INTRODUCTION
Walking biomechanics play an important role in the progression of knee osteoarthritis (OA) (Andriacchi, 2004). There remains a lack of understanding of the influence of walking mechanics on the interaction between subchondral bone and cartilage changes in osteoarthritic joints. However, this information is important since OA affects not only articular cartilage but also subchondral and trabecular bone (Lavigne, 2005). Positron Emission Tomography (PET) offers a unique opportunity to examine the metabolic activity of subchondral bone in patients with OA. Recently, $^{18}$F-fluoride PET was used to measure the skeletal response to damaging fatigue in rat ulna (Silva, 2006) and an association between the level of loading and $^{18}$F-fluoride accumulation in the damaged ulna was found.

The objective of this study was to measure the metabolic activity in bone from OA knees using $^{18}$F-fluoride and to test the hypothesis that the joint loading by walking can alter the bone metabolic activity differently between healthy and OA knees.

METHODS
Three healthy subjects (age 57±5, BMI 25.3 ±4.0, 1 female and 2 males) without history of knee injury and two bilateral medial knee OA subjects (age 60±6, BMI 29.5±0.0, 2 males) were recruited for the study. Each knee (n=10) was treated as an independent sample. The study was approved by the IRB and an informed consent was obtained from each subject prior to testing. Each subject underwent PET/CT tests on 2 consecutive days. Subjects were advised to avoid any exercise and walking before the PET/CT scans and maintain the same activity levels between the two days. On day 1, each subject rested on a chair to unload the knee for at least 30 minutes, and then received about 15 mCi of $^{18}$F-fluoride intravenously. The subject rested for an additional 60 minutes and then underwent PET/CT scan. On day 2, each subject rested for 10 minutes and then walked for 20 minutes at a normal walking speed prior to the $^{18}$F-fluoride injection. The rest of the procedure was the same as day 1.

Figure 1. (a) PET and (b) CT images in the transverse plane of the knee at femoral epicondyle level

The PET and CT data were loaded into OsiriX software (Rosset, 2004) and mean and peak values of PET standardized uptake value (SUV) were measured from five regions (three-dimensional box shape region of interest), medial and lateral femur (MF &
LF), medial and lateral tibia (MT & LT) and patella (Pat), for each knee. For each region, the mean and peak values were compared between healthy (n=6) and OA (n=4) knees with Student’s t-test at a significance level of alpha=0.05.

RESULTS
The day 1 (baseline) results showed higher metabolic activity in OA knees compared to healthy knees with the peak values significantly different in the medial femur (p<0.01) and medial tibia (p=0.02) (Fig. 2a).

![Figure 2](image)

**Figure 2.** Peak and mean SUVs for five regions in the knee on day 1

Following the 20 minutes walking exercise the bone metabolic activity at the knee increased for both the healthy and OA knees. However the increase of mean SUVs in the medial tibia (p=0.02) and lateral tibia (p<0.01) was greater for healthy knees (Fig. 3).

![Figure 3](image)

**Figure 3.** Change of peak and mean SUVs between day 1 and day 2

DISCUSSION
The finding that metabolic activity in bone of the OA knees responded with a lower increase than healthy knees following twenty minutes of walking suggest the potential for reduced sensitivity of subchondral bone to functional loading during walking in patients with knee OA. This different response to loading in OA knees could be due to the fact that the metabolic activity is already high in these knees. The higher metabolic activity in OA knees on day 1 (resting) is consistent with clinical observations of hot spots in OA knees with bone scan (Schauwecker, 2003). While the altered bone cell metabolism with OA has been investigated (Westacott, 1997), the response of the bone cells in OA joints to loading has not been understood.

A previous study using $^{18}$F-FDG could not find significant uptake in cartilage (Nakamura, 2007) which could be due to the low metabolic activity of cartilage. Bone has much higher metabolic activity than cartilage, which could be visualized in this study.

CONCLUSIONS
The differential bone metabolic response to loading in knee OA relative to healthy knees suggests the possibility for using this technique for evaluating the role of bone changes in the progression of OA.

REFERENCES


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