

## Evaluation of the Detection Sensitivity of Simulated Trabecular Bone Loss in $\mu$ MRI

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### Introduction

Patients suffering from osteoporosis or other osteodegenerative diseases experience loss of trabecular bone mass and structural integrity, leading to a decrease in the overall mechanical strength of the bone [1]. The development of the “virtual bone biopsy” (VBB), a combination of magnetic resonance micro-imaging ( $\mu$ MRI) and digital image processing techniques, has been shown to quantify topology and scale of human trabecular bone noninvasively [2, 3]. It is not known, however, whether subtle structural deterioration of the trabecular network, for example, following menopause, or conversely, improvements in response to treatment, can be detected in the limited spatial resolution and SNR of in vivo  $\mu$ MRI. The objective of the present work was to determine the extent to which different forms of bone loss, and their implications on parameters of network topology and scale, can be detected using these digital image analysis techniques.

### Materials and Methods

To evaluate the ability of VBB image processing algorithms to detect bone loss or accrual during disease progression or regression in response to treatment, in-vivo  $\mu$ MRI images of trabecular bone were simulated from ex-vivo  $\mu$ CT scans of human cadaveric bone. Nine bone specimens extracted from the femur, lumbar vertebrae and tibia of human donors were scanned by  $\mu$ CT at a voxel size of  $21 \times 21 \times 22 \mu\text{m}^3$ . From these, a control dataset was created. The  $\mu$ CT images were then threshold segmented to isolate trabecular bone and inverted to mimic MR signal intensity. To emulate in-vivo levels of noise and resolution achievable at 1.5T, the images were then downsampled in the spatial frequency domain to the spatial resolutions of  $137 \times 137 \times 410 \mu\text{m}^3$  and  $160 \times 160 \times 160 \mu\text{m}^3$  and then superimposed with random noise of SNR=12.5 and SNR=15, respectively. Finally, a dataset simulating the effects of bone loss on the control dataset was created by subjecting the original high-resolution, segmented and inverted  $\mu$ CT images to erosion algorithms before the images were downsampled and superimposed with random noise to mimic in-vivo levels of noise and resolution, as previously performed with the non-eroded data. Two types of erosion were simulated: homogeneous thinning and heterogeneous pitting. Homogeneous erosion was achieved by iteratively removing bone voxels on trabecular surfaces until a bone volume decrease of 5% was attained, while heterogeneous erosion was performed by creating pits  $60 \mu\text{m}$  in diameter centered on random trabecular surface voxels until bone volume was decreased by 5%. A schematic of the erosion and  $\mu$ MRI simulation process is illustrated in Figure 1. Lastly, the control and eroded images were analyzed using VBB processing, and two-tailed single-sample t-tests were run on the calculated structural parameters to determine whether there were significant differences between the non-eroded and eroded datasets at the same levels of noise and resolution.

### Results

T-tests of the parameters calculated from the eroded and non-eroded images showed significant differences in many structural parameters. At all levels of resolution and SNR, the parameters “bone volume fraction,” “surface density,” “surface to curve ratio,” “erosion index” and “skeleton density” were highly significantly different between control and eroded datasets (Figure 2 and Figure 3).

The results of this work indicate that, even at the limited resolution and SNR achievable in clinical trabecular bone imaging, the VBB algorithms can detect topological changes in trabecular bone caused by bone loss. Furthermore, the changes in the calculated structural parameters agree with intuitive understanding of topological changes caused by trabecular bone loss as it occurs, for example, in steroid-induced osteoporosis (homogeneous erosion) or postmenopausal osteoporosis (heterogeneous erosion) [4, 5]. As expected, the bone volume fraction decreased in good agreement with the values applied to the high-resolution images and the erosion index increased with both forms of erosion. Additionally, heterogeneous erosion was noted to cause a significant decrease in the topological surface-to-curve ratio, an intuitively logical result as the most evident effect of repeated osteoclastic resorption pitting during successive remodeling cycles.

### Conclusion

The data suggest that structural manifestations of relatively small amounts of bone loss, such as the conversion of trabecular plates to rods and impaired trabecular connectivity, can be detected in the regime of limited spatial resolution and SNR of in vivo  $\mu$ -MRI. The results have implications for the method’s potential to study the effects of aging and for the evaluation of the response to therapeutic intervention.

