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Prospective Image Registration for Automated Scan Prescription of Follow-up Knee Images in Quantitative Studies

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Abstract

Consistent scan prescription for MRI of the knee is very important for accurate comparison of images in a longitudinal study. However, consistent scan region selection is difficult due the complexity of the knee joint. We propose a novel method for registering knee images using a mutual information registration algorithm to align images in a baseline and follow-up exam. The output of the registration algorithm, three translations and three Euler angles, is then used to redefine the region to be imaged and acquire an identical oblique imaging volume in the follow-up exam as in the baseline. This algorithm is robust to articulation of the knee and anatomical abnormalities due to disease (e.g. osteophytes). The registration method is performed only on the distal femur and is not affected by the proximal tibia or soft tissues. We have incorporated this approach in a clinical MR system and have demonstrated its utility in automatically obtaining consistent scan regions between baseline and follow-up examinations, thus improving the precision of quantitative evaluation of cartilage. Results show an improvement with prospective registration in the coefficient of variation for cartilage thickness, cartilage volume, and T₂ relaxation measurements.

Introduction

Osteoarthritis (OA) is a degenerative joint disease and a leading cause of chronic disability in the United States which affects at least 20 million people(1). The World Health Organization (WHO) estimates OA to be a leading cause of chronic disability in at least 10% of population aged 60 and older(2). As a result, there is an intense interest in the medical community in developing structure modifying drugs or treatments, which not only relieve inflammation and painful symptoms of OA but also prevent disease progression(3).

Plain radiography of the knee is currently the most commonly used technique for diagnosis of knee osteoarthritis (OA), but this technique has several limitations. Early and focal changes in the cartilage and other articular tissues are not directly visible using radiographs. Cartilage loss can only be indirectly inferred in X-rays by the development of joint-space narrowing. MRI is a promising technique which offers superior soft tissue contrast and is

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capable of non-invasive evaluation of cartilage morphology as well as function, without ionizing radiation.

High-spatial resolution MR images have been used to quantify cartilage volume and thickness in OA. Eckstein et al., showed that OA patients have an approximate loss of 4–6% of cartilage volume annually(4). Stahl et al. found that OA patients had significantly lower cartilage volume and average cartilage thickness in both tibia plateaus compared to normal controls(5). Several studies also have demonstrated an inverse relationship between pain, as measured by the Western Ontario and McMaster Universities scoring system (WOMAC), and cartilage volume.

Quantitative T_2 relaxation time is a non-invasive marker of cartilage degeneration because it is sensitive to tissue hydration and biochemical composition. Loss of collagen and proteoglycan in degenerating cartilage increases the mobility of water, thus increasing its signal intensity on T_2 -weighted images(6). Several studies have found higher T_2 relaxation times in cartilage of OA patients compared to healthy(5,7) controls as well as a correlation with the severity of the disease(8,9).

Longitudinal MR studies tracking OA disease progression are often performed (5,10–12). Consistent scan prescription for MRI of the knee is very important for accurate comparison of images in a longitudinal study. For example, when imaging cartilage in OA at different time points, follow-up images acquired at the same exact orientation as baseline images would enhance the precision of measurements such as cartilage thickness, cartilage volume, and T_2 relaxation measurements. This is especially true for T_2 relaxation measurements determined from a T_2 mapping sequence, which are particularly impacted by partial volume effects due to its thick slice thickness (~4mm). However, consistent scan region selection is difficult due the complexity of the knee joint. Currently follow-up patient positioning relies on a knee holder and follow-up sequences are prescribed manually by a technologist based on three plane localizer images. This manual prescription is relative time consuming and often does not include all degrees of freedom, such as 3D rotations. In addition manual prescription is used suffers from both intra- and inter-operator variability. As a result, there is a need for an automatic prescription of MR follow-up knee scans during longitudinal studies.

Techniques to improve knee image alignment precision by adjusting scanning parameters prior to image acquisition have been previously reported(13). This technique requires a training set and uses a segmentation of certain anatomical landmarks in order to align and register images. Therefore it is limited by the population being represented by the training set and by the complexity of identifying landmarks. We propose a novel method for registering knee images based on a mutual information registration algorithm(14,15) to align images in a baseline and follow-up exam. The output of the registration algorithm, three translations and three Euler angles, is then used to redefine the region to be imaged and acquire an identical oblique imaging volume in the follow-up exam as in the baseline. The effect of the proposed automatic scan prescription on cartilage volume, thickness, and T_2 relaxation short-term reproducibility is assessed.

