MicroCT Based Bone Mineral Content Predictions can be Significantly Improved with a Change in Calibration Methods

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Introduction

The commercial availability of µCT scanning systems has led to the novel analysis of bone geometric properties and an increased interest in the mineralization of bone at the micro-structural level. The availability of this information has allowed for the development of highly-detailed heterogeneous finite-element (FE) models, used to better understand the stiffness and strength of bone specimens in-vivo, that use the mineralization level to assign elastic modulus on a voxel-by-voxel basis. Mineralization derived from µCT has also been identified as a critical input for estimating the constituents of bone in-vivo [1]. Such estimates can be used to determine bone parameters previously requiring destructive testing (e.g., dry mass, ash fraction, tissue density, percent mineralization). Unfortunately, previous studies have shown that predictions of bone mineral content (BMC) and bone mineral density (BMD) from µCT can be underestimated by as much as 40% [2], potentially influencing the performance of models and bone parameter estimates that rely on mineralization as input.

Several factors have been proposed that may contribute to the underestimation of BMC including beam hardening, the extrapolation function (i.e., linear versus polynomial) used to convert µCT measured linear attenuation to mineral density, calibration phantom design (parallel versus serially aligned calibration regions), and the background material used in the calibration phantoms for relating linear attenuation to mineral density [3]. A commercially available one-piece µCT calibration phantom with hydroxyapatite (HA) concentrations ranging from 0 to 800 mg HA/cm^3 (QRM GmbH; Germany) is commonly used with a linear extrapolation function. Considering that bone typically consists of mineral density values in the range of 900 to 1000 mg HA/cm^3 and can reach 1300 mg HA/cm^3 or greater, the extrapolation function is critical to accurately quantifying mineral density from µCT imaging.

Objective:

This study quantified the potential improvement in µCT predicted BMC related to changes in calibration phantom design (serial versus parallel orientations), inclusion of an additional high density HA calibration point, and selected extrapolation function.

Methods

Phantom Scan Parameters

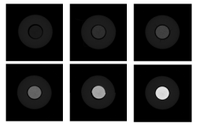
- vivaCT 40 µCT scanner (SCANCO Medical; Switzerland) 70 kVp, 114 µA, 400 msec.
- Medium resolution
  - 38.9 µm for larger 5 and 6 part phantoms.
  - 21 µm for individual rods.
- 1200 mg HA/cm^3 beam hardening correction (BHC).
- Linear attenuation coefficient (LAC) was determined as the average of the central region of each rod over multiple slices.
- Linear and 2nd order polynomial calibration curve fits between LAC and BMD were created for each of three phantoms.

Methods (continued)

Phantoms

Standard five-part Scanco phantom (0, 100, 200, 400, 800 mg HA/cm^3).

Custom six-part QRM phantom (0, 100, 200, 400, 800, 1200 mg HA/cm^3).



Individual rods (0, 100, 200, 400, 800, 1200 mg HA/cm^3).

Bone Mineral Content Prediction/Measurement

- Five 5 x 5 x 5 mm bovine cortical bone cubes.
- Scanned at 70 kVp, 114 µA, 400 msec.
  - 1200 mg HA/cm^3 BHC
  - High resolution (10.5 µm).
- Analyzed using Matlab to convert from LAC to voxel BMC, thresholded (566 mg HA/cm^3), then summed to determine the cube BMC for six candidate calibration methods.
- Each cube was dried then ashed at 800˚C for 48 hours and weighed.

Statistics

Repeated measures ANOVA with a Bonferroni/Dunn post-hoc analysis (Statview).

Results

The average BMC measurement and predictions are presented in Table 1. The gravimetric measurement was significantly larger than all predictions ($p<0.0001$). The standard Scanco 5-part linear calibration method underestimated the BMC the most (12.9%), while the serially scanned polynomial method underestimated the least (2.6%), an 80% improvement.

Table 1. Measured (gravimetric) and predicted bone mineral content for 5 cortical cow bone cubes.

	BMC (mg)	% Error
Gravimetric	140.4 (3.5)	-
5-part linear	122.3 (3.6)	-12.9 (1.1)
5-part polynomial	128.8 (3.9)	-8.3 (1.1)
6-part linear	127.7 (3.8)	-9 (1.1)
6-part polynomial	129.7 (3.9)	-7.6 (1.1)
Series linear	133.8 (4)	-4.7 (1.2)
Series polynomial	136.7 (4.1)	-2.6 (1.1)

Data presented as mean (standard deviation).

Polynomial methods were better than linear methods at predicting the BMC for all phantoms. Most values were significantly different ($p<0.0001$), except no difference was found between the 5-part polynomial prediction and either of the 6-part predictions.

Discussion

The most accurate prediction in this study used individual rods ranging from 100 to 1200 mg HA/cm^3 that were serially scanned and fit with a 2nd order polynomial. This simple change in calibration phantom and extrapolation function reduced the error by 80%.

The use of a 2nd order polynomial increased the average bone mineral density for all calibration phantoms investigated in this study (Fig. 1). This increase in density led to a significant improvement in the predictive capability when compared to the linear calibration for the same phantom. Of interest, the inclusion of the 1200 mg HA/cm^3 rod in the custom phantom did not significantly improve the BMC prediction when compared to a polynomial fit of the 5-part phantom.

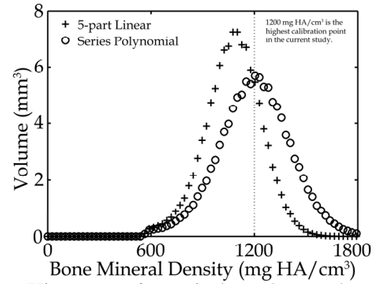


Figure 1. Histogram of a cortical cow bone cube with two of six investigated calibration methods: 1) 5-part linear, 2) Individual rods fit with a 2nd order polynomial.

In this study all BMC predictions were below the measured values suggesting that there is still a systematic deficiency in the calibration methodology. One possibility that we are investigating is that the current binder material in the mineral rods is too attenuating leading to an underestimation of BMC. Since Fig. 1 demonstrates that a substantial fraction of the mineral in the specimens is still above the 1200 mg HA/cm^3 calibration point, another possibility is that a calibration point substantially higher than 1200 may be needed. Lastly, it is known that bone does not consist solely of pure hydroxyapatite crystals [4]. Therefore, it may be necessary to account for the variation in minerals and their unique linear attenuation coefficients to get a more accurate prediction from µCT scans.

Significance: The serial scanning of calibration phantoms, addition of a 1200 mg HA/cm^3, and the use of a 2nd order polynomial fit significantly increases the accuracy of bone mineral content (BMC) prediction from µCT scans.

References

[1] Wagner et al., *Bone*, 49:931-8, 2011. [2] Kazakia et al., *Med. Phys.*, 35:3170-9, 2008. [3] Deuerling et al., *Med. Phys.*, 37:5138-45, 2010. [4] Blitz and Pellegrino, *JBJS*, 51A:456-66, 1969.

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