Systemic effects of radiation through femoral mechanical strength

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Introduction

A mission to Mars is quickly becoming an obtainable goal by NASA. Scientists around the world are working to address not only how to get to Mars, but also how to make it possible for humans to safely make the journey and live on Mars. One of the biggest threats during space travel is the increased presence of radiation, without Earth's protective barriers. Small doses, even less than 2 Gy, of space radiation can have severe effects to human health [1,2]. A well known effect of radiation is degradation of bone, but there are inconclusive data about the implications of dosage and type of radiation have on the degrading, and what this means for the mechanics of bone [3]. This study aims to better understand the overall mechanical changes in the femur due to various doses and types of radiation across time.

Methods

Study Design: All animal work was performed at Brookhaven National Laboratory and Johns Hopkins Medical University under their respective IACUC approvals. Long evans rats (n=160) were exposed to radiation or used as a sham. After completing cognitive testing at Johns Hopkins, the subjects were euthanized and hind limbs were collected for mechanical testing at significant time points.

Biomechanical Testing

Three Point Bending Tests: Right hind limbs were cleaned and stored in 70% ethanol solution, until 24 hours prior to testing, when they were hydrated in 0.1 PBS solution. An Instron universal testing frame (model 5967) was used to conduct three-point bending test until failure on each femur (Figure 1). A constant span of 15 mm with a loading rate of 0.2 mm/s was used to apply a force in the anterior to posterior direction. Force and deflection data for each sample was collected and plotted to determine linear stiffness, max force, and energy to failure.

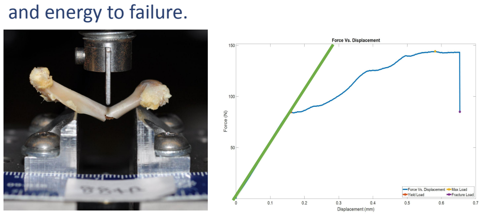


Figure 1: (Left) Three-point bending of rat specimen across a fixed span, with load applied from the top by Instron at constant rate. (Right) Force deflection curve for specimen, with relevant mechanical parameters indicated, as obtained from custom MatLab script.

Femoral Neck Tests: Proximal femur segments were completely dried then embedded vertically into epoxy. Samples were hydrated in PBS 24 hours prior to femoral neck fracture. These tests were conducted under the same specifications outline above using a custom fixture to mimic physiologically relevant femoral loading.

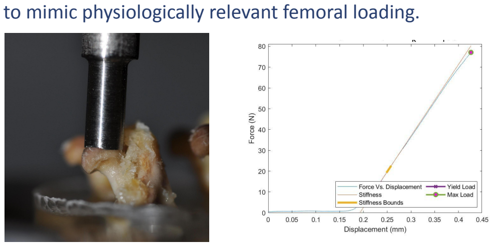
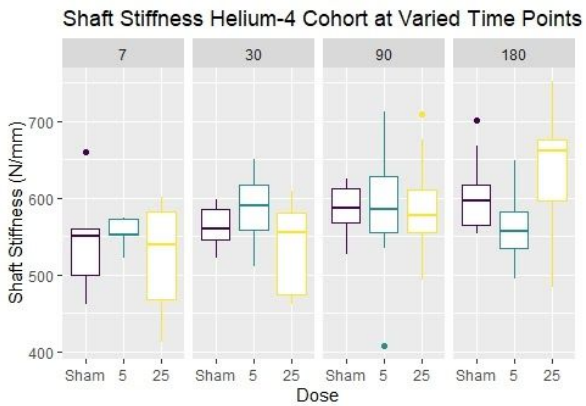


Figure 2: (Left) experimental setup for femoral neck testing with custom fixture applying load from the top.(Right) Curve for specimen, with relevant mechanical parameters indicated, as obtained from custom MatLab script.

Statistical Analysis: Two-way ANOVAs were conducted in R for each cohort, to assess differences in mechanical parameters based on dose and time point after irradiation. Data is presented as means ± SD.

