# Can Acute Galactic Cosmic Radiation-Induced Bone Loss Be Mitigated By Dietary Modulation Of Inflammatory Cytokines?

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ABSTRACT

The space environment includes weightlessness and galactic cosmic radiation (GCR), both of which can have a negative impact on bone parameters. In particular, acute exposures to space-relevant doses (2 Gy or less) of simulated GCR lead to a rapid acceleration of bone resorption activity and suppression of bone forming osteoblasts, resulting in diminished bone mineral density (BMD), strength and altered microarchitecture. A key mechanism driving these changes may be a radiation-induced increase in pro-inflammatory cytokines, such as TNF-α. Consuming a diet rich in omega-3 fatty acids has been associated with attenuated reductions in bone parameters in astronauts, mice and elderly humans with corresponding reductions in circulating inflammatory cytokines. **PURPOSE:** To test the hypothesis that a diet high in omega-3 fatty acids will mitigate radiation-induced bone loss and reduce inflammatory cytokines in bone osteocytes and serum. **METHODS:** Adult (30- to 50-week-old) female Lgr5-EGFP C57BL/6 mice (n=4-6 per group) were acclimated to a corn oil/cellulose (COC) or fish oil/pectin (FOP) diet for 3 weeks. Animals were subsequently randomized to total body low dose high-energy radiation (0.1, 0.25, 0.5 Gy of 1000 MeV/n $^{56}$Fe at 25 cGy/min at Brookhaven National Lab) or non-irradiated control (sham) and euthanized 8 weeks later. MicroCT (ScanCo, Switzerland) analyses were performed to assess bone geometry and microarchitecture at the mid-shaft and distal end of the femur. Significance was assessed using an α of 0.10. **RESULTS:** There was a significant main effect of diet on mid-shaft femur periosteal diameter (Peri.Dm) ($p=0.001$) and endocortical diameter (Endo. Dm.) ($p<0.001$). The FOP diet led to larger Peri.Dm. ($p<0.051$ for all) and Endo.Dm. ($p<0.41$ for all) than did the COC diet at all doses. We could not detect an impact of $^{56}$Fe on cortical area or cancellous bone volume at the distal femur. Irradiation with 0.25 and 0.5 Gy in the FOP mice showed significant increases in distal femur volumetric BMD ($p=0.014$, $p=0.063$) and trabecular thickness ($p=0.058$, $p=0.028$), as compared with sham FOP mice. **CONCLUSION:** Though we did not detect a significant impact of radiation on bone parameters, these early data analyses suggest some modest benefits from a diet high in omega-3 fatty acids on cortical and cancellous bone parameters.