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Research Paper

Role of subject-specific musculoskeletal loading on the prediction of bone density distribution in the proximal femur

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ABSTRACT

The typical bone density patterns in the proximal femur can be explained using bone remodeling simulations incorporating a load-adaptive response. Yet, subject-specific variations in bone density have not received much attention. Therefore, the objective of this study was to quantify to what extent subject-specific bone geometry and subject-specific musculoskeletal loading affect the predicted bone density distribution. To accomplish this goal, a computational bone remodeling scheme was combined with gait analysis and a subject-specific musculoskeletal model. Finite element models incorporating the subject-specific geometry as well as the subject-specific hip contact forces and associated muscle forces were used to predict the density distribution in the proximal femur of three individuals. Next, the subject-specific musculoskeletal loads were interchanged between the subjects and the resulting changes in bone remodeling of the proximal femur were analyzed. Simulations results were compared to computed tomography (CT) image-based density profiles. The results confirm that the predicted bone density distribution in the proximal femur is drastically influenced by the inclusion of subject-specific loading, i.e. hip contact forces and muscle forces calculated based on gait analysis data and musculoskeletal modeling. This factor dominated the effect of individualized geometry. We conclude that when predicting femoral density distribution in patients, the effect of subject-specific differences in loading conditions of the hip joint and the associated difference in muscle forces needs to be accounted for.

1. Introduction

In 1892, Julius Wolff first proposed that human bones adapt to mechanical loading during their growth and development in accordance with mathematical laws (Wolff, 2011). On the basis of Wolff's hypothesis, Frost (1987) developed the first mathematical description of mechanical adaptation of bone in the so-called Mechanostat theory. In recent years, a

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growing body of experimental evidence has supported the notion that adaptation of bone occurs as mechanical signals are transduced into biological and biochemical signals via complex mechanotransductive pathways (Huang and Ogawa, 2010). Numerous theoretical and numerical approaches have been proposed for modeling bone remodeling and adaptation in response to mechanical stimuli such as stress, strain and strain energy density (Carter et al., 1996; Cowin and Hegedus, 1976; Huiskes et al., 1987). Microdamage, disuse and overloading are believed to be some of the main driving factors that change the local mechanical environment of cells in the load-bearing human bones and cause the subsequent adaptive response (Chen et al., 2010). Both phenomenological and mechanistic formulations of mechanical adaptation of bone have been developed for further understanding this adaptive response (Doblare and Garcia, 2002; Ruimerman et al., 2005; Vahdati and Rouhi, 2009; Jacobs et al., 1997; Tsubota et al., 2009; Beaupre et al., 1990).

The mathematical descriptions of mechanically-induced bone adaptation when combined with subject-specific modeling have the potential for being important predictive tools, providing insight into bone remodeling around implants, fracture risk, pre-surgical planning, and mechanical causes of bone pathologies such as osteoporosis (Lenaerts and van Lenthe, 2009; van Lenthe et al., 2006). Particularly in recent years, there has been a paradigm shift from evaluation of medical interventions in the average patient to personalized medicine and tailored therapeutics. Patient-centered medicine and patient-oriented research allow identification of the best possible treatment for every individual according their needs, objectives and available economic resources (Sacristan, 2013; Poelert et al., 2013). To this end, subject-specific research allows improving outcomes for individual patients and avoiding/reducing ineffective treatments. For instance, a clinical problem of interest is periprosthetic bone loss which is a common complication and has been studied extensively (Huiskes et al., 1992; van Lenthe et al., 1997). Bone loss around prostheses not only is detrimental for the long-term success of the primary reconstruction, but it also causes a reduction in bone stock and thus making future revision surgery even more difficult. Mechanically-induced bone remodeling resulting from stress shielding has been shown to be the main reason for periprosthetic bone loss. Accordingly, computational tools that enable accurate prediction of bone remodeling in response to subject-specific loading may be used to optimize and personalize the design of implants and implantation techniques, thus reducing the risk of periprosthetic bone loss. Furthermore, the predictive power of subject-specific studies offers the potential for investigating the importance of intersubject variability on bone pathologies and the outcome of surgical interventions.

Algorithms for bone remodeling have been extensively utilized in finite element (FE) simulation of femur in order to test their capability for realistic prediction of bone density distribution. Not only the candidate mechanical stimuli, but also the type of loading conditions that is applied in FE simulations of femoral bone varies considerably between models presented in the literature. In order to fully harness the predictive power of bone remodeling algorithms for realistic density predictions, accurate geometry and physiologic loading conditions are essential. Kerner et al. (1999) suggested that prediction of subject-specific bone remodeling processes requires modeling of the subject-specific geometry of the femur and the implant. The use of individualized FE models is now customary when analyzing the bone remodeling processes. However, many of these analyses underestimate the effect of hip joint-loading characteristics and associated muscle forces on the predicted density distribution in the femur (Bitsakos et al., 2005; Duda et al., 1998). While simplified and generic load cases have been used for 3D simulations of bone remodeling before (Perez et al., 2010), this may not suffice to predict subject-specific bone density distribution. In one study, Jonkers et al. (2008) related regional stress distribution in the proximal femur to the applied load cases derived from gait analysis results. For the present study, we take study of Jonkers et al. (2008) one step further by including whole gait cycle loading and bone remodeling analysis. We hypothesized that a gait-based approach considering both subject-specific geometry and musculoskeletal loading would provide a more realistic representation of the mechanical environment and the subsequent mechanical adaptation of bone.

The specific goal of this study was to quantify to what extent subject-specific geometry and subject-specific musculoskeletal loading affect the bone density distribution remodeling in the proximal femur.

2. Methods

To generate subject-specific computational models of femoral bone remodeling, one must acquire and discretize geometry for the model, assign subject-specific boundary and loading conditions and choose a bone remodeling algorithm (Fig. 1). Each aspect of model development and simulation is discussed in the subsequent sections. Three healthy subjects were studied: subject A, 45 years old, female, weighing 74.3 kg; subject B, 56 years old, female, 52.6 kg and subject C, 34 years old, male weighing 82.4 kg.

2.1. *Subject-specific geometry*

In order to model the subject-specific geometry, full CT-scans of the subjects' pelvis region and femur were obtained. Semi-automatic, threshold-based segmentation was used to construct triangulated surface mesh from CT-images in Mimics™ (Materialise NV, Leuven, Belgium). During segmentation, a fixed threshold value of 226 Hounsfield Units (HU) was applied to the CT image gray values. The images were further segmented using manual editing and automated tools including morphological closing and region growing. From the resulting voxel masks, a set of triangulated surface meshes was constructed and Standard Triangulation Language (STL) files were generated (Bartels, 2011). Next, linear tetrahedral volume mesh was constructed using MSC Patran™ (MSC. Software, Santa Ana, CA, USA) after smoothing and homogenizing the surface triangles. The FE-meshes were imported into Mimics™ again and material properties were assigned by relating the HU from the CT-image to bone mineral density using a liner relationship as proposed by Bitsakos et al. (2005).