

## Dynamic Contrast Enhanced MRI of Synovium in Rheumatoid Arthritis Patients: Response to Intra-articular Therapy and Relationship to Magnetization Transfer Contrast

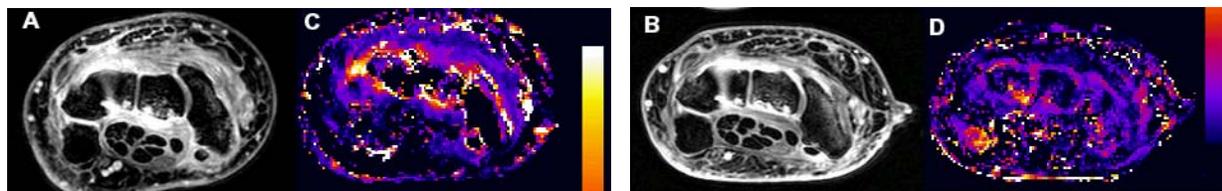
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**Purpose:** In patients with rheumatoid arthritis (RA) dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) may yield information about disease activity that is not reflected by changes in synovial volume [1]. We examined synovium after intra-articular therapy to document acute changes in standardized kinetic parameters derived from DCE-MRI. We also examined whether magnetization transfer contrast (MTC), as a potential marker of chronic synovial pannus, would bear relation to DCE-MRI features of diseased synovium.

**Methods:** 7 patients with advanced RA underwent MRI of the wrist at 3 Tesla (Phillips Intera). Imaging included T1 mapping and 3D-fast field echo (FFE) with and without off-resonance radiofrequency presaturation to generate MTC. Rapid (frame rate 4-6 sec) 3D-FFE imaging was performed during intravenous gadopentetate administration (Magnevist, 0.1 mmol / kg, 1.5 cc/sec). 4 patients were studied before and 1-2 weeks after intra-articular steroid administration. Synovitis was assigned an OMERACT [2] score.  $K_{trans}$ ,  $v_e$ , and  $v_p$  were calculated for synovial regions of interest (ROI) based on a two compartment pharmacokinetic model [3], using research software (General Electric, Cinetool). Maximal rate of enhancement (MRE) was also examined as an additional, semiquantitative enhancement parameter. Mean values for ROIs were analyzed, as well as pixel to pixel correlations within ROIs.

**Results:** The group means for  $K_{trans}$ ,  $v_e$ , or  $v_p$  measured in synovium at baseline were  $0.275 \text{ min}^{-1}$  (sd = 0.292), 0.181 (sd = 0.147), and 0.157 (sd = 0.181). The group mean for MTC at baseline was 26.3 (sd = 4.8). Baseline MTC was not correlated with MRE,  $K_{trans}$ ,  $v_e$ , or  $v_p$  based on ROI analysis. Pixel-wise correlations between MTC and these parameters were also negligible (range for mean Pearson  $r$ : 0.05, 0.15). MRE was not significantly correlated with  $K_{trans}$ ,  $v_e$ , or  $v_p$  (range for mean Spearman's  $r$ : -0.14, + 0.46) based on ROI analysis. The mean pixel-wise correlation between MRE and  $K_{trans}$  was 0.24 in synovial regions. Post treatment MRI demonstrated improvement in synovitis in all subjects (Figure 1). The mean change in OMERACT score was -2.2.  $K_{trans}$  decreased significantly ( $p < .05$ ) in 2 of 4 subjects based on ROI analysis. Changes in  $v_e$  were variable, decreasing significantly ( $p < .05$ ) in only 1 subject.



**Figure 1:** (a) Pre treatment contrast enhanced fat suppressed FFE MRI showing synovial proliferation. (b) Contrast enhanced FFE MRI showing reduced synovial volume after intra-articular therapy. (c) pre-treatment calculated  $K_{trans}$  map showing more elevated  $K_{trans}$  in deeper synovial regions. (d) post-treatment  $K_{trans}$  map. (Range for color bar = 0 to 1)

**Conclusion:** If chronic synovial inflammation results in a more fibrotic pannus, higher MTC might be associated with lower DCE-MRI markers of vascular density or capillary permeability. Our preliminary results, however, did not support this hypothesis. Any influence chronicity of synovial proliferation has on DCE-MRI characteristics remains difficult to distinguish from treatment effects. Intra-articular steroid therapy reduced synovial volume in all of our subjects on contrast enhanced MRI. There were corresponding but more variable decreases in  $K_{trans}$ . The high spatial variance of  $K_{trans}$  and other fitted parameters poses a substantial challenge to their robust summarization as outcome measures. The kinetic parameters we measured in synovium differ substantially from those reported in a recent study of juvenile rheumatoid arthritis [4]. The consistently high values we observed for  $v_p$  suggests that the validity of a two compartment model for the enhancement behavior of synovium warrants further study.

### References:

1. Cimmino MA et al. Arthritis Rheum 2003;48(5):1207-1213.
2. Tofts PS et al. J Magn Reson Imaging. 1999; 10:223-232.
3. Ostergaard M et al. J Rheumatol. 2003 Jun;30(6):1385-6.
4. Dagnachew WW et al. Magn Reson Med 2005;54:560-568.