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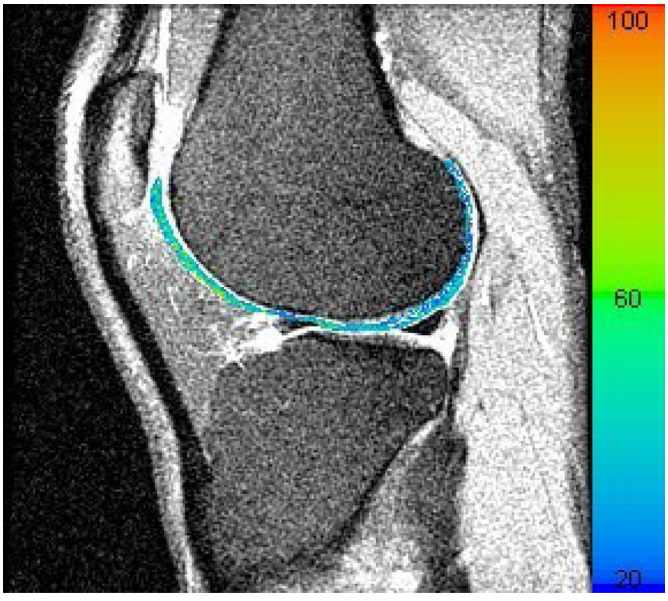
T2 MAPPING: HOW MANY ECHOES DOES IT REQUIRE?

J.K. Riek, V. Shah. *VirtualScopics, Inc, Rochester, NY,USA*

Purpose: The purpose of this study is to determine the difference between T2 relaxation times obtained from varying numbers of echoes. The results from phantoms and cartilage are compared between the varying number of echoes.
Methods: Phantoms comprised of varying concentrations of copper sulfate were placed on the anterior of the knee, just distal to the patella and offset laterally. The knee and phantom were then imagedd using a dual echo sequence, as well as multiple-echoe sequences. All imaging was performed on a GE Signa HDx 1.5T. Cartilage on one slice of the series was then identified, as well as the phantoms. T2 maps were calculated from the dual-echo using a least-squares linear fit to the natural log of the signal values. For the multiple-echo sequence, two methods were used - one where all the echoes were used in the estimate of T2, and one where the first echo was dropped. For very short T2 relaxation times (less than 2× the first echo time), all echoes were used for both cases. The mean and standard deviation of the T2 relaxation times in each of the regions was then calculated.
Results: Results are shown in the table below. The image shows an example of the T2 relaxation time for the cartilage calculated using the multiple-echo sequence.

Calculated T2 Relaxation Times

	Dual-Echo		Dropped First Echo		All Echoes	
	Mean	StdDev	Mean	StdDev	Mean	StdDev
Phantom 1	31.2	13.0	17.0	6.1	16.9	3.8
Phantom 2	41.9	4.8	44.2	9.3	39.1	4.0
Phantom 3	91.4	7.9	91.1	21.5	77.3	8.1
Phantom 4	240.3	75.7	159.9	50.2	131.0	20.4
Cartilage	50.3	19.4	37.5	17.4	36.2	13.9



Conclusions: Stimulated echoes play a large part in the variability of T2 measurements obtained from multiple-echo sequences. The effect of stimulated echoes can be mitigated in the pulse sequence by applying crusher gradients (GE's Cartigram sequence), or by ignoring the first echo in sequences that do not attempt to reduce the stimulated echoes. The disadvantage of ignoring the first echo is that it contains the most signal, and tissue with relatively short T2 relaxation times will not be estimated accurately. Using a dual-echo sequence, with a second echo that is not a multiple of the first echo, also eliminates the effect of stimulated echoes, but provides an estimate of T2 which is much more susceptible to noise. The values estimated for T2 are over-estimated for lower values of T2 because the second echo will hit the noise floor. The values are also over-estimated for areas of lower signal intensity for the same reason. This explains why the phantom values are very close between the multiple-echo sequence and the dual-echo sequence in the range of 40–90 ms, but the cartilage values in the same range are over-estimated by the dual-echo sequence.

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BONE AREA DEMONSTRATES CHANGE IN 3 MONTHS IN A VERY SMALL OA COHORT

M.A. Bowes †, P.G. Conaghan ‡. †*Imorphics Ltd, Manchester, United Kingdom;* ‡*Leeds Inst. of Rheumatic and Musculoskeletal Med., Leeds, United Kingdom*

