Effect of Galactic Cosmic Radiation on Bone Microstructural strength

Jack T. Felipe[1], Sabrina S. Vander Wiele[1], Catherine M. Davis[2], Anthony G. Lau[1]
[1]The College of New Jersey, Department of Biomedical Engineering,
[2]Uniformed Services University of the Health Sciences, Department of Pharmacology and Molecular Therapeutics

Introduction

NASA has been looking into new technology for long duration space flight to Mars [1]. Space travel has many unknowns and dangers that are both visible and invisible. Once outside of Earth's radiation shielding atmosphere, astronauts are exposed to different forms of space radiation. A form of ionizing radiation called Galactic Cosmic Radiation (GCR) is most common. Ionizing radiation has enough energy to remove electrons from orbit around their nucleus, therefore changing the chemical composition of a substance[2]. When GCR passes through humans, there is a possibility for radiation for radiation to alter the composition of the bone. Previous studies have shown that clinical radiation greatly increases a patient's chance of a fracture around the treatment area. These studies found that fracture was 65, 66, and 214% more likely in patients with cervical, rectal, and anal cancer when radiation therapy was used instead of non-radiation treatments [3]. determining the effect of GCR on the structural integrity of bone is necessary for the safety of astronauts. This study will use Finite Element Analysis to determine if there is a relationship between GCR and structural integrity of bone.

Methods

Study Design

The rats used in this experiment are Long Evans rats and were given radiation treatments at Brookhaven National Laboratory, then the hindlimbs of each rat were extracted at The College of New Jersey and stored in 70% ethanol until the time of scanning. This study consisted of a preliminary cohort of rats (n = 12). The exposed group (n = 6), consisting of 4 females and 2 males, was treated with 90-day protracted radiation. Rats from this group were exposed to protracted 50 cGy radiation. The control group (n = 6), consisting of 2 females and 4 males, was given sham treatment.

Micro-CT and Preprocessing

Each irradiated rat bone went through a micro computed tomography (CT) scan. Each scan were taken at 8 micrometer resolution with each scan being taken at 8 micrometer intervals. These scans were anatomically aligned in Mimics research 24 through 3D rotation . After alignment, the target region was analyzed by taking a 2.4mm tall section (300 slices) of bone right below the tibial growth plate (figure 1). To complete preprocessing, the bone was separated from other noise in the scans by choosing a threshold that effectively removed all unnecessary pixels. The threshold chosen for this study was 3000 to the maximum allowed value. After masking, a 3D mesh of the bone segment was produced. Each mesh was downscaled by a factor of 3, changing the interval of each slice to 24μm, due to file sizes being too large to process.

