Effects of synchrotron microbeam radiotherapy on tumour-associated neutrophil and macrophage recruitment in a mouse breast cancer model

Poster No.: R-0116
Congress: 2014 CSM
Type: Scientific Exhibit
Authors: Y. Yang¹, A. Swierczak², M. Ibahim¹, P. Paiva¹, A. Stevenson³, J. Crosbie¹, R. Anderson², P. Rogers¹; ¹PARKVILLE/AU, ²MELBOURNE/AU, ³CLAYTON/AU

Keywords: Radiation therapy / Oncology, Conventional radiography, Breast, Animal (veterinary) studies, Radiobiology, Cancer, Molecular, genomics and proteomics, Radiotherapy techniques

DOI: 10.1594/ranzcr2014/R-0116

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply RANZCR/AIR/ACPSEM's endorsement, sponsorship or recommendation of the third party, information, product or service. RANZCR/AIR/ACPSEM is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold RANZCR/AIR/ACPSEM harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, .ppt slideshows, .doc documents and any other multimedia files are not available in the pdf version of presentations.
Aim

Conventional radiotherapy (CRT) is a routine treatment for up to 50% of breast cancer patients. However, CRT may compromise anti-tumour responses by triggering inflammatory responses, increasing immune repressive molecules, and recruiting tumour-associated neutrophils (TANs) or macrophages (TAMs) to tumours. Synchrotron Microbeam radiotherapy (MRT) is a novel preclinical RT, in which synchrotron-generated X-rays are segmented by a collimator, producing intense microbeams. Animal studies have demonstrated that MRT ablates tumours but causes little or no damage to the surrounding normal tissues compared to CRT. In this study, we investigated the effects of MRT/CRT on the recruitment of TANs and/or TAMs to tumours. We hypothesized that MRT induces a different immunological response in the tumour microenvironment, which leads to less TAN/TAM recruitment compared to CRT.

Methods and materials

Balb/c mice were inoculated with $5 \times 10^5$ EMT6.5 mouse mammary tumour cells in the right hind leg. Tumours were irradiated with MRT (112 and 560 Gy peak dose) or CRT (5 and 9 Gy) and excised at 24, 48 and 120 hr post-irradiation. Flow cytometry analysis, quantitative real-time PCR and immunohistochemistry were applied to quantify TAN or TAM recruitment, and production of chemokines/cytokines responsible for immune cell recruitment.

Results

We found that there was a significant difference in both TAN and TAM recruitment in tumours irradiated with MRT and CRT at 48 hr post-irradiation. MRT induced significantly less TAN and TAM recruitment when compared to CRT ($p<0.01$). There was less chemokine (C-C motif) ligand 2 (CCL2) expression in tumours irradiated by MRT than CRT, which may be one of the mechanisms responsible for reduced tumour-associated immune cell recruitment.

Images for this section:
Fig. 1: There were less numbers of neutrophils and monocytes/macrophages in MRT-irradiated EMT6.5 tumours compared to those irradiated by CRT at 48 hr post-irradiation. Tumour bearing mice were irradiated with MRT/CRT and tumours were excised at 48 hr following irradiation as described in Figure 2A. Numbers of (A) neutrophils, (B) macrophages, (C) Ly6Chigh monocytes, and (D) Ly6Clow monocytes were quantified by flow cytometry.

Fig. 2: Less F4/80 TAMs were recruited into MRT-irradiated EMT6.5 tumours compared to those irradiated by CRT at 48 hr post-irradiation. (A) Immune staining of F4/80 in control, CRT (5 or 9 Gy) and MRT (112 or 560Gy) irradiated tumours. (B) Immune staining of BrdU and F4/80 in control, CRT (5 or 9 Gy) and MRT (112 or 560Gy) irradiated tumours.
**Fig. 3:** There was less CCL2 expression in MRT-irradiated EMT6.5 tumours than those irradiated by CRT at 48 hr post-irradiation. (A-E) Immunohistochemistry of CCL2 in control, CRT (5 or 9 Gy) and MRT (112 or 560Gy) irradiated tumours. (F) Quantitation of proportional staining area of CCL2. Images of CCL2 staining were captured and quantified by Fiji ImageJ v1.49.
Conclusion

Our results suggest that MRT may show advantages over CRT for improving tumor control through its effect on immune cell recruitment to tumours. Our results also suggest that a combined treatment of MRT with immunotherapy targeting TAMs/TANs or CCL2 will be superior to CRT with the same combinatorial treatment.

Personal information

References


