Digital Tomosynthesis of Human Vertebral Bone: The Effect of Positioning and Scan Orientation on Prediction of Cancellous Bone Stiffness.

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Disclosures:

Introduction: Clinical modalities currently available for the assessment of fracture risk in the spine largely rely on bone mineral density (BMD) measurements; however, their ability to provide information on the trabecular structure is limited. Digital tomosynthesis (DTS) is a relatively new imaging modality that has several advantages over the conventional CT and radiography, where DTS can generate stack images of a vertebra with an in-plane resolution superior to that of CT but with only 1/5th of the radiation. It has been recently reported that fractal dimension (FD), mean intercept length (MIL) and line fraction deviation (LFD) parameters obtained from DTS images of human vertebrae are correlated to 3D microstructure and stiffness of trabecular bone as determined from microcomputed tomography (μCT) [2, 3]. These correlations were achieved by using a single image slice selected at the center of a DTS stack (20 to 50 slices). The scan geometry was such that the movement of the x-ray source and the detector were transverse to the axis of the vertebra and DTS images were acquired in an anteroposterior (AP) view (resulting in a stack of coronal images). The objective of the current study was to investigate the extent to which scan orientation (transverse, parallel or oblique to the vertebral axis) and view (AP or lateral) affect the prediction of trabecular bone stiffness, independent from bone volume fraction. The results are expected to enable informed decisions about patient positioning during translation of DTS to in vivo applications.

Methods: Thoracic 6, T8, T11, and L3 vertebrae from 5 female and 5 male cadavers (age 63-90yr) were μCT scanned and reconstructed at 45 μm voxel size. In each trabecular bone region, mean bone volume fraction (BV/TV) was obtained. Cancellous bone apparent modulus (EFE) was calculated from a finite element (FE) simulation of inferior-superior compression using heterogeneous material moduli scaled with μCT gray levels [2]. The same bones were scanned using DTS (Shimadzu Sonialvision Safire II) in the AP (producing a stack of coronal plane images) and lateral (LM, producing a stack of sagittal plane images) views while aligned axially (0º), transversely (90º) or obliquely (23º) to the superior-inferior axis of the vertebrae (a total of 6 scans per spine). The vertebrae were immersed in water during scans to simulate soft tissue. A cuboidal volume of interest was cropped out of each reconstructed DTS image-stack to include as much cancellous bone as possible, similar to the volumes of interests (VOIs) from the μCT images used for the FE analysis (Fig. 1). Each cropped region was analyzed using the fractal, MIL and LFD methods. In fractal analysis, fractal dimension (FD), mean lacunarity (λ) and the slope of lacunarity vs. box size relationship (Sλ) were calculated [4, 5]. In MIL and LFD analyses, the mean (Av), standard deviation (SD), maximum (Max) and degree of anisotropy (DA, ratio of the principal measurements of MIL or LFD) were recorded for each slice (Fig 2). The central slice from each stack was also analyzed separately for a comparison between the 2D and 3D approaches.

Stepwise forward regression method was used to construct mixed multiple regression models that examined the relationship of fractal, MIL and LFD parameters with EFE. In all regression models, a subject variable was included as a random effect to account for pseudo-replication. BV/TV was introduced first and forced to stay in the model in order to examine the effect of DTS independently from bone mass. A separate analysis was performed for each scan configuration. Models with high multicolinearity (Variance Inflation Factor ≥ 5) were rejected.

Results: The models constructed using DTS parameters only (without BV/TV) ranged from nonsignificant to an explanatory capability (R2adj) of 0.89, with only the LM-oblique (R2adj =0.85) and the LM- transverse (R2adj =0.89) cases reaching a value above that is explained by BV/TV alone (R2adj =0.82). When BV/TV was present, all scan configurations provided parameters that increased the explained variability (R2adj) in cancellous bone stiffness over that is explained by BV/TV (Table 1). An exception is the oblique scans in the lateral view in which case the DTS parameters were either nonsignificant (central slice) or did not improve R2adj compared to BV/TV alone. Models from transverse scans and the LM view appeared to perform better than those from the other configurations. Parameters related to cancellous bone anisotropy (Av(MIL.DA) or, similarly, Av(MIL.SD)) were persistently present in the models from axial and transverse scans. When improvement in R2adj was observed compared to the single-slice case, the model included a term representing the slice-to-slice heterogeneity of the microstructure.

Discussion: By using the entire image stack, we were able to calculate parameters that represent the 3D heterogeneity of the microstructure. Most explanatory models of stiffness had one or more of these heterogeneity parameters, demonstrating a major advantage of DTS over 2D projection methods. A predictor set that contains BV/TV, a measure of anisotropy and a measure of heterogeneity is consistent with results from laboratory-scale high resolution imaging studies (μCT) [6]. Overall, the results are encouraging for further development of bone assessment tools using DTS.
The most explanatory model from each scan configuration included different predictor parameters. Different parts of the cancellous bone in the analysis volume and the dependence of DTS resolution on the orientation of structural features relative to the scan orientation [7] may explain these differences. The findings that DTS parameters derived from the LM views could outperform BV/TV in predicting bone stiffness and that the transverse scans from the LM view resulted in more explanatory models in the presence of BV/TV suggest that the transverse orientation in the LM view is the preferred configuration for the best assessment of cancellous bone if a single DTS scan is to be considered. However, it is likely that scans in additional orientations or views will provide information complementary to that from the LM-transverse scan and increase prediction accuracy for the fracture risk of a whole vertebra under a more complex loading than uniaxial compression.

It is not feasible in the current Safire system to position a human subject with a tilt more than 23 with respect to the scan table. However, a multi-orientation DTS scan with high resolution can be obtained (without sacrificing the low-radiation advantage) using a cone-beam system in a limited angle tomography with appropriate modifications to acquisition and reconstruction protocols. Current efforts are devoted to realization of such modifications.

**Significance:** DTS generated image stacks analyzed by fractal, MIL and LFD methods provided good to excellent predictions of in vitro vertebral trabecular bone stiffness, independent from bone mass. An orientation perpendicular to the axis of the spine in an LM view is the preferred configuration if a single scan is to be considered. Complementary microstructural information can be obtained by scanning in multiple orientations. Further development for a multidirectional DTS is feasible and may be necessary.

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Analysis volume

LM stack

AP stack

AP