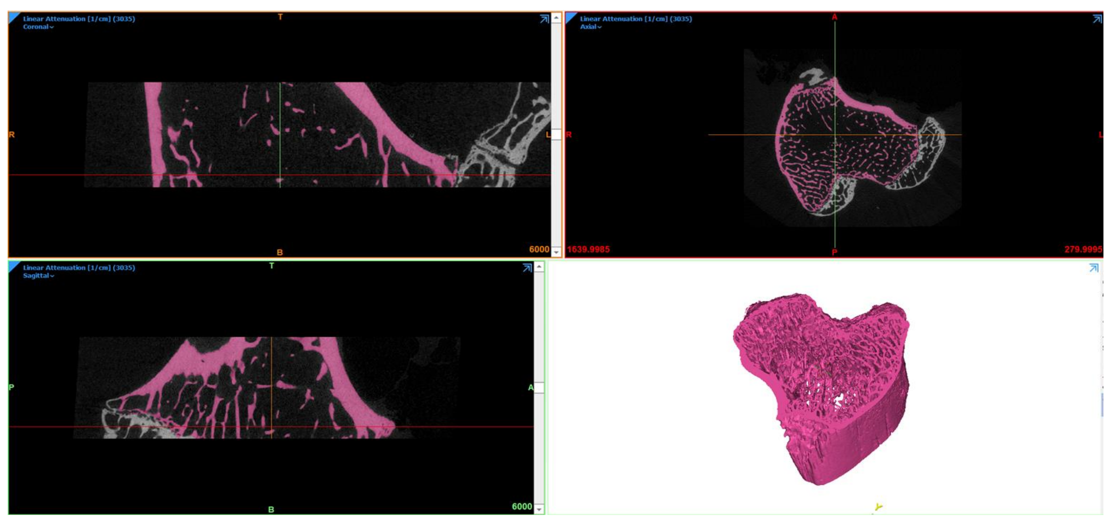

Figure 1. The Mimics research 24 program is shown. Mimics uses DICOM image data to present, coronal, sagittal, and axial views of an image. A 3D mesh (bottom right) is generated using masks (shown as purple).

Finite Element Analysis

For Finite element Analysis (FEA), the 3D mesh was imported into Abaqus 6.9 software for simulation. Bone material was assigned to each model as a nominal homogenous Young's modulus of 10 GPa and 0.3 Poisson's ratio. Superior and inferior node sets were identified, and boundary conditions were created.

A simulated axial compression test was performed by applying a 12μm downward displacement (0.5% displacement) on the superior node set (figure 2), while the inferior node set was assigned a fixed boundary condition. Abaqus software calculated the resultant forces due to the displacement and resultant force values were extracted. In addition, FE volume was calculated by multiplying the number of elements in the model by the volume of each element (24μm x 24μm x 24μm). Bone Stiffness was calculated by dividing the force reaction by the applied displacement. Bone structural efficiency was calculated by dividing bone stiffness by FE volume.

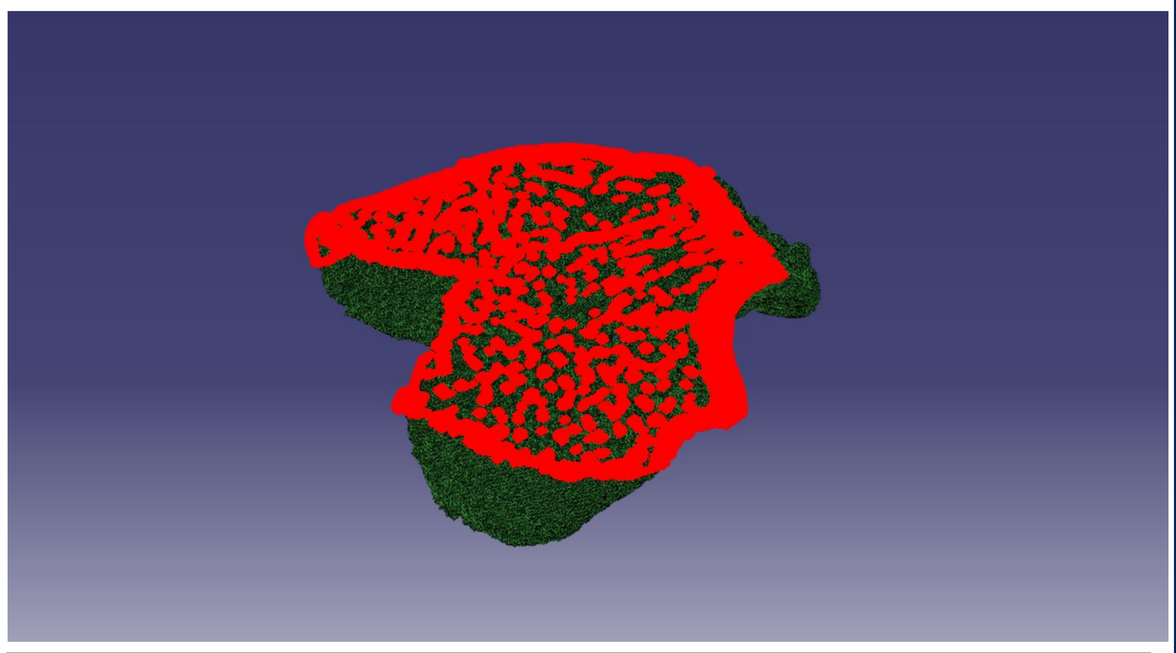

Figure 2. Image from Abaqus highlighting the superior node set.

