INTRODUCTION
We recently established a mouse osteolysis model to investigate implant wear induced inflammatory bone resorption (Ren et al., Scand. J. Rheum. 33:1-10, 2004). Histology analysis demonstrated that implant wear induce bone resorption in two patterns: limited bone erosion and extensive bone collagen depletion. The main limitation of the mouse model is its small size, and the necessity for laborious histology analyses to quantify implanted bone destruction. The purpose of this study is to determine the value of using high-resolution micro-computed tomography (μCT) technique to measure implanted bone destruction.

MATERIALS AND METHODS
Mice were assigned to two groups with 10 animals in each group. Air pouches were developed on BALB/c mice, followed by introduction of 0.5mg of UHMWPE debris suspended in saline. Two days later, a section of calvaria from a syngeneic mouse was inserted into the pouch. Mice injected with saline alone (no particles) were included as controls. Tissues were harvested four weeks after bone implantation. Paraffin tissue sections were prepared for histology analysis. Localized bone erosion was observed by Hematoxylin & Eosin (H&E) stain, and bone collagen content was analyzed by Van Gieson staining. Digital images were analyzed by a computed image analysis system. μCT images were captured using RS-9 In Vivo MicroCT Scanner (General Electric Systems, London, Ontario). Mice were scanned on the day (zero time), two weeks, and four weeks after bone implantation. The scan was done at a resolution of 0.093 mm (cubic voxel length) using manufacturer’s presetting. After data acquisition, two-dimensional projection data was re-constructed into a three-dimensional volume. The three-dimensional volumes were then reoriented in three dimensions to put all of the data sets into the same orientation for image analysis. Image data analysis was performed using Micro View (GE medical Systems, London, Ontario) software.

RESULTS
Limited bone erosions were found at areas in close contact with the UHMWPE particle-stimulated inflammatory membranes, with the invasion front formed by macrophage/osteoclasts. In contrast, implanted bone surface was remained histological normal in saline controls. (Figure 1) Van Gieson staining revealed a reduction of red staining (bone collagen content) at bone surfaces in contact with inflammatory pouch membranes. Whereas UHMWPE particle stimulated pouches showed dramatic bone collagen depletion at the bone surface compared with the center of the section, saline controls demonstrated a marked preservation of bone collagen content. (Figure 2) Quantitative measurements of bone collagen content using a computerized image analysis software revealed that saline control mice has much lower bone collagen depletion (16.6% collagen loss), in comparison with similar regions in UHMWPE particles stimulated mice (36.6% collagen loss, p<0.05). Similar to the histological findings, μCT imaging analysis of implanted bones showed a time-dependent significant alteration of plateau surface contour in pouches with UHMWPE particle stimulation, suggesting the progressive implanted bone degradation. (Figure 3) Bone mineral density (BMD) of implanted bone was found to decrease in UHMWPE particles challenged mice, as compared with saline control.

DISCUSSION
In the present study, we compared the utility of μCT with that of histology, the current “gold standard” for quantifying implanted bone degradation in this mouse model. A correlation between these methods was demonstrated. Furthermore, μCT technique allows us to obtain 3-D images of implanted bones. These images can be rotated, scaled, and sliced in various orientations interactively using MicroView software. This allows investigators the ability to identify the shape, volume, and mineral density of implanted bones. Further experiments are currently under investigation in our laboratory to verify whether in vivo μCT imaging represents a reproducible, sensitive, and rapid tool to quantify implanted bone destruction in this mouse osteolysis model.

Fig. 1 UHMWPE induced bone erosion (H&E stain, x 200)

Fig. 2 UHMWPE reduced bone collagen content
(Van Gieson stain, x 200 magnification)

Fig. 3 Comparison of 3-D morphology of implanted calvaria

(A) PBS (B) UHMWPE

Zero time

2 weeks

4 weeks