Segmentation and Analysis of Knee Femoral Cartilage for Osteoarthritis using MR Images

Revathi S A1, G Holi2

1Dept. of Computer Science & Engineering, RV College of Engineering, Bengaluru. Affiliated to Visvesvaraya Technological University, Belagavi.
2Dept. of Information Science & Engineering, Global Academy of Technology, Bengaluru. Affiliated to Visvesvaraya Technological University, Belagavi.

Email: revathisa@rvce.edu.in

Abstract. Knee Osteoarthritis (OA) is a chronic disease of femoral knee cartilage impairment and can be analyzed with Magnetic Resonance Imaging (MRI). Early detection of the disease helps patient from severe damages. Hence segmentation of knee cartilage is based on pixels of the image. We propose a Femoral Knee Cartilage degeneration method by 3 components: Preprocessing is done to standardize intensity and spatial characteristics and then Segmentation is carried out by registration, transformations and wrapping of reference image and results are verified using Dice Similarity Coefficients; Cartilage thickness is visualized by clouds using morphology and relaxometry. This paper aims at analyzing the femoral segmented cartilage thickness and volume via Pearson coefficients. Ground truth segmentation resulted in an average DICS Coefficient of 0.86. Pearson's coefficients were 0.96 for cartilage thickness and 0.98 for cartilage volume.

1. Introduction

Osteoarthritis (OA) is the most common arthritis of the knee. It is a multifactorial and heterogeneous disease and is characterized as Hyaline articular cartilage loss, progressively [1]. Magnetic Resonance Imaging (MRI) is a non-invasive technique that allows the assessment of various tissues composition and its states. In the MRI process, a patient is placed in a strong longitudinal magnetic field that aligns nuclear spins off atoms in the patient’s body, which results in a net magnetization vector. Magnetic Field Components with the radio frequency pulses transverse to the longitudinal field frequencies produced are adjusted to the Larmor Frequency of an isotope of interest are applied often. These pulses can flip spins to a higher energy resulting in a transverse component to the Magnetization vector. Responsive signals from the patient’s body can be detected when these spins return to the ground state. Characteristics of the magnetization can be measured based on the RF pulses response [2].

Evaluation of OA is carried out by plain radiographs, depicted by the joint space narrowing or gross osseous change that exist lately in the OA patients. Plain Radiographs do not show the changes of articular cartilage early. Hence the growth of joint space narrowing infers the cartilage loss indirectly, which is unreliable with proper technique of careful attention [3].

Most useful tool for direct visualization of cartilage is MRI. Morphological Imaging shows damage of cartilage at certain stage [4]. Standard sequences of MR Techniques for fat saturated T2- weighted, proton
density-weighted fast spin echo (FSE) and T1-weighted spoiled gradient echo (SPGR) sequences. Morphology assessment of knee cartilage can be done by three-dimensional double-echo steady state (3D-DESS) sequence with which slice thickness can be set. 3D-DESS makes use of 3D gradient echo technique that has simultaneous acquisition of two different steady state free precession (SSFP) echoes. These help in early degenerative of cartilage matrix changes, especially biochemical changes namely proteoglycan loss [5].

Cartilage matrix loss includes the changes in water content, loss of proteoglycans and molecular changes in collagen. Diagnosis of cartilage injury requires the ability to detect changes of collagen integrity and proteoglycan concentration before gross morphological changes happen [6].

2. Methodology

Segmentation is a major challenge in image analysis pipeline. Researchers still tend to manually or semi-automatically segment the femoral knee cartilage using tools in a tedious and non-reproducible manner. However, there are many algorithms that are developed by researchers to automatically segment the knee cartilage based on different principles namely active contours, atlas-based, graph-based, machine and deep learning and hybrid combinations. Methodology is given pictorially below which describes the workflow of the implementation carried out.