Purpose: In order to stimulate the production of novel drugs and treatments of osteoarthritis (OA), responsive measures of structural progression are required. Ideally, proof of concept studies would take no longer than 6 months and require small cohorts. Changes in bone shape and size show promise as a potential progression biomarker, which can be accurately measured using modern magnetic resonance imaging (MRI) analysis. This post-hoc study analysed the changes in bone area of knee OA, using a convenience cohort selected for high risk of OA progression, with MR images acquired at 3 months and 6 months. A previous study using this cohort demonstrated no significant change in cartilage thickness in the medial femur or tibia at either time point
Methods: 27 females with knee pain, a body mass index (BMI) $\geq$ 25 kg/m^2, radiographic evidence of medial compartment OA and varus malalignment, were recruited in a multi-centre, non-randomized, observational cohort study at four sites in the US. MR images were acquired using 3T Siemens systems, using the Dual Echo Steady State water excitation acquisition sequence. Images were automatically segmented using active appearance models (AAMs) of the femur. The primary endpoint for this study was change of the area of subchondral bone in the medial femorotibial region (MF), with a secondary endpoint of change in the lateral femur (LF) area. Repeatability of the AAM method was assessed using double baseline images, using root-mean-square coefficients of variation (CoV), and smallest detectable difference (SDD), defined as the 95% limits of agreement; the mean of the differences ± 1.96 standard deviations. Change was assessed using a paired t-test of the change at each time point, compared with the average of the 2 baseline images.
Results: Repeatability for the MF region was 0.39% (CoV) and 1.1% (SDD), and for the LF region was 0.66% (CoV) and 1.9% (SDD). Change in bone area of the MF region (the primary endpoint) was statistically significant at both 3 months and 6 months, with the 6 month change being almost twice that seen at 3 months. At 3 months, mean change was 0.29% [95% confidence interval (CI) (0.57%, 0.02%)], and at 6 months 0.58% [0.30%, 0.85]. In the LF region, the changes were not significant at 3 months 0.24% [−0.81%, 0.66], but became significant at 6 months 0.51% [0.21%, 0.81] (see Fig. 1 for comparison with previous cartilage study).

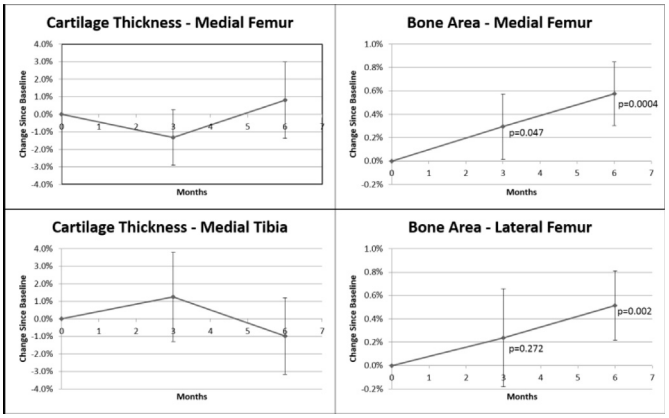

Fig. 1. Comparison of bone area change at 3 and 6 months with cartilage thickness change Charge from baseline was determined using pairwise t-test, and expressed as percentage of baseline value. P-values obtained from t-test are shown where $p < 0.05$

Conclusions: In this small cohort selected for high risk of OA progression, bone area changed in an approximately linear manner at 3 and 6 months from baseline. Bone area shows promise as a highly sensitive biomarker of OA progression, detecting change when current imaging outcomes are unable to do so, and provides a potential tool for small short-duration proof of concept studies.

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QUANTITATIVE EVALUATION OF SYNOVIAL MEMBRANE AND EFFUSION IN KNEE OSTEOARTHRITIS: NON-ENHANCED MR ASSESSMENT USING T2 MAPPING