Statistical analysis

Statistical analysis was performed in STSS using a mixed model with gender and treatment as factors for analysis. Analysis was done for bone volume, stiffness, and structural efficiency for sex, treatment, and treatment by sex.

Results

There is no statistical significance in bone Volume or stiffness between the control group and the exposed group. In addition, there was no statistical significance in the change in bone volume of stiffness between sexes of rats that were given protracted radiation as treatment. There were trending sex differences in the bone structural efficiency parameter Such trends are also seen in the box and whisker plots (Figure 2) where the structural efficiency of bone in irradiated female rats is higher than irradiated male rats.

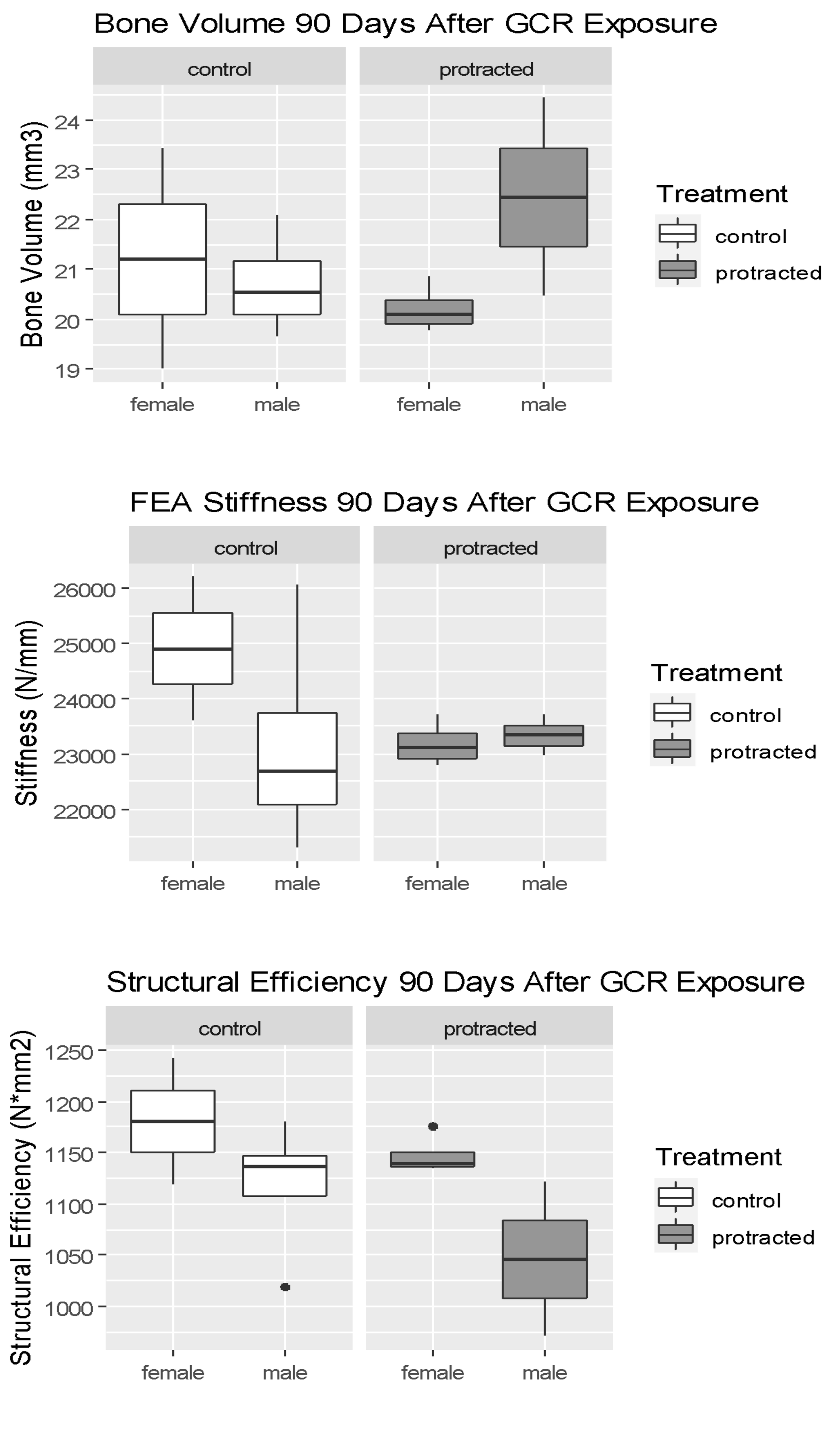

Figure 3. Box and whisker plots of bone volume, bone stiffness, and structural efficiency of bone. Each plot compares control vs. treatment groups and sex. Dots on a plot represents an outlier

Discussion

Other studies have been conducted to determine if clinical radiation affects the strength of bone. These studies determined that 54cGy of radiation over six weeks resulted in an increased likelihood of fracture [3]. However, because these studies examine clinical radiation and not GCR both forms of radiation can have different effects on the body. It is known that clinical radiation increases the likelihood of fractures, therefore further research must be done to determine if GCR has this same effect at higher doses or longer exposure times.

One limitation is that this study was conducted on a partial cohort, resulting in little statistical power. Increasing the number of animals in the study should increase statistical power. Therefore, for the results to be fully analyzed and understood a larger sample size must be used.

When analyzing these model, each bone was assigned a nominal homogonous young's modulus of 10 Gpa and a 0.3 Poisson's ratio. This assumption may not be correct for all bones. For example, there can be bones with a higher young's modulus, lower young's modulus, or even bones with a young's modulus that was assigned. Using the exact Young's modulus and Poisson's ratio for each specimen would greatly enhance the accuracy of the data and could affect significance.

