Modeling The Effects of Head Only Proton Radiation On Bone Micromechanical Properties

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Introduction

Astronauts traveling past Earth's magnetosphere are exposed to galactic particle radiation and solar particle effects. Space radiation induces high linear energy transfer, as the radiation of ionizing particles transfers into matter, it causes oxidative damages to cell structures, affecting bone homeostasis[1,2]. There is a risk of degradation of the elastic modulus of the tibial cortical bone, which is a important for weight bearing[3]. Thus, astronauts may experience the adverse effects of bone decomposition due to accumulating ionic proton radiation. The objective of our study is to investigate how microstructural changes in cortical bone of rats exposed to proton radiation affect overall mechanical behavior.

Methods

Study Design

In this study, long evans rats were exposed to head only proton radiation (100 cGy), with corresponding sham controls. Animals were euthanized 2 months after exposure and the tibia bone specimens were collected for analysis. This poster presents a subset of the overall animal study that received additional Micro CT analysis. Bones were scanned at 2µm resolution (n=2 per group) to explore microstructural changes through high resolution microCT imaging and computational micromechanical modeling.

MicroCT Image Processing

All microCT scans were taken at a 2 µm resolution of the proximal tibia just inferior to the epiphyseal growth plate. Mimics Research 21 was used for image processing. In Mimics, multiple images received from the microCT were compiled to create a single 3D model. The microCT scans were cropped down to a 50x50x50 voxel volume at 10 anatomical regions of the cortical bone, for each bone specimen in the study. Bone was segmented from the pores using a threshold on pixel intensity, bone has a higher pixel intensity than the surrounding tissue. The selected volume was exported for micromechanical analysis.

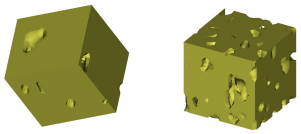

Figure 1: 3D Generated RVE of Cortical Rat Tibia: Control (left) and Irradiated (right)

Matlab Image Processing

A custom image processing code was written for MATLAB R2019a to convert voxel volumes into micromechanical models. The code recognizes the DICOM files, downsampled it to a new volume, and assigns threshold values for bone and air. The code assigns each subcell with a distinct material property of the composite material. This code writes the volume into a .mac file which can be used for MAC/GMC.

Micromechanical Modeling

NASA Glenn Research Center's MAC/GMC 4z-3.8 software was used to investigate the effective material properties based on the microstructural changes. This software was developed by NASA to study effective properties of multiphase composites in aerospace applications, we will be applying this to biological tissues. We explored two forms of homogenization with this software to determine the elastic properties using generalized method of cells (GMC) and high-fidelity generalized method of cells (HF-GMC). Bone was modeled as linear elastic with approximate material properties 10 GPa, v=0.35 as this is an exploratory study. Pores were model as linear elastic at 1 Pa due to numerical instability for using zero. The effective elastic modulus was obtained at varying levels of detail for the Representative Volume Element (RVE). From models with 50x50x50 subcells down to 10x10x10 subcells, these were both ran under traditional GMC and high-fidelity GMC. Simulations ran on a custom workstation with Intel(R) Xeon(R) W-2102 CPU @ 2.90GHz Processor with 256 GB of RAM, in a 64-bit operating system.

Statistical Analysis

A two way ANOVA was used for statistical analysis (R-4.0.5). The following treatment and Downsizing, were assigned as the independent variables and porosity was assessed as the dependent. Additionally, a post-hoc Tukey test (α=0.05) was performed to account for each individual treatment comparison.

Results

The results from the post hoc reveal a significant difference between the radiation and porosity (Fig. 2). No significant difference was observed for the RVE downsampling factor. It is important to note the large standard deviations across all groups.

