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Biological Depth Dose Studies in Electron Beam Therapy:
Effects on Anagen Mouse Hairs*

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The experiments reported here were undertaken to help elucidate the "skin-sparing" effects that have been observed when high-energy electrons are used for cancer therapy. "Skin-sparing" refers to the observation that a higher dose of electrons is required to produce the same degree of erythema caused by exposure to 200 kv X-rays.

Tapley and Fletcher have stated: "It is apparent that the skin-sparing effect with the electron beam is greater than can be explained by the demonstrated RBE of 0.8-0.9 for electrons compared with kilovoltage radiation, and may be attributed in part to the build-up factor." The experiments described in this paper are limited to a study of the build-up factor, utilizing physical and biological systems of dosimetry.

Physical Methods and Results

The electron source was the linear accelerator at the Argonne Cancer Research Hospital, The University of Chicago. This is a traveling-wave type of accelerator which was operated at an electron beam energy of 20 MeV.

The physical methods used to study dose build-up require systems of spatial resolution of about 0.5 mm since the electron beam is of the scanning type. To determine the average dose at depths near the surface, detailed measurements need to be made at the peaks and troughs of the dose distributions. Thermoluminescent dosimetry using lithium-fluoride crystals of mesh size between 100 and 200 satisfied this requirement.

Covered Teflon discs containing the lithium fluoride crystals were used as the absorbing media. The Teflon discs, centered in a 10 x 10 cm field, were scanned at a delivered dose of approximately 200 rads. The crystals were then processed and measured. The surface dose was observed to be 88 % of the plateau dose which, for these measurements with a 20 MeV electron beam, starts at

approximately 1.7 cm below the surface and appears to extend to a depth of at least 2.5 cm.

Biological Method and Results

The requirements for a satisfactory biological method of assessing build-up include quantitation, small spatial resolution, and use of the same system on the surface as in the tissue depth. Growing hairs in the mouse provide a system compatible with all of these requirements, since hair damage can be measured on one flank at the surface and on the opposite flank - about 2.5 cm distant - in the depth or at the plateau of the build-up curve.

All studies were carried out in three month old female Carworth Farms No. 1 mice according to the following technique. In this mouse strain anagen lasts 17-20 days. Initially, all animals were plucked widely over both flanks, and 24 days later, when hairs were in telogen, the mice were replucked. Twelve days later (12th day of anagen) groups of 8-26 animals received a single dose of radiation under sodium pentobarbital anesthesia. For this procedure each animal was placed in the left lateral position with the right flank exposed to the radiation source. Through-radiation was given so that the average body thickness of 2.5 cm separated entry (right flank) and exit (left flank) treatment portals. Forty-eight hours after irradiation (14th day of anagen), all animals were given 3-5 microcuries of ^3H -DL-serine intravenously. On the 24th day hairs from both flanks of each mouse were plucked for study.

Hair samples were weighed and placed in a combustion apparatus in the presence of oxygen. Volatile materials were removed in a high vacuum system and radioactivity in the remaining material was assayed as tritiated water in a liquid scintillation spectrometer. Throughout the study hair samples from control and irradiated sites were studied individually for each animal in all experimental groups.

The radiation source was the same as that described in the section on physical methods.

Low-dose exposure (300 rads) depressed serine uptake in hair almost equally at entry and exit portals (Table). At moderate doses of 500-600 rads, reduced incorporation of serine at the beam entry site was further lowered by 15% on average at the exit portal (Table).

Discussion

Serine is incorporated into keratin and into cytoplasmic and nuclear proteins. Since protein synthesis is a radiosensitive process, impaired uptake of serine is a useful indicator of radiation injury to hair.

Experimental findings for the groups of mice receiving 500 or 600 rads (Table) reveal that impairment of ^3H -DL-serine incorporation and protein synthesis on the exit side is about 15% greater than at the beam entrance site. The difference correlates well with the 12% higher plateau dose measured by physical means. The higher plateau dose is due to the well-established build-up phenomenon. It is quite possible, however, that hair damage does not exhibit the same quantitative response to radiation reflected by the degree of cutaneous inflammation and erythema produced. Clinical impressions of skin-sparing effects greater than 12-15% would most likely reflect a skin-specific RBE, perhaps primarily related to vascular reactivity, and not a substantially different build-up factor from that described above. These studies do indicate, however, that, with the instantaneous dose rates in use for pencil beam scanning, and at the dose levels studied, the physically and biologically measured build-up are in substantial agreement. Moreover, even though the linear energy transfer (LET) cannot be expected to be identical at the surface as compared with the depth, this difference has not produced a significantly different RBE at the two positions for the biological indicator used.

Reduced Levels of ^3H -DL-Serine in Mouse Hair Following Electron Beam Irradiation in Anagen. Percentages Are Expressed as an Average Ratio of DPM/mg of the Beam Entry Side (R) to the Beam Exit Side (L) for Each Individual Animal.

Dose (Rads)	Animals	DPM/mgL (Beam Exit Side)	DPM/mgR (Beam Entry Side)	R/L%	Standard Error of the Mean
300	8	2340	2044	95	13
500	9	2619	2978	118	12
600	26	322	365	113	4
No radiation (control group)	7	3131	3097	100	4