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Statistical shape modeling describes variation in tibia and femur surface geometry between Control and Incidence groups from the Osteoarthritis Initiative database

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Abstract

We hypothesize that variability in knee subchondral bone surface geometry will differentiate between patients at risk and those not at risk for developing osteoarthritis (OA) and suggest that statistical shape modeling (SSM) methods form the basis for developing a diagnostic tool for predicting the onset of OA. Using a subset of clinical knee MRI data from the osteoarthritis initiative (OAI), the objectives of this study were to (1) utilize SSM to compactly and efficiently describe variability in knee subchondral bone surface geometry and (2) determine the efficacy of SSM and rigid body transformations to distinguish between patients who are not expected to develop osteoarthritis (*i.e.* Control group) and those with clinical risk factors for OA (*i.e.* Incidence group). Quantitative differences in femur and tibia surface geometry were demonstrated between groups, although differences in knee joint alignment measures were not statistically significant, suggesting that variability in individual bone geometry may play a greater role in determining joint space geometry and mechanics. SSM provides a means of explicitly describing complete articular surface geometry and allows the complex spatial variation in joint surface geometry and joint congruence between healthy subjects and those with clinical risk of developing or existing signs of OA to be statistically demonstrated.

Keywords

Osteoarthritis; Knee; Geometry; Alignment; Statistical shape modeling

1. Introduction

Osteoarthritis (OA) is the most common form of arthritis and is a tremendous public health concern. More than half of the approximately 41 million people in the United States aged 65 and older have radiological evidence of OA in at least one joint and almost all persons over the age of 80 are expected to demonstrate OA symptoms (Bagge et al., 1992; United Nations, 2009; Van Saase et al., 1989). OA causes joint pain, swelling, and reduced motion due to degradation of the articular cartilage covering the joint surfaces (Kuettner and Goldberg, 1995).

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Conflict of interest statement

The authors do not have any potential conflicts of interest to disclose.

Current pharmacological treatments target symptoms but not the cause of OA; there does not appear to be clear evidence that current treatments inhibit the degenerative changes to joint structure (cartilage and bone) responsible for disease progression (Courtney and Doherty, 2006; Felson et al., 2000b). Furthermore, understanding disease etiology and clinical testing of new therapies is complicated by the highly variable path of OA progression in individual patients and the multitude of clinical risk factors (Pelletier et al., 2007).

It is widely believed that OA results from the local mechanical environment of the joint in general, and in the cartilage in particular, in combination with systemic susceptibility to the disease (Andriacchi et al., 2009; Felson et al., 2000b). Three dominant risk factors for early onset development of knee OA are mechanical insult to the joint, ligament damage, and obesity, all of which alter the mechanical environment of the knee joint, and it is thought that this alteration in joint mechanics is in part responsible for the accelerated degradation of cartilage (Felson et al., 2000a). However, many individuals without risk factors will develop OA later in life (Mow and Ratcliffe, 1997), leading to the hypothesis that slight differences in joint mechanics, driven by variability in joint anatomy, along with biological predisposition, is responsible for OA onset and progression (Felson et al., 2000a).

Several studies have investigated the role of femoral condyle or tibial plateau geometry in order to understand whether and how bone geometry is related to the risk and progression of OA in the knee. Previous efforts have utilized discrete, low fidelity measures such as bone volume, surface area, two-dimensional distal femur shape, condylar radius of curvature, principal surface curvature, or measures of joint malalignment or incongruity (Biscevic et al., 2005; Hashemi et al., 2008; Hohe et al., 2002; Matsuda et al., 2004; Shepstone et al., 1999; Teichtahl et al., 2007). However, discrete measures of articular surface or joint space geometry are unable to describe the complex three-dimensional articular geometry and joint congruence that directly affects knee joint mechanics.

Conversely, statistical shape modeling (SSM) is capable of describing the complex geometry three-dimensional structures. SSM has previously been applied to image processing tasks such as image segmentation, registration, object recognition, and diagnosis (Babalola et al., 2006; Benameur et al., 2005; Dornaika and Ahlberg, 2006; Ferrarini et al., 2006; Koikkalainen et al., 2007; Rueckert et al., 2003; Shan et al., 2006), and more recently extended and applied to investigating skeletal fracture risk (Bredbenner and Nicoletta, 2007a, 2007b, 2008). SSM reduces the shape dimensionality of the object of interest from a large set of highly correlated variables (typically a set of surface vertices) to a compact set of independent and uncorrelated variables. SSM provides a parametric framework for representing variability in a large number of individual complex anatomical shapes instances within a specific population or subpopulation (Lorenz and Krahnstover, 2000).

