Effects on Tissue of Mice after Irradiation with Protons ◇

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In the past much research has dealt with proton and heavy-ion effects induced in tumor and normal cell cultures, and important information about RBE, surviving fractions, DNA damage and repair has been obtained for various cell lines irradiated with particles of different LET. The response to ionizing radiation of an in vivo tumor depends on several factors (including oxygenation of tissue, nutrients, hormones and growth factors in relation with healthy surrounding tissue) that cannot be analyzed by in vitro studies. To take into account the modifications induced in an organized cellular structure such as a tissue and an organism, some experiments in tumor-bearing mice, irradiated by a proton beam, were performed.

The experimental model consisted in irradiating B16 melanoma in C57BL/6 mice. The B16 cells (200000) were subcutaneously inoculated in the right flank of the mice. When the tumor had reached an appropriate size (several mm, about 10 - 20 days later), the animals were anesthesized and the tumor was irradiated in a single session with 4 different doses (10, 20, 30 and 40 Gy). A proton beam of 20 MeV energy corresponding to a range in tissue of 4.8 mm had its Bragg peak spread out over the tumor thickness. Tumors smaller than 10 mm diameter were irradiated through a brass diaphragm with a hole of appropriate diameter; another hole of 7 mm allowed the exposure of healthy skin. For larger tumors a hole of 14 mm diameter was used.

In groups of at least 4 animals each, the mice were sacrificed 12 - 15 hours, 10 days, and 21 days after irradiation (those irradiated with 10 Gy only 15 hours), and samples of melanoma and healthy irradiated skin were taken; one half of each put in formaline and the other half frozen at -80^{0}C.

The samples will be submitted to an analysis of cell-kinetics parameters, such as ^{3}H-thymidine labelling index (TLI) and flow cytofluorimetry. Their biochemical characterization by means of parameters related to cell proliferation, as polyamines, will be performed and functional enzymes as tyrosinase will be assessed.

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