Dynamic Contrast Enhanced MRI of rheumatoid arthritis and anti-TNFalpha treatment.

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Introduction.

Dynamic contrast enhanced MRI (DCE-MRI) has been used in rheumatoid arthritis to assess disease activity, progression and response to treatment, including anti-TNFα drugs[1]. A technique to detect an early response would be useful because routine clinical assessment of anti-TNFα therapy is not performed until 3 months of treatment. Analysis of DCE-MRI data to yield values for underlying parameters including the volume transfer constant (K^{trans}), the fractional extravascular extracellular space (v_e) and the fractional plasma space (v_p) is widely performed for tumour characterisation [2]. The aim of this work is to use these techniques to determine how soon after starting treatment DCE-MRI can detect a response to anti-TNFα drugs in the inflamed synovium.

Methods

The wrists and metacarpophalangeal (mcp) joints of 10 patients with longstanding, active rheumatoid arthritis were imaged before (twice) and at 1, 2 and 4 weeks after starting anti-TNFα therapy.

Imaging was performed at 3T using a quadrature, transmit-receive coil which could image the wrist and mcp joints of one side simultaneously.

T2 weighted, fat suppressed turbo-spin-echo images were acquired with 2mm slice thickness, 0.5mm in-plane resolution, TR=4500ms, TE=33ms and 2 mins acquisition time.

3D FLASH images with TR=4.5, TE=2ms, voxel size 1mm and 13s acquisition time were acquired with nominal flip angles (α) of 3°,10°,20°,30° and 60°. To compensate for the rf field inhomogeneity, the ratio of the actual to nominal flip angle (k) was calculated from normal fatty marrow of known T_1 (365ms [3]) in the bones near the inflamed synovium by fitting to the equation for signal intensity in a FLASH image [2]:

$$\text{Signal Intensity} \propto \frac{\sin(ka).(1-e^{-TR/T_1})}{1-\cos(k\alpha).e^{-TR/T_1}} \qquad \text{Equation 1}$$

Once k was known, the same equation was used to calculate the T_1 of regions-of-interest consisting of inflamed synovium.

A dynamic series consisting of 24 sequential FLASH images with the above parameters and a 30° flip angle was acquired over approximately 5 minutes. An intravenous bolus of 0.1mmol/kg Gd-DOTA was administered immediately after the 4th image. From the fractional increase in signal intensity time t after contrast, $(S_t-S_0)/S_0$, the T_1 of the inflamed synovium at time t was calculated from equation 1. The concentration of gadolinium in the synovium $C_t(t)$ was calculated using the known relaxivity of Gd-DOTA. The concentration of gadolinium in blood in the radial artery was similarly calculated, using the known T_1 of blood. The plasma concentration of gadolinium $C_p(t)$ was calculated from this.

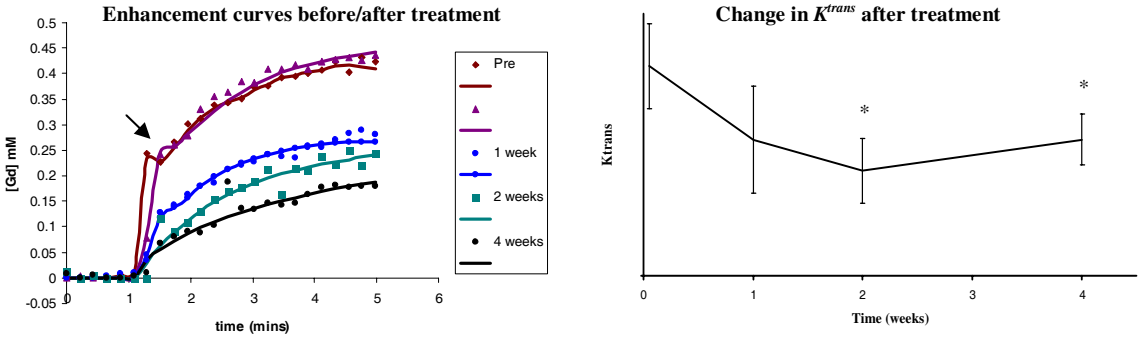
The synovial gadolinium concentration was fitted to the standard equation:

$$C_t(t) = v_p C_p(t) + K^{trans}\int_0^t C_p(t')e^{\frac{-K^{trans}(t-t')}{v_e}}dt' \qquad \text{Equation 2}$$

to yield values for K^{trans}, v_e and v_p. Since K^{trans} depends on local blood flow and vascular permeability it is expected to be a good marker for disease activity and was taken as the main outcome measure. The post treatment values were compared with the pre treatment values using the Wilcoxon signed rank significance test.

Results.

The graph on the left shows an example of the theoretical curve (line) fitted to the experimental data (points). There is a decrease in enhancement after treatment, including in the initial peak (arrow) corresponding to the left hand term in equation 2, the gadolinium in plasma in blood vessels in the inflamed synovium.



The graph on the right shows the change in K^{trans} with treatment across all patients. K^{trans} decreases with treatment and is significantly reduced by 2 weeks of therapy (p=0.02). The decrease is maintained at 4 weeks.

Conclusion.

Parametric analysis of dynamic contrast enhanced MRI in rheumatoid arthritis demonstrates a significant decrease in K^{trans} 2 weeks after starting anti-TNFα treatment.

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