Space-like radiation leads to deficits in vertebral bone density and microarchitecture in male Alzheimer's-like transgenic mice

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Irradiation and Alzheimer's are both associated with diminished bone health, though their combined effects are not fully understood. This is of consideration for long-duration space exploration missions, where chronic radiation exposure and age-associated comorbidities—such as Alzheimer's—are of great concern. The objectives of this study were to (1) compare murine bone microstructure in an Alzheimer's model to wild type and (2) to quantify late-effects of radiation exposure on bone microstructure in the Alzheimer's model.

$APP^{NL-F/NL-F}$ knock-in mice were crossed with human APOE3 floxed targeted replacement mice on a C57BL/6 background (ALZ). Male ALZ mice were exposed to 0.75Gy 5-ion mixed field beam irradiation (GCRsim) (n=9) or 2Gy gamma irradiation (n=7) at 7 months of age. Sham-treated male ALZ (n=9) or WT mice (n=6) were used as controls. Mice were sacrificed at 17 months of age; lumbar vertebral trabecular bone structure was assessed using micro-computed tomography. ANOVA with Tukey post-hoc assessed group effects; data reported as mean [95% CI]; α $p<0.05$.

ALZ-Sham mice had greater bone mineral density (198 mgHA/ccm [188, 208] vs. 171 mgHA/ccm [157, 184]; $p=0.048$) and trabecular number (4.19 [4.0, 4.4] vs. 3.72 mm^{-1} [3.5, 3.9]; $p=0.004$) than WT-Sham. ALZ-GCRsim mice had lower bone mineral density (-16%, $p=0.008$), bone volume fraction (-23%, p=0.005), trabecular number (-9%, $p=0.001$), trabecular thickness (-11%, $p=0.023$), connectivity density (-21%, $p=0.011$), and greater trabecular separation (+11%, $p=0.001$) compared to ALZ-Sham. In contrast, bone microstructure in ALZ-Gamma mice was not significantly different from ALZ-Sham.

In this ALZ model, gamma radiation did not influence bone microstructure, while GCRsim induced significant deficits in bone density and microstructure. The observed bone deficits due to GCRsim would weaken the LV, likely leading to increased risk of vertebral fracture. While this ALZ model did not have adverse effects on lumbar vertebral bone structure when compared to WT, the possible compound effects of GCRsim and ALZ should be further explored in a more severe ALZ model (APOE4 replacement). Support NIH T32GM144273, NIH T32AG023480, NASA 80NSSC18K0810.