T2, dGEMRIC and gagCEST Cartilage Assessment in an in Vivo OA Canine Model

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Target audience: Musculoskeletal imagers, physicist developing sequences for imaging OA animal models, OA specialists.

Purpose: Approximately 5% of American adults over 25 years of age and 12% over 65 years have knee osteoarthritis (OA).[1] Early detection of cartilage damage is paramount to prevent further progression. Two main processes within the hyaline cartilage are considered early events in degeneration leading to OA: the loss of glycosaminoglycans (GAG) and loss of collagen network. Several biochemical magnetic resonance imaging (MRI) techniques have been proposed to assess these processes. Delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) is used to assess the GAG content, and T2 mapping is used to evaluate the water content and damage to the collagen network. A new promising technique that does not need contrast agent administration is CEST (chemical exchange saturation transfer). CEST has been reported to measure GAG (gagCEST). In areas of GAG loss, CEST and dGEMRIC are reported to produce reduced values, while T2 values are expected to increase in damage cartilage.[2] The dog is the most studied species with respect to models of OA.[3] The purpose of this study was to use biochemical quantitative articular cartilage imaging techniques (T2, dGEMRIC and gagCEST) to serially evaluate articular cartilage in an in vivo ACL transected OA canine model.

Methods: Five Beagles underwent ACL transection via arthroscopy. The opposite, non-injured joint was used as a control. The dogs underwent MRI using a 3T whole-body system and an 8-channel knee coil. Timelines included: before surgery, 3, 6 and 12 weeks after surgery. The following sequences were acquired: T2-mapping (multi-echo TSE; 10 echoes; TE=12 to 120 ms; TR=3000ms; acquired matrix =156x174; pixel size = 0.50x0.50 mm; slice thickness = 3mm; SENSE factor 3; NSA 2). dGEMRIC (multi-flip angle SPGR, flip angles = 4, 8, 12, 16, 20°, TR/TE=6.3/3.2 ms; 148x148; 0.61x0.61 mm; slice thickness = 3mm; NSA 20) a double routine dose of Gd-DTPA (0.2 mM/kg) was administered intravenously. GagCEST (multi-shot TSE factor 12; TR/TE = 1000/8ms; 148x140; 0.61x0.64 mm; slice thickness = 3 mm; SENSE factor 2; NSA 2; pre-saturation train of 16 block pulses, each 29 ms and 630°, 33 offset frequencies from -4 to +4 ppm). Each sequence was acquired as 4 independent stacks of 1 slice each in the sagittal plane in order to image a sample of each of the 4 condyles. Statistical analyses were performed (Student T-test, ANOVA and Pearson's correlations) using IBM SPSS statistics 22. In all tests, an effect was considered to be significant if the P-value is less than 0.05

Results: T2 (ms) was higher in the ACL transected knee than the controls at 3, 6 and 12 weeks ($P < 0.05$). At 6 weeks and 12 weeks, T2 was higher than baseline ($P < 0.05$) (Fig1). Lower dGEMRIC T1 (ms) was found in the ACL versus control knees at 12 weeks ($P< 0.05$). For ACL knees, lower T1 was found at 6 and 12 weeks ($P < 0.05$) when compared to the baseline (Fig 2). Interestingly, the control knees showed lower T1 value at 6 weeks in comparison to baseline ($P < 0.05$). Followed by a significantly T1 increased at 12 weeks compared with the baseline ($P < 0.05$). The magnetization transfer ratio (MTRasym) quantification for gagCEST was not statistically significant when control and ACL knees were compared, neither among timelines. T2 and dGEMRIC correlated moderately negative (Pearson's $r = -0.386$, $P = 0.01$)

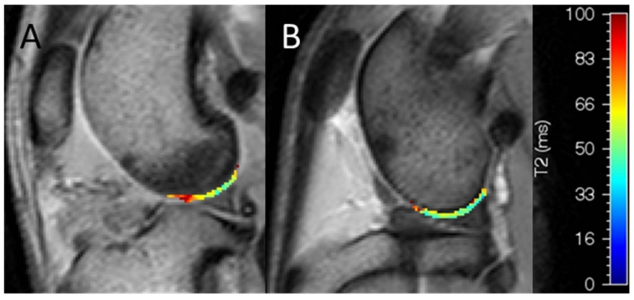

Fig 1. ACL transected left femoral condyle articular cartilage T2 ROI (A) showing a higher T2 than the control contralateral knee (B) at 12 weeks.

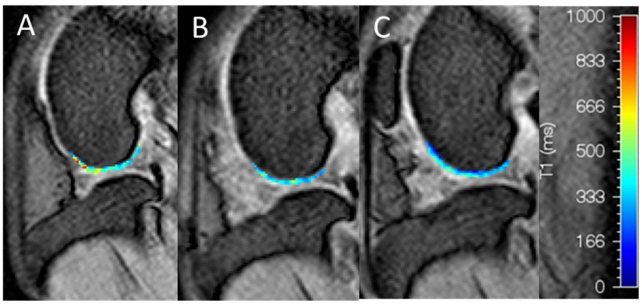

Fig 2. dGEMRIC ACL transected left femoral condyle articular cartilage ROIs at baseline (A), 6 weeks (B) and 12 weeks (C) showing a T1 (ms) decline.

Discussion: This study demonstrates that quantitative imaging techniques such as T2 and dGEMRIC can serially evaluate articular cartilage in an ACL OA canine model. The T2 increased in ACL knees as well as the T2 increased overtime might be due to an increase in water content as well as damage to the 3D collagen network in the ACL knees overtime. For dGEMRIC, lower T1 in ACL knees at 12 weeks, demonstrated evidence of GAG loss in the femoral condyle weight bearing articular cartilage. On the ACL knees, GAG loss was revealed over time with a lower T1 at 6 and 12 weeks in comparison with the baseline. The moderate negative correlation between T2 and dGEMRIC indicates that when the water content increases and the collagen network is damage, GAG content decreases. GagCEST was not significant lower in the ACL versus the control, neither showed any differences over time. This might be due to a lower signal to noise ratio (SNR) and limited scan time in an in vivo MRI under general anesthesia.

Conclusion: High field MRI T2 and dGEMRIC serially evaluated articular cartilage in an ACL OA canine model. They appear to be a potential biomarkers for an early OA diagnosis, prior to the expression of gross changes in cartilage, as well as OA assessment over time. GagCEST was not sensitive to detect GAG loss in ACL versus control neither overtime.

References:

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