modest reduction was observed in the LTP (p=0.047) and MTP (p<0.024) of the sham joints.

Conclusions: Clinical CT equipment permitted easy and non-invasive assessment of the BMD temporally (ACLT and sham) in an in vivo OA rabbit model.

312

AUTOMATIC KNEE CARTILAGE VOLUME QUANTIFICATION COMPARED TO JOINT SPACE WIDTH: BIOMARKERS OF LONGITUDINAL PROGRESSION?

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Purpose: For clinical studies, diagnostic and prognostic biomarkers are needed to select a population at the target stage of osteoarthritis (OA) with a high risk of progression; and an efficacy biomarker is needed to quantify the treatment effect. Currently, diagnostic and prognostic markers are available, but the development of progression biomarkers has proved to be challenging. The aim of this study was to evaluate whether a fully automatic cartilage volume quantification method is suitable as a biomarker for quantification of longitudinal progression of knee OA. For perspective, the results are compared to joint space width (JSW) quantification.

Methods: A study population was prospectively selected with 159 subjects with age 21 to 81 years (mean 56), BMI 19 to 38 (mean 26), and 48% female. Radiographs were acquired in a load-bearing semi-flexed position using the SynaFlex. MRI scans with near-isotropic voxels were acquired from a Turbo 3D T1 sequence on a 0.18T Esaote scanner (40° FA, TR 50 ms, TE 16 ms, scan time 10 min, resolution 0.7 x 0.7 x 0.8 mm³). Radiographs and MRI were acquired for both left and right knees at baseline (BL), after one week for a subgroup of 31 knees, and at follow-up (FU) after 21 months. After exclusion of 25 knees used for training of the computer-based method, 288 knees were in the study at BL and 245 knees at FU. Kellgren and Lawrence (KL) score and JSW were evaluated from the radiographs in the medial tibio-femoral compartment and tibial and femoral cartilage volume was quantified in the medial compartments by a fully automatic framework. JSW and volume were normalized by the tibial plateau width. At BL, the distribution of KL scores was (145,88,30,24,1) for KL 0-4. At FU, 25 knees had progressed from healthy to OA (KL>0) and 101 had remained healthy.

Results: At BL, the mean total cartilage volume was 6851 mm3 with a scan-rescan CV of 3.6% (since the method is fully automatic, the intra-scan CV was zero). The volume quantification allowed diagnostic separation at BL of healthy from OA (p<0.001) as well as from early OA (KL 1, p<0.01), see Figure 1. The BL volume predicted progression with borderline significance (p=0.08). Finally, the measured cartilage loss was higher for progressors than non-progressors (p<0.01), see Figure 2 (right). For comparison, JSW provided diagnostic separation of healthy from OA (p<0.001) and from early OA (p<0.01) - but allowed neither prognostic (p=0.3) nor progression separation (p=0.4, Figure 2 left).

Conclusions: Since JSW is an integral part of the KL score, the diagnostic ability was expected. However, the results indicated that the use of JSW as outcome measure in longitudinal studies is questionable. Cartilage volume was suitable as diagnostic marker and borderline suitable as prognostic. More importantly, the volume quantification showed increased cartilage loss for the OA progressors compared to the non-progressors (p<0.01). Thereby, the fully automatic computer-based method may be suitable for use as a treatment efficacy marker in longitudinal studies.

313

T2-STAR RELAXATION AS A MEANS TO DIFFERENTIATE CARTILAGE REPAIR TISSUE

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Purpose: The capability of magnetic resonance imaging (MRI) to visualize morphological and biochemical changes of articular cartilage give it the potential to follow-up different therapy procedures. A possible non-invasive statement about the produced cartilage repair tissue remains challenging and founded the need for modern evaluation techniques such as quantitative T2 mapping. However its clinical use with sufficient signal to noise and high resolution is limited by relatively long scan time. Underlying reliable results, T2 star mapping with its possible short scan time seems to offer a potential alternative. In a recent study of our group the accuracy and efficiency of the used T2 Star fitting algorithm was validated and the use of T2 star maps, created in clinically acceptable time frames and with resolutions that allow a detailed analysis of the cartilage, was shown. The goal of the presented feasibility study was to use T2 star mapping in the follow-up of two different cartilage repair procedures and to compare it to the established T2 mapping by a multi-echo spin-echo (SE) technique.

Methods: One group of 15 healthy volunteers and two patient
groups, each with 15 patients, after different surgical repair procedures (microfracture therapy (MFX) and matrix-associated autologous chondrocyte transplantation (MACCT)) were enrolled in this study. Ethical approval for this study was provided by the Medical University.

