## Interpatient analysis of T2 and thickness of the human patellar cartilage with hierarchical clustering

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Purpose: To investigate the value of hierarchical clustering for interindividual analysis of T2 and thickness of human patellar cartilage.

**Subjects and Methods:** Anatomical images for measurement of patellar cartilage thickness were acquired in 10 healthy volunteers with a T1-weighted FLASH sequence. T2-maps were calculated from images acquired with a fat-suppressed multi- echo sequence. A field of view of  $16 \times 16 \text{cm}^2$  and a spatial resolution of  $0.6 \times 0.6 \times 3 \text{mm}^3$  were used in both sequences. Each volunteer was measured at 7 consecutive times.

After segmenting the patellar cartilage in all acquired data sets, cartilage thickness and T2 maps of cartilage were calculated. All 7 data sets of each volunteer were registered using a rigid registration algorithm and afterwards divided into the same number of regions: 9 in the cranio-caudal (CC) direction, 4 in the anterior-posterior (AP) direction and 8 in the left-right (LR) direction for T2. Combining the regions defined in the three directions each of the 10 patellar cartilage plates was divided into  $9 \times 4 \times 8 = 288$  subregions, which included in average 71 voxels (data combined from the 7 measurements). For the cartilage thickness a similar procedure was used dividing the bone cartilage surface of each volunteer into  $8(CC) \times 9(LR)$  regions.

Each subregion is characterized by the normalized distribution density of the parameter (T2 or thickness) from all voxel included in this subregion in the 10 volunteers. The similarity between two regions can be defined as the sum of the product of their normalized distribution densities, which ranges between 0 and 1. This similarity measure contains no spatial information and permits grouping elemental regions by hierarchical clustering. Clustering consistency was assessed with the cophenetic correlation coefficient ( $\rho$ ), which is 0 for inconsistent and 1 for consistent clustering. Significance of clusters was assessed with a Kolmogorov-Smirnov statistical test.

**Results:** Clustering of the patellar cartilage based on T2 ( $\rho$ =0.85) is shown in Fig.1A-B. Clusters are spatially grouped although similarity does not contain any spatial information. The distribution of T2 values of the clusters was pair wise significantly different (p<0.005). Even more, patellar cartilage was principally clustered in the AP direction as expected from the T2 distribution from the bone cartilage interface to the articular surface (Fig 1A). The central part of the patellar cartilage exhibits the lowest T2 values with the lowest dispersion. The bone-cartilage interface and the articular surface show larger T2 variability than in the central part.

Clusters based on thickness ( $\rho$ =0.92) correctly trace the patellar geometry (Fig.1C-D). Thickness gets maximal in the central area of the patella and rapidly decreases towards the periphery (Fig.1C). Low-thickness areas have large variability whereas central areas are not affected by large deviations. As in the case of T2, clusters are spatially grouped and the distribution of thickness of the different clusters are pair wise statistically significant (p<0.005).

**Conclusions** Hierarchical clustering allows regional interindividual characterization of patellar cartilage T2 and thickness. It may provide insight into interindividual differences and in their relationship to structural properties of the cartilaginous tissue.



**Figure 1**: A. Mean T2 profile of the volunteers (solid lines) from the bone-cartilage interface (distance 0) to the articular surface (distance 1). The dotted line represents the average across all volunteers and the dashed lines the 95% confidence interval. B. Representation of the clusters found with hierarchical clustering. Colors are used for differentiation of clusters. C. Example of a thickness map of one of the volunteers. Red color corresponds to high and blue to low thickness. D Representation of the clusters obtained from cartilage thickness data. Colors are used for cluster differentiation.