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Research Paper

Reproducibility for linear and nonlinear micro-finite element simulations with density derived material properties of the human radius

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ABSTRACT

Finite element (FE) simulations based on high-resolution peripheral quantitative computed-tomography (HRpQCT) measurements provide an elegant and direct way to estimate bone strength. Parallel solvers for nonlinear FE simulations allow the assessment not only of the initial linear elastic behavior of the bone but also materially and geometrically nonlinear effects. The reproducibility of HRpQCT measurements, as well as their analysis of microarchitecture using linear-elastic FE simulations with a homogeneous elastic modulus has been investigated before. However, it is not clear to which extent density-derived and nonlinear FE simulations are reproducible. In this study, we introduced new mechanical indices derived from nonlinear FE simulations that describe the onset of yielding and the behavior at maximal load. Using 14 embalmed forearms that were imaged three times, we found that in general the in vitro reproducibility of the nonlinear FE simulations is as good as the reproducibility of linear FE. For the nonlinear simulations precision errors (PEs) ranged between 0.4 and 3.2% and intraclass correlation coefficients were above 0.9. In conclusion, nonlinear FE simulations with density derived material properties contain important additional information that is independent from the results of the linear simulations.

1. Introduction

The estimation of the patient–specific risk of fractures due to osteopenia has the potential to reduce the consequences of osteoporosis as it would allow a more precise prescription of therapies as well as the monitoring of their success (Bouxsein, 2008; Christen et al., 2010; van Lenthe and Müller, 2006). Currently bone mineral density (BMD) measured by dual energy X-ray absorptiometry (DXA) is used as a surrogate for bone mass and is used in clinics to estimate the risk of osteoporotic fractures. However, DXA measurements do not provide information on the bone microarchitecture and the functional competence of the bone. Using high-resolution peripheral quantitative computed tomography (HRpQCT) the bone microstructure can be accurately imaged in patients on a routine basis (Boutroy et al., 2005; Bouxsein, 2008; Khosla et al., 2006; Kirmani et al., 2009). Furthermore, finite element (FE) simulations based on these detailed tomographic images provide an elegant and direct way to compute bone strength (Pistoia et al., 2002). Due to the

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complex geometry of the bone on the microstructural level, these simulations are typically composed of several million elements and therefore require considerable computational resources.

FE models of the bone microstructure are typically created based on a binarized image where the bone is segmented either using a simple thresholding procedure or more complex segmentation techniques, i.e. based on contrast enhancement. These models assume a homogeneous mineralization of the bone at the tissue level and therefore a single Young's modulus is assumed (van Rietbergen et al., 1995). While this has been shown to be a valid simplification for high resolutions of up to about 30 μm, it is increasingly inaccurate for lower resolutions (Bevill and Keaveny, 2009; Homminga et al., 2001; Niebur et al., 2000, 1999). As an alternative, mappings from the tissue mineral density (TMD) to the local stiffness have been developed for FE models with lower resolution, not able to fully resolve the bone microstructure (Homminga et al., 2001; Morgan et al., 2003). In this case, the bone is no longer a single component as would be required by the FE method, but can be composed of several disjointed parts. This problem can be resolved by also considering the bone marrow in the FE model; however, only at the cost of introducing additional elements and thereby increasing the size of the simulations.

Stiffness and strength computed from linear elastic FE simulations are highly correlated with bone mass and density and therefore provide little additional information on the patient's fracture risk. The development of parallel solvers for nonlinear FE simulations allows the assessment not only of the bone's initial linear elastic behavior, but also the materially nonlinear effects due to the accumulation of plastic deformation or damage and geometrically nonlinear effects caused by deformations of the bone microstructure (Adams et al., 2003; Bevill et al., 2006; Morgan and Keaveny, 2001; Stolken and Kinney, 2003; Verhulp et al., 2008a). In a recent clinical study, we showed that nonlinear μFE simulations provide information on the risk of distal forearm fractures that was not accessible from linear μFE nor from other techniques assessing bone microstructure, density or mass (Christen et al., in press). The same study, we were also able to show that nonlinear μFE simulations were accurate when compared to experimental mechanical testing of entire human forearms in vitro. When comparing simulation and experiment in 20 forearms we found high correlations between simulated yield load and experimentally measured failure load, yield deformation and the energy dissipated before yielding. Although the reproducibility of HRpQCT measurements with respect to microstructural morphometry and linear-elastic FE simulations with a homogeneous elastic modulus has been investigated in several studies (Boutroy et al., 2005; MacNeil and Boyd, 2007; Mueller et al., 2009), it is not clear to which extend the results of the nonlinear FE simulations are reproducible.

In this study we therefore set out to investigate the reproducibility of new mechanical indices derived from nonlinear FE simulations that describe the onset of yielding and the behavior at maximal load. Furthermore, we compare simulations with elastic modulus derived from the local density to well-established linear simulations using a homogeneous Young's modulus. Finally, the additional indices derived from the nonlinear simulations are tested for orthogonality with respect to linear-elastic simulations, as this is a prerequisite to be able to improve the sensitivity in estimating fracture risk.

2. Material and methods

2.1. Material

Two different subsets of specimens originating from a collection of forearms were used in this study. The samples were donated to the Ludwig-Maximilian-University (LMU) Munich in accordance with the German legislative requirements. The donors were between 60 and 100 years old and specimens with preexisting fractures or osteosynthetic material apparent in the X-Ray radiography were excluded. The volume of interest used for the analysis in this study was defined according to the manufacturer's recommendation for human in vivo measurements. We considered 50 female forearms to compare simulations with elastic modulus derived from the local density to simulations with homogeneous Young's modulus as well as to investigate the amount of independent information in the results from nonlinear FE simulations. These samples were imaged in a previous study using a prototype HRpQCT scanner (Scanco Medical AG, Brüttisellen, Switzerland) at a resolution of 89 μm in plane and a slice thickness of 92 μm and mechanically tested up to failure (Mueller et al., 2011). To measure the reproducibility, we used a set of 14 samples (both males and females) that were imaged previously three times in an arbitrary sequence and on different days with re-positioning after each scan as part of an earlier reproducibility study for linear μFE simulations (Mueller et al., 2009). These measurements were performed with an XtremeCT scanner (Scanco Medical AG, Brüttisellen, Switzerland) providing an isotropic resolution of 82 μm.

2.2. Image processing and material properties

Two different methods were used to generate FE models from the tomographic images: either assigning 'homogeneous' or 'scaled' material properties. In the case of homogeneous FE models, the bone microstructure was segmented and constant material properties were assigned to the elements, whereas for the scaled models, the material properties were computed directly from the 3D image without any segmentation. For both approaches, the raw images were filtered by a Gaussian filter with $\sigma = 1.2$ and a support of 2 voxels to reduce the noise in the image. The resulting image was used to compute local tissue mineral density (TMD) and Young's modulus for the simulations with scaled material properties.

For the homogeneous FE models, the bone was segmented using a 3D Laplace Hamming filter and a fixed global threshold (Laib and Rüegsegger, 1999). According to the recommendation of the manufacturer, the Hamming cut-off frequency was 0.4 of the Nyquist frequency, the weighting factor was 0.5 and the threshold was set to 400/1000 of the maximal gray scale value. Using component-labeling, the largest connected component in the image was isolated and used to generate the FE mesh. The linear-elastic material properties were