Rat Root Apical Bone Resorption Model: A New Aseptic Loosening Model

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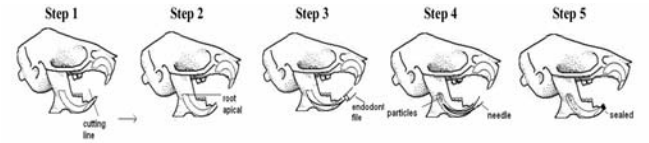
Introduction: We have developed a mouse osteolysis model[1] to evaluate ultra high molecular weight polyethylene (UHMWPE) particles-induced inflammatory osteolysis under controlled experimental condition. However, a noticeable limitation of this model is the lack of blood supply to the implanted bone. The purpose of this study is to develop a rat root apical bone resorption model that provides a more clinical relevant approach to investigate the pathogenesis of aseptic loosening.

Methods (Figure 1) Female Sprague Dawley rats were anesthetized before surgery. We exposed the lower incisor cavity by removing 3-5 mm of lower incisor crown using a dental electrical hand drill. Then we extracted pulp tissue until the root apical region could be reached easily. After cleaning the root canal by 3% H_2O_2, we injected 20 μl of either saline (left incisor) or UHMWPE particles (5 mg/ml) (right incisor) into the root apical region through the root canal cavity. After injection, the incisor cavities were sealed with filling material (glass ionomer cement). Four rats were used in this study. Rats were sacrificed two months after surgery. The mandibles (root apical portion) were collected for histology and microCT (μCT) analysis.

Figure 1. Diagram of surgery



Results: Our pilot study has shown the feasibility and reproducibility of UHMWPE particle delivery into rat lower incisor root apical region through the root canal. As shown in Figure 2, H&E stain revealed that UHMWPE induces significant inflammatory granuloma change in root apical region, associated with alveolar bone resorption, as compared with the same region with saline injection. Osteoclast- like cells, as measured by TRAP staining, were significantly increased in response to UHMWPE stimulation. The $TRAP^+$ cells were mainly located at the outer edge of the alveolar bone, and on the invasion front of granuloma tissue, where active osteolysis occurred. Van Gilson stain was performed to quantify bone matrix collagen contents. UHMWPE stimulation dramatically increased the loss of bone collagen content, in comparison with the bone collagen changes in sections of saline control. UHMWPE- induced bone resorption was further confirmed by μCT analysis. Representative 3D reconstructions of μCT image demonstrated differences in the microarchitectures of alveolar bone between rats with (right) and without (left) UHMWPE stimulation. UHMWPE stimulation resulted in weak and fuzzy surfaces with different intensities at root apical region, suggesting active bone resorption.

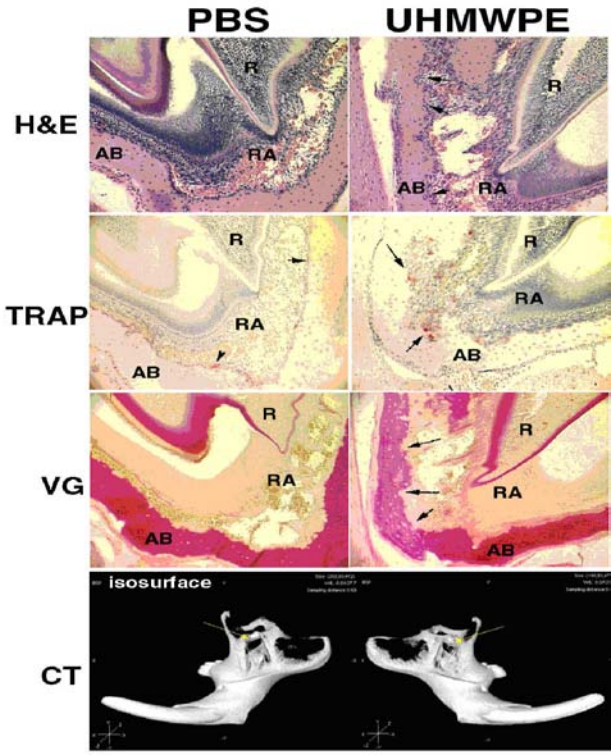


Figure 2. Histology and μCT analysis of UHMWPE–stimulated tissue inflammation, osteoclastogenesis, and bone resorption
Represent data from four rats. (A) *Histology. R,* Root; *RA*, Root apical region; *AB*, Alveolar bone (x100). H&E stain showed the general histology and inflammation change. TRAP stain was used to localize the osteoclast-like cells in the root apical tissue. The presence of red staining granules in the cytoplasm was determined as the criterion for $TRAP^+$ cells. Van Gilson stain was used to determine bone collagen content. Fixed mandible (root apical portion) samples were analyzed by using RS-9 small animal μCT Scanner (Enhanced Vision Systems, London, ON, Canada). For each sample approximately 399 micro-topographic slices with an increment of 25 μm was acquired. The scanned 3D volume was first analyzed and segmented using our developed software to highlight the root apical portion. Then we employed our texture-based volume rendering technique to directly display the segmented 3D volume data. The weak and fuzzy surfaces with different intensities can be rendered simultaneously. Reconstructed μCT images showed the difference in root apical region between the rat without (*left, arrow*) and with UHMWPE stimulation (*right, arrow*).

Discussion & Conclusions:

A novel rat root apical bone resorption model, as described here, offers a high fidelity model for the pathogenesis study of aseptic loosening, with several distinct advantages over current models, including an active blood supply, and ease and adaptability to experimental manipulation.

References:

1) Ren WP, et al. A novel murine model of orthopedic wear debris- associated osteolysis. Scand. J. Rheumatology 33:1-10, 2004