Acute effects of simulated space radiation and micro-gravity on cancellous bone loss in mice tibiae

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Space radiation and micro-gravity are the two major obstacles impeding human exploration of Mars and beyond. Long-duration space flights expose astronauts to high doses of high linear energy transfer (LET) radiation as well as prolonged periods of skeletal disuse due to weightlessness. One important consequence of both radiation exposure and micro-gravity is acute bone loss. However, biological responses to different radiation types and combined radiation and micro-gravity environments remain unknown. Thus, the purpose of this study is to compare the acute effects of different radiation species and simulated weightlessness on bone degeneration for the purpose of developing accurate risk assessments of prolonged space flight. Mouse models were used to simulate space flight-relevant doses of different radiation types as well as weightlessness via hind-limb unloading. Three groups of mice (n = 9) were irradiated with 1 Gy H^+, 1 Gy ^{56}Fe, and 1 Gy combined H^+ and ^{56}Fe (dual ion) respectively and compared to sham irradiated (n = 9) and 2 Gy ^{56}Fe irradiated positive controls (n = 6). Two groups of mice (n = 9) were hind-limb unloaded for three days and then either sham irradiated or dual ion irradiated respectively, followed by subsequent hind-limb unloading for 11 days. Cancellous tissue from tibiae metaphyses were harvested 11 days post-irradiation for *ex vivo* micro-computed tomography analysis. Microarchitecture parameters including bone volume to total volume ratio (BV/TV), trabecular thickness (Tb.Th), trabecular number (Tb.N), trabecular spacing (Tb.S), and connectivity density (Conn.D) will be quantified using a novel automated segmentation procedure developed in our lab. The anticipated results will be instrumental in developing counter-measures against micro-gravity and radiation-induced bone loss. Moreover, possible synergistic effects may provide insight into underlying mechanisms mediating biological response.

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