![Methodology Diagram](image)

**Figure 1.** Methodology

In the pipeline of image analysis, segmentation is challenging. Most papers tend to segment femoral knee cartilage manually or semi-automatically, using commercialized or in-house software tools, in a monotonous and unrepeatable process. However, there are many algorithms that have been evolved to perform segmentation automatically for knee cartilage. In the literature and in published reviews [7-11], we have found 29 pertinent publications that suggest new algorithms for segmentation of femoral knee cartilage. These algorithms are based on various principles, namely atlas-based, active contours, machine and deep learning, graph-based and hybrid combinations, which was developed by various research groups worldwide.

2.1. Preprocessing

Raw Dataset of Knee MR Images was available from the OAI (Osteoarthritis Initiative) are preprocessed using spatial and intensity preprocessing. Spatial preprocessing transforms the image to right-anterior inferior (RAI) orientation. Intensity Preprocessing correct the image inhomogeneity to a static magnetic field (B0). Intensities are rescaled to a range of [0-100]. Cartilage edges are preserved and smoothed using curvature flow. Preprocessing the spatial and intensity property of images is done to provide high quality images to the segmentation algorithm. Figure 2 below is the result of standardization of spatial information and intensity of images used as the fundamental step in preprocessing.
2.2. Atlas Based Segmentation

Atlas-based segmentation is used here to segment (reference image) image of the dataset, registration to segment each image (moving image) is used. Registration is done using elastix software. A different approach to calculate the cartilage spatial prior, multi-atlas registration is used. Every atlas is a separate expert for segmentation of cartilage and bone. Majority voting, locally weighted and non-local patch-based fusion are the three popular Label-fusion methods.

Atlas-based segmentation can be described as matching of its corresponding segmentation and an original image [12]. There are three categories namely single, average and multi-atlas-based methods [13]. Foreground and Background are the two labels for binary segmentation, which leans to combine touching objects if spatial regularity is imposed. Objects can be separated using multi-label segmentation and are applicable to segment touching objects. Most of the severe OA patients have the femoral and tibia cartilage touching each other in the MR Images, hence three-label segmentation method is used to keep away feasible merging. Multi-shape-atlas registration is used for computing the cartilage spatially. Here femur segmentations $S_{FB}$ for query image $I$.

First the atlas bone segmentations $S_{FB}$ are registered bone segmentations $S_{FB}$ segregated by affine transforms of the query image. Using majority voting [14] and label fusion [15], the registered cartilage atlas segmentations average calculates the spatial priors is calculated next

$$p(FC) = \frac{1}{N} \sum_{i=1}^{N} T_{FB}^i o S_{FC}^i$$  \hspace{1cm} (1)

Implementing a locally weighted label fusion approach [15], gives better accuracy of segmentation than a majority voting technique. Here the atlases are chosen which suits for the local cartilage likelihoods $p(f(x)|FC)$ from the classification by probability. For the femoral cartilage variation of spatially weighting functions $\lambda_{FC}^{i}$ is computed as

$$\lambda_{FC}^{i} = \frac{1}{a[|T_{FB}^i o S_{FC}^i - p(f(x))| - \varepsilon]$$  \hspace{1cm} (2)

Succeeded by a minor amount of diffusion smoothing. In this case, $a = 0.2$ and $\varepsilon = 0.001$ is considered for execution. For each cartilage the spatial prior is the weights of the propagated atlas cartilage segmentations and averaged [16]

$$p(FC) = \frac{1}{N} \sum_{i=1}^{N} \frac{\lambda_{FC}^{i}}{\sum_{i=1}^{N} \lambda_{FC}^{i}} (T_{FB}^i o S_{FC}^i)$$  \hspace{1cm} (3)

Coupé P et al. [17] and Rousseau F et al. [18] proposed non-local patch-based label fusion techniques. Across the training atlases, in a predefined neighborhood a label was obtained using surrounding patches, the label is determined in each propagated atlas from the same voxel location. Patches are assigned the distance of the target patch and the selected patches weights. Resulting in registration errors given by local robustness.
At voxel $x$, the spatial prior of femoral cartilage (i.e., $p_{FC}$) denoted by $p_{FC}(x)$. In search of a pre-specified neighborhood $N(x)$, the propagated labels are weighted, averaged and probabilities across $N$ warped atlas are computed. Focused local patch similarities give the weights. Assume $S_i^{FC} = T_i^{FB} \circ S_i^{FC}$ and $I_i^{FC} = T_i^{FB} \circ I_i$. The atlas index $i$, loops from 1 to $N$, $S_i^{FC}$ denotes the segmentation of femoral cartilage of the $i$-th atlas, and $I_i$ is the $i$-th atlas appearance. Femoral cartilage is formulated,

