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# A novel approach to estimate trabecular bone anisotropy using a database approach

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ABSTRACT

Continuum finite element (FE) models of bones have become a standard pre-clinical tool to estimate bone strength. These models are usually based on clinical CT scans and material properties assigned are chosen as isotropic based only on the density distribution. It has been shown, however, that trabecular bone elastic behavior is best described as orthotropic. Unfortunately, the use of orthotropic models in FE analysis derived from CT scans is hampered by the fact that the measurement of a trabecular orientation (fabric) is not possible from clinical CT images due to the low resolution of such images. In this study, we explore the concept of using a database (DB) of high-resolution bone models to derive the fabric information that is missing in clinical images. The goal of this study was to investigate if models with fabric derived from a relatively small database can already produce more accurate results than isotropic models.

A DB of 33 human proximal femurs was generated from micro-CT scans with a nominal isotropic resolution of 82 μm. Continuum FE models were generated from the images using a pre-defined mesh template in combination with an iso-anatomic mesh morphing tool. Each element within the mesh template is at a specific anatomical location. For each element within the cancellous bone, a spherical region around the element centroid with a radius of 2 mm was defined. Bone volume fraction and the mean-intercept-length fabric tensor were analyzed for that region. Ten femurs were used as test cases. For each test femur, four different models were generated: (1) an orthotropic model based on micro-CT fabric measurements (gold standard), (2) an orthotropic model based on the fabric derived from the best-matched database model, (3) an isotropic-I model in which the fabric tensor was set to the identity tensor, and (4) a second isotropic-II model with its total bone stiffness fitted to the gold standard. An elastic-plastic damage model was used to simulate failure and post failure behavior during a fall to the side.

The results show that all models produce a similar stress distribution. However, compared to the gold standard, both isotropic-I and II models underestimated the stress/damage distributions significantly. We found no significant difference between DB-derived and gold standard models. Compared to the gold standard, the isotropic-I models further underestimated whole bone stiffness by 26.3% and ultimate load by 14.5%, while these differences for the DB-derived orthotropic models were only 4.9% and 3.1% respectively.

The results indicate that the concept of using a DB to estimate patient-specific anisotropic material properties can considerably improve the results. We expect that this approach can lead to more accurate results in particular for cases where bone anisotropy plays an important role, such as in osteoporotic patients and around implants.



## 1. Introduction

Patient specific continuum finite element (FE) models have become a standard pre-clinical tool to study mechanical behavior of bone alone or with implants. Such models usually implement material properties with elastic and strength properties that are based on the local bone density as quantified by Hounsfield units in clinical CT images (Keyak, 2001; Liebschner et al., 2003; Taddei et al., 2007; Yosibash et al., 2007). Empirical power–law relationships are then used to derive the elastic and strength properties (Carter and Hayes, 1977; Helgason et al., 2008; Keller, 1994; Lotz et al., 1991; Wirtz et al., 2000; Zannoni et al., 1999). In virtually all studies done so far, material properties assigned to the bone elements are chosen

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as isotropic based on bone density distribution only. Experimental and computational studies, however, have shown that bone can be highly anisotropic, particularly in cancellous bone regions, and that its elastic behavior is best described as orthotropic. In most cases, the experimentally derived power–law relationships are determined only after aligning the measurement direction with the anatomical direction. As such these power–laws may well represent the stiffness and strength in the principal load carrying direction, but will likely overestimate these values in other directions. It was demonstrated that models that account for this anisotropic behavior better predict whole bone stiffness and stress distributions than isotropic models (Hazrati Marangalou et al., 2012; Kabel et al., 1999; Pahr and Zysset, 2009; Turner et al., 1990). The anisotropy of cancellous bone is largely determined by its microstructural organization. Theoretical and experimental studies demonstrated that the orthotropic principal directions and the anisotropic stiffness tensor can be well predicted from a second rank fabric tensor that describes the average orientation of this trabecular microarchitecture (Cowin, 1985; Cowin and Mehrabadi, 1989; Gross et al., 2013; Harrigan and Mann, 1984; Kabel et al., 1999; Odgaard et al., 1997; Zysset, 2003; Zysset et al., 1998). Measurement of such fabric tensors, however, requires images with a resolution that is good enough to resolve the trabecular architecture. For bone in-vivo, this presently is possible only for the peripheral skeleton (Boutroy et al., 2005; Burghardt et al., 2011; Burrows et al., 2010; Liu et al., 2010; MacNeil and Boyd, 2008). Although recent studies have introduced approaches to calculate such microstructural properties from clinical CT (Saha and Wehrli, 2004; Tabor et al., 2013; Tabor and Rokita, 2007) and high-resolution flat-panel CT systems (Bredella et al., 2008; Mulder et al., 2012), the accuracy of such measurements still has to be established.

In this study, we explore a different approach to derive patient-specific fabric information by using a database of high-resolution bone models. By combining the density information measured from a patient CT scan with fabric information from the database, patient-specific anisotropic properties can be defined. Presently, only a rather limited number ($n=33$) of bones are available for this database. The goal of this study therefore was to investigate if models with fabric derived from such a limited database can already produce more accurate results than isotropic models. To investigate this, we compared the stress and damage distribution as well as the whole bone stiffness and strength for FE models with fabric derived from the actual bone with those of model with fabric mapped from the database or isotropic mechanical properties.

