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Subject-specific bone loading estimation in the human distal radius

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ABSTRACT

High-resolution *in vivo* bone micro-architecture assessment, as possible now for the distal forearm, in combination with bone remodelling simulation algorithms could, eventually, predict patient-specific bone morphology changes. To simulate load-adaptive bone remodelling, however, physiological loading conditions must be defined. In this paper we test a previously developed algorithm to estimate such physiological loading conditions from the bone micro-architecture. The aims of this study were to investigate if realistic boundary forces and moments are predicted for the scanned distal radius section and how these predicted forces and moments should be distributed to the scanned section in order to obtain a load transfer similar to that *in situ*. Images at *in vivo* resolution were generated for the clinically measured section of nine distal radius cadaver bones, converted to micro-finite element models and used for load estimation. Models of the full distal radius were created to analyse tissue loading distributions of the sections *in situ*. It was found that predicted forces and moments at the boundaries of the scanned region varied considerably but, when translated to equivalent radiocarpal joint forces, agreed well with values reported in the literature. Bone tissue loading distribution was in best agreement with *in situ* distributions when loading was applied to an extra layer of material at both ends of the clinical scan region. The agreement of the predicted loading to previous studies and the wide range of predicted loading values indicate that subject-specific bone loading estimation is possible and necessary.

1. Introduction

The human distal radius is a clinically important site to assess bone micro-architecture in patients, *e.g.* in order to diagnose bone disorders such as osteoporosis. With the advent of high-resolution peripheral quantitative computed tomography (HR-pQCT), it is now possible to scan part of the forearm *in vivo* at high resolution and therefore reconstruct the detailed three-dimensional bone micro-architecture of a patient's distal radius and ulna (Boutroy et al., 2005; Boyd, 2008; Khosla et al., 2006). Such measurements thus allow patient-specific investigations of morphometric parameters in the healthy and pathological state as well as patient-specific calculations of bone strength using micro-finite element (micro-FE) analysis (Liu et al., 2010; Mueller et al., 2011; Mueller et al., 2009a; Pistoia et al., 2002; Varga et al., 2010). In combination with bone remodelling simulation models, it would even be possible to predict changes in bone micro-architecture and strength over time.

For bone remodelling simulations, however, patient-specific physiological bone loading conditions should be defined, but such *in vivo* loading conditions in the human distal radius of patients are usually not known. Although some progress has been made to calculate these forces using inverse modelling strategies (Dennerlein et al., 2007; Desroches et al., 2010; Qin et al., 2011; Slavens et al., 2011), the many assumptions that are needed with such strategies makes it difficult to assess their accuracy, in particular in a patient-specific manner. Most direct techniques for force measurements, on the other hand, have the disadvantage of being invasive. Using a pressure-sensor device, forces at the radioulnocarpal joint were measured *in vivo* in healthy human volunteers under physiological loading conditions (Rikli et al., 2007). Total forces ranged from 31 to 245 N depending on the position of the wrist, and forces at the radial centre ranged from 11 to 93 N. During grasping, however, the forces at the wrist increase due to additional muscle forces acting in the hand. Assuming that during grasping the main loading is transferred

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via the lunate and scaphoid carpal bones to the radius as measured in cadaver forearms (Markolf et al., 1998), most of the grip force would be translated to the radius as well. Grip forces can therefore lead to considerably higher forces at the radius. For example, maximum handgrip strength was experimentally measured using a hydraulic handgrip dynamometer showing values ranging from 302 to 472 N in men and 173 to 281 N in women with considerable between subject variation (Foley et al., 1999). This indicates that the loading at the radius should also show highly variable values in that range. Partly this variation is due to differences in sex and age, but also due to idiosyncratic variation (White and Folkens, 2000). These large differences indicate that a patient-specific determination of the forces will be needed in order to represent realistic loading conditions for bone remodelling simulations. Also it is not clear how forces acting at the wrist joint transfer to the small region of the radius that is usually scanned in clinical practice.

Earlier studies proposed algorithms to estimate external bone loads based on the bone density by scaling unit forces until a homogenous tissue loading distribution was reached using optimization methods (Bona et al., 2006; Fischer et al., 1995; Fischer et al., 1998, 1999) and more recently also using artificial neuronal networks (Campoli et al., 2012). These approaches use continuum models and therefore estimate the actual bone micro-architecture and tissue stress from the bone density and continuum stress, respectively. Accounting also for the bone micro-architecture and thus the local tissue loading, we also have proposed a bone loading estimation method (Christen et al., 2012b). With our algorithm it is assumed that bone strives for homogeneous tissue loading. After defining a set of plausible external load cases, micro-FE analysis is used to calculate the local tissue stress/strain condition for each load case, and based on these combined results, an optimization algorithm is employed to scale the magnitude of the forces such that the most homogeneous bone tissue loading distribution is found. In this earlier study, this approach has provided reasonable estimates for the forces applied externally to vertebrae in an *in vivo* animal experiment (Christen et al., 2012b; Lambers et al., 2011). It was also successfully used to predict forces for a patient-specific bone remodelling study based on human bone biopsies taken from a clinical cohort of patients (Christen et al., 2012a).