J. Kim. *Osaka Univ. Graduate Sch. of Med., Osaka , Japan*

Purpose: Symptom and functional disability in knee osteoarthritis are mainly related with disorders in several principal structures such as articular cartilage, meniscus, ligament, and bone. Among those disorders, synovial inflammatory activities are strongly influential on severity of pain and prognosis of osteoarthritis. For assessment synovial inflammation, fluid-sensitive fat-suppressed MR proton density or T2 -weighted imaging were often employed. However, recent MRI studies indicated that contrast-enhanced MR sequences are necessary to distinguish between synovial membrane and synovial fluid in synovial inflammation, due to similar demonstration of synovial membrane and fluid on non-enhanced MR sequences. However, use of contrast-enhanced MR sequences had inherent disadvantages including cost and risk of acute adverse reactions. We hypothesized that T2 mapping of knee joints may be useful to discriminate synovial membrane and fluid without using contrast agent, due to remarkable variations of T2 values among those structures.
The aim of the current study was to assess volume of synovial membrane and synovial fluid on non-enhanced T2 mapping and examine associations of synovial inflammation activity with clinical symptom and structural disorders of the articular cartilage and meniscus.
Methods: MR imaging of the knee was obtained in 8 patients who showed knee mild or advanced osteoarthritis on plain radiographs and provided consent to this preliminary study. There were 2 males and 6 females, and the mean age of patients was 55 years (range; 40 to 70 years). 3D-FIESTA-C images (TR/TE:12.7/6.3 ms; slice thickness: 1.5 mm; FOV: 12 cm; acquiring time: 10 min 27 sec.) and 2D consecutive sagittal T2 map images (TR: 1500 ms; TE: 8 echoes between 10–80 ms; slice thickness: 3 mm; FOV: 12 cm; acquiring time: 12 min54 sec.) were obtained using 3.0-T MRI system. Previous studies showed mean T2 value of synovial fluid as approximately 650 ms ± 110 and that of articular cartilage or subcutaneous fat as approximately 50 ms ± 1 ms. Therefore, on T2 mapping images, we defined synovial fluid as region with T2 value more than 430 ms, and synovial membrane as region with T2 value between 100 ms and 430 ms. Manual segmentation of each synovial membrane and fluid was performed for joint cavities at the suprapatellar recess and femoro-tibial joints on a slice-by-slice basis using our custom-made software (Baum globe, Osaka Univ.), by one observer [Fig. 1(A, B and C)]. Then total volumes of synovial membrane and fluid were calculated by multiplication of each segmented region with the image section thickness. Ratio of synovial membrane volume to fluid volume (M/F ratio) was calculated in each patient. On 3D WATS images, knee structural disorder in meniscus and articular cartilage was assessed semiquantitatively using the Whole-organ Magnetic Resonance Imaging Score (WORMS). Volume of synovial membrane, synovial fluid, and M/F ratio were correlated with WORMS scores of meniscus or cartilage, and knee pain scores
Results: In all cases, synovial membrane and fluid were easily differentiated on T2 mapping images. Mean volume of synovial membrane was 13.4 ml ± 4.7. Mean volume of synovial fluid was 4.3 ml ± 2.3. Mean M/F ratio was 4.2 (range; 2.2 to 9.8). Mean WORMS score of cartilage was 36.6 ± 5.2, and mean WORMS score of meniscus was 4.38 ± 0.70. Volume of synovial membrane or fluid showed no significant correlations with WORMS score of meniscus / cartilage, or knee pain scores. However, there was positive correlation between M/F ratio and knee pain scores ($r = 0.577$, Fig. 2).
Conclusions: Volumes of synovial membrane and fluid in this study were calculated similarly to previous studies using contrast-enhanced MR sequences. Furthermore, high correlation between M/F ratio and knee pain score suggested that synovial membrane inflammation was more influenti l on pain worsening than fluid accumulation. Although further extensive studies for validation of segmented volume against the gold standard of reference are needed, T2 mapping of knee joint can be expected to provide reliable quantitative assessment of synovial

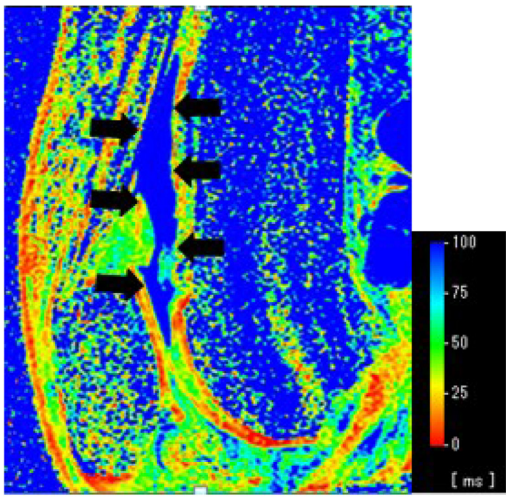

Fig.1A

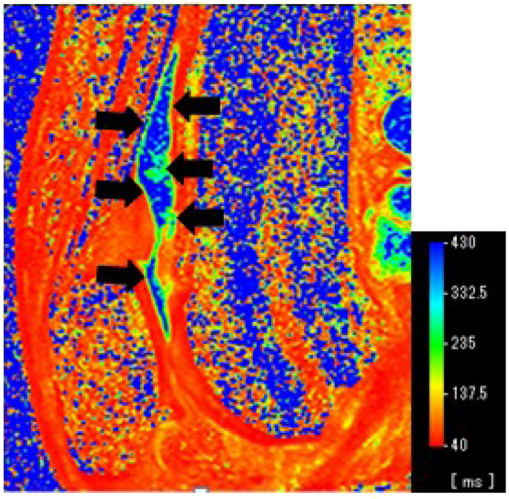

Fig.1B

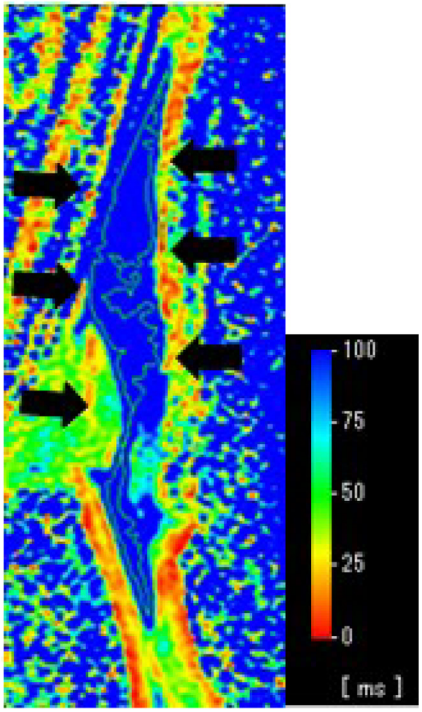

Fig.1C