Based on evidence that bony changes in osteoarthritic joints precede changes in articular cartilage by months or years (Hutton et al., 1986), we hypothesize that variability in knee subchondral bone surface geometry will differentiate between patients at risk and those not at risk for developing OA. Furthermore, we propose that SSM methods will form the basis of a predictive method for determining the risk of developing OA with greater sensitivity and specificity than current predictive approaches based on discrete measures of joint or joint component geometry.

Using a subset of clinical knee magnetic resonance imaging (MRI) data from the Osteoarthritis Initiative (OAI) database (publicly available at <http://www.oai.ucsf.edu/>), the objectives of this study were to (1) utilize SSM to compactly and efficiently describe variability in knee articular surface geometry and (2) determine the efficacy of SSM and

rigid body transformations to distinguish between patients who are not expected to develop OA and those who have clinical risk factors for OA.

2. Methods

Twelve age and body mass index (BMI) matched female participants aged 55–69 were randomly selected from both the Control and Incidence (e.g. at risk) groups of the OAI database (mean age: 62.4 years; mean BMI: 22.8). During MRI scanning, each of the 24 participants was positioned with the study leg in a relaxed, neutral position with the foot vertical and sandbags were used to retain positioning (Osteoarthritis Initiative, 2006). Clinical MRI data (sagittal 3D Double Echo Steady State (DESS)) was obtained for the right knee of each of the 24 subjects at study baseline using a Siemens Trio 3.0 Tesla MRI scanner and reformatted to generate axial slice data sets ($0.365 \times 0.365 \times 1.5 \text{ mm}^3$) (Osteoarthritis Initiative, 2006). Each data set was filtered using a noise reduction median filter and semi-automatically segmented to separate the distal femur and the proximal tibia from cartilage and surrounding soft tissue and to generate triangulated surfaces describing the outer bone boundaries of each individual femur and tibia (Amira 4.1.2, Visage Imaging, Inc., Andover, MA). All surfaces were smoothed using a Laplacian smoothing filter (MeshLab 1.2.2, <http://meshlab.sourceforge.net>).

Tibia surfaces were transected at a level proportionate to the vertical distance from the proximal-most aspect of the intercondylar eminence to the superior-most aspect of the medial rim of the tibial plateau using custom code developed in MATLAB (MATLAB R2008b, The Mathworks, Inc., Natick, MA) (Fig. 1). Similarly, femur surfaces were transected at a level proportionate to the vertical distance from the proximal-most aspect of the lateral epicondyle to the distal-most aspect of the femoral condyles (Fig. 2). Transected tibia and femur surfaces were closed and decimated to generate proportionally sized bone surfaces based on individual subject knee anatomy. A new set of vertices was mapped on to each bone surface and repositioned such that all tibia and femur surfaces were described using 4102 vertices and all vertices were positioned at corresponding anatomical locations between surfaces for like bones (Heimann et al., 2006).

Differences in average femoral and tibial bone geometry were investigated by comparing average bone surfaces determined for the Control and Incidence groups. Pointwise surface variation between the average Control bone surface and the average Incidence bone surface was described with the magnitude and direction of vectors between corresponding surface vertices.

Variation in high-dimensional bone surface morphology between groups was investigated using statistical shape models (SSMs) separately generated from sets of triangulated bone surfaces for the distal femur and proximal tibia. Joint point distribution models were constructed from all individual triangulated surfaces in the set of 24 knees. Each triangulated surface was described by a shape parameter vector

$$\mathbf{p}_i = [v_{1x}, v_{1y}, v_{1z}, \dots, (v_{jx}, v_{jy}, v_{jz})] \quad (1)$$

where $v_{j(xy)}$ are the three-dimensional coordinates of the nodes on the surface mesh, $j=1, \dots$, number of nodes in the triangulated surface, and $i=1 \dots n=24$ are each instance of the 24 femur or tibia surface models in the sample sets. The mean shape of all bones in each sample set is defined as the average mesh

$$\bar{\mathbf{p}} = \frac{1}{n} \sum_{i=1}^n \mathbf{p}_i \quad (2)$$

and the correlation between triangulated surfaces in the set is given by the empirical covariance matrix

$$\mathbf{S} = \frac{1}{n} \sum_{i=1}^n (\mathbf{p}_i - \bar{\mathbf{p}})(\mathbf{p}_i - \bar{\mathbf{p}})^T \quad (3)$$

