

## Dental X-rays Identify Women with Low Hip and Spine BMD

S. Liew<sup>1</sup>, D. Steines<sup>1</sup>, M. Jeffcoat<sup>2</sup>, G. Adams<sup>1</sup>, R. Vargas-Voracek<sup>1</sup>, P. Lang<sup>1</sup>, C. Arnaud<sup>1</sup>, P. Hess<sup>1</sup>

1. Imaging Therapeutics Inc., Foster City, CA, USA

2. University of Alabama, Birmingham, AL

### Introduction

It is estimated that less than 30% of postmenopausal women in the US with osteoporosis have been diagnosed. While numerous diagnostic technologies exist, the cost effectiveness in utilizing these techniques for mass screening is still debatable.

We have developed an automated computer based technique to estimate the relative bone mineral density of hip and spine using digitized, calibrated, periapical dental x-rays. Regular dental x-rays are taken with a phantom embedded in the film holder. Films are then developed and digitized using a desktop scanner (UMAX PowerLook 1100) at 1200 dpi. Figure 1 illustrates the process of the ImaTx Mandibular Bone Assessment. It measures the calibrated bone density as well as a number of parameters that characterize the mandibular trabecular pattern.

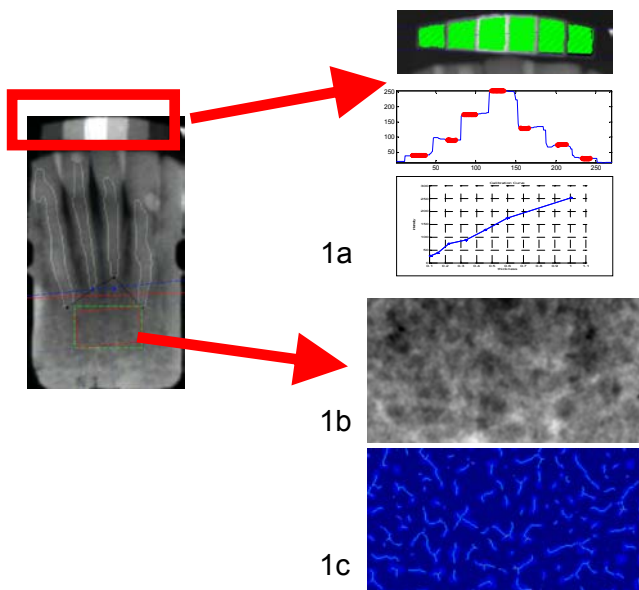


Figure 1a. The calibration phantom and region of interest is automatically recognized and evaluated on a digitized anterior mandibular x-ray. A calibration curve generated from the phantom is used to normalize the radiographic intensity in the region of interests.

Figure 1b (left). Calibrated intensity ROI provide BMD statistics (mean, median, std. dev, min, max).

Figure 1c (left). Extracted structure provides morphology information such as structure perimeter, length, thickness, number of nodes and segments. More specific BMD values are also derived by calculating density of extracted structures and background.

## Method

In a prospective optimization trial to develop this technology, hip and spine DXA BMD were measured in 48 postmenopausal women, and each had 2 periapical x-rays of the anterior mandible taken. The group had a mean spine BMD T-score of  $-1.4$  ( $sd=1.5$ ), mean hip BMD T-score of  $-1.8$  ( $sd=1.3$ ), mean age of  $60.5$  ( $sd=14.5$ ), and a mean BMI of  $23.9$  ( $sd=5.1$ ).

A multivariate stepwise linear regression algorithm (Matlab Statistics Toolbox, Mathworks, MA) was used to select a combination of mandibular measurements that correlates with hip and spine T-scores. Since the definition of osteoporosis is having either spine or hip BMD T-score of less than  $-2.5$ , the minimum of the hip and spine BMD T-score was used as the independent variable. The stepwise regression process selected three parameters. They are: standard deviation of ROI density, background density (BMD), and normalized structure perimeter. A composite parameter, Mandibular Index (MI) was formed using these three measurements.

