## Reproducibility of trabeculae bone structural parameters at two resolution regimes

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#### Introduction

High-resolution magnetic resonance imaging ( $\mu$ MRI) of trabecular bone (TB) is capable of discerning changes in the TB microstructure due to disease [1] and treatment [2]. The ability to detect small microstructural changes in TB, such as the conversion of plates to rods, is limited by the trade-off between SNR and resolution. For example, slice resolution is often relaxed to gain SNR, leading to decreased sensitivity to detection of trabeculae oriented transverse to the slice direction [3]. The measurable change in a structural parameter is also dependent on the reproducibility of the imaging protocol. Sources of error in capturing structural parameters in  $\mu$ MRI of TB include: 1) variations in SNR; 2) subject motion; and 3) poor overlap/alignment of the analysis volume. Here, a new clinical protocol for TB imaging at 3T in the distal tibia has been designed to minimize these error sources and explore the potential of isotropic imaging. The reproducibility of TB structural parameters has been assessed for both, an anisotropic (A) and isotropic (I) fast large-angle spin-echo imaging protocol in repeated scans of five healthy volunteers.

### Methods

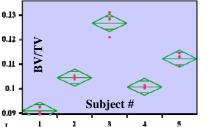
The imaging protocol was implemented on a 3T Siemens TIM Trio scanner (Erlangen, Germany) with a four-channel RF coil (Insight MRI, Worcester, MA). The five volunteers consisted of 1 female and 4 males, ranging from 30-42 years of age. The onehour protocol consisted of 2D localizers to ensure correct coil positioning, a 3D fast-GRE acquisition for prospective registration [4], and two high-resolution acquisitions based on a modified FLASE pulse sequence [5]: 1) a standard 16-minute scan with an anisotropic voxel size 137x137x410µm<sup>3</sup> over a 70x64x13mm<sup>3</sup> FOV; and 2) an 18-minute scan employing GRAPPA with an isotropic 160µm voxel size over a 80x64x10mm<sup>3</sup> FOV. To improve the reproducibility, the following improvements had been implemented: a new ankle immobilization device bolted to the scanner table; prospective image registration [4] to maximize anatomic overlap between baseline and follow-up scans; and in-plane translational motion correction via navigator echoes [6]. Each image was manually masked and the common masked volume was determined using a rigid registration technique [7] prior to computation of the apparent bone volume fraction (BV/TV) and the surface-to-curve ratio (S/C) from each acquisition[8]. The coefficient of variation (CV) and the intra-class coefficient (ICC) were computed as metrics of reproducibility.

# **Results and Conclusions**

Image quality (SNR, artifacts, and degree of motion) was consistent over the course of the study. Only one of the fifteen scans displayed minor blurring attributed to rotational motion, suggesting effectiveness of immobilization. Minor translations of <3 pixels were detected and corrected using navigator projections. The average common volume retained for analysis after retrospective registration was approximately 64% of the total available analysis volume for both A and I.

Good visual reproducibility and anatomical alignment is demonstrated in Figs. 1a-c. In Table 1, parameter means calculated across all fifteen scans; CVs averaged over the five volunteers, and ICCs are provided. The mean BV/TV and S/C values are higher in I than in A. Additionally, the parameters derived from I are less reproducible

than those from A. The lower reproducibility is attributed to the reduced analysis volume (75% of the analysis volume of A) and the lower SNR (voxel size is halved at approximately the same scan time). Still, ICC for BV/TV (0.95-A/0.85-I) and S/C (0.95-A/0.93-I) suggest between-subject to dominate over within-subject variances in both A and I



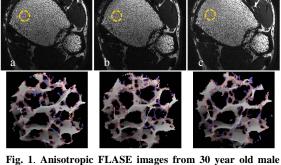


Fig. 1. Anisotropic FLASE images from 30 year old male subject at three time points: a)baseline; b)follow-up 1; and c)follow-up 2. Segmented cores from approximately the same location show good reproducibility of curve voxels in blue, surface voxels in grey, and surface edges in red.

	Scan	Mean	CV(%)	ICC
BV/TV	A	0.107	1.78	0.95
	I	0.116	3.59	0.85
S/C	A	7.78	3.77	0.95
	I	7.92	4.45	0.93

Table 1. Mean values, CVs and ICC for BV/TV and S/C from three repeated anisotropic (A) and isotropic (I) scans in five subjects.

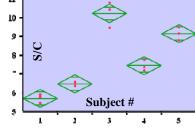


Fig. 2. a)
Distribution of
BV/TV and b) S/C
showing wide
variation between
subjects and small
within-group
variation.

(Fig. 2a&b) despite the narrow age range of the subjects (30-42 years of age). CVs (2-4%) and ICCs (0.82-0.95) obtained here (for both A and I) suggest considerably better reproducibility than previously reported [8] in the distal tibia at 1.5T (CVs of 4-7% and ICCs of 0.68-0.92) using a  $137x137x410\mu m^3$  voxel size.

The present data demonstrate substantially better reproducibility than previously reported at 1.5T. The ability to distinguish means between five young healthy subjects suggests the TB structural parameters determined with the two protocols to have adequate sensitivity in the clinical setting for the evaluation of treatment response. While isotropic scanning provides somewhat lower reproducibility, it may offer superior sensitivity for the detection of subtle topological changes.

### References

[1] Boutry et al., Radiology 227, 3 (2003). [2] Chesnut et al., JBMR 20, 9 (2005). [3] Wald et al., Proc. of ASBMR, Montreal, QC 2008. [4] Rajapakse et al., MRM 59, 1120 (2008). [5] Magland et al., In Press (2008). [6] Song and Wehrli, MRM 41, 947 (1999). [7] Magland and Wehrli, Acad. Radio. In Press (2008). [8]Gomberg et al., IEEE TMI 19, 166 (2000). [9] Gomberg et al., Bone 35, 266 (2004). Acknowledgements: NIH F31EB74482, RO1 AR41443, RO1 AR53156