Knee Osteoarthritis Progression Evaluated by Magnetic Resonance Imaging and a Novel Quantification Software Tool

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Introduction

Osteoarthritis (OA) is a prevalent disease characterized mainly by cartilage degradation. There is no known cure for OA. However, research is under way to find a therapeutic agent that will slow or stop the progression of the disease. Unfortunately, evaluating the efficacy of such agents is not an easy, straightforward process. Presently, the gold standards to evaluate the progression of knee OA are either complex radiographic methods for measuring joint space width, such as the Buckland-Wright method, or Arthroscopy. On the surface, these methods would seem reliable and sensitive to changes, but they have such large variability that studies need thousands of patients followed over many years to bring reliable results.

In this abstract, we show the first application of a method to quantify OA progression that combines high resolution MRI and active contour segmentations and registrations.

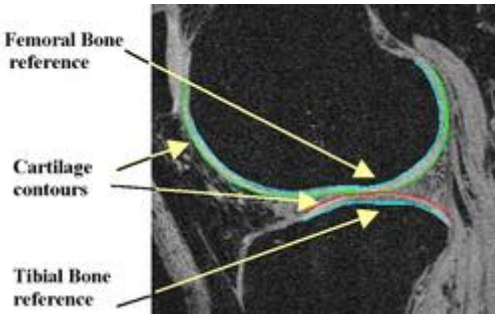
Methods

1. MRI: In addition to standard clinical MR acquisitions, each patient has a high resolution 3D scan. This is an optimized 3D FISP acquisition with fat suppression. All parameters were set to produce images with highest cartilage contrast and SNR within a reasonable acquisition time: TR=42ms, TE=7ms and flip angle=20°, 98Hz per pixel bandwidth, matrix size 410x512 and the field of view was set at 160mm and was rectangular whenever possible. Finally, we had ~110 1.0mm thick partitions for a total acquisition time of 24 to 31 minutes.

We kept a strict positioning and immobilizing protocol to reduce the chances of movement during this long acquisition. Movement has not been a problem and, in the hundreds of scans we have made in the last 2 years, very few had to be redone.

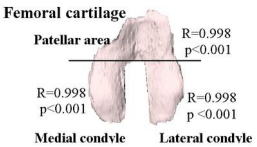
Two small high precision geometrical phantoms are positioned around the knee to monitor eventual changes in the scanner gradient calibrations.

2. Cartilage segmentation: We use a 3 step method. First, the bone/cartilage interfaces (tibial, femoral and patellar) are delineated using a sub-pixel accuracy active contour method[1,2]. The process is semi-automatic to allow reader interventions for difficult areas.



Second, the cartilage/tissues interfaces are delineated in a similar way. Last, when all the segmentations are done for all a patient's visits, the bone segmentations of the first visit are chosen as references and registered onto each visit. It is then possible to build a 3D model of the knee and automatically compute the cartilage volumes and thicknesses for all regions.

Results



1. Test-retest: 12 patients with symptomatic OA of the knee had 2 MRI at 1 to 2 hours interval. The segmentations were done in a random order. The resulting volumes were compared using correlation analysis with the results shown above. We can see that the correlations between the 2 scans are excellent in all areas.

2. Cartilage volume losses (in %): 35 patients with symptomatic OA of the knee were scheduled to have 3 MRIs : baseline, 6-month and 1-year follow-ups. Inclusion/Exclusion criteria similar to RCTs on knee OA. Internal compartment with joint space width between 2 and 4 mm on semi-flexed standing X-rays. Treatment according to standard care.

The cartilage was segmented in a random order, the reader being completely blinded as to the subject and visit. We show in the table below the change in % of the volume for the lateral and medial condyles, and for the global cartilage. We have used a paired t-test for the difference between the baseline and the 6 month measurement, and an anova test for repeated measurements to evaluate the cartilage volume progression using all 3 time points.

Cartilage volume loss per region (in %)

MRI Location	Mean (s.e.m.)	Median	t-value	p-value
0-6 months: n= 35				
Medial Condyle	-3.34 (0.96)	-2.12	-3.48	0.001*
Lateral Condyle	-2.11 (0.48)	-1.99	-4.35	0.0001
Global	-1.81 (0.43)	-1.49	-4.23	0.0001
0-6-12 months: n= 34				
Medial Condyle	-5.03 (1.33)	-2.39	-3.79	0.001**
Lateral Condyle	-2.65 (0.76)	-2.46	-3.49	0.001
Global	-2.38 (0.51)	-1.50	-4.64	0.0001

* paired t-test ** Anova Repeated Measures.

We have found that, as expected, the progression was largest for the central portion of the medial condyle. Less expected though, we have also found that the progression of the cartilage volume for the tibial plateau and the patellar area was not significant within the time frame of the study.

Discussion

Change of cartilage volume over time was our main criteria for disease progression evaluation. Comparing the patient to himself in a paired study is a statistically robust method to measure small changes.

The Reader has always been kept blinded as to the time sequence.

The assumption that the bone reference was stable has borne out to be mainly true. Qualitatively, only a few subjects had any observable osteophyte growth which, if taken in consideration, would reduce even more the cartilage volume.

Using our results, we calculated the minimum number of patients that would be required to measure the efficacy of a treatment in a 1 yr study. Using the expected Global-Cartilage Volume loss, the treatment efficacy power calculations (alpha=0.05, 1-beta=0.80) and a 40 % difference at 1 year yields N= 150 per group.

These results are quite promising. They indicate that cartilage volume losses are detectable and are statistically significant at 6 months and 1 year. Further analyses are needed, however, to establish the correlation of the cartilage losses with the clinical parameters. Nonetheless, the tool should be useful to evaluate the progression of knee osteoarthritis and the therapeutic efficacy of "chondroprotective" agents in clinical trials.

References

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