Simplifying 3D Architectural and Mechanical Changes in Human Trabecular Bone During Menopause

INTRODUCTION

The reduced level of estrogen during menopause leads to an increase in bone remodeling activity and a subsequent decrease in bone mass, despite normal bone formation activities [1]. However, dynamic simulations of bone remodeling have indicated that both a maintained increase in bone remodeling activation and a transient imbalance in local bone remodeling (i.e., a small, local deficit between bone formation and bone resorption) are required to predict the clinical course of bone mineral density loss during post-menopausal osteoporosis [2]. The later assumption has not been supported by the available bone histomorphometric data that the resorption depth in older women is the same as in young women. Interestingly, a three-dimensional (3D) simulation of age-related bone remodeling using micro-CT images of trabecular bone also suggests that a bone formation deficit is a dominate cause of post-menopausal bone loss [3]. However, the mechanism of post-menopausal bone loss is still uncertain. In this study, a rigorous 3D image topological analysis technique has been incorporated into the 3D simulation of trabecular bone remodeling with a specific consideration of three types of microscopic bone loss: trabecular perforation, breakage, and isolation. The available literature in bone biology suggests that perforated holes in trabecular plates, broken trabeculae, or small isolated bone volumes broken off from the main architecture are not re-filled or re-connected during the remodeling process. In this study, we simulate the bone remodeling process during and after menopause by a detailed 3D human trabecular bone model and quantify the amount of the bone loss due to each mechanism.

MATERIALS AND METHODS

Eight human trabecular specimens were obtained from one 3rd lumbar vertebra (52 y.o. male), two proximal femurs (two singles: 64 y.o. male and 44 y.o. male) and one proximal tibia (69 y.o. male) and scanned at 21µm resolution using a vivaCT 40 µCT system. The central –4x4x4 mm cubical sub-volume was extracted and a global thresholding technique was applied to binarize grayscale µCT images. The isolated voxels or voxel-clusters in binarized µCT image were removed using clustering analysis [5].

Bone remodeling simulation consisted of a 40-day bone resorption period (1 cycle) and a 160-day bone formation period (4 cycles). The simulation started 5 years before and ended 15 years after menopause. The bone remodeling activation frequency during menopause was based on the latest literature (Figure 1) [6]. Five steps were involved in each remodeling cycle: (1) the current bone surface was labeled; (2) resorption cavities (42 µm deep and 126 µm in diameter) were created and distributed randomly over the bone surface. The total number of cavities were determined by current activation frequency; (3) each cavity went through a digital topological detection [7] and the cavity caused a perforation or a disconnection of trabeculae was identified (Figure 1); (4) for every cavity which didn’t cause topological change in architecture, refilling was completed in 4 cycles; (5) isolated voxels or voxel-clusters were removed at the end of each cycle by clustering analysis [5].

For each sample, 3D images of -5, 0, 5, 10 and 15 years of remodeling simulation were converted to voxel-based finite element models and subjected to linear analysis to determine the Young’s modulus (E) along the principal trabecular orientation. Based on digital topological analysis, the plate fractions (pf), defined by plate bone volume over total bone volume, were also calculated for those images.

RESULTS

The bone volume fractions (BVF) of eight trabecular bone samples vary from 10.5% to 34.9% with the Young’s modulus ranging from 0.337 to 3.31 GPa. The variations in architecture result in a range of plate fractions from 86.0% to 95.2%. The percentages of bone loss attributed to different mechanism are shown in Figure 2. It suggests that the primary bone loss is due to the perforation of trabecular plate and secondary due to broken trabeculae. With the increased bone remodeling activation rate, the trabecular bone remodeling simulation predicts decreased BVF, elastic modulus and plate fraction (Table 1). The rate of bone loss is consistent with previous clinical studies [6].

It is also interesting that although each bone sample undergoes same in bone remodeling, the BVF reduction rates are different (Figure 2). Denser bone with higher plate fraction goes through a slower bone loss and results in a lower fracture risk in prospect.