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A Novel, Fully 3-Dimensional Dynamic Contrast MRI Method in the Hand Reveals Details of Synovial Inflammation and Provides a Sensitive Measure of Change

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Background: Quantitative analysis of tissue microvascular function using dynamic contrast enhanced MRI (DCE-MRI) shows promise for improved understanding of synovial pathophysiology in rheumatoid arthritis (RA). Most studies to date used 2D measures, and do not use physiologically-interpretable measures such as k^{trans}.

Objectives: Develop a 3D method for DCE-MRI, using validated quantitative parameters. Provide precise and consistent regions of interest (ROI) that are unaffected by hand position in the coil using active appearance models (AAMs)

Methods: MR images of the hand were acquired pre- and post-contrast (Gd) in 27 patients with established RA who had recently commenced the same biological therapy. Subjects were imaged at 0,3,6 months. MRI protocol included pre- and post-Gd high-resolution 3D FLASH acquisitions. DCE-MRI scan protocol included 3 FLASH images for baseline T1 measurement. 15 sequential volumes were acquired over 5 minutes (flip angle =35°), during which a bolus of gadolinium (0.1 mmol/kg) was administered at 2 ml/s at the beginning of the 5th volume measurement. Concentration of contrast agent was determined via T1 measurement. The Extended Kety model was applied to each voxel concentration-time series within ROIs, allowing voxelwise estimates of the capillary transfer coefficient of contrast agent (k^{trans}). Pre-contrast T1 images were searched using 3D AAMs to identify bones and capsular structures and generate 3D ROIs. Images from the dynamic series were registered to the high resolution pre-contrast images, providing standardised 3D ROIs for each of the RAMRIS joints. 3D visualisation was performed by dividing voxels into 3 k^{trans} bins: (High >0.2 min^{-1}, Medium 0.1-0.2 min^{-1}, Low <0.1 min^{-1}), displayed over AAM-identified bone surfaces. RAMRIS scoring was performed by a single experienced reader blinded to time point.

Results: Change in k^{trans} from baseline (95% CI) at 3 months was -0.007 min^{-1}(0.001,-0.015), p=0.06, at 6 months -0.012 (-0.004,-0.020), p=0.005 (Fig 1). This indicates a reduction in joint perfusion and capillary permeability associated with reduced inflammation. RAMRIS scoring showed no significant change at either 3 or 6 months. 3D visualisation of individual participants revealed extra details of the response to the biological treatment. For example, the total amount of synovial tissue with a k^{trans} value >0 decreased by 40% in 6 months in one participant (Figure 2); DCE-MRI revealed that most of the remaining “synovitis” at 6 months was of Low permeability class with almost all of the High permeability class of synovitis disappearing after drug treatment.

Conclusions: Novel 3D DCE-MRI measures are practical in RA MR imaging trials, and offer sensitivity to differential tissue response not visible with other methods. Full hand coverage maximises the potential to monitor disease, and allows the pharmacokinetic modelling of drugs used in RA.

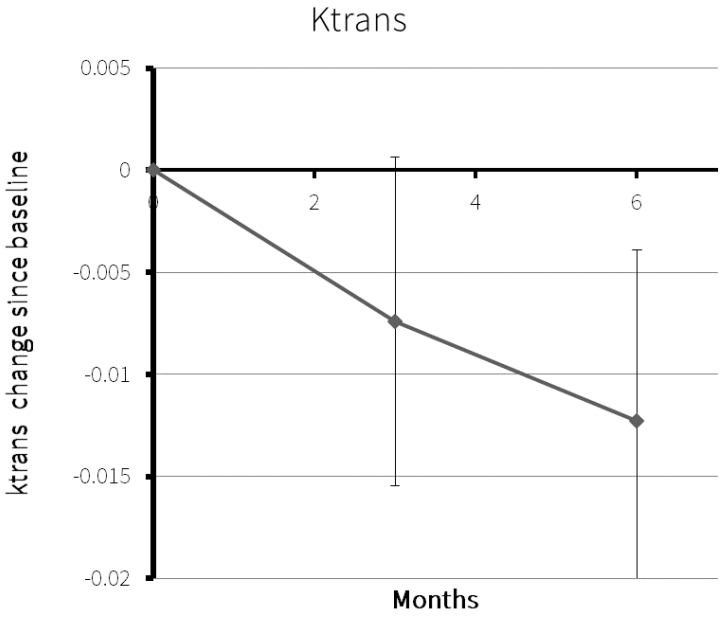

Figure 1 - Change from baseline. Change from baseline. Graphs show change in synovitis volume (microliters or mm3) for the two measures, showing 95% confidence limits for change from baseline using a paired t-test.

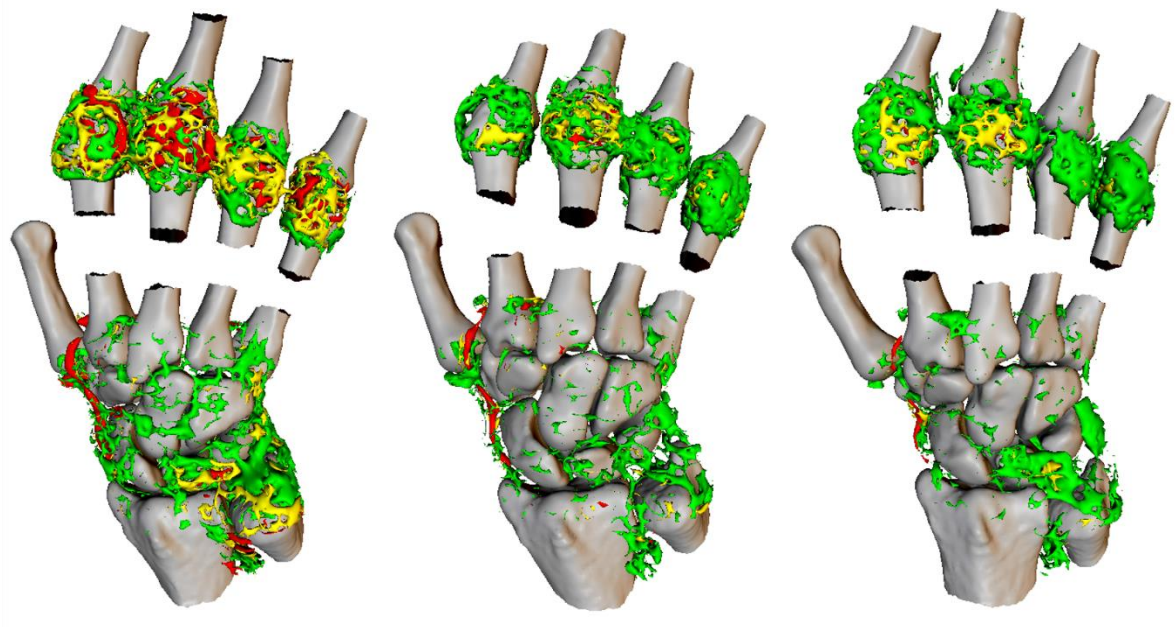

Figure 2 – Response of individual patient at 0, 3 and 6 months following biological treatment. Voxels are coloured based on k^{trans}. Red (high) >0.2 min^{-1}, Yellow (medium) 0.1 - 0.2 min^{-1}, Green (low) <0.1 min^{-1}. At 6 months synovial volume has decreased by around 40%, but remaining tissue is less permeable than the tissue at baseline.