INTRODUCTION
Medial compartment knee osteoarthritis (OA) affects a substantial portion of the population (estimated 20-40%) over the age of 65 [1]. Yet the primary treatment for OA addresses the symptoms rather than the disease. Disease modifying interventions for OA have been limited since the appearance of clinical symptoms (pain and radiographic) often occur too late in the disease process. Given that pain is often the first reported clinical symptom of OA and the “wear and tear” nature of the disease, an examination of pain associated with regional patterns of cartilage thinning in the context of walking mechanics offers the opportunity to gain new insight into the degenerative pathway of the disease.

The purpose of this study was to examine patterns of cartilage thinning in patients with varying grades of medial compartment knee OA in regions that are frequently loaded during walking and to determine whether pain, stiffness, and limited function correlate with regional patterns of thinning. Specifically, the following hypotheses were tested: (1) patients with more severe medial compartment knee osteoarthritis will have thinner cartilage in medial compartment weight bearing regions during walking (anterior-middle femur and anterior tibia) compared to less severe patients and control subjects, and (2) the clinical score will correlate with regional patterns of thinning.

METHODS
21 patients (10 male, 11 female; age: 60.4 ± 9.9 yrs; height: 1.69 ± 0.07 m; mass: 74.7 ± 13.3 kg) with less severe medial compartment osteoarthritis (Kellgren Lawrence, KL; grade of 1 or 2); 13 patients (8 male, 5 female; age: 59.3 ± 8.3 yrs; height: 1.71 ± 0.09 m; mass: 85.1 ± 13.5 kg) with more severe medial compartment osteoarthritis (KL grade of 3 or 4); and 16 healthy individuals (7 male, 9 female; age: 59.2 ± 6.4 yrs; height: 1.72 ± 0.11 m; mass: 73.9 ± 15.6 kg) participated after giving written consent in accordance with the Institutional Review Board. Subjects with plain radiographic evidence of lateral compartment osteoarthritis were excluded. If patients with OA were affected bilaterally, their more severely affected side was used for analysis.

Three dimensional cartilage thickness maps were created using a previously described method [2] to measure the average thickness of the medial femoral and tibial cartilages from magnetic resonance (MR). MR images were acquired using a 3D spoiled gradient-echo sequence in the sagittal plane with fat-saturated, TR=60 ms, TE=5 ms, flip angle=40°. matrix 256x256, rectangular FOV 14x14 cm, slice thickness 1.5 mm, 60 slices. Load bearing regions during walking on the medial femoral condyle (Figure 1) and medial tibial plateau were defined based on the regions that would be in contact during the stance phase of walking (extension to 30 degrees flexion) [3].

Figure 1: Definition of the weight-bearing regions of the femoral cartilage.

Average regional thicknesses were normalized to subject height. Multivariate analysis of variance (MANOVA; α = 0.05) was used to detect differences in normalized cartilage thickness values of the femoral and tibial load-bearing regions between healthy control subjects, less severe patients, and more severe patients. Upon significant result of the MANOVA, Bonferroni adjusted t-tests were used for post hoc analyses (α = 0.01). The second hypothesis was tested using a subset of OA patients (N=21; 12 male, 9 female; age: 57.0 ± 9.1 yrs; height: 1.70 ± 0.08 m; mass: 79.7 ± 15.0 kg) that completed WOMAC functional improvement-based ratings [4] to assess pain and function. Linear regression analysis (α=0.05) was used to test the correlation between normalized regions of cartilage thickness and total WOMAC score.

RESULTS
Patients with more severe medial compartment OA had thinner cartilage in the anterior femoral condyle (35.6% reduction, P=0.003 and 35.3% reduction, P=0.003) and middle femoral condyle (24.7% reduction, P=0.004 and 29.7% reduction, P<0.001) compared to controls and less severe patients, respectively. No differences in normalized cartilage thickness were seen for the tibial regions between groups. No differences in age, height, or weight were found between the groups. Patients with a higher total WOMAC score, indicating more pain and disability, had thinner cartilage in the anterior region of the medial femoral condyle where a significant correlation (R²=0.39, P=0.003) was found between the thickness in this region and total WOMAC score (Figure 2). No other medial load bearing region (femur or tibia) was correlated with WOMAC score.

Figure 2: Correlation between normalized medial femoral anterior cartilage thickness and total WOMAC score.

DISCUSSION
The results of this study support the conclusion that cartilage thinning occurs in the regions that sustain load during walking. The region specific thinning suggests that both the loading and the number of repetitive cycles of load that occur in a local region of the cartilage during walking should be considered for understanding both the cause and treatment of osteoarthritis [3]. The results of this study that suggest disease progression in medial compartment knee OA starts on the femoral side of the joint agree with recent studies finding more rapid femoral cartilage thinning in OA progression [5,6]. The finding that increased pain and reduced function were associated with localized thinning in the anterior region of the medial femoral condyle is important in understanding the degenerative pathway of OA. For example, imaging methods such as MRI that can focus on the anterior region of the medial femoral condyle may provide a more sensitive method in detecting the disease at an early stage than is possible with traditional frontal plane radiographs. In addition, the often confounding findings between reports of pain and radiographic appearance of the disease might be related to the fact that pain is sensitive to localized regional thinning rather than the more global changes that can be measured from radiographs. Further these results suggest other conditions such as bone marrow edema that have been associated with pain in knee OA should be examined on a regional basis.

In summary, the results of this study support the conclusion that the local regions of the knee loaded during walking are important for understanding the degenerative process of the disease. Further, the finding that cartilage loss occurs earlier on the femur and is correlated with clinical findings indicates the potential for MR imaging to be important for revealing region specific thickness changes and their relation to clinical disease state in knee osteoarthritis.

REFERENCES

ACKNOWLEDGEMENTS
This study was supported by VA grants # A02-2577R and A04-3583R.