Results

The only significant differences were found with respect to time point after irradiation. Specifically, there was a significant increase in shaft stiffness in the Helium-4 cohort and protracted GCR cohorts. There was also significance within the Helium-4 cohort for femoral neck analysis with regard to time for stiffness, and energy to failure. The graphs below are shown because they demonstrate some form of significant difference



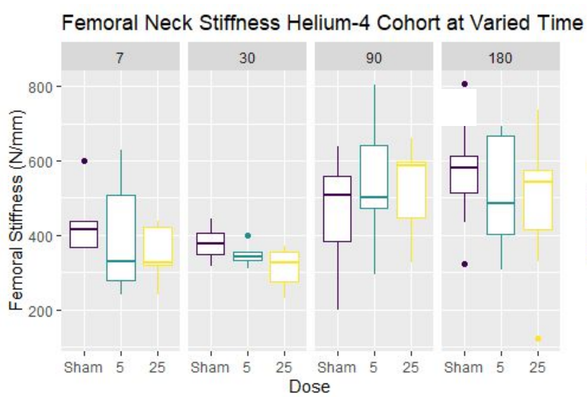


Figure 3: (Top): Shaft stiffness values across varied time points at each dose within the Helium cohort. Significant differences were only observed for factors of time. In this trial, there were significant differences between the 180 day and 7 day (p=0.0148), as determined through post-hoc Tukey tests. (Bottom): Femoral neck stiffness values across a range of time points and doses within the Helium-4 cohort. Significant differences evaluated between the 180 and 7 days (p=0.00978), 90 and 30 days (p=0.0035), and 180 and 30 days (p=0.00031).

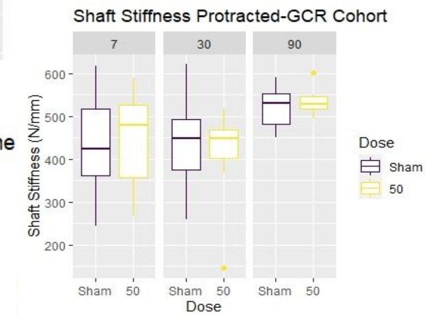


Figure 4: Mean and standard deviations for shaft stiffness within the protracted GCR cohort. Significant differences determined between time points, specifically between the 90 day and 30 day (p=0.0313). General trends are also evident, including those showing an increase in stiffness with age in the sham group. This is also evident in the treatment groups, along with a decrease in variability.

Discussion

While there is limited significance within the data, general trends shared among each cohort are still telling of the generalized effects of radiation. Within the shaft analysis alone, Helium-4 data had on average, the highest values for each mechanical parameter, suggesting that higher weighted irradiation may be more detrimental. Also there were consistent trends showing increase mechanical strength among the sham groups with time. This accounts for the higher influence of time, as the rats got stronger with age. Energy showed no trends within three-point bending analysis, however, femoral neck failure energy was one of the few tests to show significant increases with time. Similarly to the overall bone mechanics, there were increasing strength trends with time observed across multiple ions and parameters.

The lack of significance, primarily within the galactic cosmic radiation (GCR) groups, may be due to the fact that these are preliminary cohorts. Tukey test showed that majority of the changes within the He-4 cohort were changes in time-points compared to 180 days. Additionally, cognitive decline for all specimen is being analyzed. This data could be matched, on a per specimen basis, to better understand which subjects had a systemic reaction to radiation. With this, data clusters will be identified such that more accurate statistical analysis can be performed.

Figure 5: Example of experimental microindentation set up that has found similar time dependent changes in material strength after radiation treatment. This work will be continue to further correlate with large scale mechanical data.

Conclusion

This study continues to explain the systemic effects of radiation on physiological function. This data supported preliminary microindentation results, however, there is far more experimental and statistical analysis to be conducted. Linear mixed models, with a full set of cognitive and mechanical data will clarify observed trends in time points across all cohorts of radiation.

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References

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