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Quantitative Computed Tomography Protocols Affect Material Mapping and Quantitative Computed Tomography-Based Finite-Element Analysis Predicted Stiffness

Quantitative computed tomography-based finite-element analysis (QCT/FEA) has become increasingly popular in an attempt to understand and possibly reduce vertebral fracture risk. It is known that scanning acquisition settings affect Hounsfield units (HU) of the CT voxels. Material properties assignments in QCT/FEA, relating HU to Young's modulus, are performed by applying empirical equations. The purpose of this study was to evaluate the effect of QCT scanning protocols on predicted stiffness values from finite-element models. One fresh frozen cadaveric torso and a QCT calibration phantom were scanned six times varying voltage and current and reconstructed to obtain a total of 12 sets of images. Five vertebrae from the torso were experimentally tested to obtain stiffness values. QCT/FEA models of the five vertebrae were developed for the 12 image data resulting in a total of 60 models. Predicted stiffness was compared to the experimental values. The highest percent difference in stiffness was approximately 480% (80 kVp, 110 mAs, U70), while the lowest outcome was ~1% (80 kVp, 110 mAs, U30). There was a clear distinction between reconstruction kernels in predicted outcomes, whereas voltage did not present a clear influence on results. The potential of QCT/FEA as an improvement to conventional fracture risk prediction tools is well established. However, it is important to establish research protocols that can lead to results that can be translated to the clinical setting. [DOI: 10.1115/1.4034172]

Keywords: material assignment, vertebral fracture, finite-element modeling, CT resolution

Introduction

Finite-element analysis has become increasingly popular in an attempt to predict and reduce the incidence of vertebral fractures and their associated functional limitations in the elderly [1–5]. More specifically, quantitative computed tomography-based finite-element analysis (QCT/FEA) has been used to predict fracture loads and stiffness of bones with high accuracy [6]. These improvements in predicted outcomes, compared to the gold standard dual X-ray absorptiometry (DXA), have been achieved due to the advantages of QCT-based models including precise characterization of the three-dimensional heterogeneity of bone and accurate material property assignment to the models.

It is well established that varying computed tomography acquisition settings (current time (mAs), voltage (kVp), reconstruction algorithms, scanner type, and table height) will affect the gray scale value, measured in Hounsfield units (HU), of the CT voxels [7–9]. It is also known that CT imaging on patients in a clinical setting is performed with varying CT acquisition parameters on the basis of a diagnosis evaluation while keeping an acceptable radiation dose (ALARA, “as low as reasonably achievable”). On the other hand, research groups developing new techniques for

fracture risk prediction and treatment using QCT and FEA implement imaging protocols that improve bone contrast and image quality. Furthermore, material properties assignments for the finite elements relating HU from the CT images to Young's modulus are performed by applying empirical equations (Fig. 1) [10,11]. These equations may depend on QCT acquisition protocols and parameters used, thus, introducing variability, affecting material properties' assignments, and possibly resulting in an inaccurate fracture risk prediction. Understanding the effect that CT scanning parameters might have on QCT/FEA outcomes is important to overcome differences in scanning protocols between researchers from different institutions and valuable when developing a technique that implements research specifications and is intended to be translated to a patient population.

A previous study has demonstrated that QCT/FEA predicted bone strength and stiffness can vary between models developed with high-resolution scans, used in the research community, and low-resolution scans, used in the clinical setting [12]. Furthermore, estimated volumetric bone mineral density (vBMD) values used for material properties' assignments in finite-element models measured from CT images were also shown to depend on scanning protocols [13]. The purpose of this study was twofold: (1) to evaluate the effect of QCT scanning parameters and postprocessing settings on regression parameters obtained from calibration phantoms and (2) to evaluate the effect of these QCT settings on predicted stiffness values from finite-element models.

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Table 1 Summary of scanning and post processing settings

Scanning		Postprocessing	
Voltage (kVp)	Current (mAs)	Reconstruction kernel	Slice thickness
80, 120, 140	110, 200	U30, U70	0.5

We hypothesized that these factors will induce differences in predicted QCT/FEA outcomes possibly resulting in inaccurate estimations of fracture. These factors need to be considered when implementing finite-element models from QCT scans for fracture prediction and osteoporosis research.