For the scanned section of the distal radius, however, the plausible forces and moments do not represent well-defined external forces such as the ones acting at the joints, but net internal forces and moments working in a cross-section of the radius. To calculate the tissue loading generated by these internal forces, they will have to be distributed to the cross-sectional ends of the micro-FE models. It seems likely that the way in which this is done (*e.g.* as a prescribed stress or strain), can play an important role in the distribution of bone tissue loading, and thus can affect the load estimation. In order to reach a natural distribution of the forces and moments, such as they would occur for the scanned region *in situ*, we here propose to add an extra layer of material at both loaded ends to which boundary conditions are prescribed. This extra layer could also compensate for the loss of stiffness at the loaded ends that is expected due to cutting of the trabeculae. It is presently unclear, however, what layer stiffness would result in the best representation of the *in situ* load transfer.

For the purpose of the present study, we defined two goals. The first goal was to investigate the accuracy of the internal forces and moments that are predicted at the ends of the clinical scan region. This was done by comparing predictions to measurements reported in the literature. Since experimental force measurements are mainly available from the radiolunate and radioscaphoid joints, we used force equilibrium conditions to translate the estimated forces at the scanned region to forces at these joints. The second goal was to find an optimal value for the layer stiffness. This was achieved by comparing the calculated tissue loading conditions in the scanned region with those calculated for the scanned region *in situ*. Since the results of the load estimation will also depend on the stiffness of these additional layers, we will first determine the optimal layer stiffness and then use that value in all further models to determine bone loading estimates. These predictions are then compared to literature values to reach our first goal.

2. Materials and methods

2.1. Bone samples

A randomly selected subset ($n=9$) of HR-pQCT images of human cadaveric forearms (Fig. 1a) from another study was used (Mueller et al., 2009b). The subset includes scans from 5 women with ages ranging from 78.5 to 94.3 years and 4 men with ages ranging from 64.9 to 91.5 years (Table 1). Prior to death, all donors had agreed to dedicate their body to the Institute of Anatomy of the Ludwig-Maximilians-University (LMU) Munich (Eckstein et al., 2007; Hudelmaier et al., 2005; Lochmuller et al., 2008a; Lochmuller et al., 2008b). In the previous study, scanning was performed at an in-plane resolution of 89 μm and slice thickness of 93 μm. Laplace–Hamming filtering and a fixed global threshold (41.5% of the maximum grayscale intensity value) were used for segmentation (Laib and Ruegsegger, 1999). Based on the HR-pQCT images, micro-FE models were created for the full distal end of the radius (Fig. 1a) in order to calculate the *in situ* loading conditions, and the cross-sectional region that is recommended for clinical measurements (Fig. 1b) using a voxel-conversion technique (van Rietbergen et al., 1995). A 3-voxel thick layer was added at both ends of the clinical model.

2.2. Layer stiffness definition

In order to define the appropriate layer stiffness in the clinical model (Fig. 1b), mean strain energy density (SED) was compared when applying a compressive force of 100 N in the axial direction to the full and clinical micro-FE models. Micro-FE results from the common region of the full and clinical model were compared using linear regression. For the clinical region, test models were created with a Poisson's ratio of 0.3 and a layer stiffness of 10, 100, 1000, 6800 MPa, and one model with no layers. Mean SED of each test model were related to those of the full model in the linear regression and the appropriate layer stiffness was defined based on the slope of the regression trend line which should be as close as possible to 1. Additionally, also the local SED distribution of the test models was correlated to the full model by calculating the Pearson product-moment correlation coefficient, R. Bone material was modelled with a Young's modulus of 6800 MPa and a Poisson's ratio of 0.3 (Macneil and Boyd, 2008). Articular cartilage in the full model was modelled as linear elastic with a Young's modulus of 12 MPa and a Poisson's ratio of 0.45 (Chegini et al., 2009; Moglo and Shirazi-Adl, 2003). For the full model, a distributed load was prescribed at a stiff plate connecting the lunate and scaphoid bone at the distal end whereas displacements at the proximal end were fixed in all directions. For the clinical model, frictionless displacement was prescribed at the distal end whereas displacements at the proximal end were fixed in all directions. Model creation and micro-FE analysis were performed using Image Processing Language (IPL, Scanco Medical AG, Brüttisellen, Switzerland).

2.3. Bone loading estimation algorithm

Based on the assumption of uniform tissue loading distribution quantified by SED and calculated using micro-FE analysis, the loading history can be estimated by scaling a set of n predefined unit loads until the most homogeneous tissue loading distribution is found. This is formulated as an optimization problem by finding scaling factors, s_i, that minimize the residual function, $r(s_i)$:

$$\min_{s_i} r(s_i) = \int \left(\sum_{i=1}^{n} (s_i U_{i_{unit}}(x)) - k \right)^2 dV \quad (1)$$

Where $U_{i_{unit}}(x)$ is the SED distribution due to unit load i and k is a reference value for physiological local tissue loading which was set to 0.02 MPa in this study (Mullender and Huiskes, 1995). Scaling factors are calculated using non-negative linear least square optimization technique (Lawson and Hanson, 1974) (MATLAB, The MathWorks Inc., Natick MA, USA). In the present study, loading was estimated using the clinical model (Fig. 1b) where forces and moments, prescribed as displacements and rotations, in the three orthogonal directions were considered as unit load cases. Positive z, x, and y directions of the coordinate system were oriented distally, anteriorly, and medially respectively. It was assumed that these load cases act equally long over time and are applied sequentially. Therefore, the loading magnitude, α, considering the 6 unit load cases was calculated according