1415 THORACIC FLASH RADIOTHERAPY SIGNIFICANTLY SPARES PERIPHERAL BLOOD LYMPHOCYTES AND IMPROVES PROLIFERATION OF BONE MARROW STEM/PROGENITOR CELLS AND LYMPHOPENIA RECOVERY

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Background Conventional radiation treatment (RT) causes severe lymphopenia and normal lung and heart damage in patients with lung and breast cancers. This study is designed to compare effects of FLASH and Conventional RT on lymphocytes, bone marrow (BM) stem/progenitor cells (HSPCs) and their potential mechanisms.

Methods We performed electron irradiation to the whole thorax in C57BL/6 mice using 17 Gy conventional vs. FLASH (>300 Gy/s) dose-rates using the FLASH Mobetron (IntraOp). Lymphocytes and BM HSPCs were detected by multicolor flow cytometry analysis. Fibrosis was examined using Masson's Trichrome Staining.

Results First we determined that we were able to generate the effects of FLASH RT by significantly reducing the fibrosis in both normal lung and heart tissues by six months after treatment compared to conventional dose rate RT. Under the same condition, conventional dose rate RT caused severe lymphopenia in all the subsets of CD3, CD4, CD8, NK cells and CD19 positive B cells, and had minimal recovery over time except the B cells until two months after treatment. FLASH radiation also resulted in severe lymphopenia on day 3 after treatment, however, the levels of lymphocytes in the peripheral blood gradually recovered to nearly baseline levels by day 31. In fact, the levels of lymphocytes in the FLASH group were significantly greater than those in conventional dose rate group even at day 3 after radiation. Moreover, we found that conventional dose rate RT caused significantly suppression of out-field (femur) BM HSPCs at day 6, which didn't show increase until day 21 after radiation. On the contrary, FLASH RT did not suppress the levels of out-field BM HSPCs at day 6 but increased the levels from day 13 after radiation; and the levels of BM HSPCs in FLASH group were significantly greater than those in the conventional group.

Conclusions Together, our results indicate that thoracic FLASH RT significantly spared peripheral blood lymphocytes and triggered greater proliferation of BM HSPCs and lymphopenia recovery. This implies that FLASH radiation may not only reduce late normal tissue complications but also have the potential to improve immunologic fitness after radiation therapy.

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