Anabolic Changes in Vertebral Trabecular Microstructure in Osteoporotic Postmenopausal Women Treated for 2 Years with Human Parathyroid Hormone Fragment (hPTH 1-34) as Determined by a New, Automated, Noninvasive Imaging Technology that Uses Ordinary Lateral Spine Radiographs

C. Arnaud[1], S. Liew[1], D. Steines[1], R. Vargas-Voracek[1], S. Sanchez[2], P. Hess[1]

1. Imaging Therapeutics Inc., Foster City, CA, USA
2. University of California, San Francisco, CA, USA

Introduction

Until recently, quantitative assessment of trabecular structure required either bone biopsy followed by microscopy or 3-dimensional micro computed tomography (3D µCT). Non-invasive options include the use of expensive capital equipment such as magnetic resonance imaging (MRI) of peripheral bones. We developed a new, noninvasive, automated 2D image analysis technology that uses ordinary radiographs that can measure surrogate trabecular parameters comparable to those measured by 3D µCT. In general, it involves x-ray digitization, identification of regions of interest, background subtraction, and trabecular pattern extraction. Parameters of trabecular structures are measured using computer algorithms. In previous work, we applied this novel technology to ordinary radiographs of cores of proximal cadaveric femora showing that 2D measurements of trabecular structure correlate well with 3D µCT measurements. Those 2D measurements also correlate with biomechanical failure loads applied to those cores as well to whole proximal femora (JBMR; Abst # 1218, Abst # 107; 18 Suppl 2; 2003). We applied the same technology to in-vivo lateral vertebral radiographs obtained in a previously performed study of the effect of hPTH (1-34) on the bone density of estrogen treated postmenopausal osteoporotic women (JBMR; Abst #1019; 14 suppl 1; 1999).

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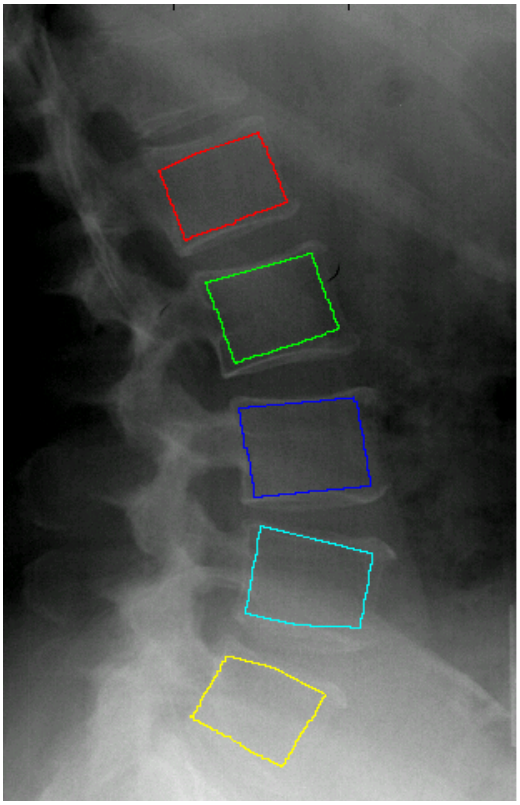

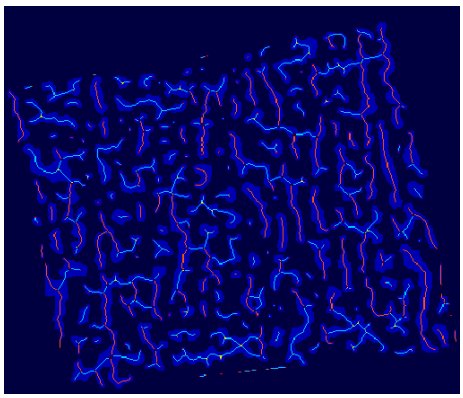

Figure 1. Regions of interest are semi-automatically placed on lumbar vertebrae (L1 – L5). The operator clicks on the approximated center of each vertebral body. The software then automatically characterizes the curvature of the spinal columns and places the regions accordingly (left). Structure analysis on each vertebra includes differentiation of vertical vs. horizontal structures (above).