A principal components analysis of the covariance matrix, $\mathbf{S}$, results in a set of $k=n-1$ eigenvalues (λ_k) and eigenvectors ($\mathbf{q}_k$), which are the principal directions spanning a shape space centered at the mean, $\bar{\mathbf{p}}$. The proportion of the total variance described along each eigenvector is equal to its corresponding eigenvalue divided by the sum of all eigenvalues; eigenvectors corresponding to the largest eigenvalues describe the majority of the variance. Thus, triangulated surfaces for each bone in the set were described in terms of the average mesh and a weighted linear combination of uncorrelated shape components as

$$\mathbf{p}_i = \bar{\mathbf{p}} + \sum_k b_{ik} \mathbf{q}_k \quad (4)$$

where for each individual bone

$$b_i = \mathbf{Q}^T (\mathbf{p}_i - \bar{\mathbf{p}}) \quad (5)$$

are scores and $\mathbf{Q}^T$ contains the k eigenvectors. Weighting factors for each individual model were determined by dividing the k scores by the square root of the corresponding eigenvalue

$$c_{ik} = \frac{b_{ik}}{\sqrt{\lambda_k}} \quad (6)$$

where $\sqrt{\lambda_k}$ is the standard deviation of the shape from the mean along the corresponding eigenvector. All variability within the original set of surfaces is contained in the weighting factors for each tibia or femur.

Wilcoxon rank sum tests were used to detect significant differences between principal shape modes using mean tibia and femur weighting factors for each group (MATLAB R2008b, The Mathworks, Inc., Natick, MA). Contributions of significant weighting factors to tibia and femur geometry were investigated as

$$\mathbf{p}' = \bar{\mathbf{p}} + \sum_{k'} \bar{c}_{k'} \sqrt{\lambda_{k'}} \mathbf{q}_{k'} \quad (7)$$

where $\bar{c}_k$ are the average Incidence weighting factors for the subset of k' significant principal shape modes. In the case of multiple significant shape modes, surfaces $\mathbf{p}'$ were determined using each significant shape mode separately and as the combination of all significant shape modes. Pointwise surface variation was described between shapes $\mathbf{p}'$ using means of the significant Incidence weighting factors and the average Control group surface.

Stepwise logistic regressions were used to select sets of femur and tibia shape modes based on statistical significance in regressions of weighting factors against group label (*i.e.* Control or Incidence) (MATLAB R2008b, The Mathworks, Inc., Natick, MA) (Draper and Smith, 1998). Pointwise surface variation was described between shapes generated using Eq. (7) with principal modes selected using stepwise logistic and the average Control group surface.

A three-dimensional joint coordinate system was established to investigate differences in three-dimensional anatomical alignment between knees in the Control and Incidence groups (Grood and Suntay, 1983). Based on knee anatomy, orthogonal tibial coordinate frames were defined for each tibia and orthogonal femoral coordinate frames were similarly defined for each femur. Positioning of the femur with respect to the tibia was determined using rigid body transformations between the femur and tibia coordinate systems and reported in terms of clinical rotations and translations (Grood and Suntay, 1983). Wilcoxon rank sum tests were used to detect significant differences between mean clinical rotations and translations of the Control and Incidence knees (MATLAB R2008b, The Mathworks, Inc., Natick, MA).

Combined effects of bone geometry and knee alignment on joint space were investigated by repositioning corresponding tibia and femur surfaces in the scan orientation and determining the average knee for each group. The average Incidence tibia was registered to the average Control tibia using a Procrustes analysis without scaling (MATLAB R2008b, The Mathworks, Inc., Natick, MA). The resulting transformation was applied to the average Incidence femur so that the average Incidence knee was registered to the average Control knee in a coordinate system defined by the average Control tibia (Grood and Suntay, 1983; Kadaba et al., 1989; Newell et al., 2008). Differences in joint space of the average Control and Incidence knees were investigated by determining vectors between corresponding surface vertices and cumulatively evaluating changes in the tibial and femoral articular surfaces.

3. Results

Noting that all individual bone models were proportionally-sized based on anatomic landmarks, the overall height (*i.e.* distance from the superior aspect of the intercondylar aspect to the transaction level) of the average Incidence group tibia was less than the overall height of the average Control group tibia, except for the medial intercondylar eminence and a small postero-lateral region. However, the anterior-posterior and medial-lateral measures of tibial plateau width for the average Incidence group tibia are greater than the same measures for the average Control tibia (Fig. 3).