Material and Methods

Quantitative Computed Tomography (QCT) Scanning.

After approval from our Institutional Review Board at Mayo Clinic, one fresh frozen cadaveric torso (female, 101 years old) was obtained from the anatomy department and thawed at room temperature for 48 h. The torso was then imaged using a General Electric Lunar Prodigy DXA scanner in the anterior–posterior position to obtain areal bone mineral density (aBMD) measurements and calculate a *T-score*. A *T-score* is the number of standard deviations representing the difference between the aBMD measured in the lumbar (L1–L4) spine and a healthy young adult with normal bone density. It can range from -2.5 and below in osteoporosis, between -2.5 and -1 in osteopenia, and above -1 in normal bones. The torso and a QCT calibration phantom (Mindways Inc., Austin, TX) were then scanned six times using a Siemens Somatom Definition CT scanner (Siemens Healthcare, Forchheim, Germany). A total of twelve sets of image data were obtained for the torso for model comparison based on the scanning parameters and various image reconstruction settings. The scanning and postprocessing settings, described in Table 1, consisted of three voltage levels, two current levels, and two reconstruction kernels. The scanning acquisition parameters were chosen based on protocols routinely used in the clinical setting which do not pose any eventual additional risk to the patients. The calibration phantom was used to obtain linear regression parameters (σ_{CT} and β_{CT}) for each scan and convert Hounsfield units (HU) to equivalent K_2HPO_4 density (Eq. (1)), assumed to be equal to bone ash density [12,13]:

$$\rho_{ash} = \rho_{K_2HPO_4} = \frac{1}{\sigma_{CT}} \times \mu_{ROI}(HU) - \frac{\beta_{CT}}{\sigma_{CT}} \quad (1)$$

Experimental Testing Procedure. Five vertebrae (T8, T11, T12, L1, and L3) from the torso were excised and all soft tissue and posterior elements were removed. These vertebrae were selected to include the thoraco-lumbar region, area where most osteoporotic fractures occur, and thoracic and lumbar vertebrae of different sizes. To prepare the specimens for testing, both upper

and lower regions were embedded in polymethylmethacrylate (PMMA), as previously described [14]. The vertebral bodies were wrapped, kept moist with physiologic saline solution, and stored at -20°C until testing was performed. Prior to testing, the specimens were thawed at room temperature for 24 h. The vertebrae were compressed between two aluminum platens at a rate of 5 mm/min using a Mini Bionix 858 servohydraulic test machine (MTS, Eden Prairie, MN) to failure, signaled by a sudden drop in the force–displacement curve. Vertical reaction force was collected at 102.4 Hz from the MTS single axis load cell, and vertical displacement was measured using the MTS linear variable differential transformer (LVDT) system. Stiffness was calculated from the linear portion of the force–displacement curve, i.e., between 30% and 70% of the peak force.

Specimen-Specific QCT/FEA Models

Segmentation and Mesh Generation. QCT-DICOM images obtained from the scanning and reconstruction process were imported into Mimics image processing and editing software (Materialise US, Plymouth, MI). Since the highest scan resolution (140 kVp, 200 mAs, U70) showed the best contrast compared to all other scanning acquisition settings (Figs 2(a) and 2(b)), it was used to create the segmentations and outlines of the five vertebrae computer models. First, a standard Hounsfield unit (HU) window ($HU > 225$) was used for all models, and each slice was then manually edited to include the entire cortical bone region and generate a 3D geometry of each vertebrae. Triangular surface meshes were generated using the Mimics FEA module with a maximum element length of 2.5 mm. Unstructured tetrahedral volume meshes were automatically generated from the triangular surface meshes with 3-Matic (Materialise US, Plymouth, MI) using ten-noded tetrahedral elements of 2.5 mm size. A preliminary sensitivity analysis with tetrahedral meshes of 2, 2.5, 3, 3.5, and 4 mm element size showed that the 2.5 mm element mesh produced converged results while not being computationally expensive. For each of the five vertebrae, the same 3D mesh of 2.5 mm element size was then imported into the 12 corresponding image data in Mimics to assign material properties, resulting in a total of 60 QCT/FEA models and results sets (Figs 2(c) and 2(d)).