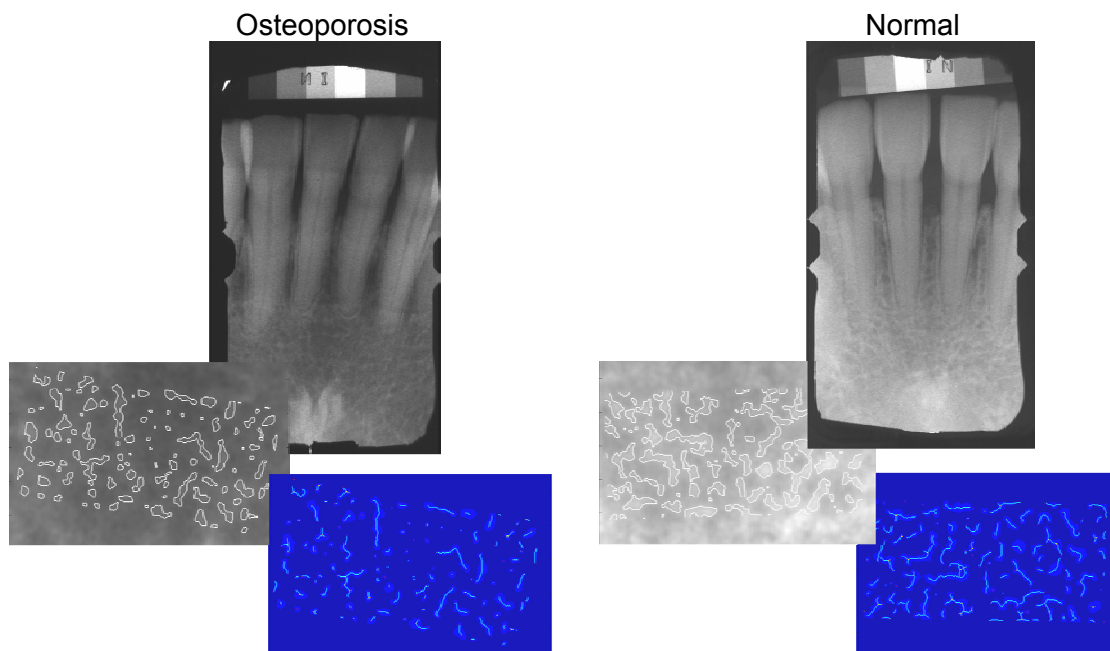


Figure 2. Examples of dental x-rays of osteoporotic (left) and normal (right) subjects. Both density and structural features differ between the two.

## Results

MI correlates with spine DXA BMD T-scores ( $r=0.66, p<0.001$ ). This correlation coincides with the correlation of spine BMD with hip BMD ( $r=0.66, p<0.001$ ) in this study. MI also correlated with hip BMD T-scores ( $r=0.57, p<0.001$ ). Correlating MI with the minimum of spine and hip BMD T-score provided  $r = 0.65$ . Charts below show these correlations.