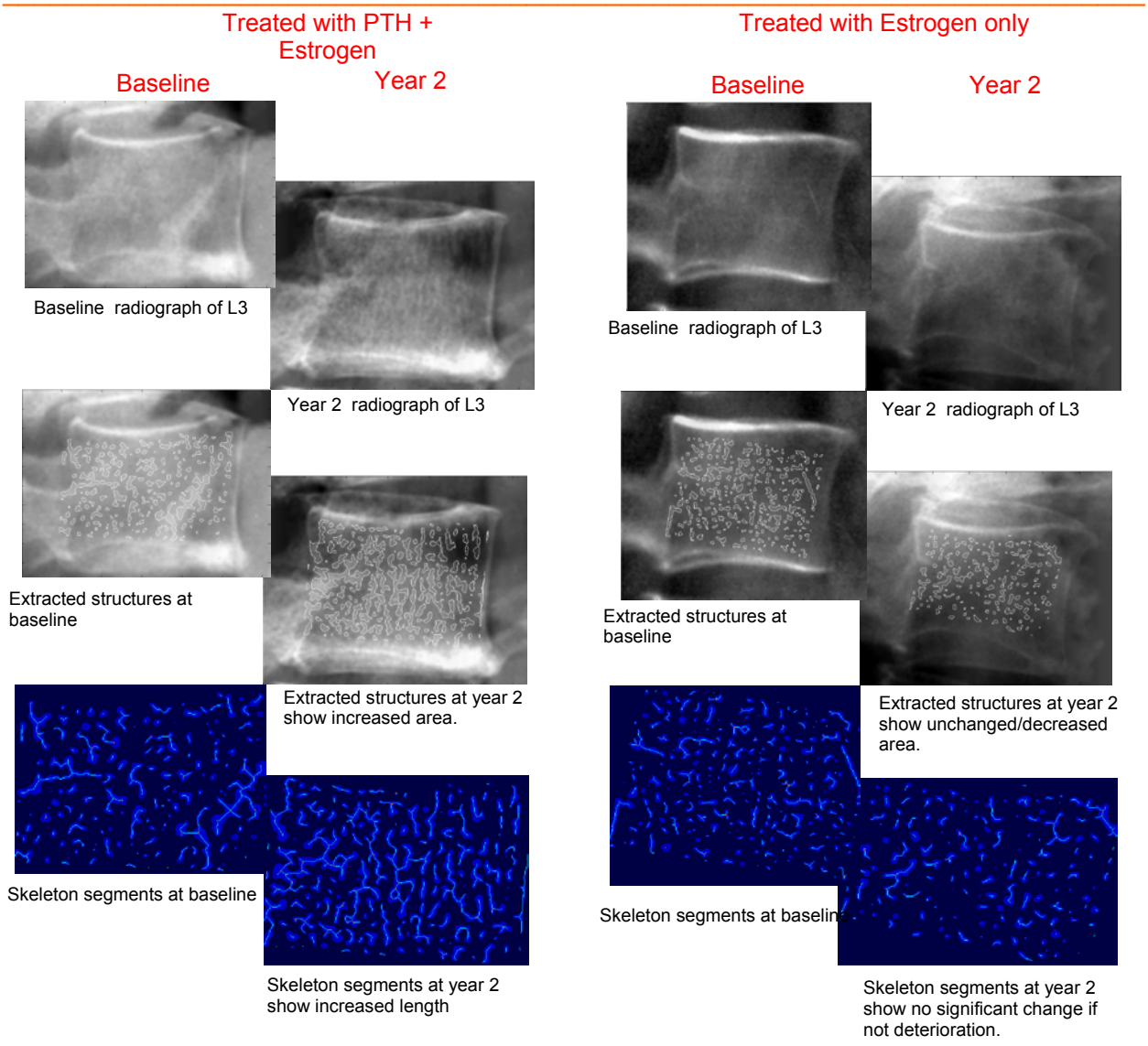

Figure 2. Visual comparison of baseline to year 2 images and extracted structures reveals obvious changes in the PTH group and relatively minor changes in the control group.

Method

The radiographs used are from a two-year study which involved postmenopausal women with osteoporosis that were undergoing estrogen replacement therapy. Thirty-seven subjects were treated with daily injections of hPTH(1-34) for the first year and thirty-seven controls were not. Lateral thoracolumbar radiographs were taken at baseline and at 24 months. BMD measurements were taken at baseline, 12-months and 24 months using DXA and QCT.

In this study we digitized (Powerlook 1100, Umax Technologies Inc., TX, USA) and analyzed available radiographs of 24 treated and 27 controls at baseline and 24 months using ImaTx Vertebral Structure Assessment (VSA) software. Regions of interest were semi-automatically placed (Fig. 1) and were inspected by an expert observer. Trabecular patterns on the vertebrae were extracted and measured for features reflecting the thickness, length, connectivity and number of fragments.