Methods

Subjects and Clinical Assessment

The subjects in this study were 5 health volunteers (3 female, 2 male, mean $\pm$ std age = 36.16 $\pm$ 10.26 years) with varying degrees of cartilage degeneration. Pathologic findings at the knee joint were analyzed based on the high-spatial resolution SPGR sequence using a modified WOMS score(17) by a radiologist to demonstrate that subjects had a range of

cartilage quality, from normal to severe degeneration and osteophytes (Table 1). The 15 compartments in the original WOMBS score were merged to a total of 7 compartments as performed by Stahl et al.(18).

Registration Framework

The registration method requires two inputs: a baseline and a follow-up low-spatial resolution fat suppressed sagittal SPGR ($0.62 \times 0.62 \times 1 \text{ mm}^3$) image of the knee. The registration technique initially identifies a region containing only the distal femur by a process depicted in Figure 1. First, a threshold is chosen for each slice based on the maximum value of the corresponding histogram. The connected components of the resulting binary image are then determined(16). The connected components which connect to the left and right edges of the images are removed and the largest connected component within the top region of the image is isolated. The result is a binary image with the proximal femur approximately isolated. The smallest box which contains the proximal femur is then identified and used as the region for the mutual information calculation in the registration algorithm. This ensures that the registration is performed only on the distal femur and is not affected by the proximal tibia or soft tissues. Additionally the isolation of the distal femur in this manner allows the algorithm to be robust to articulation of the knee and anatomical abnormalities due to disease (e.g. osteophytes). With the region for the mutual information calculation identified, the registration, which is implemented with the Insight Tool Kit (ITK), is then performed. The output of a registration algorithm is three translations and three Euler angles.

MR Imaging

Sagittal images of the knee joint of the 5 volunteers were acquired on a 3T GE Signa MRI scanner using a 8 channel phase array knee coil. The scanning procedure is depicted in Figure 1. Three baseline scans were obtained. The first baseline scan was a low-spatial resolution 3D T1-weighted fat suppressed spoiled gradient-echo (SPGR) sequence (matrix 160×160 , FOV = 16 cm, slice thickness = 1mm, time = ~2min) acquired for the image registration. The second baseline scan was a high-spatial resolution 3D T1-weighted fat suppressed 3D SPGR sequence (matrix 512×512 , FOV = 16 cm, slice thickness = 1mm, time = ~10min) acquired for quantification of cartilage morphology. The final baseline scan was a 3D T₂ mapping sequence (matrix 256×128 , slice thickness = 4 mm, four different images acquired with TE = 4.1/14.5/25/45.9 ms, time = ~7min) obtained using an acquisition protocol based on a 3D SPGR sequence, as previously reported in [3], which was acquired to quantify the biochemical composition of cartilage. The volunteer was then removed from the scanner and repositioned for the follow-up scan where five follow-up scans were obtained. The first follow-up scan was a low-spatial resolution fat suppressed SPGR acquired with the same protocol as in the first baseline scan. Using the mutual information based registration method, the low-spatial resolution baseline and follow-up scans were registered. The registration provided the translation and rotation parameters which were inputs into the modified follow-up pulse sequences for the automated prescription of an oblique follow-up scan. The next two follow-up scans were acquired with the same parameters as the last two baseline scans except for input parameters from the registration. The final two follow-up scans were also acquired with the same parameters as the last two baseline scans but required a manual scan prescription.

Post-processing

Cartilage segmentation was performed using in-house software(19) developed in MATLAB (The Mathworks, Natick, MA). Based on the high-spatial resolution SPGR images, articular cartilage was segmented using a semi-automatic technique based on local propagation of line profiles and cartilage thicknesses between contiguous slices, and was defined in five

distinct regions: Medial/Lateral Femur Condyle (MFC/LFC), Medial/Lateral Tibia (MT/LT) and Patella (P). Following segmentation, cartilage was transformed into a 3D binary mask with isotropic voxels by using shape-based interpolation with distance fields. The cartilage thickness was then determined by calculating the minimum Euclidean distance from each point on the articular surface to the bone-cartilage interface. The average thickness was calculated for each slice and then averaged for all the slices(30). The cartilage volume was determined by multiplying the total number of voxels encompassing the cartilage by the actual volume of each voxel.

