Dietary supplement attenuates radiation-induced osteoclastogenic and oxidative stress-related responses and protects adult mice from radiation-induced bone loss

Ruth Globus1, Ann-Sofie Schreurs1, Candice Tahimic1, Yasaman Shirazi-Fard1, Joshua Alwood1, Mohammed Shahnazari2, and Bernard Halloran1,2
1Space Biosciences Research Division, NASA Ames Research Center, 2Endocrine Research Unit, University of California, San Francisco

Abstract
Our central hypothesis is that oxidative stress plays a key role in cell dysfunction and progressive bone loss caused by radiation exposure during spaceflight. In animal studies, excess free radical formation is associated with pathological changes in bone structure, enhanced bone resorption, reduced bone formation and decreased bone mineral density, which can lead to skeletal fragility. We previously reported that exposure to low or high-LET radiation rapidly increases expression levels of pro-osteoclastogenic and oxidative stress-related genes in bone and marrow, followed by pathological changes in skeletal structure. To screen various antioxidants for radioprotective effects on bone, 4 month old, male C57Bl6/J mice were treated with a dietary antioxidant cocktail, injectable α-lipoic acid, or a doped plum-enriched diet (DP). Mice were then exposed to 2 Gy 137Cs total body radiation and one day later marrow cells were collected and the relevant genes analyzed for expression levels. Of the candidates tested, DP was most effective in reducing bone resorption-related gene expression. Microcomputed tomography revealed that DP also prevented the radiation-induced deterioration of skeletal microarchitecture, as indicated by percent bone volume, trabecular spacing and trabecular number. DP had similar protective effects on skeletal structure, post-exposure to protons (0.5 Gy, 150MeV/n) and 56Fe 0.5Gy, 600 MeV/n. When cultured ex vivo under osteogenic conditions, bone marrow-derived cells from DP-fed animals exhibited increased colony numbers compared to control diet-fed animals. These findings suggest that DP exerted pro-osteogenic effects apart from previously identified anti-resorptive actions, which may contribute to radioprotection of skeletal tissue. In conclusion, a diet enriched in certain types of antioxidants and polyphenols such as DP may be useful as an intervention to protect tissues from degenerative effects of ionizing radiation.

Purpose of the study
- Assess the ability of selected antioxidants to mitigate radiation-induced bone loss
- Determine the mechanisms underlying radiation-induced bone loss

Overview

High doses of radiation lead to progressive bone loss

Conclusions
- Radiation induces acute and persistent damage to bone and associated tissue.
- Radiation-induced bone loss is to some extent driven by the early increase in bone resorption response as well as oxidative stress and that and the capacity to prevent these early responses can effectively mitigate bone loss.
- These early markers are useful tools to assess and screen for candidate interventions against bone loss.
- Plum supplementation can positively alter the skeletal response to radiation.

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