• Dosimetry of Internal Emitters

The Dosimetry of Internal Emitters Program endeavors to refine the correlation between radiation dose and observed biological effects. The program is presently engaged in the development of studies that will demonstrate the applicability of microdosimetry models developed under the Microdosimetry of Internal Sources Program. The program also provides guidance and assistance to Pacific Northwest Laboratory's Biology Department in the dosimetric analysis of internally deposited radionuclides. The investigators work closely with the Biology Department staff and collaborate on the Microdosimetry of Internal Sources Program.

MICRODOSIMETRY--A TOOL FOR INTERPRETING THE DOSE-RESPONSE FROM INTERNAL EMITTERS

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Although the concept of absorbed dose is commonly used in radiation biology as a parameter for comparing the toxic effect of different levels of radiation on a system, situations exist where absorbed dose by itself is inadequate, and additional dose distribution information is needed to explain the observed biological effect. An example of such a situation is the irradiation of cells by alpha particles from internal emitters. This report describes a case where microdosimetry methods were used to reinvestigate the dosimetry of two very similar experiments with apparently contradictory dose-response results.

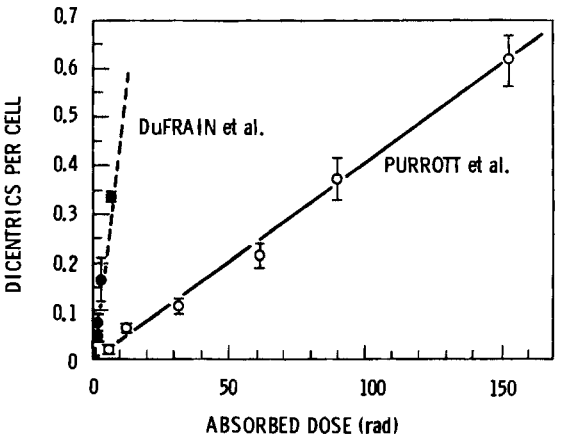

FIGURE 1. Frequency of Dicentric Chromosomes as a Function of Absorbed Dose from Alpha Particle Irradiation *In Vitro*

Figure 1 shows a plot of dicentric chromosome aberration yields induced in human blood lymphocytes following in vitro exposure to dissolved americium or plutonium. The experiments were performed at two separate research laboratories (DuFrain et al. 1979; Purrott et al. 1980). Although each irradiation produced linear dose-response functions, the slopes of the best-fit lines (Figure 1) are different by a factor of about 12. This disparity was totally unexpected. The relative biological effectiveness (RBE) of alpha particles compared to ^{60}Co gamma radiation for a dicentric yield of 0.1 per cell reported by Purrott et al. was approximately 10 times lower than the value obtained by DuFrain et al. for the same cell type and mode of irradiation.

We re-evaluated the dosimetry of the two studies using an internal microdosimetry computer code (Roesch 1977). For each experiment, we assumed that the lymphocytes were randomly distributed in a unit-density solution of americium or plutonium, and that the activity was well dissolved and uniformly mixed in. We also assumed that the cells were completely separated from the solution of alpha emitter at the end of the exposure period.

During such an irradiation, only a certain percentage of the cells are hit by alpha particles. The alpha particle energy imparted to individual cells is highly variable. Both the probability that a cell was hit, and the probability that a specific amount of energy was deposited, were calculated using the computer code for internal microdosimetry. In Table 1 the predicted fraction of irradiated cells is compared to the fraction of damaged cells observed in each of the two cell irradiation studies.

We are not yet able to correlate specific energy with discrete biological effects, but we can, as a first approximation, assume that the early effects will occur in that fraction of cells that are irradiated. Table 1 shows that a higher fraction of cells were damaged than were calculated to have been irradiated. It would not be possible, therefore, for the activity in the study of DuFrain et al. to have been uniformly distributed in the solution, as was earlier assumed.

TABLE 1. Summary of Predicted Fraction of Cells Irradiated and Frequency of Observed Cytogenetic Damage in Two Experiments

Experiment	Absorbed Dose (rad)	Irradiated Cells (predicted)	Damaged Cells (observed)
DuFrain *et. al.*	0.85	0.016	0.10
	1.71	0.031	0.13
	3.42	0.061	0.23
	6.84	0.118	0.32
Purrott *et. al.*	6.50	0.105	0.016
	13.0	0.198	0.070
	33.0	0.430	0.110
	65.0	0.665	0.181
	95.0	0.796	0.299
	160.0	0.931	0.442

For DuFrain et al. to have obtained the observed chromosome aberrations, quite possibly one or both of two events also transpired during the irradiation of lymphocytes: (1) settling of the cells and activity in the solution may have occurred because it was not agitated; and (2) the activity may have been attracted to the cell membrane of the lymphocytes. Either situation leads to higher specific energy densities in the cells and increased probabilities that the cells were irradiated and damaged. Thus, microdose distribution is an important determinant of biological effect.

