Spatial Analysis Of Articular Cartilage In MR Knee Images Through The Development Of A Two-Channel Template

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Disclosures: Study funded by NIH/NIAMS (1R21AR074094).

INTRODUCTION: Osteoarthritis (OA) creates a massive health burden on the global population, with a total number of prevalent cases sitting at close to 530 million people in 2019. Magnetic resonance (MR) imaging is a common tool used to study OA due to its high soft tissue contrast and its ability to effectively visualize articular cartilage affected by OA. While this is an effective technique, differences in personal anatomy and variability in MR image coordinate systems make it challenging to accurately align and compare spatial changes in articular cartilage across individuals, limiting the ability to detect consistent patterns in large cohorts or at the population level. To get around this problem, many MRI-based studies segment images into regions of interest (ROIs) or utilize anatomical standardization of a population of images. Anatomical standardization via template allows for voxels from individuals to be placed on a common coordinate system defined by the template to study population data in the context of the template anatomy. This method – statistical parametric mapping (SPM) - allows for the analysis of statistically significant ROIs to not be restricted to predetermined regions or those that fail to be identified due to the lack of dominance within a predetermined ROI. This has been an effective technique in studying functional MRI and PET signals in the brain, but the knee has proved to be slightly more difficult to standardize due to greater variations in anatomy between individuals. In this study, we propose a two-channel method of constructing an anatomical knee template utilizing both MR knee images and bone label images segmenting the tibia and femur to facilitate the goal of a higher detail spatial analysis of the cartilage surface. Using this template, we will also show the ability to register multiple MR imaging modalities to the anatomical template regardless of resolution or signal values.

METHODS: ***Image Acquisition*** Double echo steady state (DESS), T1ρ MAPSS, and single echo spin echo T2 MR knee images were taken on a 3T Magnetom Prisma (Siemens) with a 15-channel Siemens knee coil (TX/RX Knee Coil 15 FLAIR 3T) during the same scan session. Quantitative T1ρ/T2 relaxation maps were fit to the MR signal equation via linear regression in the logarithmic space from four-dimensional T1ρ/T2 volumes containing four different relaxation times (spin lock(T1ρ)/spin echo(T2)). ***Bone Labeling*** DESS knee images were used to label the tibia and femur, critical structures in the knee registration workflow. This labeling was done via a 55-layer U-net image segmentation network trained on 46 investigator labeled DESS knee images and binary label maps in a train/validation/test split of 40/5/1 images. ***Knee Template Creation*** The knee template was created as an anatomical average of 21 DESS uninjured knee images using Advanced Normalization Tools (ANTs) (University of Pennsylvania) that minimized the deformation distance between the calculated anatomical template and all individual DESS images. The workflow utilized two image channels, the DESS image and the bone label image defining the tibia and femur, in a greedy B-spline symmetric image normalization deformable registration through five iterations (Figure 1). ***Registration of Individual Knee to Two-Channel Template*** Registration of an individual subject's knee to the template utilized ANTs in a three-step transformation process (rigid, affine, deformable) to determine a deformable mapping from its intrinsic coordinate system (subject space) to the template coordinate system (template space). Transformations were calculated by finding a deformable mapping that, when applied, maximized the mutual information between the DESS image and the anatomical template. Four T1ρ/T2 relaxation time volumes were then warped with the calculated transform to fit the template and used to calculate a quantitative T1ρ or T2 map in the template space. ***Validation of Template Effectiveness*** Five subject's T1ρ and T2 3D quantitative relaxation maps were warped into the space of the anatomical template. Binary label maps defining tibial and femoral cartilage were created using the same U-net segmentation network this time trained on 34 investigator labeled DESS knee images in a train/validation/test split of 30/3/1 images. Femoral and tibial cartilage of the template was then labelled in the same manner in template space. Subject 3D binary label maps were then transformed into template space utilizing the previously calculated deformable mappings. Knee cartilage anatomy as defined by the subject's DESS derived binary label map was evaluated for shape consistency with the template anatomy via a DICE score. Scores for subjects (n=6) were then compared via a two sample t-test with DICE scores calculated between the subject space label maps and the template label maps in template space to determine if the deformable mapping effectively moved the individual's cartilage shape toward the calculated standardized anatomy.