$$p_{FC}(x) = \sum_{y \in N(x)} w_{FC}(x, y)$$

where the $p_{FC}(x)$ patch centered at $x$ for the voxel $x'$ a voxel in the $p_{FC}$ patch centered at $y$ and $h_{FC}(x)$ is denoted by

$$h_{FC}(x,y) = \min_{(x',y') \in N(x)} \left( \sum_{y' \in p_{EP}(x, y')} \left( I(x') - I_i^{FC}(x') \right)^2 + e' \right)$$

### 2.2.1. Registration Framework

Important step in medical image processing is registration of medical images. Different modalities of MRI are aligned to process the data sets, varying time points like following-up of scans and/or from separate subjects for studies [15]. A Parametric Approach which is based on the number of feasible transformations is bounded by a parametrization of transformations. Mathematical Formula for the registration problem.

Multi-Atlas Segmentation, training set images are included with the corresponding manual segmentation. Cartilage spatial prior is computed by multi-atlas registration. Every single atlas is a single segmentation of bone and cartilage. Popular label fusion methods are majority voting locally weighted and non-local patch-based fusion.

Segmentation here consists of two parts: 1) Femur Bone Segmentation to initialize cartilage segmentation. 2) Cartilage segmentation. Segmentation process is carried out in three steps as mentioned below.

#### Step 1: Registration of image to reference. Moving image is registered to the reference image. Femoral Cartilage Segmentation $S_i^{FC}$, Femur Segmentations $S_i^{FB}$ for $N$ atlases of Query image $I$. First, $S_i^{FB}$ atlas bone segmentations are recorded to the $S_i^{FB}$ bone segmentations of the query image are separated by $T_i^{FB}$ affine transforms. Registered cartilage is averaged using atlas segmentations for spatial computations, which is required for label fusion calculated using Eq (1).

#### Step 2: Invert transformations. Parametric technique is used in the elastix software; parametrization transformation is initiated by binding feasible number of transformations. The problem of registration is given by an optimization of cost function $C$ reduced with $T$.

$$\hat{\mu} = \arg \min_{\mu} C(T_{\mu}; I_F, I_M)$$

Parameterized transformation is indicated by subscript $\mu$. Transformation parameters are contained in the vector $\mu$. Overview of nonparametric methods [19] and [20] is referred. Iterative optimization process is used to resolve the minimization problem in a multi resolution setting.

Users can specify the titles of the components required in a text file passed as parameter. Using similar parameter settings, moving images and passing of file names of fixed images as arguments to command-line, so that registration of many image pairs is done.

Registration output such as $I_M \left( T_\mu(x) \right)$ saves the moving image deformed and intermediate progress information. The resulting transformation is applied to data sets other than the moving image. It is ITK based. Cost Function is measured by comparing between the transformed moving image and the fixed image.
where the fixed image domain $\Omega_f$, $N$, is the sampled number of voxels $X$ from the fixed image domain. Selection of the samples $X$ by sampler. Identical intensities of two images i.e. with same modality, only for those images MSD is suited.

The $T_\mu$ coordinate transformation parameters decide the degrees-of-freedom deformation. Affine transformation prototype permits the images for scaling, translation, skew, and rotation.

$$T_\mu(X) = AX + t$$

where the matrix $A$ and the vector of translation $t$. The parameter $\mu$ vector is framed by the translation vector and the matrix elements $a_{ij}$. In 2-D, this represents a vector of 6 dimensions: $\mu(a_{11}, a_{12}, a_{21}, a_{22}, t_x, t_y)^T$. In 3-D, it comprises 9 matrix elements and 3 translational components.

