicitly.

<sup>2</sup> The term *energy imparted* will be restricted to  $\epsilon_r$ , i.e. it refers to a region of radius  $r$ . The term *imparted energy* will be used in the general sense of deposited or absorbed energy in the exposed medium.

<sup>3</sup> Formally  $\epsilon_i$  can be defined as the difference between the loss of kinetic energy of the incoming ionizing particle due to a collision at the point  $T_i$  and kinetic energy of the ionizing particles released in this collision. — An even shorter definition is that  $\epsilon_i$  is the limit value of  $\epsilon_r$  at the point  $T_i$  as  $r$  goes to zero.

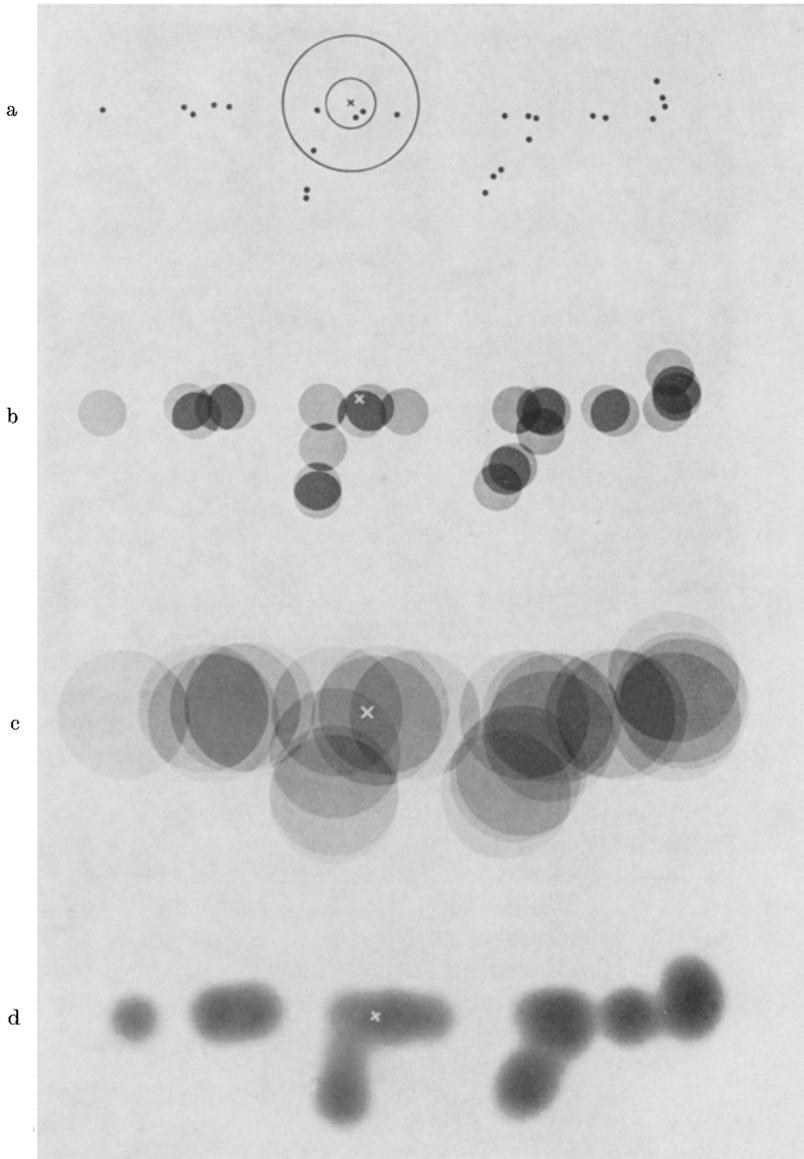


Fig. 1. Schematic diagram of a microscopic pattern of energy deposition. a) The inchoate distribution. The transfer points,  $T_i$ , are represented by dots. The cross represents a randomly chosen reference point, the circles spherical sites of two different radii around this point. b) The distribution of local concentration which results from a dissipation corresponding to the smaller radius. c) The distribution of local concentration which results from a dissipation corresponding to the larger radius. d) The blurred distribution of local concentration resulting from a more realistic diffusion process

in this interpretation. This is in analogy to the term local energy density which had been used when the quantity  $z$  was originally introduced [15]. However, the word energy is omitted in the present context to indicate that the concept refers not necessarily to a dissipation of the imparted energy due to energy transport in the true sense, it applies equally to diffusion of free radicals or other radiation-induced chemical species, or to intracellular movement of sublesions. A condition for the applicability of the concept is merely that these radiation products are proportional to the imparted energy.

