

Effects of Low, Medium, and High Dose-rate Whole Body Irradiation on Hematopoietic Environment in Murine Bone Marrow

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Abstract

It is known that hematopoiesis in the bone marrow and spleen is highly sensitive to radiation. Our previous study showed that whole body low dose-rate (LDR) radiation exposure resulted in a decrease in the number of hematopoietic stem cells (HSCs). In vivo, HSCs in the bone marrow are surrounded by a microenvironment (a hematopoietic niche) that is composed of various cells controlling the balance between self-renewal and differentiation of HSCs. Although there are a few studies on alterations in the hematopoietic niche, gene expression analysis has suggested that the decrease in the number of HSCs after LDR irradiation is associated with alteration of biomolecules that control the cell cycle and differentiation of HSCs, such as cytokines and hormones. This study aims at clarifying the effect of LDR irradiation on the hematopoietic niche. We exposed eight-week-old male C3H/HeN mice to gamma-rays at low (LDR: 20 mGy/day), medium (MDR: 400 mGy/day) and high (HDR: 770 mGy/min) dose-rates, and collected the bone marrow at pre-determined intervals for examination. Sections of fresh bone marrow tissue from the femur and humeri were prepared following Kawamoto's method and stained with hematoxylin and eosin. Compared to age-matched non-irradiated controls, bone marrow exposed to MDR of 400 mGy/day showed a decrease in bone marrow cell counts at day 1 (dose received = 400 mGy), but on day 10 (dose received = 4000 mGy), the bone marrow cell counts were not significantly different from the non-irradiated control. No significant difference in bone marrow cell counts was observed at day 20 (dose received = 8000 mGy), day 35 (15 days post-irradiation, dose received = 8000 Gy) and day 50 (30 days post-irradiation, dose received = 8000 Gy). We also found no change in both HDR at 5000 mGy and LDR at 2000 mGy (day 100). We are now analyzing compositional and qualitative changes in bone marrow cells using fluorescent antibody immunostaining. Furthermore, we have started an ex vivo HSC culture to study the function of extracellular biomolecules that was predicted by the gene expression analysis.

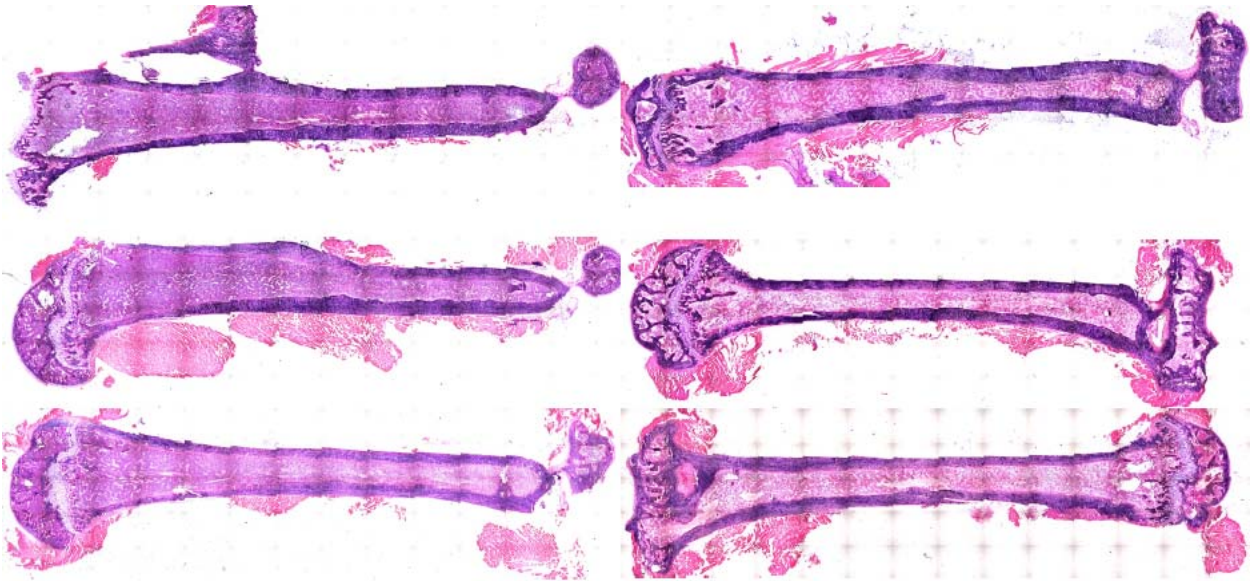


Fig. 1 Fresh frozen tissue sections of the bone marrow (H&E Stain). Photos on the left are from non-irradiated mice, while those on the right are from mice exposed to MDR of 400 mGy/day after 1 day.

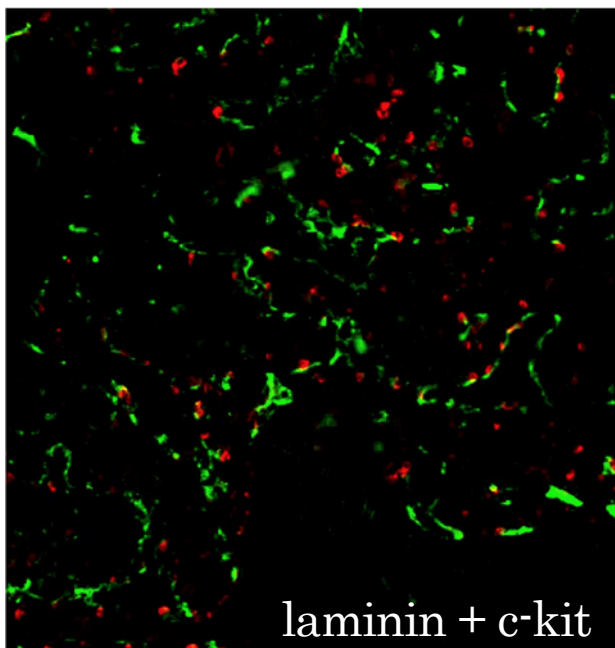


Fig. 2 Fluorescent immunohistochemical staining showing blood vessels (laminin^{pos}: green) and hematopoietic stem cells (c-kit^{pos}: red)

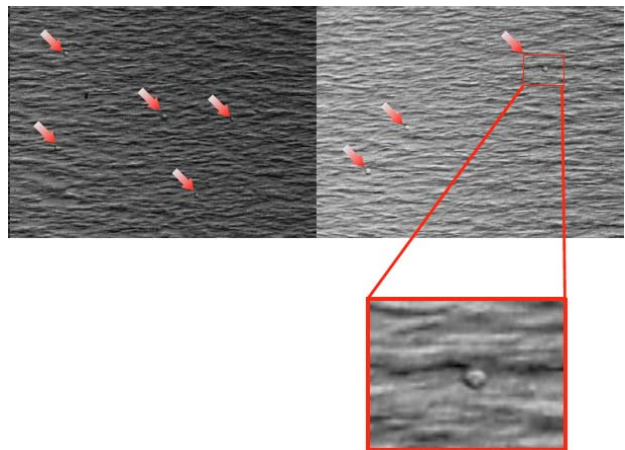


Fig. 3 Cultured hematopoietic stem cells (arrows) in Preset VECCELL™.