Optimization: To solve Eq. (7), an iterative optimization step is used. In each $k$ iteration, the parameter $\mu_k$ is current transformation revised by considering $d_k$ in direction of search.

$$\mu_{k+1} = \mu_k - a_k d_k$$

with $a_k$ a scalar that signifies the step size. A broad span of optimization techniques can be planned such that distinct terminologies of $a_k$ and $d_k$ are specified[24]. An option for the direction search is the cost function derivative $\frac{dc}{d\mu}$ assess at the $\mu_k$ current position Eq. (4) decreases gradient descent procedure.

Step 3) Reference mask is wrapped to the moving image. Inverted transformations are applied to the reference image mask to obtain a moving image mask.

The reference image is selected as a result of a convergence study. Here femur mask and femur cartilage masks of the reference image are present and checked. Segmentation process is carried out by segmenting bone and then the cartilage (Figure 3).

Figure 3. Femur Cartilage Segmented Image.

Segmentation quality is measured quantitatively by Dice Similarity Coefficient (DSC) measured by the overlap between a newly segmented mask (NM) and the corresponding ground truth segmentation (GT).

$$DSC = \frac{2 |NM \cap GT|}{|NM| + |GT|}$$

2.3. Morphology

Cylindrical shape of the cartilage in the MR Images, a template of reference is designed by mapping the identical points to copy 2-Dimensional cartilage shape array and then changing the value thickness
anatomically at each point described by regions of normal thickness [15]. Cartilage thickness Wear-maps are of great help in identifying the thinning regions of cartilage as shown in Figure 3. Visualization and subsequent cluster analysis projection maps [19] were created. From each segmented slice, bone-cartilage interface was extracted and subsided into a single sagittal plane. Using the least-square approach circle was fit into the data and the center and circle radius to generate a fitting cylinder for the femoral condyles was used. Every slice recognized the value of the Anterior proximal from the original segmented data and rays were marked from this point at 1° increase to 245°, which resulted in creating 245 angular bins. This range made sure that the cartilage is encompassed. Pixel data was averaged from the cartilage that was within this range. An area-based-weighted-average for pixels that fell within multiple bins are used. Using angular bins Projection maps were created versus slice number plotting. 1*10 interpolation factors were used on the slice direction to get maps of isotropic projection. The angular bin direction using low pass 1*5 blurring filter to reduce the effect of noise.

At different time points projection maps were subtracted to obtain Difference maps, which reduced magic angle effects present after the registration step at a band of about ±10° degrees around a ±54° angle from projection maps of static magnetic fields of 46° and 144°. Due to small differences in the cartilage edge segmentation any pixel without corresponding pixel was eliminated by utilizing a 7-pixel wide disk erosion [19].

The cartilage plate’s focal lesions were identified for cluster analysis. Clusters were classified by thresholds i.e. Intensity and size either as increased or decreased. Increased and decreased clusters, thresholds were set at +2σ for both T2 and T1p relaxation times, where the healthy groups’ difference map the mean standard deviation σ. A cluster is termed as pixels set above or below the thresholds that are separated by one corner, pixel or edge.

The T1p feature vectors of the cAB (bone-cartilage interface) is non-shape interpolated cartilage is considered and put in a matrix with same number of rows and cartilage layers d, same number of columns and number of points in the cAB. A feature vector of d elements associated with each point in the cAB. This approach is referred to the perpendicular or normal approach [10]. Arbitrarily the Cluster Area threshold is selected, focal defects were identified though 85th percentile noise was removed. The percentage of identical clusters covered in the projection map is Term Percent Cluster Area (%CA). There are two Classifications of %CA, area covered above intensity threshold of clusters is %CA+; second is %CA- values is the area covered below the intensity threshold of clusters. Cartilage surface is extracted from the binary mask. Subchondral bone surface is visualized as flattened yellow point cloud and articular surface blue point clouds as shown in Figure 4.

2.3.1. Statistical Analysis
The %CA difference map of healthy and OA affected patients. Relaxation time values T2 and T1p was executed for both %CA+ and %CA- and analyzed. Statistical significance p was initialized to <0.05 and analysis was carried out. Positive skew of patient data and small sample size was chosen for Non-parametric analysis.