T₂-maps were computed on a pixel-by-pixel basis from the T₂ mapping sequence based on the following equation:

$$S(TE) \propto S_0 * \exp(-TE/T_2)$$

where S is the signal intensity in a T₂-weighted image with a certain TE, and S₀ is the signal intensity when TE=0 ms. Cartilage segmentations were resampled and superimposed on the T₂-map to define the regions of interest for T₂ relaxation assessment. Areas of partial volume effects due to fluid and areas of cartilage lesions appeared as visible clusters with elevated values and were manually excluded from the respective maps. The average T₂ relaxation time was determined for each of the five compartments.

Statistics

The coefficient of variation (CV)(20) and the intra-class correlation coefficient (ICC) were determined for baseline and follow-up images for average cartilage thickness, cartilage volume, and T₂ relaxation with and without registration to quantify the improvement in measurement precision.

Results

By image subtraction, the improvement in image alignment can be assessed. Figure 2 shows representative results of the prospective registration. The baseline high resolution scan is shown for comparison (Figure 2a and d) next to the corresponding high resolution follow-up images without registration (Figure 2b) and with prospective registration (Figure 2e). The improvement from the registration can be seen by inspecting the subtraction images (Figure 2c and f). It can be seen in the results that the follow-up scan with registration is more closely oriented with the baseline scan. For example, in Figure 2c the edges of the bone are misaligned with higher intensity in the subtraction image and in Figure 2f, the high intensity differences within the femoral edge are reduced.

Figure 3 demonstrates the improvement in registration for the distal femur with the selection of a region including only the distal femur for the calculation of the mutual information measure in the registration algorithm. The difference image without the region selection contains higher intensities in the subtraction image at the edges of the distal femur due to a less accurate alignment.

Our study observed differences between cartilage thickness, volume, and T₂ relaxation measurement determined from the manual prescription images and the prospective registration images. Table 2 shows the improvement in CV and Table 3 shows the improvement in ICC. The CV for volume, thickness, and T₂ relaxation was improved with the use of prospective registration between 2.9%–6.4%, 1.5–5.1%, and 1.5–5.9% respectively.

Discussion

Knee MR images acquired in longitudinal studies examining OA disease progression are currently obtained by a trained MR technologist who manually determines the scan prescription. The procedure is difficult due to the complex shape and angulations of the knee making accurate scan prescription time consuming and unreliable. However, sufficient anatomical coverage and optimal slice orientation is critical to quantify thin structures such as cartilage. This study demonstrates the feasibility of using a novel mutual information based method to register MR images of the knee to automatically determine the follow-up scan prescription. This registration method is performed only on the distal femur and is not affected by the articulation of the proximal tibia or soft tissues.

In sectional images of cartilage, the local cartilage thickness and volume depend on the orientation of the cartilage to the imaging plane. The true thickness of the cartilage may be overestimated due to the angle between the images and the cartilage layer(21). Because identical local regions and orientations could not be obtained in longitudinal studies, quantitative analysis was primarily global. The changes in cartilage volume, thickness, and T_2 relaxation are determined for the entire joint rather than at specific locations(5,10). This study proposes a prospective registration technique which ensures that follow-up images are acquired with the same orientation as baseline images and will allow for a more precise local examination of cartilage longitudinal changes due to disease.

A number of prospective registration methods have been previously proposed for the brain(22,23), spine(24), and tibia(25,26). Only one study has investigated the feasibility of prospective registration for knee images in clinical practice(13). The registration is based on an active shape model which requires triangular meshes obtained from the mean shape of bone surfaces from a pre-segmented image set, a training set of at least 15 knee MRI studies positioned by an experienced technologist, and segmentation of certain anatomical landmarks in order to align and register images(27). Therefore it is limited by the population being represented by the training set, as well as by the complexity of identifying landmarks and therefore may fail for anatomical deformations due to disease or surgery. In the proposed method, no training set or atlas is required and segmentation of the knee is not needed allowing it to be successful for knees with severe OA. Additionally, the reproducibility and the impact of prospective registration in quantitative studies assessing knee cartilage had not yet been evaluated.