With future research, the entire cohort of rats will be examined for changes in bone volume, bone stiffness, and bone structural efficiency. The trend seen in structural efficiency of bone in the sex parameter should be studied as well. The box plot in figure 3 showing structural efficiency 90 days after GCR exposure shows that the mean structural efficiency is lower for radiated groups compared to sham groups. In addition, when comparing sex, structural efficiency has a greater decrease in male irradiated rats compared to females.

Further research will examine the effect of 90-day acute radiation on bone strength. In addition, future research must be done to examine how longer exposure to acute and protracted radiation affect bone strength.

Conclusion

With deep space travel on the horizon, it is important to understand how space radiation affects the human body. Studies such as this one are new and must be investigated further. Exposure to protracted radiation does not significantly affect volume, stiffness, or structural efficiency of bone 90-days after exposure. There were trending differences in bone structural efficiency between the male and female subjects. Future work will expand the cohort as well as investigate dose-rate effects for radiation exposure (acute vs protracted).

Acknowledgements

We would like to thank our funding sources: The College of New Jersey's Mentored Undergraduate Research Experience (MUSE), the New Jersey Space Grant Consortium (NJSGC), National Space Biomedical Research Institute (grant MA02802), and the NIH (R01 AR068132, R37 AA0011290, and F32 AA023422).

References

[1] Dunbar, B. (2018, November 30). NASA's Exploration Campaign: Back to the Moon and on to Mars. NASA. https://www.nasa.gov/feature/nasas-exploration-campaign-back-to-the-moon-and-on-to-mars/

[2] Zeitlin, C., Hassler, D. M., Cucinotta, F. A., Ehresmann, B., Wimmer-Schweingruber, R. F., Brinza, D. E., … Reitz, G. (2013). Measurements of energetic particle radiation in transit to mars on the mars science laboratory. Science, 340(6136), 1080–1084. https://doi.org/10.1126/science.1235989\

[3] Willey, J. S., Lloyd, S. A., Nelson, G. A., & Bateman, T. A. (2011). Ionizing Radiation and Bone Loss: Space Exploration and Clinical Therapy Applications. Clinical reviews in bone and mineral metabolism, 9(1), 54–62. https://doi.org/10.1007/s12018-011-9092-8