The Normal Tissue Sparing Effect of Microbeams on Rat Skin

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Introduction: Despite considerable recent progress in the field of conformal radiation therapy, radiation treatment of the carcinomas of the head-and-neck tumors remains a significant clinical problem due to the collateral damage to the normal tissues surrounding the tumor. Studies with Microbeam Radiation Therapy (MRT), an experimental radiotherapy modality that uses segmented, planar, synchrotron-generated x-ray beam slices, has indicated that the method spares normal tissue and preferentially damages the tumor using single-fraction, unidirectional irradiations. A limitation of the microbeams has been their dose penetration to the tissue, which is lower than that of the Mega Volt x rays of the clinical electron linacs because of their lower beam energy (70-200 keV). The effect results in an elevated skin dose during therapy. The present study evaluated the tolerance of the normal rat's skin to unidirectional microbeams for estimating the significance, if any, of the dose-penetration in MRT

Methods and Materials: Preliminary evaluation of skin's response (rat model) to microbeam irradiation was carried out using a microplanar beam width of 90 μm and a beam spacing of 300 μm at the X17B1 beamline. The white beam was filtered with 3-mm Si and 6.25-mm copper, producing a median spectral energy of about 120 keV and a dose rate of about 26 Gy/s at 200 mA current of the synchrotron storage ring. The biological end point used in the study was moist desquamation caused by the breakdown of the surface layer (epidermis) of the skin.

Results: The moist desquamation effect observed was shallower and more transient compared to that from broad beams. Histopathological analyses of skin sections indicated focal breakdown of the epidermis in the direct path of microplanar beams. For surface scoring of the skin, this disruption is manifested as "hair clumping" due to leakage of exudate from small, localized sites of denuded epidermis. To characterize the dose-response pattern of skin to 90/300 μm microbeams, 8 groups of rats (6 per group) aged 12 weeks were irradiated at skin doses of 912.5 Gy, 925 Gy, 937.5 Gy, 950 Gy, 962.5 Gy, 975 Gy, 982.5 Gy, and 1000 Gy. Hair clumping appeared 13-17 days after irradiation. Other responses of the skin were erythema, dry desquamation, and hair loss, which were palliated very quickly within 1-2 weeks. Visible re-growth of hair occurred progressively on the irradiated skin around 4 weeks after irradiation. The rat skin was also irradiated with an unsegmented beam of the same energy spectrum. The resulting moist desquamation was much more pronounced and also less transient than the atypical changes seen in the rats exposed to microbeams. The estimated ED50 (50% incidence dose) using moist desquamation as the end point was about 43.5 Gy for broad beams from the X17B1 beamline after irradiation with unsegmented synchrotron x rays (broad beams). The microbeam-irradiated rats developed "clumping hair" at 937.5 Gy and larger doses, but they did not develop the type of moist desquamation seen in the broad beam at doses up to 2000 Gy. This represents a skin-sparing dose which is at least a factor of 23 higher with microbeams compared with the broad beam. It represents an about 7-fold advantage when the microbeam dose is normalized to take into account the volume of tissue between the microplanar beams.

Conclusions: The result is significant because the surface dose from MRT, which is larger than that from conventional radiotherapeutic modalities (due to lower beam energy), has been a concern. The advantage of tolerance to the MRT exposure is much larger than the extra skin dose the subject will receive from MRT.

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