Articulation, bending of the knee, is limited to a few degrees due to the MR scan setup and knee coil. However, slight differences in knee articulation between baseline and follow-up scans in a longitudinal study are possible so that a global rigid transform may not adequately align the entire image. In the proposed method, the registration algorithm focuses on the distal femur by isolating a region for the registration's mutual information calculation. If the articulation of the knee has not changed between the baseline and follow-up, then the proximal tibia will also be aligned. However, if the knee articulation has changed, an additional post-scan registration to align the proximal tibia may be necessary.

While the workflow proposed in this study is straightforward and fast (adding only ~1:30 min to the baseline exam and ~5min for the follow-up exam), there are several improvements to be implemented in future. The current software can be implemented on any scanner and does not require the transfer of data offline. However, in this study we modified the pulse sequences to automatically read in the inputs, the three translations and rotations, directly from a text file created by the registration software. This allows for a automated workflow with minimal user input or user errors. But there is no opportunity for the technologist to review the suggested automated scan prescription and make modifications.

Additionally, only pulse sequences which are modified are compatible with the proposed technique. Improvements in workflow could be implemented to more smoothly interact with the scanner's scan prescription interface to allow a review of the prospective registration scan prescription and allow compatibility with any pulse sequence without requiring a modification.

It is possible to implement a prospective registration technique into a hospital routine so that it is not too time consuming and provides an advantage for a radiologist. The proposed technique currently only adds ~1:30 min to the baseline exam and ~5min to the follow-up exam. By optimizing the software and writing the code to run registration iterations in parallel, the time still can be substantially improved. For a radiologist the main advantage is that the images will be acquired in the same orientation when comparing baseline and follow-up images to assess changes over time. Changes in anatomy such as cartilage thickness or bone marrow edema can be more accurately assessed when images are acquired at the same orientation. For a clinical cartilage evaluation, axial images are also often desirable. It is feasible with the current implementation to transform the output of the registration (three translations and three Euler angles) from the sagittal plane to the axial plane so that follow-up axial images can also be acquired in the same orientation as baseline images.

The proposed registration algorithm does not account for scaling or shearing, but the transform could be modified to account for such changes. However the registration is primarily performed based on the shape and intensity of the proximal femur and since bone remodeling affecting the shape is relatively slow, the expectation is that a rigid body algorithm is adequate.

Reproducibility without prospective registration for volume, thickness, and T₂ relaxation ranged from 1.4–10.2%, 2.1–5.8%, and 2.3–11.3% respectively. Glaser et al (28) reported a reproducibility of 2.11–3.8% for patellar cartilage volume and thickness and 3–7% for T₂ relaxation in healthy subjects. Similarly Eckstein et al. (29) reported a reproducibility of 1.3–3.4% for cartilage volume in healthy subjects. The lower reproducibility for measurements without prospective registration in this study compared to those studies may be due to the amount of cartilage degeneration of subjects. It has been observed that precision errors are generally higher for OA patients than for healthy volunteers(31). While other studies reported reproducibility for only healthy subjects with normal cartilage, in this study not all subjects were normal as denoted by the range of WOMS scores (Table 2). The reproducibility for volume, thickness, and T₂ relaxation was improved with the use of prospective registration to 2.9%–6.4%, 1.5–5.1%, and 1.5–5.9%, respectively. The improvement in reproducibility was higher for volume than for thickness which may be due to averaging during the calculation of the cartilage thickness. The calculation for volume does not require averaging of values and therefore is more sensitive to differences in the volume of interest.

Consistent scan prescription for MRI of the knee is very important for accurate comparison and quantitative analysis of images in a longitudinal study. This study demonstrates the feasibility of using a mutual information based method to register MR images of the knee without segmentation and automatically determine the follow-up scan prescription. This registration method is performed only on the distal femur and is not affected by the proximal tibia or soft tissues. Results show an improvement with registration in the coefficient of variation for cartilage thickness, cartilage volume, and T₂ relaxation measurements.