Material Property Assignment. Ash density and elastic modulus were grouped into 42 discrete material property bins and mapped to the QCT/FEA models using the Mimics FEA module, as previously described [14,15]. The mean HU number of each finite element was averaged from the values of the contained CT voxels. A Young's modulus value (E , [MPa]) was assigned to each element based on a density-dependent elastic modulus relationship established by Morgan et al. [10], assuming a ratio between ash and apparent density of $\rho_{ash}/\rho_{app} = 0.6$ (Eq. (2))

$$E_{average} = 4730 \times \rho_{app}^{1.56} \quad (2)$$

Poisson's ratio was set to 0.4 for all material bins. Histograms were generated showing the number of elements per material bin.

Fig. 1 QCT/FEA process. Assignment of material properties (step 4) to the finite elements of the models is based on Hounsfield unit values from the CT images and estimated bone mineral densities obtained using a calibration phantom.

Fig. 2 Axial view of a vertebral body using high resolution scans (140 kVp, 200 mAs) reconstructed with (a) sharp (U70) and (b) smooth (U30) kernels. The smooth reconstruction kernel shows a lower image quality and contrast compared to the sharp kernel. (c–d) Same finite-element mesh was imported into the different CT image data for material properties assignment.

Finite-Element Modeling. Models were imported into ABAQUS v.6.14 (Dassault Systèmes Simulia Corp., Providence, RI), and simulations of each QCT/FEA model were conducted by applying boundary conditions matching the constraints from the experimental testing as described in more details in a prior publication

[14] and summarized here for convenience. The inferior vertebral surface nodes embedded in PMMA were constrained in all directions. The superior surface nodes embedded in PMMA were constrained in the mediolateral/anteroposterior translations and all three axes of rotation while allowing a vertical displacement.

Table 2 Summary of results. Material properties for the models were estimated from measured Hounsfield unit values from the CT images and regression parameters obtained using the calibration phantom.

				Regression parameters		ρ_{ash} Estimation parameters	
Voltage (kVp)	Current (mAs)	Slice thickness	Reconstruction kernel	Slope (σ_{CT})	y-intercept (β_{CT})	Slope ($1/\sigma_{\text{CT}}$)	y-intercept ($\beta_{\text{CT}}/\sigma_{\text{CT}}$)
80	110	0.5	U30	1.96	49	0.51	25.00
			U70	1.69	24	0.59	14.20
	200		U30	1.96	48	0.51	24.49
			U70	1.72	7	0.58	4.07
120	110		U30	1.43	53	0.70	37.06
			U70	1.26	7	0.79	5.56
	200		U30	1.43	52	0.70	36.36
			U70	1.26	6	0.79	4.76
140	110		U30	1.31	50	0.76	38.17
			U70	1.14	6	0.88	5.26
	200		U30	1.31	50	0.76	38.17
			U70	1.14	5	0.88	4.39

Fig. 3 Estimated vBMD versus Hounsfield unit values. Calibration curves obtained from the calibration phantoms for varying scanning and image reconstruction algorithms. Hounsfield unit values are extrapolated to 3000 [HU] to represent cortical values. Solid and dotted lines represent sharp (U70) and soft (U30) kernels, respectively.

To mimic loading of the platen on the vertebrae, reference nodes were visually placed, respectively, at the superior and inferior endplates of the specimens. Superior and inferior surface nodes from the vertebrae and the reference nodes were selected to form rigid bodies and create a kinematic coupling. A vertical displacement to the superior reference node was applied and stiffness was calculated from the simulated load–displacement curve. Stiffness from each QCT/FEA model was compared to the experimental values.

Statistical Analysis. Analysis of variance (ANOVA) was used to investigate the relationship between imaging and regression parameters. A three-way interaction was assumed to not be present, and a model with main effects and all possible two-way interactions was considered. The level of significance was set at 0.05. Descriptive plots of predicted stiffness results were developed and compared to experimentally measured values.

