Introduction

- Alzheimer’s Disease (AD) and Osteoporosis are common degenerative diseases of aging. Previous research has found that AD and osteoporosis may overlap [4].
- Observational studies demonstrate a correlation between the osteoporosis and AD that suggest, rather than one condition causing the other, both conditions are related by a common underlying mechanism [4].
- Previous studies have investigated bone mass in mouse models that recapitulate the pathology of AD [4].
- This study focuses on the 5xFAD mouse model, another AD mouse model that exhibits a more aggressive form of AD. Thus, the 5xFAD mouse model rapidly recapitulates major pathologies that are driving the effects seen in those mouse models. Future work is necessary to identify the role of Aβ pathologies that are driving the effects seen in those mouse models.

Material and Methods

5xFAD and Wild-Type (Control) Mice Tissues
The 5xFAD mouse model is a validated model of familial Alzheimer’s disease.

Micro-Computed Tomography (μCT)
The right femur of the wild-type (control) mice and 5xFAD mice were scanned and analyzed using μCT. Trabecular bone architecture was measured in a proximal region. Primary trabecular parameters included bone volume per total volume (BV/TV). Cortical geometry was measured in a 100 slice region at the midshaft at 50% of the total length of the femur. Primary cortical parameter includes cortical area (mm²).

Bone Histological Analysis:
After μCT scanning, the bones were prepared for histological investigation by dehydration and decalcification of the femoral tissues. After all the calcium from bones were removed, samples were embedded in paraffin, cut into sections and mounted for tartrate-resistant acid phosphatase (TRAP) and Sudan Black B staining.

Results and Discussion

Trabecular Bone
Male 5xFAD mice exhibit a decrease in trabecular bone density over time in contrast to Wild-Type (WT) mice (Figure 3). Older female 5xFAD mice exhibit a lower trabecular bone density than the WT mice.

Cortical Bone
μCT analyses show that over time male 5xFAD mice do not have a decreased cortical bone are in comparison with WT mice. Older female mice exhibit a lower cortical bone area than WT mice.

Conclusion and Future Work

- We are currently performing TRAP staining, which is a method to identify active osteoclasts.
- Considering other mouse models that recapitulate AD exhibit similar effects in trabecular and cortical bone, our current model could share the same mechanisms and pathologies that are driving the effects seen in those mouse models. Future work is necessary to identify the role of Aβ and RANKL Pathway in the 5xFAD model.
- We are also performing Sudan Black staining to investigate senescence, a process known to occur in the brains of AD patients, to understand whether the bone resorption is due to cellular aging.

Bone loss has not been studied nor published before in the 5xFAD model. Although AD and osteoporosis are not commonly considered linked diseases, past research presents compelling information that they are interconnected. Continuing to investigate the AD mouse models is crucial to further our understanding of these two devastating diseases of aging.

References