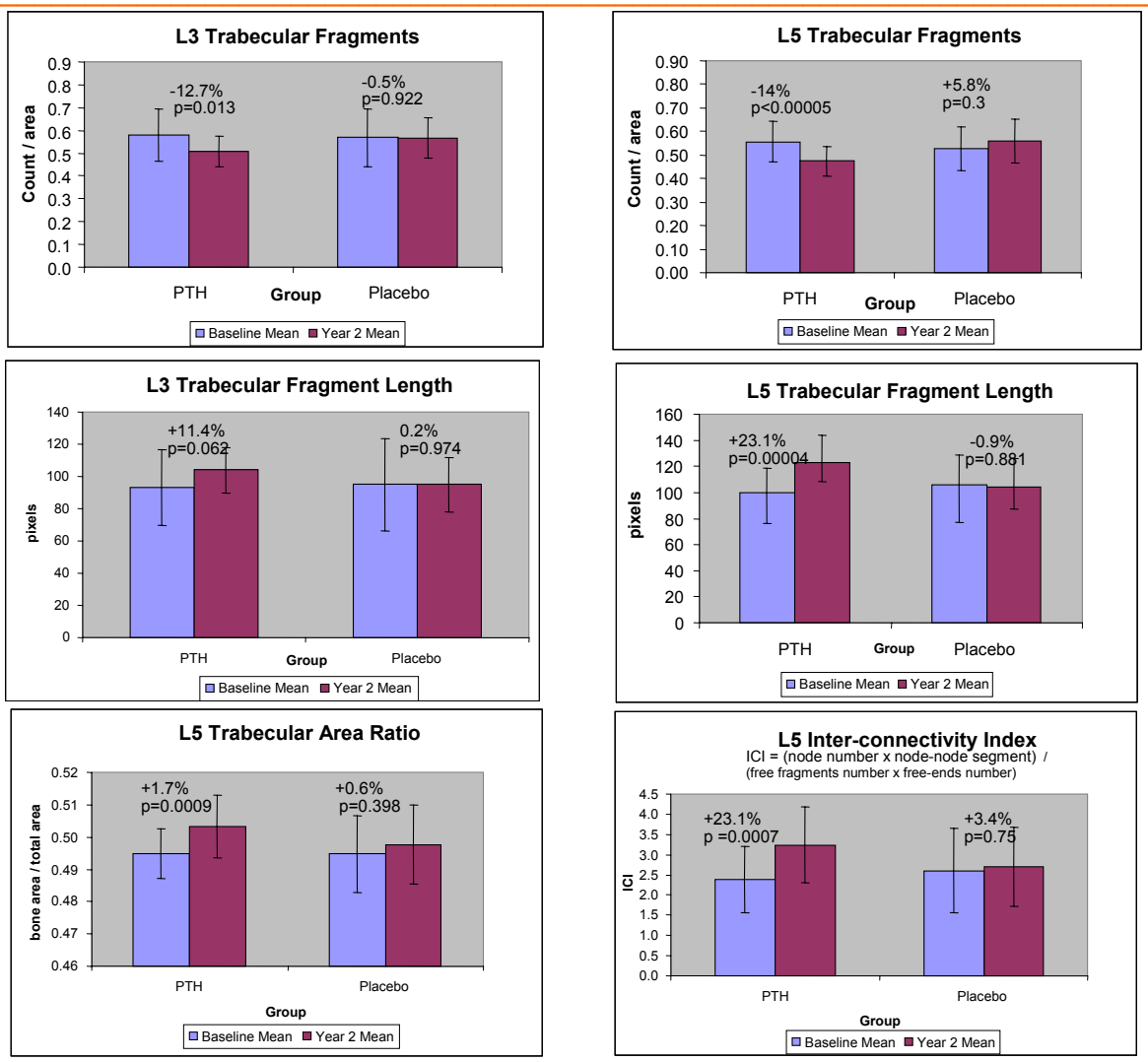

Figure 3. Parameters measured in L3 and L5 show significant changes in the PTH group and no significant change in the placebo group.

Results
Features that show the most significant change in the PTH group after 2 years is Trabecular Fragment Length measured in L5 at +23%, while no significant change is shown in the placebo group. As shown in Fig. 3 below, the number of Trabecular Fragments, Interconnectivity Index, and Area Ratio also show significant changes in the PTH group and no significant change in the placebo group.

According to the results from the previous study, the median changes in BMD of the lumbar spine by QCT and DXA in the PTH group at 24 months was +74% and +24.5%, respectively. Meanwhile, the placebo group had median changes of -3% (QCT) and +1.5% (DXA).

Conclusions
The 2D trabecular parameters shown above demonstrated highly significant changes from baseline in the PTH group, whereas none of the corresponding parameters changed significantly in the placebo group. The results indicate that hPTH (1-34) dramatically reduces trabecular fragmentation, while increasing the Trabecular Bone/Area Ratio, the Interconnectivity Index and the Trabecular Network Length. These changes are consistent with those shown in PTH treated subjects reported previously by others using 3D μCT in bone biopsies and provides strong evidence that noninvasive vertebral x-ray 2D image analysis can play a major role in the future, noninvasive, clinical evaluation of bone structure.