MR imaging was performed on a 3 T MR scanner. The protocol for the groups was identical and consisted of a multi-echo spin-echo (SE) sequence using 6 echoes for the standard T2 mapping and a GRE sequence using 6 echoes for assessment of the T2 Star maps. T2 and T2 star maps were obtained using a pixel wise, mono-exponential non negative least squares (NNLS) fit analysis. Regions of interest analysis for both T2 methods was evaluated and statistically analyzed.

Results: As control values healthy appearing cartilage could be assessed in all three groups and a strong and significant correlation between T2 and T2 star relaxation with a Pearson coefficient of 0.800 could be shown (p < 0.001). In the patient group after MFX lower T2 and T2 star values could be assessed (p < 0.05), whereas after MACT T2 and T2 star values showed no change (p > 0.05). Again a strong and significant correlation was found between T2 and T2 star. Furthermore spatial resolution was high enough for T2 and T2 star to assess zonal variation within healthy/control cartilage and cartilage repair tissue.

Conclusions: The use of T2 star allows maps to be created in clinically acceptable time frames and with resolutions that allow a detailed analysis of the cartilage. It is this detailed analysis which reveals most strikingly the differences between different cartilage repair techniques. However T2 star relaxation times were shorter whereas sex did not.

Following the final advantage of the T2-star method is that it is somewhat faster than the T2 method allowing a greater spatial resolution to be measured. In conclusion the preliminary results for our study show the possible value of T2 star as a diagnostic marker that is superior to both JSW and individual MRI markers.

Methods: The diagnostics markers were evaluated on a cross-sectional study including 159 subjects (age 21 to 81 years with mean 56, BMI 19 to 38 with mean 26, and 48% female). From these, 288 left and right knees were used for evaluation and 25 knees were used for training of the fully automatic computer-based framework.

The medial tibio-femoral compartments were quantified as follows. For each knee, radiographs were acquired in a load-bearing semi-flexed position (using the SynaFlex) and Kellgren & Lawrence score (KL) and JSW were determined by a radiologist. MRI scans were acquired using a 0.18T Esaote scanner (40° FA, TR 50 ms, TE 16 ms, scan time 10 min, resolution 0.7 x 0.7 x 0.8 mm³). From each MRI, the automatic framework quantified tibial and femoral volume, surface area, and homogeneity (a measure of structural integrity); and tibial thickness, surface smoothness, and congruity (a measure of the 3D surface curvature). All morphometric measures were normalized by the tibial plateau width. The aggregate markers were constructed by linear discriminant analysis (LDA) and evaluated in terms of p-value, sample size (n), and area under the ROC (AUC) for separation of the groups of healthy (KL 0) and OA (KL > 0) knees. P-values were estimated by MANOVA; n and AUC by repeated random sampling of disjoint training and test sets in order to avoid over-fitting in the LDA.

Results: AUC and n are listed in the table. For each MRI marker, only the compartment offering best separation is listed.

In addition, BMI and age allowed separation (p < 0.0001) whereas sex did not.

The figure below illustrates that compared to JSW, the MRI-based markers had less within-class variation - particularly so for the aggregate marker combined volume, homogeneity, and congruity.

314

AN IMPROVED DIAGNOSTIC MARKER OF KNEE OA BASED ON MULTIPLE CARTILAGE MARKERS FROM A FULLY AUTOMATIC MRI FRAMEWORK

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Purpose: Joint space width (JSW), age, and clinical symptoms are typically used to select study populations in clinical osteoarthritis (OA) trials. These criteria are essential for defining a population at the proper stage of OA that a potential treatment is targeting. A poor choice of selection criteria can cause a clinical study to fail - irrespective of the actual treatment effect.

Recently, much research has been focused on finding MRI-based markers that are more sensitive to OA related changes than JSW. The aim of this study was to investigate whether combinations of multiple imaging-based cartilage markers can provide an aggregate diagnostic marker that is superior to both JSW and individual MRI markers.

Methods: The diagnostics markers were evaluated on a cross-sectional study including 159 subjects (age 21 to 81 years with mean 56, BMI 19 to 38 with mean 26, and 48% female). From these, 288 left and right knees were used for evaluation and 25 knees were used for training of the fully automatic computer-based framework.

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Results: AUC and n are listed in the table. For each MRI marker, only the compartment offering best separation is listed.

In addition, BMI and age allowed separation (p < 0.0001) whereas sex did not.

The figure below illustrates that compared to JSW, the MRI-based markers had less within-class variation - particularly so for the aggregate marker combined volume, homogeneity, and congruity.