

Histopathology of Normal Rat Skin after Irradiation with Arrays of Microplanar X-ray Beams

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Beamline(s): **X17B1**

Introduction: The experimental radiotherapy method Microbeam Radiation Therapy (MRT) is described in accompanying abstracts in this report. In particular, our comparisons of the tolerances of the skin of the normal rat to microbeams and to broad beams of the same energy spectrum from the X17B1 beamline showed that the ED50 (50% incidence dose) of single-fraction irradiation for developing moist desquamation on the skin of the thigh is 43.5 Gy for broad-beam irradiation, and more than 1000 Gy for microbeams (90- μ m beam width and 300- μ m beam spacing). Desquamation appears 2-3 weeks after irradiation. The present study was designed to explore the underlying mechanisms for this extraordinary resistance of the skin of normal rat to radiation damage from arrays of parallel x-ray microbeams.

Methods and Materials: Normal rats were irradiated at 12-weeks of age on the external side of their thigh with microbeam arrays of 90 μ m beam width and 300 μ m center-to-center beam spacing from the X17B1 beamline. There were two groups, each with 12 rats. Group A was irradiated with a 937.5 Gy in-slice skin-entrance dose, and Group B with a 987.5 Gy dose. Two rats from each group were euthanized at the following times after the irradiation: 24 hrs, 48 hrs, 72 hrs, 6 days, 12 days, and 1 month. The irradiated thigh skin on the external side then was then removed, fixed in Formalin, and embedded in paraffin. Tissue sections were prepared and stained with hematoxylin and eosin, then examined using light microscopy.

Results: The findings are the following. First, there was no morphologically significant difference between group A and group B at any of the time points. Second, no morphological changes were observed during the first 24 hrs. During the period from 24 hrs to the 6th day, the basal and the spinous cell populations were progressively lost; in contrast, the thickness of the granular and the corny cell layers progressively increased. At 72 hrs, both the sebaceous glands and the hair follicles still appeared like those in the unirradiated skin. At 6 days, clear changes became evident; the skin was covered only by several layers of granular and corny cells; and sebaceous glands were on longer seen. The structure of hair follicles gradually became distorted, and morphologically necrotic/pyknotic cells started to appear in the matrix of the follicles. At 12 days, the skin displayed epithelial hyperplasia that led to multiple layers of spinous and granular cells and a thicker-than-normal layer of corny cells. At this stage, epithelial cell islands about 50-300 μ m long, developed and spaced regularly at 300-500 μ m from center-to-center; most of these islands were connected to hair follicles. Also, the density of hair follicles decreased from the day 6 to the day 12, and no sebaceous glands remained by day 12. By one month, the thickness of the epidermis and the densities of the hair follicles and sebaceous glands had returned to normal, reaching the same levels as those in the unirradiated control rats. The histology results are consistent with our observation that only transient moist desquamation develops on the rats from both these doses. We observed small areas of "hair clumping", which is evidenced by occasional acellulose crust above the regenerated epidermis. The results suggest that the resistance of the rat's skin to damage from microbeams, and its fast recovery from moist desquamation, are caused by rapid regeneration of the surviving clonogenic basal cells between the microbeams, a process that does not occur with the broad-beam damage. From this we speculate that the tolerance of the microbeams by other normal tissues (see accompanying abstracts) may arise from the regeneration of the endothelial cells of microvasculature that survive between microbeam.

Conclusions: We conclude that after microbeam irradiation the rat's epidermis experiences a very short period of degeneration (1-6 days post-irradiation), and then regeneration, (6 -12 days post-irradiation), and, possibly, post-regeneration hyperplasia. The surviving clonogenic basal cells lying between direct paths of microbeams appears to proliferate and regenerate the epidermis, a process followed by epidermal hyperplasia.

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