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References

1. Lawrence RC, Helmick CG, Arnett FC, Deyo RA, Felson DT, Giannini EH, Heyse SP, Hirsch R, Hochberg MC, Hunder GG, Liang MH, Pillemer SR, Steen VD, Wolfe F. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. *Arthritis Rheum.* 1998; 41(5):778–799. [PubMed: 9588729]
2. Organization WH. Global Economic and Health Care Burden of Musculoskeletal Disease. 2001.
3. McAlindon TE, LaValley MP, Gulin JP, Felson DT. Glucosamine and chondroitin for treatment of osteoarthritis: a systematic quality assessment and meta-analysis. *JAMA.* 2000; 283(11):1469–1475. [PubMed: 10732937]
4. Eckstein F, Cicuttini F, Raynauld JP, Waterton JC, Peterfy C. Magnetic resonance imaging (MRI) of articular cartilage in knee osteoarthritis (OA): morphological assessment. *Osteoarthritis Cartilage.* 2006; 14 (Suppl A):A46–75. [PubMed: 16713720]
5. Stahl R, Blumenkrantz G, Carballido-Gamio J, Zhao S, Munoz T, Hellio Le Graverand-Gastineau MP, Li X, Majumdar S, Link TM. MRI-derived T2 relaxation times and cartilage morphometry of the tibio-femoral joint in subjects with and without osteoarthritis during a 1-year follow-up. *Osteoarthritis Cartilage.* 2007; 15(11):1225–1234. [PubMed: 17561417]
6. Konig H, Sauter R, Deimling M, Vogt M. Cartilage disorders: comparison of spin-echo, CHES, and FLASH sequence MR images. *Radiology.* 1987; 164(3):753–758. [PubMed: 3615875]
7. Li X, Benjamin Ma C, Link TM, Castillo DD, Blumenkrantz G, Lozano J, Carballido-Gamio J, Ries M, Majumdar S. In vivo T(1rho) and T(2) mapping of articular cartilage in osteoarthritis of the knee using 3 T MRI. *Osteoarthritis Cartilage.* 2007; 15(7):789–797. [PubMed: 17307365]
8. Dunn TC, Lu Y, Jin H, Ries MD, Majumdar S. T2 relaxation time of cartilage at MR imaging: comparison with severity of knee osteoarthritis. *Radiology.* 2004; 232(2):592–598. [PubMed: 15215540]
9. David-Vaudey E, Ghosh S, Ries M, Majumdar S. T2 relaxation time measurements in osteoarthritis. *Magn Reson Imaging.* 2004; 22(5):673–682. [PubMed: 15172061]
10. Hunter DJ, Niu J, Zhang Y, Totterman S, Tamez J, Dabrowski C, Davies R, Le Graverand MP, Luchi M, Tymofyeyev Y, Beals CR. Change in cartilage morphometry: a sample of the progression cohort of the Osteoarthritis Initiative. *Ann Rheum Dis.* 2009; 68(3):349–356. [PubMed: 18408248]
11. Hellio Le Graverand MP, Buck RJ, Wyman BT, Vignon E, Mazzuca SA, Brandt KD, Piperno M, Charles HC, Hudelmaier M, Hunter DJ, Jackson C, Kraus VB, Link TM, Majumdar S, Prasad PV, Schnitzer TJ, Vaz A, Wirth W, Eckstein F. Subregional femorotibial cartilage morphology in women--comparison between healthy controls and participants with different grades of radiographic knee osteoarthritis. *Osteoarthritis Cartilage.* 2009; 17(9):1177–1185. [PubMed: 19341831]
12. Wluka AE, Stuckey S, Snaddon J, Cicuttini FM. The determinants of change in tibial cartilage volume in osteoarthritic knees. *Arthritis Rheum.* 2002; 46(8):2065–2072. [PubMed: 12209510]
13. Lecouvet FE, Claus J, Schmitz P, Denolin V, Bos C, Vande Berg BC. Clinical evaluation of automated scan prescription of knee MR images. *J Magn Reson Imaging.* 2009; 29(1):141–145. [PubMed: 19097115]
14. Maes F, Collignon A, Vandermeulen D, Marchal G, Suetens P. Multimodality image registration by maximization of mutual information. *IEEE Trans Med Imaging.* 1997; 16(2):187–198. [PubMed: 9101328]
15. Viola RA, Wells GA, Peterson J. The effects of fluid status and fluid therapy on the dying: a systematic review. *J Palliat Care.* 1997; 13(4):41–52. [PubMed: 9447811]
16. Haralick, RM.; Shapiro, LG. *Computer and Robot Vision.* Vol. 1. Addison-Wesley; 1992. p. 28-48.

