The nanomechanical material properties of iliac crest biopsies from bisphosphonate-treated patients with severely suppressed bone turnover (SSBT) differ from normal and untreated osteoporotic subjects

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INTRODUCTION:

Bisphosphonates (BPs) are commonly prescribed drugs for the treatment of osteoporosis, a condition of increased fracture risk. BPs inhibit bone resorption, and decrease bone turnover and bone loss. Long-term use of BPs may be associated with changes in the mechanical integrity of the bones of some patients. Odvina et al (2005) were the first to report on a group of nine patients who suffered spontaneous non-vertebral fractures with delayed or absent fracture healing while on long term (3 to 8 years) alendronate, a commonly prescribed BP. The patients received alendronate alone or in combination with estrogen or prednisone, resulting in severely suppressed bone turnover (SSBT). Several cases and case series have since been published. We hypothesized that the compromised integrity of SSBT bone is associated with differences in the mechanical properties of the tissue from normal. In this study, we aimed to characterize and compare the micro-mechanical properties of iliac crest biopsies taken from SSBT patients, and three comparison groups: untreated osteoporotic fracture patients, age-matched and young normal subjects.

METHODS:

Fifty five iliac crest biopsies were analyzed for tissue-level elastic modulus (E) and hardness (H) using nanoindentation. All biopsies were from female patients or normal subjects with the exception of one male SSBT patient. Biopsies were from 12 SSBT patients (aged 49-77y), 11 age-matched osteoporotic patients with vertebral fracture (aged 53-76y), 12 age-matched normal subjects (aged 49-74y), and 20 young normal subjects (aged 20-40y). SSBT biopsies were from patients reported in two publications [1,2]. The three comparison groups (osteoporotic fracture patients, and the young and age-matched normal subjects) were not treated with BPs. Biopsies were prepared at Henry Ford Hospital (Detroit, MI) and Southwestern Medical Center (Dallas, TX), where they were embedded in poly methyl-methacrylate (PMMA) and analyzed for bone histomorphometry.

Nanoindentation is a method by which mechanical properties of a material are probed by monitoring the load and displacement of an indenter tip into a surface at high resolution. Thirty or more indents were made in both trabecular and cortical bone regions of each biopsy (Figure 1). Indents were made to 500 nm maximum depth. Modulus and hardness were calculated using the Oliver-Pharr method [3].

RESULTS:

One-way ANCOVA (Factor=Group, Covariate=PMMA modulus) of trabecular bone properties averaged by biopsy indicated that the groups had significantly different modulus and hardness (p=0.012, p=0.002, respectively). Takey post-hoc pair-wise analyses indicated that SSBT trabecular bone was harder than the three comparison groups, and SSBT bone was stiffer than that of young normals and age-matched osteoporotics (Figure 2). Cortical bone properties did not differ among the groups for either elastic modulus or hardness. PMMA modulus was included as a covariate in the ANOVA analyses because the biopsies were prepared in two laboratories using different embedding protocols, yielding stiffer plastic properties in Detroit samples compared to Dallas samples.

DISCUSSION:

The analysis of micro-mechanical properties of iliac crest bone tissue indicated that mechanical properties of SSBT trabecular bone are different from that of untreated osteoporotics and normal controls. Notably, the differences were detected only in the trabecular bone. Specifically, the SSBT trabecular bone is harder and stiffer than the trabecular bone of three comparison groups, and stiffer than the bone of young normal subjects and age-matched osteoporotics with vertebral fracture.

However the magnitudes of the differences are rather small in relation to the wide ranging clinical presentations and fractures among SSBT, old and young normal subjects, and osteoporotic fracture patients. SSBT bone modulus was 7.0% and 7.7% greater than that of osteoporotic patients and young normal subjects, respectively. Hardness of SSBT bone was 13.8% to 17.8% greater than the three control groups. We suggest that the tissue-level mechanical properties are unlikely to be the sole cause for the unusual fractures in SSBT, and hence other aspects of bone quality must be considered to explain the differences in fracture patterns among the groups analyzed.

Despite our demonstration that SSBT patients have distinct iliac crest trabecular bone material properties, the data presented here do not establish a causal connection between the use of bisphosphonate, the differences in material properties and the SSBT condition.

Low bone turnover is associated with a larger proportion of aged bone tissue of high mineral content, than the bone tissue remodeling at a normal rate. We conclude that trabecular bone material properties are different among SSBT, untreated osteoporotics, and young and older normal subjects. The primary conclusion is that trabecular bone tissue from patients with SSBT has high modulus and hardness due to aging of the bone tissue from reduced bone turnover.

ACKNOWLEDGMENTS:

National Institutes of Health grant: AR040776 (DPF).

REFERENCES: