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

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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 currently used Broad Beam (BB) modality. A comprehensive investigation on the mechanisms and side effects of these modalities have not currently 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 γH2AX assay. For both modalities the levels of γH2AX foci in unirradiated tissues of irradiated mice, varied in comparison to irradiated animals. Overall, MRT and BB induced an elevated γH2AX 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. Results show 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 or phrases (comma separated)

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Summary

Primary author(s) : Mrs VENTURA, Jessica (Molecular Radiation Biology Laboratory, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia)

Co-author(s) : Dr IVASHKEVICH, Alesia (Centre for Innate Immunity and Infectious Diseases, MIMR, Monash University, Clayton, VIC, Australia;Radiation Oncology, Canberra Hospital, Garran, ACT, Australia); Dr GEORGAKILAS, Alexandros G (Department of Physics, National Technical University of Athens, Athens, Greece); Dr SMITH, Andrea (Molecular Radiation Biology Laboratory, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia); Mr NTARGARAS, Andreas (Department of Physics, National Technical University of Athens, Athens, Greece); Dr STEVENSON, Andrew (Australian Synchrotron/ CSIRO); Dr SPRUNG, Carl.N (Centre for Innate Immunity and Infectious Diseases, MIMR-PHI, Monash University, Clayton, VIC); Dr HALL, Christopher (Australian Synchrotron); Dr FORRESTER, Helen (Centre for Innate Immunity and Infectious Diseases, MIMR-PHI, Monash University, Clayton, VIC); Mr MASON, Joel (Molecular Radiation Biology Laboratory, Peter MacCallum Cancer

Centre, Melbourne, VIC, Australia); Mrs BEST, Nickala (Molecular Radiation Biology Laboratory, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia); Prof. MARTIN, Olga (Molecular Radiation Biology Laboratory, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; Sir Peter MacCallum Department of Oncology, the University of Melbourne, Melbourne, VIC, Australia; Division of Radiation Oncology and Cancer Imaging, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia); Dr LOBACHEVSKY, Pavel (Molecular Radiation Biology Laboratory, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia;Sir Peter MacCallum Department of Oncology, the University of Melbourne, Melbourne, VIC, Australia); Mr KOTSARIS, Vasilis (Department of Physics, National Technical University of Athens, Athens, Greece)

Presenter(s) : Mrs VENTURA, Jessica (Molecular Radiation Biology Laboratory, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia)

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