17. Peterfy CG, Guermazi A, Zaim S, Tirman PF, Miaux Y, White D, Kothari M, Lu Y, Fye K, Zhao S, Genant HK. Whole-Organ Magnetic Resonance Imaging Score (WORMS) of the knee in osteoarthritis. *Osteoarthritis Cartilage*. 2004; 12(3):177–190. [PubMed: 14972335]
18. Stahl R, Luke A, Li X, Carballido-Gamio J, Ma CB, Majumdar S, Link TM. T1rho, T2 and focal knee cartilage abnormalities in physically active and sedentary healthy subjects versus early OA patients--a 3.0-Tesla MRI study. *Eur Radiol*. 2009; 19(1):132–143. [PubMed: 18709373]
19. Carballido-Gamio J, Bauer J, Lee KY, Krause S, Majumdar S. Combined image processing techniques for characterization of MRI cartilage of the knee. *Conf Proc IEEE Eng Med Biol Soc*. 2005; 3:3043–3046. [PubMed: 17282885]
20. Gluer CC, Blake G, Lu Y, Blunt BA, Jergas M, Genant HK. Accurate assessment of precision errors: how to measure the reproducibility of bone densitometry techniques. *Osteoporos Int*. 1995; 5(4):262–270. [PubMed: 7492865]
21. Eckstein F, Gavazzeni A, Sittek H, Haubner M, Losch A, Milz S, Englmeier KH, Schulte E, Putz R, Reiser M. Determination of knee joint cartilage thickness using three-dimensional magnetic resonance chondro-crassometry (3D MR-CCM). *Magn Reson Med*. 1996; 36(2):256–265. [PubMed: 8843380]
22. Benner T, Wisco JJ, van der Kouwe AJ, Fischl B, Vangel MG, Hochberg FH, Sorensen AG. Comparison of manual and automatic section positioning of brain MR images. *Radiology*. 2006; 239(1):246–254. [PubMed: 16507753]
23. Itti L, Chang L, Ernst T. Automatic scan prescription for brain MRI. *Magn Reson Med*. 2001; 45(3):486–494. [PubMed: 11241708]
24. Pekar V, Bystrov D, Heese HS, Dries SP, Schmidt S, Grewer R, den Harder CJ, Bergmans RC, Simonetti AW, van Muiswinkel AM. Automated planning of scan geometries in spine MRI scans. *Med Image Comput Comput Assist Interv Int Conf Med Image Comput Comput Assist Interv*. 2007; 10(Pt 1):601–608.
25. Blumenfeld J, Carballido-Gamio J, Krug R, Blezek DJ, Hancu I, Majumdar S. Automatic prospective registration of high-resolution trabecular bone images of the tibia. *Ann Biomed Eng*. 2007; 35(11):1924–1931. [PubMed: 17705036]
26. Rajapakse CS, Magland JF, Wehrli FW. Fast prospective registration of in vivo MR images of trabecular bone microstructure in longitudinal studies. *Magn Reson Med*. 2008; 59(5):1120–1126. [PubMed: 18421688]
27. Bystrov, D.; Pekar, V.; Young, S.; Dries, SPM.; Heese, HS.; van Muiswinkel, AM. Automated Planning of MRI Scans of Knee Joints. SPIE Medical Imaging; San Diego: 2007.
28. Glaser C, Mendlik T, Dinges J, Weber J, Stahl R, Trumm C, Reiser M. Global and regional reproducibility of T2 relaxation time measurements in human patellar cartilage. *Magn Reson Med*. 2006; 56(3):527–534. [PubMed: 16894587]
29. Eckstein F, Westhoff J, Sittek H, Maag KP, Haubner M, Faber S, Englmeier KH, Reiser M. In vivo reproducibility of three-dimensional cartilage volume and thickness measurements with MR imaging. *AJR Am J Roentgenol*. 1998; 170(3):593–597. [PubMed: 9490936]
30. Carballido-Gamio J, Bauer JS, Stahl R, Lee KY, Krause S, Link TM, Majumdar S. Inter-subject comparison of MRI knee cartilage thickness. *Med Image Anal*. 2008; 12(2):120–135. [PubMed: 17923429]
31. Eckstein F, Burstein D, Link TM. Quantitative MRI of cartilage and bone: degenerative changes in osteoarthritis. *NMR Biomed*. 2006 Nov; 19(7):822–54. [PubMed: 17075958]