Figure 4. Cartilage Thickness Map
Figure 5. Cartilage Thickness visualized using Color-map
Table 1. Cartilage Thickness Average

| subjects          | volume |
|-------------------|--------|
| 01_DESS_01_prep_fc | 8716   |
| 01_cubeQuant_01_prep_fc | 7905   |

Above table indicates thickness average of the cartilage.

2.4. Relaxometry

Cartilage was segmented using atlas-based segmentation sagittal SPGR images. Calculation of cartilage average thickness and volume for each region by an iterative minimization process. Following segmentation, the next process was generating a medial line for each region of cartilage [21]. Cartilage thickness is determined by shortest distance from medial point line to cartilage boundary. Cartilage thickness average was computed by averaging each slice.

Cartilage volume was set by multiplying the volume of each voxel by all the voxels surrounding the cartilage. This algorithm’s intra-observer root mean square CV is in the range of 2.4%-3.6% as recorded previously [22]. Volumetric variations are minimized by the knee size, axial (spoiled gradient-echo) SPGR images determine the epicondylar distance to normalize the cartilage [24].

Figure 6. Relaxometry Graph

The scaling of the elements is represented by Relaxation and diffusion over time (T1 relaxation is an add-on factor to the DC longitudinal term, Z0) and shifting of transverse coefficients $F_n$ is Gradient effect. Scaling is defined by the decay effect of $\frac{T_1}{T_2}$ and diffusion, on state $n$.

Here, repetition $TR$ and echo time $TE$, flip angle $\alpha$, diffusivity $D$, unbalanced gradient is represented by $\Delta k = \gamma G \tau$ inducing dephasing per unit length, where spoiler amplitude $G$ and duration $\tau$, and gyromagnetic ratio $\gamma$. Relationship between the two Double Echo in Steady State Scan (DESS) signals is determined by the echo pathway of the visible signal immediately before the pulse, $F_0^-$, as well as the components that contributed to it. Loop this till the visible signal immediately after the pulse, $F_0^+$ [23].

Cartilage Volume and average thickness for each region was computed by an iterative minimization process as in [25]. Cartilage volumetric variations are minimized by normalizing the epicondylar distance from axial SPGR images. The T1ρ map was structured by fitting the pixel-by-pixel image intensity using Levenberg-Marquardt mono-exponential fitting algorithm equation.
and is shown in Figure 7.

\[ S(TSL) \propto \exp \left( \frac{-TSL}{T_{1p}} \right) \]  \hspace{1cm} (12)

Linear fitting is faster as logarithmic transform of data and linear interpolation. Linear fitting is less accurate compared to exponential fitting as the nonlinear transform of their log has more weight to outliers. Fitting is computed after registration of the acquired images. X-variable is echo times for each voxel and Y-variable is intensity of voxels in each acquisition.

3. Results and discussion
Dataset used here was OAI1, OAI2 and a few MR Images. 19 DESS images and T2-weighted spin-echo images acquired at year 4 of the OAI1. Ground Truth segmentation was done using Atlas-based technique. At 1-year follow-up, 88 DESS images obtained at baseline in OAI2. Internals images were 4 obtained using DESS and CubeQuant Protocols. Images have been divided into two sets of OAI1 i.e. DESS and T2. Similarly, for OAI2, first is Baseline (BL) and Follow-up (FU).

Table 2. Segmentation results

| Images     | DSC (Dice Similarity Coefficients) | Mean Standard Deviation |
|------------|-----------------------------------|------------------------|
| OAI1-DESS  | 0.86                              | 0.02                   |
| OAI1-T2    | 0.76                              | 0.04                   |
| OAI2-BL    | 0.73                              | 0.04                   |
| OAI2-FU    | 0.72                              | 0.04                   |

Morphology results were calculated by cartilage thickness and volume by finding their correlations of cartilage thickness computed from segmentation and ground truth. Computed Pearson Coefficients of Cartilage thickness and volume are shown in the table:
Table 3. Pearson Coefficients of Cartilage thickness and volume

|                  | OAI1- DESS | OAI1-T₂ | OAI2- BL | OAI2- FU |
|------------------|------------|---------|----------|---------|
| Cartilage Thickness | 0.95       | 0.66    | 0.65     | 0.66    |
| Cartilage Volume  | 0.98       | 0.84    | 0.89     | 0.88    |

Relaxometry maps were calculated by the following procedure: Shortest echo time images were registered with longest echo time for OAI1-T₂ and similarly for T₁ρ maps with shortest time-of-spinlock. OAI-T₂ images T₂ maps were done by extracting masks values of ground truth, which was compared by Pearson’s Coefficient = 0.51.