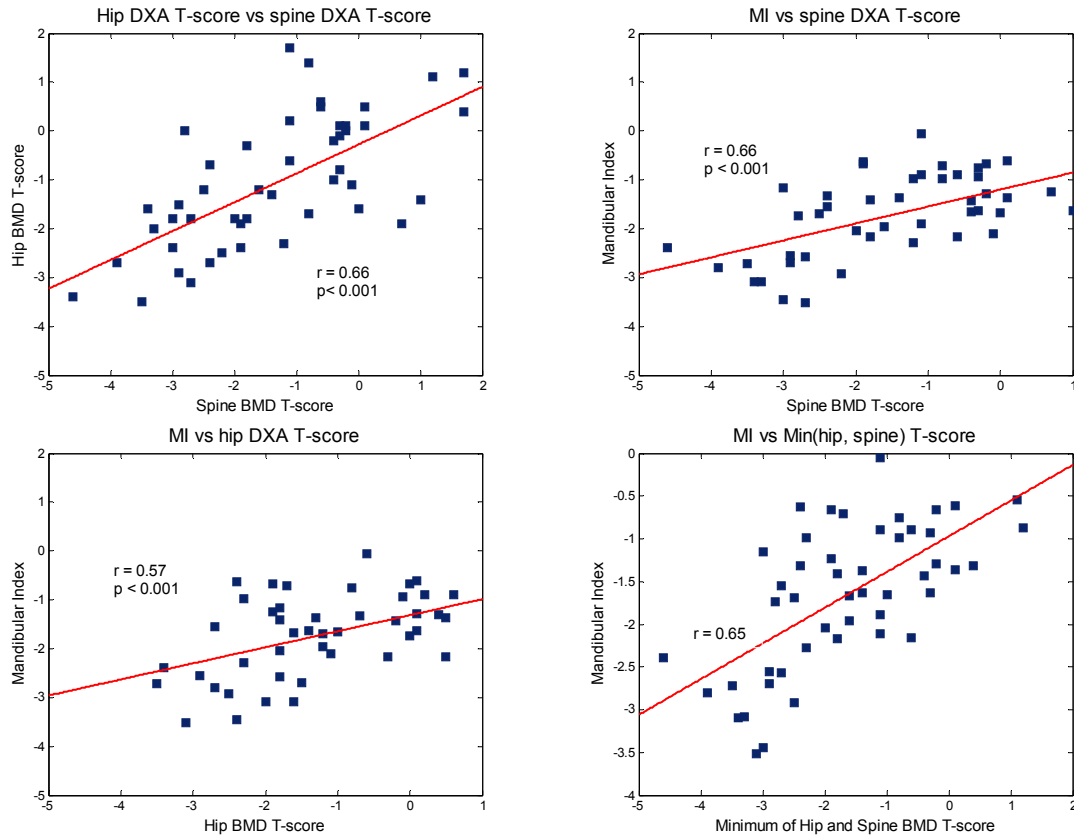


Figure 3. Correlations of MI with spine and hip DXA BMD.

We applied a leave-one-out cross validation process to identify patients with osteoporosis (hip or/and spine BMD T-score  $\leq -2.5$ ) using MI. As illustrated Fig. 4, ROC curves showed that the MI can provide sensitivity of 81% (95% CI 59-94%, AUC=0.88) with 80% specificity. Age and BMI given the same specificity provided a sensitivity of 39% (95% CI 14.5-69.2%, AUC=0.70). Age slightly improves identification of osteoporotic subjects when added to MI (AUC=0.90).

Identification of subjects with T-score cutoffs of less than or equal to -2, -1.5 and -1 achieved sensitivity levels of 74%, 64%, and 57% respectively, using MI, given an 80% specificity level.

Short-term reproducibility was gauged by correlating measurements obtained from the first x-ray to those from the second x-ray from 44 subjects. Mandibular BMD correlated at  $r = 0.84$  ( $p < 0.001$ ) while MI correlated at  $r = 0.79$  ( $p < 0.001$ ).