Results

Bone densitometry measurements showed normal bone density values in the lumbar spine (L1–L4: 1.175 g/cm^2 , $T\text{-score} = -0.2$). Table 2 summarizes the regression parameters (σ_{CT} and β_{CT}) obtained from the calibration phantom and the calculated slopes and intercepts ($1/\sigma_{CT}$ and β_{CT}/σ_{CT}) used for conversion of HU to ash density for each scan setting. Summary statistics of the regression parameters are presented in Table 3. Analysis of the slope parameter showed a significant interaction between kernel and voltage ($P = 0.0006$). A model, including main effects only, found significant differences in slope values for voltage and reconstruction kernels ($P < 0.0001$). No two-way interactions were significant when looking at the intercept parameter. However, main effects model showed significant differences in the intercepts values for kernels ($P < 0.0001$).

Figure 3 illustrates representative curves for vBMD estimation versus Hounsfield unit values from the images obtained using $[1/\sigma_{CT}]$ and $[\beta_{CT}/\sigma_{CT}]$ from Table 2. The HU values are extrapolated to 3000 [HU] to cover the entire spectrum from trabecular bone (low density, low HU values) to cortical bone (high density, high HU values). For ease of visualization, because current (mAs) does not affect the estimated values and regression parameters, only one current setting is shown. Figure 4 shows the predicted and experimentally measured stiffness outcomes. There is not a clear visual distinction between voltage differences on stiffness values, as shown by Figs. 4(a) and 4(c). Figures 4(c) and 4(d) show the percent difference between measured and predicted values for each specimen. The highest percent difference was approximately $\sim 480\%$ on T12 with scanning parameters of 80 kVp, 110 mAs, and U70 kernel. The lowest percent difference corresponded to T11 with $\sim 1\%$ error and scanning parameters of 80 kVp, 110 mAs, and U30 kernel. There is a clear distinction between reconstruction kernels and predicted outcomes, as shown in Figs. 4(b) and 4(d). The smooth reconstruction kernel (U30) showed smaller percent errors when compared to the sharp U70 kernel.

Figure 5 shows histograms of the numbers of finite elements in each bin for two vertebrae based on kernel (Fig. 5(a)) and voltage (Fig. 5(b)) differences. The vertical (“y”) axis corresponds to the element frequency, and the horizontal (“x”) axis represents the material bin number, with bin number 1 corresponding to the elements having the least dense material (smaller density and Young’s modulus). Analysis of the histograms showed the sharp kernel (U70) models to contain a larger number of elements at the first bin and high bin numbers, corresponding to low and high densities. On the other hand, the smooth kernel (U30) models contained more elements in the middle bin range. Figure 5(b) shows the element frequency in the models as a function of voltage differences. Middle and high voltages (120 and 140 kVp) were characterized by a large number of elements in the middle density range, with a decreasing number of elements with increasing density. There was a similar element frequency distribution trend between middle- and high-voltage values. In contrast, low-voltage models showed more elements allocated to higher densities with fewer elements in the middle and low density range.

Discussion

The purpose of this study was to assess if there were any differences in predicted stiffness outcomes from finite-element models when implementing varying QCT scan settings. Scanning and postprocessing parameters were varied, and QCT/FEA models were developed for five vertebrae. Results showed that there exist important differences in estimated stiffness values from diverse scanning and reconstruction settings. Initial analysis of the results showed that the slope of the calibration equation used for conversion of Hounsfield unit values to ash density was affected by voltage and reconstruction kernel. However, the intercept was only affected by the kernel (Table 3). Although differences were observed in predicted stiffness when implementing different voltage settings, there were evident inconsistencies between smooth

Table 3 Summary statistics of regression parameters. Mean (SD) slope and y-intercept values are shown for voltage, current, and reconstruction kernels.

