Dr. Emily Stein

Osteoporosis is a major complication of glucocorticoid (GC) therapy. Osteoporotic fractures, common in patients using GCs, significantly worsen morbidity and increase mortality. GCs increase fracture risk most in postmenopausal women, who are already at high risk for fractures because of estrogen deficiency and aging. Individuals who use GCs fracture at higher areal bone mineral density (aBMD), measured by dual energy x-ray absorptiometry (DXA), than those who do not, suggesting that increased fracture risk in patients taking GCs is not completely accounted for by reductions in aBMD.

High-resolution peripheral computed tomography (HRpQCT) is a new noninvasive imaging technology available at few centers worldwide and at only six in the US. HRpQCT can separately measure trabecular (Tb) and cortical (Ct) vBMD at the distal radius and tibia, and has sufficiently high resolution (voxel size ~82 microns) to image Tb microarchitecture. Individual trabeculae can be imaged and classified as plates and rods by a novel procedure, individual trabecula segmentation (ITS). In addition, HRpQCT scans can be computationally modeled by Finite Element Analysis (FEA) to assess the contributions of Ct and Tb parameters and Tb plates and rods to bone stiffness (mechanical competence). We have used this technique to show that postmenopausal women with a history of fractures have lower vBMD, microarchitectural deterioration, decreased stiffness, preferential reductions in Tb plate bone volume, number, and connectivity, loss of axially aligned trabeculae, and a more rod-like Tb network compared to those without fractures, despite similar aBMD by DXA. These novel and powerful tools have not been applied to patients treated with GCs, yet have the potential to greatly expand our understanding of microstructural mechanisms by which GCs adversely affect bone strength.

The goal of this research proposal is to use HRpQCT to elucidate the effects of GCs on bone microstructure and strength in postmenopausal women. We hypothesize that GC therapy will be associated with disrupted bone microstructure and reduced mechanical competence independent of aBMD by DXA. We will test these hypotheses in a cross-sectional, case-control study of postmenopausal women with and without GC use and with and without a history of fragility fracture.