Comments on "An Assessment of the Role of Microdosimetry in Radiobiology"


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Dr. Goodhead proposes to give in his review "a perspective of the evolving role of microdosimetry in the study of radiation effects in mammalian cells," but he also states his intention to "confine this paper to the earlier more narrow usage," i.e., the site concept. A treatment that focuses on a first step that was presented more than a decade ago hardly provides a perspective on a developing theory.

In our original paper (1) we primarily treated the site model but pointed out that it was an approximation to the more general distance model. Like any approximation it has limited validity, and it should not be applied when energy deposition in a site is grossly nonuniform. In the meantime and concurrently with designing the molecular (associated) ion experiment, we did develop the generalized version (the distance model).

However, in dealing with these and various other issues major mistakes and misconceptions are propagated which are enumerated below. Items (1) and (2) reflect lack of familiarity with experimental microdosimetry; (3) is a misconception relating to an elementary application of microdosimetry to radiobiology; (4) is a misrepresentation of the essence of our theory; (5) is an incorrect definition of a function basic to Dr. Goodhead’s argument; (6) is an erroneous specification of the nature of this function; (7) and (8) equate the theory of dual radiation action with the site model approximation, and specifically, (8) purports to show disagreement of experimental results with the theory when it is misapplied in the form of an unsuitable approximation; (9) implies that the theory of dual radiation action supports the "linear hypothesis" of dose–effect relations in radiological protection. Apart from being based on faulty reasoning this is diametrically opposed to our position.

(1) On p. 49, in the discussion of the proportional counter: "The chamber is filled with gas at a sufficiently low pressure so that the enclosed mass of gas is the same as that of a small sphere of tissue (of say 1 μm diam.)." The mass of the gas exceeds the mass of the equivalent tissue sphere by a factor of $10^8$ to $10^{10}$.

(2) Footnote (4) to the same paragraph is also erroneous; the principal reason why

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proportional counters cannot be used at low pressures is the impossibility of achieving sufficient and uniform multiplication in the counter volume; this is the case for all types of radiation.

(3) On p. 51: "If the probability of the biological effect increases exactly proportionally to the energy deposited in the simulated tissue volume, then the frequency mean should be appropriate." This is a wrong analogy to the correct statement in the subsequent sentence. The microdistribution of energy imparted would be irrelevant if effects were to be proportional to energy imparted, and a linear dose–effect relation independent of radiation quality would have to result. The frequency mean is relevant under the entirely different condition that any energy deposition regardless of its magnitude can bring about the effect.

(4) On the bottom of p. 51 it is stated as an assumption of the theory of dual radiation action that "... the shape of the dose–effect relationship for a given biological effect is not modified by any subsequent biological processes. ..." It has been one of the main points of the theory that a variety of complex biological factors can enter into the dose–effect relation, and this has been the very reason to emphasize the study of RBE–dose relations that can help to eliminate factors influencing the dose–effect relation.

(5) On p. 64: \( \gamma(x) = s(x)g(x) \). As defined in our analysis of the experiment (2), \( \gamma(x) \) is proportional to \( s(x)g(x)/x^2 \).

(6) \( \gamma(x) \) is the probability that two energy transfers separated by \( x \) produce a lesion and not as stated in Fig. 17 the probability of interaction of sublesions; that quantity has been defined as \( g(x) \). The issue is not clarified by Fig. 17b since its quality is such that we cannot tell whether this is a plot of \( \gamma(x) \) or of what Dr. Goodhead incorrectly claims \( \gamma(x) \) to be; but in any case peaking of the function \( \gamma(x) \) at short distances implies the dominance of short-range interactions for the intratrack damage. For reasons cited by Dr. Goodhead, a long-range interaction is also required to explain the curvature of the dose–effect relation, i.e., the intertrack action. Contrary to the impression generated this applies regardless of the postulated mechanisms, and it would also have to be part of any eventual quantitative formulation of "saturable repair models."

(7) In Fig. 7 and its legend, \( g(x) \) needs to be removed and the words "according to the site model" need to be added. But the figure is irrelevant because the biologically meaningless step of the function \( g(x) \) is by no means required in the site model.

(8) In Fig. 12a the words "Dual Action Prediction" need to be replaced by "Site Model Prediction."

(9) Figure 20 and p. 69: what may well be the most unfortunate aspect of this publication are its implications to radiation protection. Regardless of any specific theory, microdosimetric considerations make it evident that sufficiently low absorbed doses must result in proportional cellular damage of any kind (and this, incidentally, must also apply to the "repair model" proposed by Dr. Goodhead). However, this does not mean that this relation holds for such important radiation effects as carcinogenesis. We pointed this out more than 10 years ago (3), and although we have continued to stress this point in many publications the misconception has persisted.
as a fundamental flaw in arguments relating to radiation protection. It is being perpetuated in Dr. Goodhead's article.

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REFERENCES