



Contribution ID: 208

Type: Poster

Synchrotron Broad Beam and MRT radiation induces DNA damage in normal mouse tissues distant from the irradiated volume

Thursday, 26 November 2015 13:30 (45 minutes)

Microbeam radiation therapy (MRT) is a novel, preclinical modality; with a unique ability to generate less radiation damage to neighbouring normal tissues, while providing efficient ablation to the tumour mass; compared to the conventionally used Broad Beam (BB) modality. A comprehensive investigation on the mechanisms and side effects of these modalities has currently not been established. Here we compared the radiation-induced bystander effect (RIBE) of BB and MRT irradiation, generated by the Imaging and Medical Beamline at the Australian Synchrotron in C57BL/6 mice. Animals were irradiated with 10Gy or 40Gy peak dose of BB or MRT, in an 8x8, 8x1 and 2x2mm area on the right hind leg, using an X-ray beam with a dose rate of 49Gy/sec and constant current of 200mA. At 24 and 96hrs post-irradiation, we collected irradiated skin and an assortment of unirradiated tissue; these were processed for DSB detection, using the gammaH2AX assay. For both modalities the levels of gammaH2AX foci in unirradiated tissues of irradiated mice, varied in comparison to irradiated animals. Overall, MRT and BB induced an elevated gammaH2AX response at 10Gy, while inhibiting this response at 40Gy. Oxidative clustered DNA lesions (OCDL) in tissues were measured using constant field gel electrophoresis, where genomic DNA was treated with purine, pyrimidine and abasic site-specific enzymes. We found a marked increase of OCDLs in a variety of unirradiated tissues. We will discuss the role of irradiated volume, dose, and beam modality in the manifestation of the in-vivo RIBE.

Keywords

Microbeam Radiation Therapy, Broad beam, DNA damage, gamma H2AX, Cancer

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Session Classification: Poster Session 1

Track Classification: Radiotherapy and Radiobiology