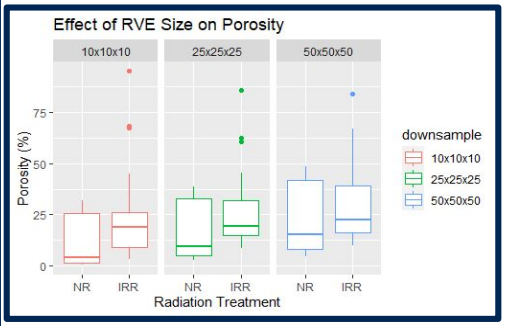

Figure 2: Radiation Treatment vs. Porosity. NR depicts the sham irradiated and IRR represents the 100 cGy proton irradiated group. Effects of RVE downsmapling can also be observed individually.

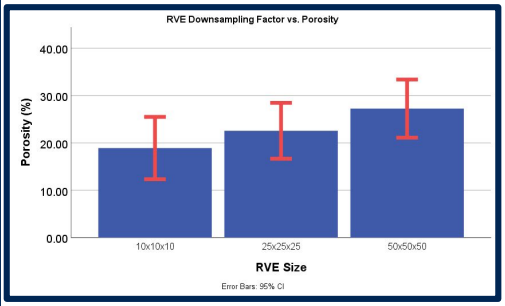

Figure 3: The effect RVE size on the average porosity

Treatment	Porosity (Air/Total Volume)		
	50x50x50 RVE (i = 1)	***25x25x25 RVE (i = 2)***	***10x10x10 RVE (i = 5)***
Non-Irradiated (Sham)	23.1 ± 17.1 %	17.2 ± 14.5 %	12.2 ± 12.5 %
Irradiated (IRR)	31.4 ± 20.7 %	27.9 ± 20.7 %	25.7 ± 24.9 %

Table 1: The result porosity percentage due to the effects of downsampling on RVEs. Each RVE is influenced by the downsampling index. RVE is determined by dividing the volume to the downsampling index.

Discussion

This is the first study to investigate the effects of radiation on the material properties of bones through micromechanical modeling. The study results show that there is a significant difference in porosity between radiation treatments. The study shows a trend that irradiated groups correlate to significantly reduced elastic moduli.

The main limitation to this study was the limited sample size. Only a total of 4 rats were scanned resulting in an n=2, for each treatment. This small sample size has led to a high amount of variance as shown by the results. The large standard deviation and variability of the samples, shown in Figure 2, is due to the partial volume effect and unique geometry of the tibia bone volume. Threshold values must be carefully chosen.

Across the 4 samples, at 10 distinct locations (repeated measures), none of the bones are identical. The bones' microarchitecture displays patterns of interstitial pores, consisting of penetrable and isolated pores[4]. When constructing the RVE in Mimics, the volume must be within the cortical regions of the tibia and needs to avoid the empty zones of the microCT file or risk skewing the data. In the micromechanical modeling phase, the algorithm takes into account all three dimensions of the volume and approximates an effective modulus given the two phases (i.e. bone and air).

Table 1 displays the porosity downward trend as downsampling index increases. As the RVE model size decreases, the amount of detail of the model decreases. This may in turn affect the results of the micromechanical analysis, leading to increased stiffness as RVE model size decreases. Problems may also arise due to local changes in microstructure. The cortical region is not homogeneous and where the RVE is chosen affects the overall results.

The next steps in this study are to finalize the RVEs and analyze them using the MAC/GMC code. In term of user define homogenization, HF GMC allows for shear coupling, thus we predict more consistent and accurate results with High Fidelity Analysis. Although HF-GMC may result in more accurate results, it is computationally taxing. Memory usage is high and run times increase with model size. Our study will seek to quantify the differences in the traditional micromechanical analysis and HF, assessing whether or not the extra computational stress affects the end moduli results.

Conclusion

While the micromechanical analysis code was developed for aerospace applications, it can be applied to biological materials, especially bone. Material data may be collected which could be used to homogenize bone material. This bone material could be applied to Finite Element Analysis (FEA), allowing for the analysis of large scale bone failure mechanics.

Acknowledgements

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