Imaging parameter		Slope (σ_{CT})	p-value	y-intercept (β_{CT})	p-value
Voltage (kVp) ^a	80	1.83 (0.15)	<0.0001	32.0 (20.28)	0.5720
	120	1.35 (0.10)		29.5 (26.56)	
	140	1.23 (0.10)		27.75 (25.70)	
Current (mAs)	110	1.47 (0.31)	0.7598	31.5 (21.99)	0.3059
	200	1.47 (0.31)		28.0 (24.14)	
Reconstruction kernel ^a	U30	1.57 (0.31)	<0.0001	50.33 (1.86)	<0.0001
	U70	1.37 (0.27)		9.17 (7.31)	

^aSignificant interaction ($P = 0.0006$)

Fig. 4 Predicted and experimental measured stiffness. Stiffness difference for all models versus predicted stiffness based on (a) voltage parameters and (b) reconstruction kernels. Percent different for all models and vertebral level based on (c) voltage parameters and (d) reconstruction kernels.

(U30) and sharp (U70) kernels in predicted results. Finally, a histogram of the element distribution showed differences in the allocation of elements and material property assignment for smooth versus sharp kernels (Fig. 5(a)), as well as for 80 versus 120 and 140 kVp (Fig. 5(b)). In the smooth kernel, a larger number of elements were assigned to bins 2–5, corresponding to low density elements ($\sim 0.01\text{--}0.11\text{ g/cm}^3$) when compared to the sharp kernel. However, a larger number of elements were allocated to high density bins (seven and higher, $\sim 0.16\text{--}1.57\text{ g/cm}^3$) when using the sharp kernel. Interestingly, a large number of elements were assigned to the first bin, corresponding to low HU values, when reconstructing the images with a sharp kernel. As Fig. 5(b) shows, scanning with a high voltage distributes a larger number of elements between bins two and five, while using a low voltage setting places a larger number of elements at higher density bins (eight and higher). Element frequency distribution is clearly represented by the results shown in Fig. 4(b) and 4(d). A sharp kernel, having more elements assigned high density values, therefore larger Young's modulus, showed a higher percent difference, thus predicted stiffness, when compared to the experimental measured results. On the contrary, models reconstructed with a smooth kernel, with the majority of the elements at the low density range, resulted in a lower percent error. Although it is evident by observing Fig. 5(b) what the element frequency distribution is depending on the voltage acquisition, this difference in voltage and predicted stiffness is not apparent when observing Fig. 4(a). This may be due to the significant interaction between the voltage and the reconstruction kernel.

Reconstruction kernels describe the type of filtering applied to the raw data to obtain a final image. The sharp reconstruction

kernel (U70) has the advantage of high image contrast and sharp edges allowing for a better cortical definition and distinction from the trabecular bone. On the other hand, the smooth kernel (U30) reduces the contrast and makes it harder to segment the geometry and observe bone tissue local inhomogeneities. The sharpness of the image is controlled by the number in the type of kernel; the higher the number, the sharper the image [16]. However, a sharp filtering process will introduce noise to the image. Several studies have reported the effect of scanner and CT acquisition settings on the gray value (HU) of the voxel and image quality. Cann [7] compared HU values from CT scanners of different manufacturers and showed that results from one equipment could not be compared to results from other CT scanner, unless a correction factor was applied. Similarly, using a chest phantom, Paul et al. showed reconstruction kernels and slice thickness to affect image quality [9]. Some of our previous work showed that the effect of high- and low-resolution scanning protocols on predicted strength and stiffness of QCT/FEA models was significantly different [12]. Over an entire femoral dataset of osteoporotic, osteopenic, and normal bones, stiffness predicted values from high-resolution scans were consistently larger than those obtained from low-resolution scans. Furthermore, it has also been demonstrated that estimated vBMD measurements from rabbit femurs were affected by voltage and kernel but not by current, proving a significant difference in the estimated vBMD values obtained with different scanning acquisitions [13]. The latter study presented mean estimated vBMD values obtained from large bone segmentations. Although the calibration phantom corrected for voltage differences when analyzing the mean measurements, the large noise in the images and segmented regions could affect the estimated vBMD

Fig. 5 Number of elements per material bin for two representative vertebrae. The thoracic vertebra shows a smaller number of total elements compared to the lumbar vertebra as described by the relative frequency at each bin. Element density and Young's modulus for each scan will vary according to the different values of Hounsfield units acquired at each bin and the different calibration equations corresponding to each combination of scan parameters (Table 2).

values when small voxels are selected for finite-element model development. The results in the current study support this observation and demonstrate that large noise in the image leads to an incorrect stiffness prediction.

