The Effects of Polyethylene Particles at a Weight-Bearing Rat Tibia Bone-Implant Interface

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Introduction:
Osteolysis leading to aseptic loosening is problematic for many patients who have undergone total joint arthroplasty. A better understanding of the pathogenesis of this phenomenon, in particular the effects of polyethylene microparticles on bone and tissue, is necessary in order to limit osteolysis and develop treatments. Rat pin models have been widely used for the investigation of periprosthetic osteolysis because of the similarity to the human immune system, the resemblance to human aseptic loosening, and the relative ease of implanting a “prosthesis” into the rodent tibia. The purpose of our study was to evaluate the in vivo effects of polyethylene particles on bone using mechanics and micro computed tomography (μ-CT) in rats implanted with tibial pins.

Methods:
After obtaining approval from our institution’s Animal Care Committee, titanium pins were surgically implanted in the tibia of 9 week old female Sprague Dawley rats with either 0.03 ml solution of 1% normal rat serum in phosphate buffered saline (NRS/PBS) or in the same solution containing ultra-high molecular weight polyethylene (PE) wear particles at a concentration of 5 mg/ml. Pin placement and bone regeneration were measured by assessing the trabecular bone structure surrounding the titanium pin two days and 60 days after surgery using a μ-CT (vivaCT 40, Scanco Medical, Bassersdorf, Switzerland). 3-D analyses of the μ-CT image data were performed to calculate percent bone volume/total volume ratio (BV/TV), and trabecular number, separation, and thickness. To maintain simulation of wear-debris, intra-articular injections of control or PE solutions were performed at 2 week intervals. Rats were sacrificed at 60 days and tibias removed. The distal end of the tibia was potted in a custom fixation device. The pin was pulled in line with the tibia using a materials testing machine (Instron, Norwood, MA). Statistical analysis was performed by the Student’s t test. A p value of less than 0.05 was considered significant.

Results:
As shown in Figure 1A-C, when comparing baseline to day 60, the rats injected with PE had a statistically significant increase in trabecular separation, a decrease in trabecular number, and an increase in trabecular thickness; no significant difference was observed in BV/TV (Figure 1D). In rats with NRS injection, no significant difference was seen in trabecular separation, trabecular number, trabecular thickness or BV/TV, as compared to their baseline (Figure 1). When comparing the PE injected rats with those injected with NRS at day 60, the PE injected rats had a reduced BV/TV, decreased amount of trabecular bone, thinner trabecular bone, and increased trabecular space; however, these differences were not statistically significant (Figure 1). Regarding pull out testing, no statistically significant difference was detected between the two groups; nevertheless it took more force on average to remove the pins implanted in the NRS rats (PE rats 13.33N and NRS rats 19.95N).

Discussion:
Three statistically significant differences were observed in this study, two of which (an increase in trabecular separation and decrease in the number of trabecular bone in PE injected rats) indicated that the PE exposure appeared to decrease bone formation. This finding was also observed when comparing PE and NRS injected rats. Although not statistically significant, a trend was seen in other markers for decreased bone formation (reduced BV/TV, trabecular number, trabecular thickness, and increased trabecular space in the PE group). It was consistent that the pull out strength decreased with the negative changes in the bone. This combination of μ-CT characterization and biomechanics may be used in the future alone or in combination with biomolecular evaluation to assess effects of other particulate or treatment measures for osteolysis. Finally, this rat model of weight-bearing tibia implantation provides a tool to study the effects of PE wear debris on bone. Our data (trabecular space in the PE rats) had a negative effect on bone formation and mechanical stability, based on both quantitative μ-CT and biomechanical pull out testing. The establishment of these quantitative outcome measurements is critical for the evaluation of drug efficacy of implant wear-induced osteolysis using this rat model.

Summary of results. Statistical significance assessed by the Student’s t test.

Significance:
Our data showed the quantitative outcome measures of PE particle-induced osteolysis, which is reproducible and validated. This knowledge is essential for the future pharmaceutical investigation using this rat pin implantation model.