The first principal mode in the tibia statistical shape model described 82.8% of the total geometric variability and the first two modes described 96% of the variability (Fig. 4). The means of tibia mode 15 weighting factors were significantly different between Control and Incidence groups (p -value=0.046). Group means of all other modes were not significantly different. Mode 15 explained 0.06% of the total variance within the study sample. While mode 15 described the majority of the differences in tibial geometry between groups, the magnitudes of pointwise variation were not fully described (Figs. 3 and 5).

Stepwise regression of tibia weighting factors against group membership led to the inclusion of principal modes 2, 8, 10, 15, and 21. Surface geometry generated using these tibia shape

modes more fully described the radial difference between group average tibias; however, the variation patterns in tibial plateau and intercondylar eminence geometry were described less successfully than when using mode 15 alone (Fig. 6).

The average Incidence femur model surface was outside the average Control femur model surface indicating that the average Incidence femur was larger, particularly in the posterior condylar region and the lateral epicondylar region (Fig. 7). The first femur principal mode described 58.2% of the variability in geometry and the first 7 modes described 96% of the variability (Fig. 8). The means of principal modes 9 and 11 were significantly different for the femur (p -value=0.019 and 0.040, respectively); all others were not significantly different. Shape mode 9 explained 0.50% of the total variance and mode 11 explained 0.43% of the variance within the study sample. Distal femur shapes generated using femur modes 9 and 11 separately (Figs. 9 and 10) and in combination (Fig. 11) described qualitatively similar spatial patterns of geometry differences when compared to the average Control femur geometry. As with the tibia, the significant femur modes qualitatively described the spatial distribution of differences in femur articular surface geometry between groups (Fig. 7), although the variation magnitudes were not fully described.

Stepwise regression of femur weighting factors against group membership led to the inclusion of modes 1, 9, 11, 12, and 20. Variation in pointwise surface geometry between the average Control femur and the femur geometry generated using these significant shape modes was identical to that of the comparison between average group femurs, suggesting that this set of shape modes described all variability in femur articular geometry between groups (Fig. 12).

Differences between group means with respect to orientation or distance between subchondral bone surfaces of the femur and the tibia were not statistically significant (Table 1). Quantitative investigation of pointwise variation in average knee joint space between groups demonstrated that the joint space for the Incidence group was smaller overall than the Control group, particularly in the lateral condylar region (Fig. 13).

4. Discussion

This study demonstrated that quantitative differences in tibia and femur geometry were observed between surface models based on clinical MRI data for subjects at risk of developing OA (*i.e.* Incidence group) and Control group subjects. Furthermore, SSM is capable of efficiently describing variability in this complex knee articular surface geometry. Differences in knee joint space between groups did not appear to be related to non-weight-bearing alignment and relative orientation of the tibia and femur. Rather, results of the present study suggest that variability in individual bone geometry may play a greater role in determining joint space geometry and underscore the importance of considering geometry of the individual bones and other structures comprising the knee joint in advancing the understanding of knee OA.

Low fidelity measures of geometry are not capable of fully describing the complex three-dimensional joint geometry that exists in the knee and other articulating joints. As such, subtly complex differences in joint geometry may not be detected and it may be these differences that contribute most to differences in mechanics that may lead to the development or progression of knee osteoarthritis. Numerous studies have demonstrated the role of mechanical loading factors in onset and advancement of OA (Andriacchi et al., 2004; Arokoski et al., 2000; Sharma et al., 1999; Vos et al., 2009; Yang et al., 2009), and clinical studies have demonstrated that joint incongruity is related to early cartilage degeneration (Harris, 1986; Hohe et al., 2002; Mankin et al., 1971).

SSM provides a means of explicitly describing complete joint surface geometry and allows for statistical investigation of the spatial variation in articular geometry and joint congruence between healthy subjects and those with clinical risk of developing or existing signs of osteoarthritis. Quantitative investigation of variation in average bone geometry between subjects in the Control and Incidence groups illustrates the regional nature of the complex differences in bone geometry and suggests that spatial geometry variation may serve to further differentiate between persons developing OA symptoms and those remaining healthy.