It is important to note that the material equation relating bone mineral density to Young's modulus [10] will affect the stiffness results. Stiffness outcomes will change depending on the material equation used, and although in the current study the average value of the referenced equation was chosen and applied to all models when comparing the CT settings, this might not be the optimum equation to be used when optimizing the models. However, the study shows that using only one equation with varying CT scanning settings and reconstruction parameters, the predicted stiffness values differ. The use of QCT/FEA as a tool for fracture prediction has been well established by various research groups [2,3,15,17–20]. However, several “optimum” material equations exist between and within groups, and these differences might be due to the different scanners or scanning parameters used. Furthermore, missing information in scanning acquisition protocols is sometimes encountered in published literature. Combining the unavailability of complete scanning information and the variable material equations available might lead to an erroneous estimation of mechanical properties. Additionally, there might exist a mismatch between what is optimum in the research community and the available resources in the clinic when translating the ideal model parameters including material and fracture properties, imaging settings, and model development (segmentation, meshing, boundary, and loading conditions [21]). Diagnostic images are usually acquired and reconstructed in order to maximize dose reduction in patients while reducing image artifact without affecting the diagnostic process. This may potentially mean using a smooth kernel, lower voltage and current and most possibly differing even within the same institution and more importantly between institutions.

This study has several limitations. First, our sample number used for the analysis was small, possibly preventing us from capturing differences that could be presented between normal, osteopenic, and osteoporotic bones. However, we believe that the presented results using five vertebrae illustrate the important differences in predicted stiffness between CT scanning settings and reconstruction parameters. Nevertheless, future studies with a larger sample population containing a wider range of bone mineral densities will help to better understand any difference arising from image acquisition and modeling of vertebral fracture. Second, although we believe stiffness is a very important aspect to consider in fracture risk prediction, we did not model the fracture process. Despite not modeling a vertebral failure load, understanding differences in stiffness outcomes based on image acquisition processes will further our understanding of the steps needed to be able to translate research outcomes into a clinical setting. Third, only one scanner was used in this study and, although the table height was kept constant, only a single position was evaluated. There will be a variety of scanner manufacturers within and between institutions, and image reconstruction algorithms together with scanning protocols will also differ. Although BMD estimations of larger cortical and trabecular regions could be partially corrected by cross-calibrating scanners [22], differences in HU values at a smaller scale might highly affect the fracture properties estimation. If similar methods are used by researchers from different institutions, which may include different material equations and failure criteria, depending on the CT-measured ash densities, stiffness and strength prediction may result in widely diverse estimations. Finally, the effect of patient size was not evaluated. Attenuation of X-rays will vary depending on the amount of tissue present, and although this might have a small effect in the measured HU value, it could still affect the predicted outcomes.

In summary, this study demonstrated that there are differences in the regression parameters obtained from a calibration phantom when implementing different image acquisition settings. More importantly, differences in stiffness estimations from QCT/FEA models might potentially lead to misleading bone properties results. These results indicate that researchers implementing QCT/FEA as a tool for fracture risk prediction may obtain dissimilar equations relating the conversion of HU values to Young's modulus, and possibly failure criterion equations to predict fracture, depending on their CT settings and reconstruction parameters. Body size and cadaveric tissue degradation over time can potentially affect the attenuation coefficient (HU) of bone in the CT imaging process. Although the stiffness values presented in this study might not perfectly mimic those observed in an in-vivo situation, we still expect differences to be observed in the predicted outcomes depending on the implemented acquisition and reconstruction protocols. It is well established the potential of QCT/FEA as an improvement to conventional fracture risk prediction tools. However, we believe it is important for the research community to come up with a standard implementation of CT acquisition protocols for bone material properties and fracture prediction that come close to those used in the clinic, and to further understand these differences so that additional protocols can be implemented to translate the findings in the research environment to the needs of clinicians.

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