Image preprocessing was successful for all the images while segmentation failed for few images. Average DSC for OAI1 - 0.81, OAI2 - 0.73. Analysis of morphology and relaxometry had an impact from the outcome of segmentation. Cartilage Volume had higher Pearson’s Coefficient than thickness. T₂ relaxation was low because of higher dependency on segmentation quality for intensity-based measurements. Though there are hybrid machine learning segmentation algorithms which give higher DSC than atlas-based segmentation. Here atlas-based algorithm is advantageous to analyze cartilage volume and thickness.

4. Conclusion
Preprocessing implemented using spatial and intensity attributes of knee images, results in standardized high quality images for segmentation. Dice Similarity Coefficient is used to evaluate the quality of segmentation using the ground truth images and newly segmented images. Contours of the cartilage mask is extracted as a point cloud and interpolated to a cylinder of each cartilage side using nearest neighbor algorithm. Thickness is associated to the point cloud to visualize as 2D map. Volume of the cartilage is the mask's voxels number multiplied by the voxel volume. Exponential or Linear fitting are used to calculate T₁ρ maps from T₁ρ-weighted images and T₂ maps from T₂-weighted images.

5. References
[1] Brandt, KD.; Doherty, M.; Lohmander, L.S., “The economics of Osteoarthritis”. New York: Oxford University Press Inc.; 1998
[2] W Chen, YX Wang, J Baiyan “Quantitative magnetic resonance imaging relaxometry with suppression of blood signal” - US Patent 10,557,906, 2020 - Google Patents.
[3] Rogers J, Watt Dieppe P. “A comparison of the visual and radiographic detection of bony changes at the knee joint” BMJ 1990;300:367–368. [PubMed: 2106987]
[4] Chan WP, Lang P, Stevens MP, Sack K, Majumdar S, Stoller DW, et al. “Osteoarthritis of the knee: comparison of radiography, CT, and MR imaging to assess extent and severity” Ajr Am J Roentgenol 1991;157(4):799–806. [PubMed: 1892040]
[5] Gray ML, Eckstein F, Peterfy C, Dahlberg L, Kim YJ, Sorensen AG. “Toward imaging biomarkers for osteoarthritis”. Clin Orthop Relat Res 2004;(427)(Suppl):S175–181. [PubMed: 15480063]
[6] Dijkgraaf LC, de Bont LG, Boering G, Liem RS. “The structure, biochemistry, and metabolism of osteoarthritic cartilage: a review of the literature”. J Oral Maxillofac Surg 1995;53(10):1182–1192. [PubMed: 7562173]
[7] Monu UD, Jordan CD, Samuelson BL, Hargreaves BA, Gold GE, McWalter EJ. Cluster analysis of quantitative MRI T2 and T1rho relaxation times of cartilage identifies differences between healthy and ACL-injured individuals at 3T. Osteoarthritis and Cartilage. 2017;25(4):513–520. pmid:27720806
[8] Liukkonen MK, Mononen ME, Tanska P, Saarakkala S, Nieminen MT, Korhonen RK. Application of a semi-automatic cartilage segmentation method for biomechanical modeling of the knee joint. Computer Methods in Biomechanics and Biomedical Engineering. 2017;20(13):1453–1463. pmid:28895760

[9] Heimann T, Morrison B. Segmentation of knee images: A grand challenge. Proc Medical Image Analysis for the Clinic: A Grand Challenge Beijing, China. 2010; p. 207–214.

