Detecting statistically significant changes in cartilage thickness with sub-voxel precision

J. G. Raya[1], A. Horng[2], L. König[3], M. F. Reiser[2], and C. Glaser[2]
[1]Josef Lissner Laboratory for Biomedial Imaging, University of Munich, Munich, Germany, [2]Department of Clinical Radiology, University of Munich, [3]Technical University of Munich

Introduction: MRI-based quantification of the cartilage thickness is a robust and well validated technique for the assessment of cartilage degradation in osteoarthritis [1], and for the analysis of cartilage deformations after exercise [2]. Nowadays changes in cartilage thickness are evaluated by comparing averaged thickness over regions defined on an anatomical basis [1]. However, the combination of high-field MRI, sub-voxel segmentation techniques and the use of registration methods allow an accurate voxel-based detection of changes in cartilage thickness. The aim of this work was to establish a method to track statistically significant changes in the cartilage thickness in longitudinally acquired datasets based on the measurement of the errors in thickness.

Methods: To detect significant changes in the thickness at a voxel-basis in longitudinally acquired datasets a good knowledge of the errors in thickness is mandatory. Errors are calculated with repeated measurements on healthy volunteers (n = 10, (26±4) y). Each volunteer underwent four imaging sessions in a 3 T-MRI scanner (Magnetom Verio, Siemens Healthcare, Erlangen, Germany) at four different time points. Images were acquired sagittally to cover all cartilage plates (femur, tibia lateral and medial and patella) using a 3D T_1-weighted FLASH sequence with water-excitation pulses (TE/TR = 7.2/14.2 ms, flip angle = 15°, matrix = 512×512×56, resolution=0.31×0.31×1.5 mm³, GRAPPA acceleration factor=2, 24 reference lines, bandwidth = 130 Hz/pixel, acquisition time = 5:34 min). Segmentation of all cartilage plates was performed using an in-house written semiautomatic segmentation program, which allows sub-voxel segmentation and demonstrated in phantom measurements an accuracy better than 9 µm [3]. For each voxel of the bone-cartilage interface (BCI) the cartilage thickness was calculated as the minimum distance to the articular surface (AS). The four BCIs obtained from the same cartilage plate of each volunteer were pairwise registered (6 different pairwise registrations) using a rigid 3D registration method with sub-voxel accuracy [4]. After registration, there are two thicknesses associated to each voxel at the BCI: the original thickness and the thickness of the registered datasets. All pairs of thicknesses of the same cartilage plate of all patients were pooled together according to the original thickness in units of 0.1 mm. The standard deviation of the differences in thickness measured for each groups is a measurement of the error in thickness. If the difference in thickness after registration exceeds two times the standard deviation, a significant (P<0.05) change has occurred. The method was used to assess significant changes in cartilage thickness in five volunteers, which were asked to squat for 20 min. Volunteers were imaged before and directly (<1:30 min) after squatting. Maps of significant changes were calculated for each cartilage plate. Changes in thickness were assessed with the significant change in volume (sCV), i.e. the change in volume caused by the voxels whose thickness changed significantly.

Results: Fig. 1A shows the calculated error (standard deviation) for each cartilage plate. These errors include all sources of errors (registration, segmentation, thickness calculation…) and range between one third of and slightly more than the voxel size, thus demonstrating the power of working with a sub-voxel precision. Errors of around 1 voxel size occurred only for voxels with thickness lower than 0.8 mm, which were located at the periphery of the cartilage. These regions were difficult to segment because of partial volume effects. This was especially accentuated for the patellar and the medial tibial cartilage due to the angulation of the images. In the volunteers examined before and after squatting (Fig. 1B) a significant decrease on the lateral facet of the patellar cartilage (averaged over all volunteers sCV = -68.6 mm³ corresponding to -2.25% of the volume) and in the lateral femoral condyle (mean sCV = -30.3 mm³ corresponding to -1.34% of the volume) was observed. The averaged sCV in all other compartments was lower than 0.4% of the cartilage volume, thus indicating not systematic pattern of deformation.

Conclusions: Working with sub-voxel precision on high-field images of the cartilage allow detecting changes in the cartilage morphology at scales lower than a voxel size, so that datasets can be analyzed on an anatomical basis. The use of the techniques presented here could improve our knowledge of the natural history of OA and our understanding of the mechanical loading of the cartilage.

References:

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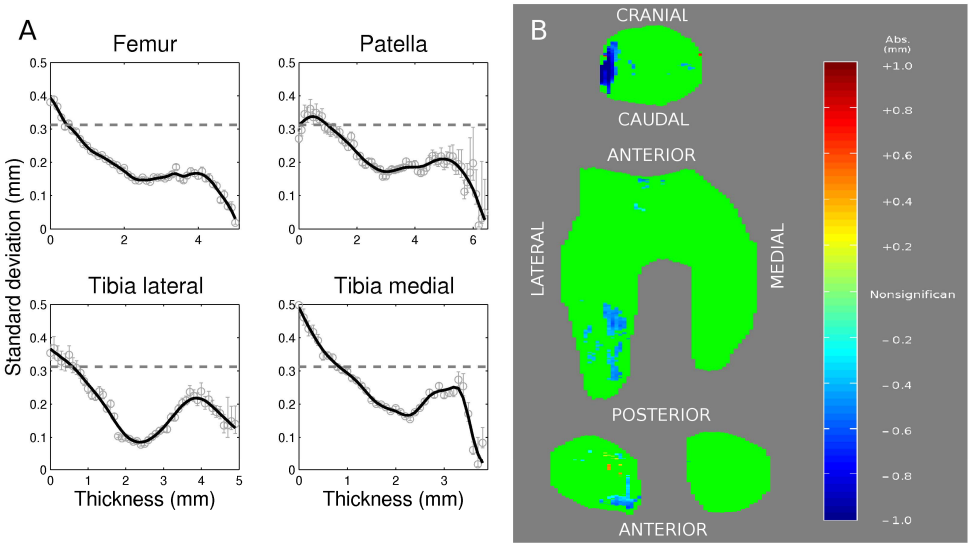

Figure 1. 1A. Error in thickness obtained for each cartilage plate as a function of the cartilage thickness. Circles represent the measured error and the errorbars the 95%-confidence interval of the error. Measured points have been fitted by a spline for practical use (black line). The dashed line represents the voxel-size (0.31 mm). **1B.** Example of the significant (P<0.05) changes observed in one of the volunteers. Green represents no significant changes. A significant reduction of the cartilage thickness between 0.4 and 0.9 mm was found in the lateral extreme of the patellar cartilage, in the medial part of the lateral femur condyle and in the anterior part of the lateral tibial cartilage.