## 2. Material and methods

### 2.1. Material

A database (DB) of 33 human cadaver femurs (mean age: 77.8 ± 10.0 year) obtained from 17 female and 16 male donors was generated for all these bones. Micro-CT scans (XtremeCT, Scanco Medical AG, Brüttisellen, Switzerland) of the most proximal part (9–12 cm in length) were made with a nominal isotropic resolution of 82 μm. Images were filtered and processed according to the protocol recommended by the manufacturer. Compartments of cortical and cancellous bone were identified using masks. A first mask comprising the whole bone was made based on the periosteal contour. In order to find the cortical shell, original images were filtered using a strong Gauss filter (sigma = 5, support = 5 voxels) and segmented using a threshold of 15% of the maximum gray-value, leaving only the cortical bone. This image was used to identify the cortical shell in the original mask. In addition, the most periosteal 1 mm region of the original mask was identified as part of the (sub)cortical compartment. The remainder of the mask was considered the cancellous compartment.

### 2.2. Creation of FE models

Continuum finite element models of the 33 proximal femurs were generated based on contours of the bone periosteal surface as obtained using software provided with the micro-CT scanner (IPL V5.16, Scanco Medical AG, Brüttisellen, Switzerland). Isotopological models were generated for each bone segment using a pre-defined mesh template based on a generalized femur geometry that contained approximately 300 thousand second order tetrahedron elements with a typical edge length of 2 mm. This mesh template was morphed onto the bone surface extracted from the micro-CT scan by identifying a minimum of 8 anatomical landmarks. After morphing, each element number identifies an element that, with good approximation, is at the same specific anatomical location in all samples (Grassi et al., 2011). Since the mesh template comprises the whole femur while the micro-CT scans only covered the most proximal part of these, the number of elements on the proximal femur models was less and varied from approximately 80,000–90,000 depending on the scan length.

To each element a volume fraction and morphological properties were assigned using a homogenization technique described earlier (Hazrati Marangalou et al., 2012). In summary: first, we determined whether the element was in the cortical or cancellous compartment. If an element was at the cortical/cancellous interface, we calculated what fraction of its volume was in each of both compartments. For each element that was at least partly within the cancellous bone, a spherical volume of interest around the element centroid with a diameter of 4 mm was defined (Harrigan et al., 1988). Trabecular bone architectural parameters, including bone volume fraction (BV/TV) and the mean intercept length (MIL)-based fabric tensor, were analyzed for the volume of interest as far as it was within the cancellous compartment using the image processing software provided by the micro-CT system. Measured morphological parameters were then assigned to the elements. For elements in the cortical compartment, only a volume fraction for the volume comprised by the element itself was defined whereas a rule of mixture was used for elements that cover both compartments based on the portion of the element volume within the cortical/cancellous compartments. Fig. 1 depicts mesh generation and bone morphology analysis procedures.

Ten femurs were randomly taken from the database as test cases. For each test case, three different FE models were generated. In the first model, orthotropic material properties were specified based on the actual fabric and density measurements of that bone. In the second FE model, orthotropic material properties were specified based on the actual density measurement and fabric derived from a corresponding DB model. To do so, the DB model with a density distribution most similar to that of the test bone was selected and its fabric was mapped to the test model. The test model itself was excluded from the database during the selection process. In the third FE model, isotropic material properties were specified based on the actual density measurements only (Fig. 2).

To select a DB model $j$ with a density distribution most similar to that of the test bone $i$, we selected the DB model that minimized the root-mean-square error

$$Err_i = min_{j=1}^{32}\left(\sqrt{\frac{\sum_{k=1}^{N_{elements}}(\rho_{i,k}-\rho_{j,k})^2}{N_{elements}}}\right) \tag{1}$$

with $N_{elements}$ the number of elements and $\rho_{i,k}$ the density of element $k$ of model $i$.

Whereas the use of the template enables an easy mapping and comparison of scalar properties between models, the mapping of tensor properties, such as fabric

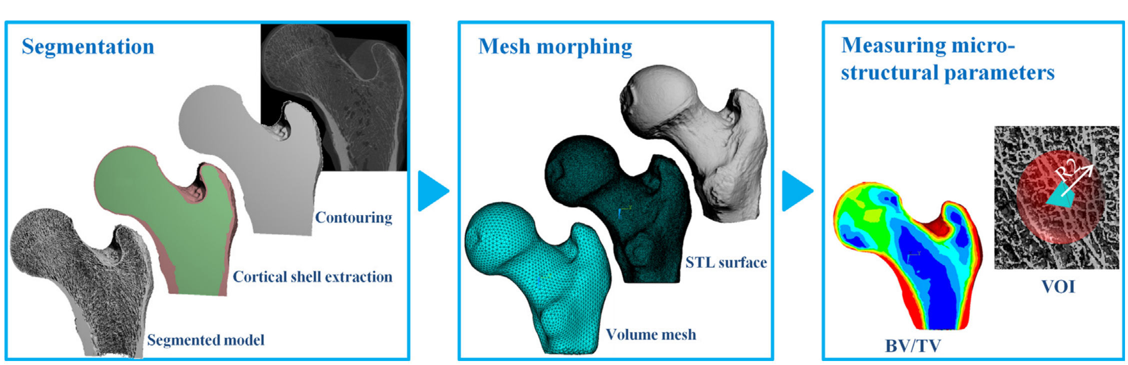


**Fig. 1.** FE models creation procedure for proximal femur models.