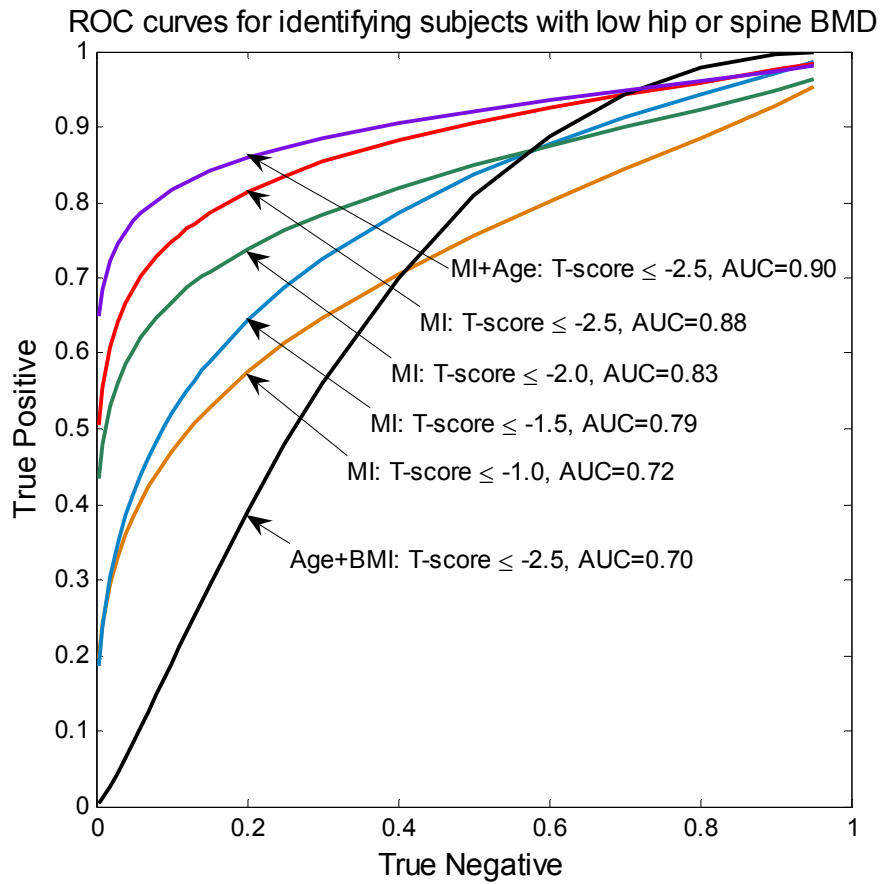


Figure 4. (above) ROC curves showing classification performance for identifying subjects that have low central DXA BMD T-scores. Label arrows are pointing at the various sensitivity levels at 80% specificity.

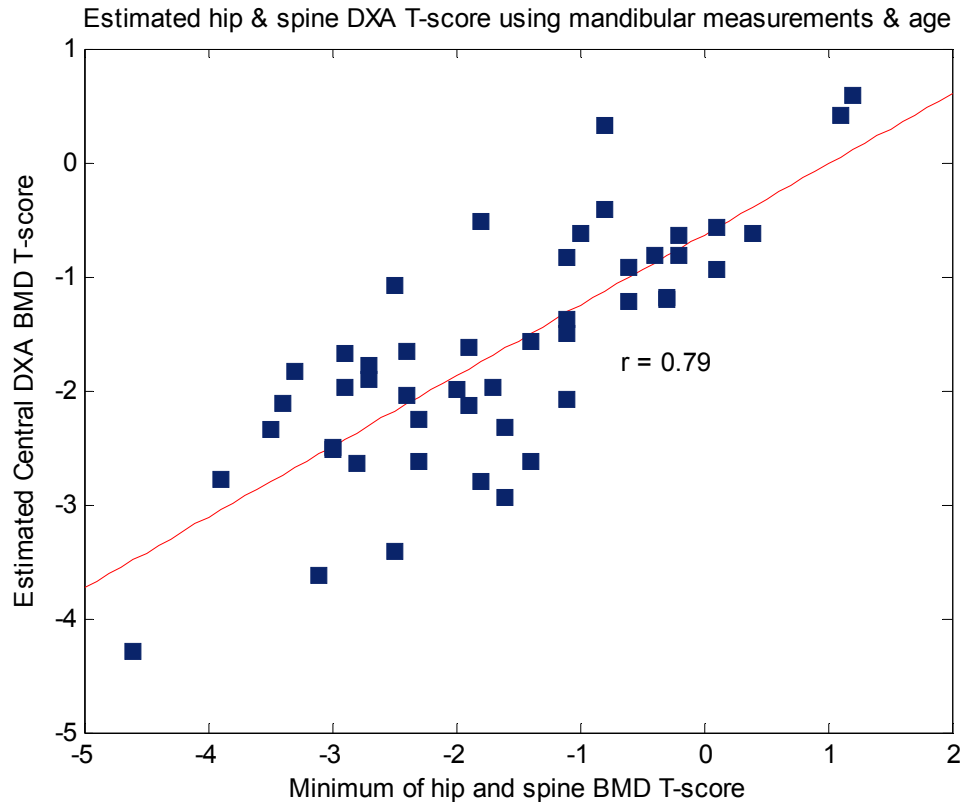


Figure 5. (below) Age combined with Mandibular Index improves estimation of hip and spine BMD T-scores.

### Discussion

The results, while preliminary because of the limited sample size and the unblinded optimization study design, provide clear evidence that systemic bone loss can be detected in the mandible by systematically harvesting biologically relevant features shown on dental x-rays. The mandibular BMD measured here, by excluding density of extracted structures in the calculation, may be reflective of primarily the cortical bone density. Separate measurements on trabecular features, weighted appropriately, are then combined to provide a more complete picture of bone health. This approach makes biological sense since trabecular bone loss rate may not necessarily coincide with cortical bone loss rate and may differ at various stages of osteoporosis.

### Conclusions

These results suggest that MI measurements correlate with hip and spine BMD to a similar degree as spine with hip BMD and can be more accurate than age and BMI in identifying women with osteoporosis. MI measurements do not require expensive capital equipment and can be employed during patient's routine dental exams to screen for osteoporosis. A prospective study is in progress to establish the population reference values and to further validate the technique.