# Sexual Dimorphism in the Skeleton of Adult and Aged Mice with Alzheimer's Disease-Related Mutations

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**Background and Hypothesis**: Alzheimer's disease (AD) is a progressive neurological disease characterized by gradual impairment in cognition and memory. Osteoporosis is another common degenerative disease in aging populations. Recent research has uncovered links between AD and bone biology, as well as potential sex-linked differences in disease progression, but the mechanisms behind this are yet to be fully understood. We hypothesize that at both 4 and 13 months of age, female mice with AD-related mutations will have more age-related adverse effects on bone microstructure and geometry than their male counterparts.

**Project Methods**: Male and female mice expressing humanized forms of AD-linked mutations (Swedish/Artic/Austrian) in the Amyloid Precursor Protein (APP-SAA) were raised until either 4 or 13 months of age to accelerate plaque formation. Dxa/Piximus data was collected for body weight, total bone mineral density (BMD), femur BMD, and spine BMD for both age groups and sexes. Trabecular bone from distal femora and cortical bone from femoral mid-diaphyses were then analyzed by μCT. Sexes were analyzed separately by 2-way ANOVA (Tukey's post-hoc multiple comparisons) or unpaired t-test.

**Results**: Our results show that among mice with AD-related mutations, female sex is associated with more pronounced age-related effects on bone. Both sexes displayed increases in tissue and marrow area, point of maximal inertia, and tissue mineral density, but females showed a more detrimental effect with age. The deleterious effects of age were more apparent in trabecular bone than cortical, with female APP-SAA mice also displaying significantly lower BV/TV, Tb.N., Tb.Th., and higher Tb.Sp. than male APP-SAA mice at both ages.

**Conclusion and Potential Impact**: AD and osteoporosis are prevalent and debilitating diseases affecting millions of patients throughout the United States. The results from this study will help to understand the relationship between them and identify potential interactions between sex and disease progression.