RESULTS: The four-dimensional T1ρ and T2 volumes were effectively warped into template space (Figure 2). The average DICE score of individual's template space cartilage anatomy with the template cartilage was 0.723 ± 0.02. This was a significant ($p = 7.35e-7$) difference from the DICE score between the average individual's subject space cartilage anatomy and the template cartilage of 0.144 ± 0.117.

DISCUSSION: When the final quantitative T1ρ/T2 map is fully warped, it mimics the anatomical structure of the template with the DESS image resolution – anatomically standardizing the cartilage in the T1ρ/T2 map of a subject's individual knee as seen via DICE scores. The DICE scores also became far more consistent between subject and template as seen by the decrease in standard deviation (0.02 vs. 0.117) after subject's anatomies were placed in template space, indicating a more consistent spatial shape and location. The most consistent and clean transformation of the cartilage is at the bottom of the femoral condyle and the top of the tibial condyle while cartilage located towards the anterior/posterior sides of the femoral condyle resulted in slightly more blurring in the template cartilage anatomy (Figure 3). This can be attributed to the anatomical variation in individual subject's knees. Some individuals had significant variations in femoral condyle shape compared to the sample average. Also, separate from femoral condyle shape, the extent of certain individual's cartilage along the anterior/posterior side of the femur varied greatly from the sample average. This variation in condyle shape and cartilage extent may lead to a less defined soft tissue-cartilage interface in the template on the anterior/posterior sides of the femoral condyle (Figure 3). Conversely, the ends of condyles, where the distance between the femur and tibia was much more consistent between individuals, led to a more defined soft tissue-cartilage interface in that area of the template. Despite this, the T1ρ/T2 map was able to be successfully warped in most cases to match the cartilage anatomy to that of the template despite the differences in intra-slice (0.4375mm x 0.4375mm to 0.3125mm x 0.3125mm) and inter-slice (4mm to 1mm) resolution. The method of transforming and averaging a sample set of MR knee images and bone labels created a two-channel knee template allowing for the anatomical standardization of an individual subject's knee. This standardization ultimately allows for the future goal of creating a more spatially specific analysis of the cartilage surface over a population.

SIGNIFICANCE/CLINICAL RELEVANCE: Using SPM in the knee, we can provide more detailed spatial analysis of the articular cartilage than confining ourselves to predefined areas. This will potentially give more insight into how tibial and femoral articular cartilage respond to changes in kinematics caused by ACL injury and reconstructive surgery, thus shedding light on mechanisms behind posttraumatic OA commonly correlated with this injury.

IMAGES AND TABLES:

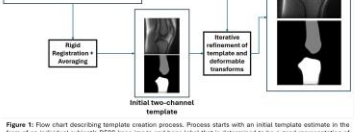

Figure 1: Flow chart describing template creation process. Process starts with an initial template estimate in the form of an individual subject's DESS knee image and bone label that is determined to be a good representation of the population's average knee anatomy. All 21 DESS knee images and bone labels are then rigidly registered to these initial estimates and averaged to form an initial estimate of the template. The 21 DESS knee images and bone labels are then warped via a deformable transform towards this estimate and then averaged together to form the 1st iteration of the template. This process is repeated (minus the initial rigid registration and averaging) four more times until the final template of the DESS image and bone label is created.

Figure 2: A) Unwarped quantitative T1rho relaxation time map of the knee. B) Quantitative T1rho relaxation time map of the knee warped to the template space. C) Two-channel knee template for reference. The unwarped knee in A retains its original anatomy. However, when warped, the knee anatomy becomes slightly wider and condyle shapes change to more closely match that of the knee template.

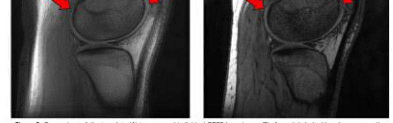

Figure 3: Comparison of the template (A) to a warped individual DESS knee image (B). Areas labeled with red arrows are the posterior and anterior sides of the femoral condyle. These areas of the cartilage show slightly more blurring along the cartilage-tissue interface in the template than the cartilage towards the ends of the condyle between the tibia and femur. Because of this blurring, the warping of the cartilage in the individual DESS image does not quite match up with the cartilage in the template as these regions display noticeably thicker cartilage than the anatomy of the template. This is once again contrasted with the tibial cartilage and cartilage at the bottom of the femoral condyle, which match up well with the cartilage in these areas of the template. It is also worth noting that the patellar cartilage (which was not a focus of this study) is also not well defined in the template, which could contribute to some of these inaccuracies in the warped image.