

Intermittent PTH Treatment Increases Intracortical Microporosities in Ovariectomized Rats

Steven M. Tommasini¹, Andrea Trinward¹, Alvin Acerbo^{1,2}, Lisa M Miller², Stefan Judex¹

¹*Biomedical Engineering, Stony Brook University, Stony Brook, NY, USA* ²*National Synchrotron Light Source, Brookhaven National Laboratory, Upton, NY, USA*

Some pharmaceutical treatments for osteoporosis have the potential to deteriorate mechanical properties of the skeleton by altering specific aspects of bone's tissue quality. Whether cortical tissue quality is modulated by intermittent treatment of PTH is largely unknown. Here, we hypothesized that PTH treatment alters bone quality, specifically intracortical porosity, which has been linked to the stiffness and strength of cortical bone. Using an OVX rat model, we combined conventional desktop μ CT with synchrotron radiation-based nanoCT to quantify changes in macro and microscopic bone structural properties. The improvement in spatial resolution from synchrotron light allows imaging of bone porosities and vascular channels that, at least in bones from small animals, go undetected with conventional μ CT.

Six-month old female Sprague Dawley rats were assigned to either: baseline controls, age-matched control, untreated OVX, or OVX treated with 15 μ g/kg/d hPTH(1-34). Rats in the OVX groups were ovariectomized 4wk prior to starting the experimental protocol. Treatment duration was 6mo and all rats were sacrificed at 12mo of age (n=5/group). Changes in abdominal fat volume were determined by *in vivo* μ CT. Femoral diaphyseal cortical geometry and tissue mineral density (TMD) were determined via desktop μ CT (36 μ m resolution). The porosity of the medial quadrant of the diaphysis was assessed using synchrotron nanoCT (0.98 μ m resolution).

There were no significant differences in any of the cortical geometrical or compositional parameters among groups. Even though no differences in overall porosity were detected, prolonged PTH treatment maintained a greater number of small (<25 μ m²) and large (>50 μ m²) pores/area compared to OVX and controls (p<0.05). Correlations between porosity and bone composition revealed that TMD was inversely related to the number of pores/area (r=-0.83). PTH-treated rats also had significantly lower fat volume/body weight (BW) compared to age-matched controls and OVX (p<0.01).

Together, these data suggest that prolonged PTH treatment alters aspects of bone quality not detected by conventional μ CT. The higher number of larger pores in PTH rats may be the result of intracortical remodeling events, explaining the inverse relationship observed between the number of pores and TMD. Fewer remodeling sites are associated with higher TMD because the level of mineralization increases with tissue age. The mechanical consequences of the greater number of small pores are yet to be established, but do not necessarily have a negative impact on bone's ability to resist load. For instance, very small pores have the potential to delay crack propagation by absorbing shear forces. The origin of these small pores is currently unclear, but would be consistent with an increase in osteocytic osteolysis previously reported with continuous PTH treatment. Also, the lower fat/BW ratio in PTH-treated rats suggests the greater number of small pores may be related to changes in metabolic rate, which has been correlated with osteocyte density. However, further study is needed. Therefore, a combination of assays including measures of energy expenditure (RT-PCR), new bone formation (SEM), and microscopic compositional changes (FTIRI), are currently being correlated with bone mechanical properties (nanoindentation) to better understand how different osteoporosis treatments alter bone quality and thus bone strength.