Figure 1.
Scanning Procedure for the prospective registration

Figure 2. Comparison of baseline images to follow-up with and without registration. (a & d) high-spatial resolution baseline SPGR (b) high-resolution follow-up without registration (c) subtraction of baseline from follow-up without registration (e) high-resolution follow-up with registration (f) subtraction of baseline from follow-up with registration.

Figure 3.
Difference images with (left) and without (right) distal femur region selection for metric calculation in registration algorithm.

Table 1

WORMS scoring of patients

Patient	# 1	# 2	# 3	# 4	# 5
Knee	Left Knee	Left Knee	Left Knee	Left Knee	Right Knee
Effusion	0	0	1	0	1
Loose Body	0	0	3	0	0
ACL	0	0	1	0	0
PCL	0	1	1	0	0
Patellar Tendon	0	0	0	0	0
Popliteal Tendon	0	0	0	0	0
Meniscus					
Medial	0	0	5	0	1
Lateral	0	0	0	0	0
Cartilage Lesions					
P	0	0	5	2	0
T	0	0	5	0	0
MFC	0	0	5	0	0
LFC	0	0	3	0	0
MT	0	0	5	0	0
LT	0	0	1	0	0
Bone Marrow Edema					
P	0	0	0	2	2
T	0	0	0	0	0
MFC	0	0	1	0	3
LFC	0	0	0	0	0
MT	0	0	2	0	0
LT	0	0	0	0	0
Subcondral Cyst					
P	0	0	0	0	0
T	0	0	0	0	0
MFC	0	0	1	0	0

Patient		# 1	# 2	# 3	# 4	# 5
Knee		Left Knee	Left Knee	Left Knee	Left Knee	Right Knee
	LFC	0	0	0	0	0
	MT	0	0	0	0	0
	LT	0	0	0	0	0
Osteophytes	P	0	0	7	0	0
	T	0	0	7	0	0
	MFC	0	0	7	0	0
	LFC	0	0	7	0	0
	MT	0	0	7	0	0
	LT	0	0	7	0	0

Table 2

Coefficient of Variation (CV %) for cartilage volume, thickness, and T₂ relaxation measurement for each of the five compartments: Medial/Lateral Femur Condyle (MFC/LFC), Medial/Lateral Tibia (MT/LT) and Patella (P).

Volume	LFC	LT	MFC	MT	P
Without Registration	10.2%	6.1%	8.3%	10.1%	1.4%
With Registration	3.5%	3.2%	5.6%	6.4%	2.9%
Thickness					
Without Registration	3.2%	4.6%	3.2%	5.8%	2.1%
With Registration	4.0%	4.5%	2.2%	5.1%	1.5%
T ₂ Relaxation					
Without Registration	2.6%	3.1%	7.5%	11.3%	2.3%
With Registration	1.5%	3.5%	5.9%	5.8%	3.2%

Table 3

ICC values for cartilage volume, thickness, and T_2 relaxation measurement for each of the five compartments: Medial/Lateral Femur Condyle (MFC/LFC), Medial/Lateral Tibia (MT/LT) and Patella (P).

Volume	LFC	LT	MFC	MT	P
Without Registration	0.830	0.930	0.957	0.918	0.992
With Registration	0.984	0.984	0.975	0.970	0.995
Thickness					
Without Registration	0.830	0.930	0.972	0.956	0.988
With Registration	0.908	0.736	0.962	0.966	0.995
T_2 Relaxation					
Without Registration	0.898	0.752	-0.002	0.329	0.880
With Registration	0.974	0.812	0.427	0.826	0.880