QUANTIFYING SEX-RELATED CHANGES OF BONE MASS IN CLINICAL TRIAL CT SCANS USING VOXEL-BASED MORPHOMETRY

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Introduction

Fragility fractures in the hip are a growing risk for older adults [1] which potentially could be mitigated by better understanding local bone quality changes in the proximal femur. Current methods are often limited to regional analyses, such as volumetric (vBMD) or areal bone mineral density (aBMD) in the femoral neck or greater trochanter. Voxel-Based Morphometry (VBM) can be used to compare similar but different images at the voxel-level [2] and is a powerful tool for quantifying sub-regional bone quality changes in the femur.

In this study, we demonstrate the use of VBM on quantitative computed tomography (QCT) scans of the proximal femur to investigate sex-related sub-regional bone quality changes over an 18-month period.

Methods

QCT scans from 67 females and 32 males (ages 65-85; BMI 27-45 kg/m^2) were selected from the UPLIFT clinical trial [3]. All subjects underwent an aerobic exercise and caloric restriction intervention targeting 10% weight loss. No subjects were osteoporotic at study entry. Baseline scans and 18-month follow-up QCT scans were available for all selected subjects. A single template right femur was generated from 10 random baseline scans [4]. Every scan was manually segmented and, using the Advanced Normalization Tools (ANTsPy 0.3.1), deformably registered to this template using a symmetric normalization transformation and cross-correlation as the optimization metric. The registered images were smoothed with a Gaussian filter (σ = 3mm) which renders the data more normally distributed [2]. Bone density differences for each subject were calculated by subtracting registered baseline scans from the registered 18-month follow-up scans, and an image of averaged bone density changes was created for males and females. These were compared using a two-sided t-test for each voxel, and a False Discovery Rate control of $q<0.05$ was used to address multiple comparisons [5].

Results

Local bone changes ranged from -0.011 to 0.023 g/cm^3 for females and -0.005 to 0.022 g/cm^3 for males. Both groups showed bone density increases on the anterior and posterior aspects of the cortical bone along with the posterior aspect of the femoral neck (Figure 1B and D). The average female showed a large density decrease in the greater trochanter (Figure 1A). The significantly different bone density changes between the males and females are mostly located in the femoral head and trochanter, and all have negative values, meaning the average female femur lost significantly more bone than the average male femur (Figure 1E).

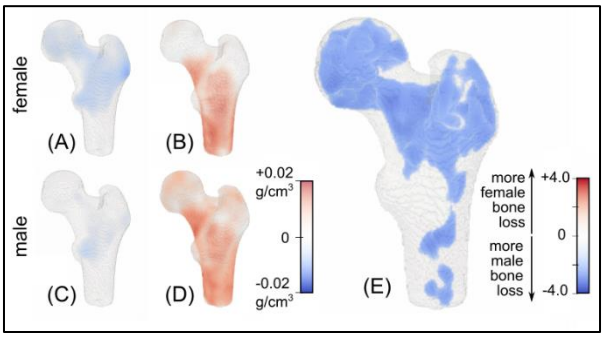

Figure 1: (A) Female average bone loss; (B) Female average bone gain; (C) Male average bone loss; (D) Male average bone gain; (E) T-values of the difference between female and male bone changes. Non-significant bone changes are transparent.

Discussion

This is the first weight loss trial to quantify longitudinal sub-regional bone changes at the voxel level using VBM. While other longitudinal bone quality studies show regional bone loss, we found that there is also substantial local bone gain that may be overlooked in previous work. In many regions of the femur, females lost bone at a significantly higher rate than males. However, this is not uniform, and these areas may be a reason for the increased fragility fracture risk women have compared to males. Future studies should investigate if these regions are associated with increased fragility fracture risk (e.g., finite element analyses). VBM may a useful tool for studying other effects (e.g., age or pharmaceutical treatment) on local bone changes and could be used to develop personalized bone change and fragility fracture risk models.

References

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