The small sample size of knees is an obvious limitation of the present study and it remains to be seen whether morphological differences observed between average Control and Incidence groups have predictive value in the clinic. Additionally, it is unknown whether differences in knee geometry measures and the ability to describe these differences using a small set of principal shape modes will be capable of disease status classification in longitudinal data. Similarly, the Progression group in the OAI database was not considered in the present study because we expect that morphological changes between the Progression group and the Control or Incidence groups may reflect effects of disease rather than provide predictive capability. Finally, joint alignment measures in the current study were determined from MRI scan data collected during non-weight-bearing conditions. Although measures of tibia–femur alignment in the current study provide a means of comparison between participants, it is unknown how weight-bearing conditions would affect the results of this comparison. Work towards a more comprehensive treatment of the knee anatomy geometry is necessary. Numerous studies have demonstrated the important role of the meniscus in cartilage mechanics and in protecting and preserving cartilage integrity in both healthy individuals and those demonstrating early and progressive signs of OA disease (Biswal et al., 2002; Cicuttini et al., 2002; Ding et al., 2007; Hunter et al., 2006; Pelletier et al., 2007). Further description of the structural geometry and the accompanying increase in variability of the knee structure will lead to changes in mechanical loading factors expected to lead to manifestation of OA and provide improved predictive capability. Application of multi-object SSM to comprehensively describe relevant cartilage, meniscal, ligamentous, and muscular structures along with the bone surfaces and subsequent analysis of the kinematic and mechanical loading environment of the knee joint will likely provide a direct pathway towards advancing the understanding of OA etiology.

In conclusion, SSM provides a means of explicitly describing complete articular surface geometry and allows the complex spatial variation in joint surface geometry and joint congruence between healthy subjects and those with clinical risk of developing or existing signs of OA to be statistically demonstrated. SSM methods provide an innovative and important step towards describing differences in knee surface and joint space geometry that may directly lead to understanding and differentiating between the causes and effects of OA.

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Fig. 1.
Frontal view of the proximal tibia demonstrating positioning of the transection plane.

Fig. 2.
Frontal view of the distal femur demonstrating positioning of the transection plane.

Fig. 3. Pointwise differences in average tibia surface geometry between Control and Incidence groups. (Left: antero-medial view, right: articular surface view.)

Fig. 4. Cumulative total geometry variance explained by principal modes of the tibia SSM.

Fig. 5. Pointwise differences in surface geometry between the average control tibia and the surface generated using the average tibia mode 15 weighting factor for the incidence group. (Left: antero-medial view, right: articular surface view.)

Fig. 6. Pointwise differences in surface geometry between the average control tibia and the surface generated using the average tibia modes 2, 8, 10, 15, and 21 weighting factors for the Incidence group. (Left: antero-medial view, right: articular surface view.)

Fig. 7. Pointwise differences in average femur surface geometry between Control and Incidence groups. (Left: antero-medial view, right: articular surface view.)

Fig. 8.
Cumulative total geometry variance explained by principal modes of the femur SSM.

Fig. 9.
Pointwise differences in surface geometry between the average control femur and the surface generated using the average femur mode 9 weighting factor for the Incidence group. (Left: antero-medial view, right: articular surface view.)

Fig. 10. Pointwise differences in surface geometry between the average control femur and the surface generated using the average femur mode 11 weighting factor for the Incidence group. (Left: antero-medial view, right: articular surface view.)

Fig. 11. Pointwise differences in surface geometry between the average control femur and the surface generated using the average femur modes 9 and 11 weighting factors for the Incidence group. (Left: antero-medial view, right: articular surface view.)

Fig. 12. Pointwise differences in surface geometry between the average control femur and the surface generated using the average femur modes 1, 9, 11, 12, and 20 weighting factors for the Incidence group. (Left: antero-medial view, right: articular surface view.)

Fig. 13.
Pointwise differences in average knee joint space between Control and Incidence groups.

Table 1

Comparison of knee alignment measures between Control and Incidence groups.

Clinical measure	Control cohort	Incidence cohort	<i>p</i> -Value
Flexion (deg.)	-3.95±2.63	-4.18±2.49	0.51
Tibial rotation (deg.)	-2.84±4.74	-2.40±5.27	0.89
Adduction (deg.)	0.21±0.65	0.37±0.80	0.34
Lateral tibial displacement (mm)	1.95±1.35	1.11±1.61	0.10
Anterior tibial drawer displacement (mm)	-7.23±1.48	-7.53±2.43	0.54
Joint distraction (mm)	9.17±1.57	8.23±1.09	0.19

Note: Values are given as mean ± standard deviation.