3D STATISTICAL SHAPE MODELING FOR CLASSIFICATION OF TREATMENT EFFECTS ON OSTEOPOROTIC MOUSE BONE GEOMETRY

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Introduction

In preclinical studies, murine bone models simulate osteoporosis and test different treatment strategies. Morphometric analysis using *in vivo* longitudinal micro-Computed tomography (μCT) scans typically measure the treatments effects on bone geometry. This method accounts for scalar changes such as cortical thickness [1], leading to unrepresentative measure of the treatment impact due to this geometric approximation. This study develops a Principal Component Analysis (PCA)- based model to enable: 1) localized quantification of the 3D geometric variations, given by the PCA modes, 2) classification of the most important treatment effects.

Methods

The examined population consisted of two groups, the treated after ovariectomy, "ML" (N = 6) and the untreated, "OVX" (N = 5). The "ML" group received mechanical stimulus at week 19 and 21. The right tibiae were scanned using *in vivo* μCT (10.4μm/voxel) every two weeks between week 14 and 24 [2]. Two time points, week 18 and 24, were included. Image slices from the midshaft were selected [3]. The proposed pipeline extracted surface meshes from images to represent the bone shapes. A bone structure at week 18 was used as reference. 3D image samples were rigidly registered, binarized and processed to enforce topological equivalence. The reference surface mesh was extracted from the surfaces in the reference image. This reference mesh was mapped to each bone sample by applying the displacement field found with elastic image registration (spatial resolution equal to 5 voxels) [4]. The mapped reference mesh on each bone composed the rows of the PCA-input matrix.

The PCA temporal modes were primarily classified by score clustering and measuring the individual score changes (δa) over time. "a" denotes the scores and "δ" the differences. The scores were firstly normalized and clustered over the cohorts. Treatment-related modes were determined when the score changes are different in magnitude in the "ML" from those in the "OVX" group. Important treatment modes were identified by further performing paired two-sided Wilcoxon tests of the scores before and after treatment. For these modes, a pairwise analysis complemented the classification. The averaged Cohen's effect sizes were also calculated.

Results and Discussion

The reference surface mesh was composed by tetrahedral elements with 8934 nodes. The first PCA 6 modes described 90% of the total variance. The first and sixth mode described significant treatment effects detected on the anterior crest and on very localized scattered features across the section, respectively ($p<0.05$) (Fig. 1a). Modes 1 and 6 captured 50% of the overall variance, and the effect sizes for their scores before and after the treatment were 1.9 and 2.4, respectively. Other treatment modes captured the endosteal resorption and periosteal apposition at the medial aspect (mode 2) and at the lateral aspect on the distal end (mode 4). Mode 5 captured the opposite change at the anterior crest on the distal end. The above changes (modes 2, 4 and 5) occur to a less extent as there is a noticeable trend of temporal score changes, but not statistically significant. The remaining modes described other minor sources of variation. Fig. 1b is the pairwise plot of the score changes for both cohorts and for the significant modes, highlighting the achieved clustering.

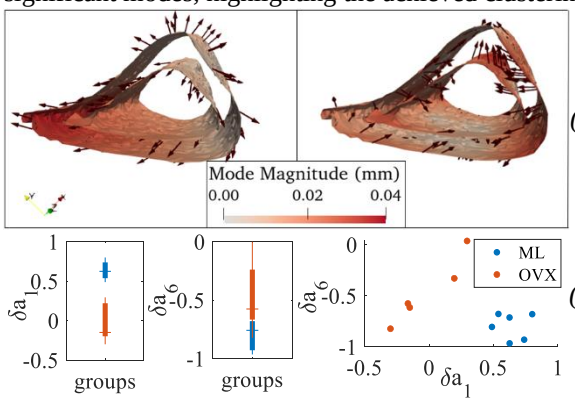

Figure 1: (a) Modes 1 and 6 illustrated as vectors on top of the mean shape. Contour colors show the vector magnitude. (b) Boxplots of score changes (δa) for mode 1 and 6 and scatter plot.

Conclusions

This study identified new 3D features that capture the main bone adaptation patterns to mechanical stimulus. The methodology has the potential for testing all treatment strategies in murine studies.

References

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