Disease modifying therapy of osteoarthritis (OA) represents an unmet clinical need. Appropriate outcome measures are required to robustly identify patients with different OA phenotypes who may benefit from specific therapies. APPROACH is an exploratory, European, 5-centre, 2-year prospective follow-up cohort study. It entails extensive clinical, imaging, biomechanical and biochemical parameters, in a cohort recruited using machine learning models based on retrospective patient data to display a high likelihood of radiographic JSW loss and/or knee pain over the course of the study.

**Purpose:**
(1) To report baseline test-retest reliability for cartilage thickness and composition (T2) by MRI, and (2) to identify potential differences between the participating sites.

**Methods:**

- 3 volunteers had both knees imaged at 4 of 5 sites (2 with 1.5T MRI: A Coruña and Oslo; 2 with 3.0T MRI: Leiden and Utrecht; Table 1).
- 26 participants across the 5 sites had test-retest MRI with repositioning of the knee (Table 2).
- Sagittal 3D WAT3, 3D FFE, or FLASH MRIs were acquired for determining cartilage thickness (57-120 1.5 mm slices; 0.31mm in-plane resolution; TR 17ms, TE 7ms, FA 12-15°; Fig 1).
- Sagittal multi echo spin echo (MSE) were acquired for generating T2 maps (21 3.0 mm slices with 3.5 mm gap; 0.27-0.31 mm in-plane; TR 2700ms, 5-7 echoes between 0-70ms; Fig 1).
- Segmentation of the total weight-bearing femoro-tibial joint was performed using Works 3.0 software (Chondrometrics GmbH, Airing, Germany) to measure cartilage thickness (1).
- 3 central MRI slices were analyzed in the medial (MFTC; Fig 1) and lateral femorotibial compartments (LFTC) for determining cartilage T2 (2), given lack of full anatomical coverage.
- Sets of inter-site comparison images and test-retest pairs, were read by the same reader, in 1 session, with reference to each other.
- The root-mean-square (RMS) standard deviation (SD) and coefficient of variation (CV%) were used to estimate measurement variability (3).

**Results:**

- 1 volunteer of the inter-site calibration study displayed motion in most images, so that only 4 knees of 2 participants were available (Table 1).
- The mean cartilage thickness in the MFTC was 3.00-3.11 mm across 4 sites, and that in the LFTC 3.33-3.47 mm (Table 1).
- The test-retest reliability was 45um (RMS SD) or 1.5% (RMS CV%) in the MFTC (range 1.2% to 2.9%) across the 3 sites. Test-retest errors in the LFTC were somewhat lower (Table 2).
- The inter-site variability (RMS SD and CV%) for cartilage thickness was somewhat greater than the average test-retest errors (Tables 1 & 2).
- The cartilage T2 was consistently longer in the superficial than deep layer, and consistently longer in the LFTC than in the MFTC (Table 1).
- There were differences in the T2 values between sites, exceeding the variability of the 4 knees.
- Longer TEs were apparent at 1.5T (A Coruña) compared with 3.0T (Leiden & Utrecht; Table 1).
- The inter-site variability of cartilage T2 was substantially greater than the T2 test-retest errors, and T2 test-retest errors substantially larger than for cartilage thickness (Table 2).

**Conclusions:**

In this pilot study, we have explored inter-site differences and test-retest reliability of cartilage thickness and composition (T2) analysis by MRI.

A limitation is the small sample, but few multicenter studies have thus far made an effort to ascertain measurement variability across sites.

Cartilage thickness measures displayed small differences between sites and were well reproduced with repositioning.

Cartilage T2 also showed reasonable test-retest reliability, but notable differences between sites, particularly between 1.5 and 3.0T.

Hence, in contrast to cartilage thickness measurement, T2 should not be pooled across sites for cross-sectional statistical analysis.

**References:**


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**Authors:**


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**Table 1: Inter-site Comparison**

<table>
<thead>
<tr>
<th>Site</th>
<th>Mean ±/SD at each site, and RMS SD (and CV%) across 4 of the 5 sites</th>
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**Table 2: RMS SD (%) of test retest acquisitions at each site, and across all 5 sites**

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**Image References:**

- Fig 1: Top row: Sagittal gradient echo MRI with water excitation for T1 suppression acquired for determining cartilage thickness; bottom row: Sagittal multi echo spin echo (MSE) acquired for generating the cartilage transverse relaxation time T2.
- Figure 2: Mean obtained by MRI for cartilage thickness and composition (T2) analysis by MRI.

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**Image Dimensions:**

- Image 1: 12x2901 to 191x3161
- Image 2: 38x2804 to 2384x3368
- Image 3: 59x282 to 218x380
- Image 4: 797x285 to 947x377
- Image 5: 1025x290 to 1156x372