Fig. 1 is a two-dimensional representation of the distribution of imparted energy in an exposed medium. In Fig. 1a a pattern of points is given which stands for the transfer points, *i.e.* for ionizations or excitations. The energy imparted,  $\epsilon_r$ , at a point,  $P$ , chosen at random in the medium is equal to the sum of all transfers,  $\epsilon_i$ , belonging to those transfer points which lie inside the sphere of radius  $r$  around  $P$ . One randomly chosen reference point,  $P$ , is indicated in Fig. 1a by a small cross, and spheres around  $P$  are symbolized by two circles of different radii,  $r$ . In this example the energy imparted for the smaller radius is the sum of the 2 transfers contained in the smaller sphere, while the energy imparted for the larger radius is the sum of the 5 transfers contained in the larger sphere. The specific energy is the sum of the transfers inside the region divided by the mass of the region.

If instead of energy imparted one considers the number of ionizations, and if for this purpose it is assumed that all the points in the pattern of Fig. 1a symbolize ionizations, the value of the variable,  $n_r$ , for the smaller radius is 2 and for the larger radius 5. This example corresponds to the situation in microdosimetric measurements with spherical proportional counters.

Figs. 1b and 1c illustrate the alternative interpretation. Here the discs indicate the spheres of energy dissipation around the transfer points. At the reference point,  $P$ , which is again symbolized by a small cross the value of the quantity energy imparted is the sum of the individual overlaps at this point weighed by the corresponding transfers,  $\epsilon_i$ . The specific energy is obtained if one weighs each overlap by  $\epsilon_i/m$ , where  $m$  is the mass of the sphere of dissipation. If all transfer points are assumed to be ionizations, then the value of  $n_r$  at the reference point is equal to the multiplicity of overlaps at this point. In agreement with the conclusion from Fig. 1a this is 2 for the smaller radius (see Fig. 1b) and 5 for the larger radius (see Fig. 1c).

The total volume represented by the spheres in Figs. 1b and 1c resembles the structure which Lea has termed associated volume [5]. In fact, it is identical to Lea's associated volume if one considers ionizations only. Since a term which designates the total volume covered by the spheres in Figs. 1b and 1c is desirable, the word associated volume will also be used in the more general sense. Whether the term is used in the more narrow sense of Lea's definition or in the general sense, will be understood from the context.

Lea [5], among others, has observed that in the cell one may deal not with well-defined sensitive sites but with "diffuse" targets. Similarly it may be more realistic to consider a dissipation process which results in a blurred distribution rather than a uniform distribution over a sphere. Such a blurred distribution is symbolized in Fig. 1d; it will be further considered in the next section.

### Formalization of the Definitions

The relations between the discrete increments  $\varepsilon_i$  at the transfer points,  $T_i$ , and the variables  $\varepsilon_r$  and  $z_r$  can be formalized in the following way: Let  $h(x)$  be what might either be called a dissipation function or a radial profile of the reference site:

$$h(x) = \begin{cases} 1/V_r & \text{for } x \leq r \\ 0 & \text{for } x > r, \end{cases} \quad (2)$$

where  $V_r = 4/3 \pi r^3$  is the volume of the sphere of radius  $r$ .

Then the specific energy,  $z_r(\mathbf{x})$ , at a point in the medium with the coordinate vector  $\mathbf{x}$  is:

$$z_r(\mathbf{x}) = \frac{1}{\varrho} \sum_i \varepsilon_i h(|\mathbf{x} - \mathbf{x}_i|); \quad (3)$$

$\varrho$  is the density of the irradiated medium,  $\mathbf{x}_i$  stands for the coordinate vector of the transfer point  $T_i$ . The summation extends over all transfer points.

It is readily seen that the equation agrees equally with the interpretation in terms of geometrically defined sites or in terms of a dissipation process over spherical regions. The corresponding relations for  $\varepsilon_r(\mathbf{x})$ ,  $y_r(\mathbf{x})$  or  $n_r(\mathbf{x})$  involve analogous expressions and need therefore not be spelled out.

