

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

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Abstract

The hematopoietic stem cell (HSC) niche is the microenvironment essential for hematopoiesis in the bone marrow. While it is known that radiation exposure induces hematopoietic injury, there are few reports on its effects on the HSC niche, particularly the effects of low dose-rate (LDR) radiation. Chronic radiation exposure at a low dose-rate of 20 mGy/day has been shown to be leukemogenic, but its effect on the HSC niche in the bone marrow is unknown. We compared the effects of high-dose-rate (HDR), middle-dose-rate (MDR) and LDR radiation in the bone marrow, using both *in vivo* and *ex vivo* experimental approaches.

In vivo analyses focused on bone marrow cellularity (ratio of hematopoietic (non-fat) tissues) and blood vessels. The bone marrow from the femurs of 8-week-old C3H males exposed at the dose-rates of 750 mGy/min (acute HDR), 400 mGy/day (chronic MDR) and 20 mGy/day (chronic LDR) were histologically analyzed. Decreased cellularity was noticed at 10 days after the HDR exposure (total dose: 8000 mGy) and at 50 days after the beginning of the MDR exposure (total dose: 20000 mGy). At lower total doses or at earlier time points, the disintegration of basement membranes of venous sinuses, but not decreased cellularity, was observed. So far, we have not detected any effects of the LDR exposure.

Ex vivo cultures of HSCs, isolated from 16-week-old C3H males and exposed at 870 mGy/min (acute HDR) to a total dose of 4290 mGy or at 359 mGy/day (chronic MDR) to a total dose of 4667 mGy, showed lower cell counts after 20 days in culture. Thus, isolated HSCs might be more radiosensitive than *in vivo* HSCs in the niche.

These results suggest that radiation exposure could alter the hematopoietic microenvironment and that these alterations could influence the fate of HSCs in the bone marrow.

Table 1 *In vivo* analyses of femoral bone marrow

	750 mGy/min acute irradiation (5000 mGy)	750 mGy/min acute irradiation (8000 mGy)	400 mGy/day chronic irradiation	20 mGy/day chronic irradiation
Decreased cellularity	no change	From day 10 post- irradiation	From day 50 of radiation exposure	no change
Disintegration of basement membranes of venous sinuses	From day 15 post- irradiation	From day 1 post- irradiation	From day 1 of radiation exposure	no change

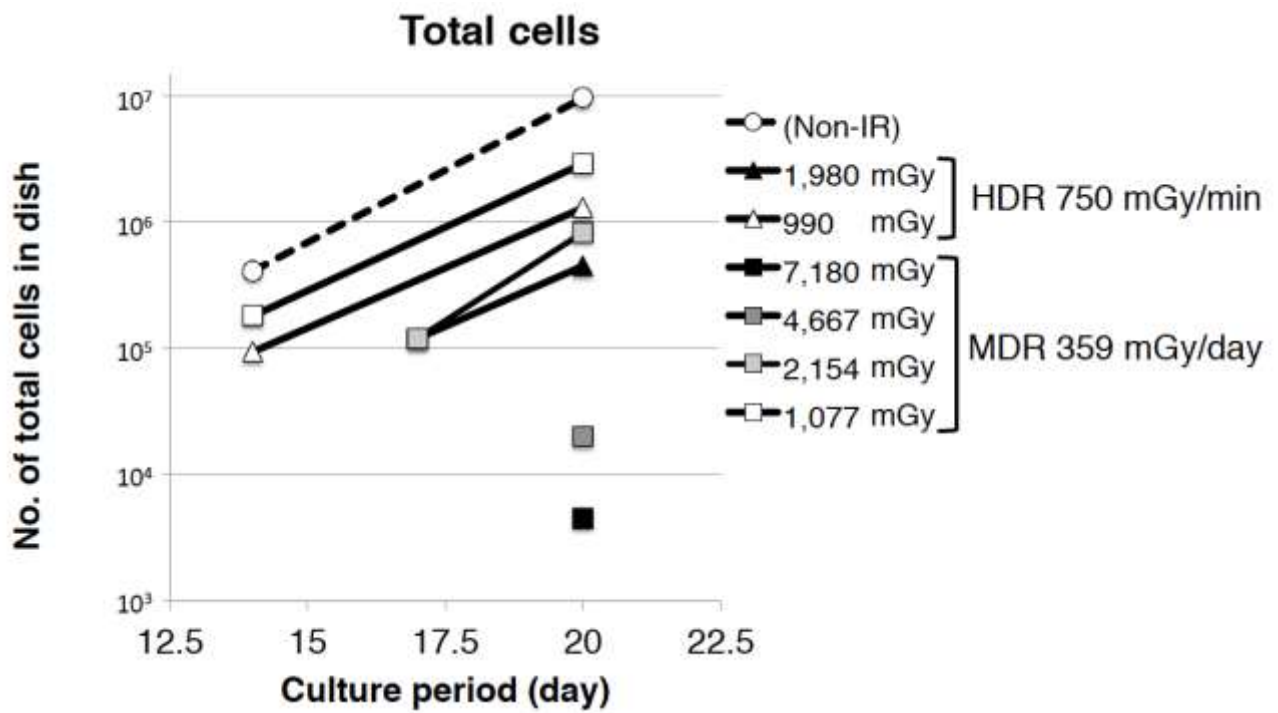


Fig. 1 Cell counts of HSCs cultured for 20 days *ex vivo* after exposure to acute HDR [870 mGy/min; total doses = to 990 (△) and 1980 mGy (▲)] or chronic MDR [359 mGy/day; total doses = 1077 (□), 2154 (■), 4667 (■) and 7180 mGy (■)] radiation compared to the non-irradiated control (○).