### References

[1] Seeman E, et al., *N Engl J Med* **354** 2250-61 (2006). [2] Wehrli FW, et al., *Proc IEEE* **91** 1520-42 (2003). [3] Wehrli FW, et al. *NMR Biomed* **19** 731-64 (2006). [4] Aaron JE, et al. *Clin Orthop Relat Res* **243** 294-305 (1989). [5] Parfitt AM, et al. *J Clin Invest* **72** 1396-409 (1983).

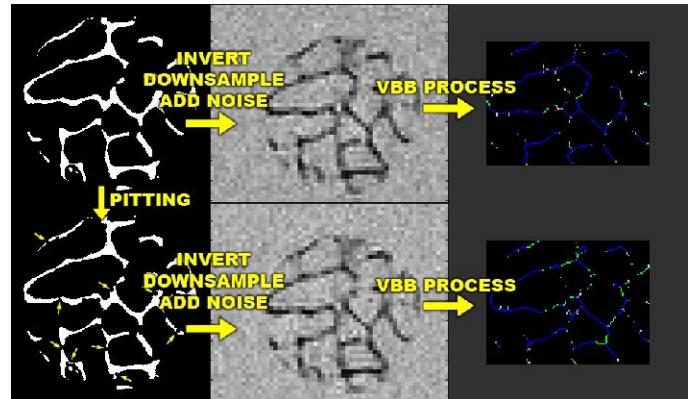


Figure 1. Illustration of erosion, downsampling to mimic in-vivo  $\mu$ MRI, and VBB processing, resulting in topological classifications of trabeculae into surfaces (blue), surface edges (green), curves (light blue), etc.

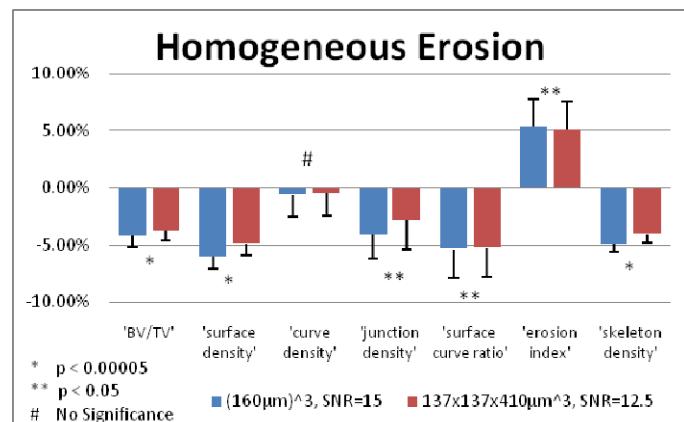


Figure 2. Detected changes in structural parameters at in vivo resolution and SNR after simulated homogeneous erosion for a net loss of 5% in bone volume fraction. Error bars represent standard deviations.

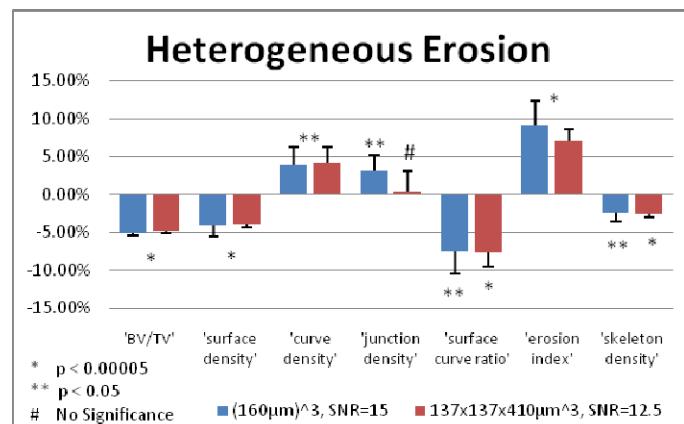


Figure 3. Detected changes in structural parameters at in vivo resolution and SNR after simulated heterogeneous erosion for a net loss of 5% in bone volume fraction. Error bars represent standard deviations.