The increments,  $\varepsilon_i$ , of imparted energy together with the coordinates of the transfer points,  $T_i$ , represent the original spatial pattern of imparted energies which results solely from the energy transport and transfer by ionizing particles. This spatial distribution which exists prior to any subsequent dissipation processes (see Fig. 1 a) will in the following be termed *inchoate* distribution.

From Eqs. (2) and (3) it is apparent how the definitions of the microdosimetric quantities have to be modified to apply to sites without sharp boundaries or to a realistic diffusion process which leads to a blurred distribution. The modification consists in choosing an appropriate form of the function  $h(x)$ . The most obvious choice is a Gaussian distribution:

$$h(x) = e^{-x^2/r^2}/V, \quad (4)$$

where the normalization factor

$$V = \int_0^\infty 4 \pi x^2 e^{-x^2/r^2} dx = \pi^{3/2} r^3 \quad (5)$$

can be considered as an effective volume of the diffuse site or of the domain of dissipation.

With this definition one obtains the following relation instead of Eq. (3):

$$z_r(\mathbf{x}) = \frac{1}{\varrho V} \sum_i \varepsilon_i e^{-(x-x_i)^2/r^2}. \quad (6)$$

The usual assumption in microdosimetry of a step function for  $h(x)$  will in the following be called the sharp boundary model, the assumption of a Gaussian  $h(x)$  will be termed the blurred boundary model. In a later section certain mean values of the specific energy will be considered which are relevant to radiobiology. It will be seen that the mean values of  $z$  in the sharp boundary and the blurred boundary model are closely related. This will be taken as an indication that it is usually sufficient to use the simple step function in Eq. (3). However, a second

conclusion is equally relevant, namely that it is not always essential in microdosimetric measurements to measure the ionization in regions with sharp boundaries. Somewhat diffuse boundaries, as they are unavoidable with wall-less proportional counters, will not necessarily invalidate the results.

The following part of this investigation will deal with the definition and interpretation of microdosimetric distributions.

*Acknowledgement.* We are indebted to Dr. Harald H. Rossi for numerous discussions and helpful suggestions.

### Appendix

The description of the inchoate distribution in terms of the transfers  $\varepsilon_i$  together with the coordinates of the transfer points,  $T_i$ , is limited insofar as it can not represent continuous energy loss processes of charged particles. While such processes, if they indeed exist, may be of little practical significance, it is still desirable to admit them in a generalized concept. For this purpose one can introduce the inchoate energy density,  $z_0(\mathbf{x})$ :

$$z_0(\mathbf{x}) = \frac{1}{\varrho} \sum_i \varepsilon_i \delta(|\mathbf{x} - \mathbf{x}_i|), \quad (\text{A.1})$$

where  $\varrho$  is the density of the irradiated medium. The summation extends again over all transfer points, and  $\delta(|\mathbf{x} - \mathbf{x}_i|)$  is the delta-function with the property that its volume integral is equal to unity:

$$\int_V \delta(|\mathbf{x} - \mathbf{x}_i|) d\mathbf{x} = 1, \quad (\text{A.2})$$

where  $V$  is any volume which contains the point with the coordinate  $\mathbf{x}_i$ . The index 0 in  $z_0(\mathbf{x})$  indicates that this inchoate density is the limit of  $z_r(\mathbf{x})$  as the radius,  $r$ , approaches zero.

Continuous energy loss processes, when they occur, are automatically accounted for if  $z_0(\mathbf{x})$  is defined not in terms of Eq. (A.1) but as the limit of  $z_r(\mathbf{x})$ :

$$z_0(\mathbf{x}) = \lim_{r \rightarrow 0} z_r(\mathbf{x}). \quad (\text{A.3})$$

If one uses the inchoate density  $z_0(\mathbf{x})$ , Eq. (3) is replaced by:

$$z_r(\mathbf{x}) = \int_{\mathbf{x}'} h(|\mathbf{x} - \mathbf{x}'|) z_0(\mathbf{x}') d\mathbf{x}', \quad (\text{A.4})$$

where the integration extends over the surrounding of  $\mathbf{x}$  that contributes to the integral.

In practice Eqs. (3) and (A.4) are equivalent; it will be sufficient to use Eq. (3) in numerical computations.

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Dr. Albrecht M. Kellerer  
Radiological Research Laboratory  
630 West 168th Street  
New York N.Y. 10032  
U.S.A.