Average dose to a biological system of cells and body fluids can therefore be a misleading concept unless the microdistribution of activity with respect to sensitive biological sites is adequately defined. Care must be taken in the interpretation and extension of dose response curves, particularly in the case of internally deposited alpha particle emitters. Microdosimetric evaluations are recommended for all cell studies involving alpha-emitting radionuclides.

REFERENCES

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Purrott, R. J., A. A. Edwards, D. C. Lloyd and J. W. Stather. 1980. "The Induction of Chromosone Aberrations in Human Lymphocytes by In Vitro Irradiation with α-Particles from Plutonium-239." Int. J. Radiat. Biol. 38(3):277-284.

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IN-VITRO ALPHA-PARTICLE MICRODOSIMETRY

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We have begun experiments which will allow us to demonstrate the applicability of microdosimetry calculations to radiation protection. Microdosimetry, extended to the dosimetry of internal emitters at this laboratory (Roesch 1977), utilizes the stochastic quantity "specific energy (Z)." The specific energy is the value of the energy actually imparted divided by the mass of the site.

Experiments to verify microdosimetric calculations can be applied to cells either in vivo or in vitro. In our experiments we are utilizing two types of radioactive sources. The first is a zirconium oxide microsphere labeled with plutonium. The second source type is a polystyrene microsphere labeled with ^{244}Cm. The former has been generously supplied by Dr. L. M. Holland of Los Alamos Scientific Laboratory. The latter microspheres are being developed at this laboratory. Polystyrene microspheres have the relative advantages of being smaller, having a density closer to the density of tissue, and causing less attenuation of the alpha particles.

The present experiments utilize the zirconium microspheres dispersed among Chinese hamster ovary (CHO) cells growing on the bottom of plastic flasks. The experiments are designed so that in all cases the average energy deposited in the system remains constant while microscopic energy distributions are varied. This is done by varying the concentration of the microspheres inversely with their activity. That is, microspheres with high activity will be in a lower concentration than that of microspheres having a lower activity. Thus, the total number of alpha particles emitted is nearly the same in all cases, as is the average radiation dose. However, as the activity of individual particulate sources is increased and the number of sources is correspondingly decreased, the probability of a cell being hit decreases; but if hit, the amount of energy deposited in a cell will be greater.

We anticipate that the response of CHO cells to radiation (e.g., cell survival and mutation rate) should correlate better with the specific energy (Z) and the probability of a cell being hit than with the absorbed dose. We hope that these experiments will demonstrate the applicability of microdosimetry to internally deposited radionuclides.

REFERENCE

Roesch, W. C. 1977. "Microdosimetry of Internal Sources." Radiat. Res. 70:494-510.

DEPOSITION OF INHALED ^{239}Pu-NITRATE IN KIDNEYS OF BEAGLE DOGS

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The deposition of plutonium in the kidneys of beagles that had inhaled ^{239}Pu-nitrate was studied to determine the extent to which plutonium accumulated in the kidney. Accumulation, if it occurred, would increase the dose to the kidney.

The data were obtained from beagle dogs which had inhaled ^{239}Pu-nitrate aerosol (Cannon et al. 1979). The data were grouped according to the number of days past exposure at the time of sacrifice. Then the percentage of the body burden in the kidney was computed for each group, as shown in Figure 1.

This study indicates that less than one percent of the body burden at sacrifice is deposited in the kidney, and that this organ burden is also present shortly after the inhalation. No trend of increased deposition of plutonium in the kidney was found between three and 1310 days post inhalation. Based on these data, it appears that the fraction of inhaled plutonium nitrate deposited in the kidney is small and remains fairly constant following an exposure.

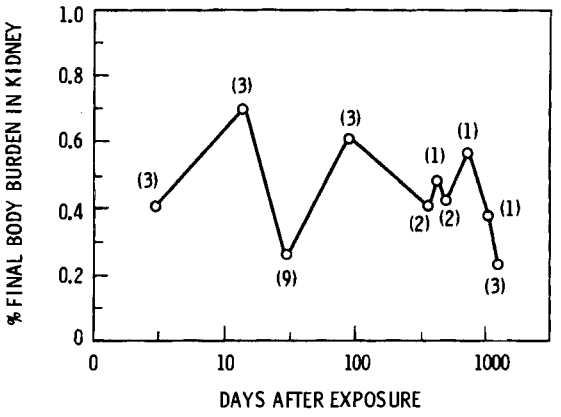

FIGURE 1. Deposition of Plutonium in Dog Kidneys Following Inhalation. Numbers in parentheses indicate number of dogs.

REFERENCES

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