[10] Pdeoia V, Majumdar S, Link TM. Segmentation of joint and musculoskeletal tissue in the study of arthritis. Magnetic Resonance Materials in Physics, Biology and Medicine. 2016.

[11] Zhang B, Zhang Y, Cheng HD, Xian M, Gai S, Cheng O, et al. Computer-aided knee joint magnetic resonance image segmentation—A survey, 2018.

[12] Aljabar P, Heckemann RA, Hammers A, Hajnal JV, Rueckert D. “Multi-atlas based segmentation of brain images: atlas selection and its effect on accuracy”. NeuroImage. 2009;46:726–738.

[13] Išgum I, Staring M, Rutten A, Prokop M, Viergever MA, van Ginneken B. “Multi-atlas-based segmentation with local decision fusion—application to cardiac and aortic segmentation in CT scans”. IEEE Trans Med Imag. 2009;28:1000–1010.

[14] Rohlffing T, Brandt R, Menzel RCR, Maurer J. “Evaluation of atlas selection strategies for atlas-based image segmentation with application to confocal microscopy images of bee brains”. NeuroImage. 2004;21:1428–1442.

[15] Sled JG, Zijdenbos AP, Evans AC “A nonparametric method for automatic correction of intensity nonuniformity in MRI data”, IEEE Trans Med Imaging. 1998 Feb;17(1):87-97.

[16] J. H. Kellgren and J. S. Lawrence “Radiological Assessment of Osteo-Arthrosis” Ann Rheum Dis. 1957 Dec; 16(4): 494–502.

[17] Coupé P, Manjkn J, Fonov V, Prusessner J, Robles M, Collins D. “Patch-based segmentation using expert priors: application to hippocampus and ventricle segmentation”. Neuroimage. 2011;59.

[18] Rousseau F, Habas P, Studholme C. “A supervised patch-based approach for human brain labeling”. IEEE Trans Med Imag. 2011;30:1852–1862.

[19] Uchechukwuka D. Monu, Caroline D. Jordan, Bonnie L. Samuelsøn, Brian A. Hargreaves, Garry E. Gold, and Emily J. McWalter “Cluster Analysis of Quantitative MRI T2 and T1ρ Relaxation Times of Cartilage Identifies Differences between Healthy and ACLinjured Individuals at 3T” Osteoarthritis Cartilage. 2017 April ; 25(4): 513–520.

[20] Carballido-Gamio J, Link TM, Majumdar S. “New techniques for cartilage magnetic resonance imaging relaxation time analysis: texture analysis of flattened cartilage and localized intra- and inter-subject comparisons” Magn Reson Cartilage. 2017 Apr ; 25(4): 513–520.

[21] Akhtar S, Poh CL, Kitney RI. “An MRI derived articular cartilage visualization framework”. Osteoarthritis Cartilage. 2007; 15:1070–85.

[22] Carballido-Gamio, J.; Bauer, JS.; Lee, KY.; Krause, S.; Majumdar, S. “Combined Image Processing Techniques for Characterization of MRI Cartilage of the Knee”. Shanghai, China: 2005 Sep 1–4.

[23] Blumenkrantz G, Lindsey CT, Dunn TC, Jin H, Ries MD, Link TM, et al. “A pilot, two-year longitudinal study of the interrelationship between trabecular bone and articular cartilage in the osteoarthritic knee”. Osteoarthritis Cartilage 2004;12(12):997–1005. [PubMed:15564067].

[24] Buxton RB. “The Diffusion Sensitivity of Fast Steady-State Free Precession Imaging. Magnetic Resonance in Medicine”. 1993; 29:235–243. [PubMed: 8429788]

[25] Sveinsson B, Chaudhari AS, Gold GE, Hargreaves BA. “A simple analytic method for estimating T2 in the knee from DESS”. Magn Reson Imaging. May;38:63-70. 2017.

Acknowledgements
We would like to thank OAI (Osteoarthritis) for providing the dataset and also Serena Bonaretti. Links for the dataset:
https://nda.nih.gov/oai
https://www.doi.org/10.5281/zenodo.2530608
https://github.com/sbonaretti/pyKNEEr/tree/master/publication/data.