Nonlinear modelling of Dynamic Contrast Enhanced Gd imaging data in Rheumatoid Arthritis: extraction of Ktrans

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Hypothesis: Dynamic Contrast Enhanced (DCE) Gd imaging data in Rheumatoid Arthritis (RA) can be analysed using the concept of transfer constant K^{trans} that is established in tumours

Introduction: Nonlinear K^{trans} estimation is a preferred way to analyse T_1w DCE Gd uptake data in tumours[1,2]. K^{trans} represents the combined effect of blood flow and capillary permeability in transferring Gd tracer to the Extravascular Extracellular Space (EES). This is an intrinsic quantitative biological parameter, in principle independent of the particular MRI machine and study centre; thus serial and multi-centre studies are possible. Recently DCE has been used in Rheumatoid Arthritis (RA) to study inflammatory locations, and analysed using linear modelling [3]. Nonlinear modelling allows the full dynamic range of the signal vs concentration curve to be exploited, thus increasing signal-to-noise ratio. Here we investigate the applicability of K^{trans} analysis to RA data.

Methods: **MRI:** Subjects had clinically active RA with synovitis at the imaged wrist. On a 1.5T Philips Achieva imager, with in-vivo 4 channel wrist array coil, volume datasets were collected every 8.4s, TR=3.6ms, FA=30°, TE=1.3ms, voxel size 0.8 x 0.8 x 0.6 mm, FOV=100mm with 80% RFOV, Gd dose 0.16 mmole/kg. ROI's were placed on the radial artery and several locations of visible tissue enhancement in the synovium.
Modelling: The signal from a spoilt gradient echo sequence is:

$$S(t) = \frac{S_0\left(1 - \exp(-R_1(t)\,TR)\right)\sin(\theta)}{1 - \exp(-R_1(t)\,TR)\cos(\theta)}; \quad R_1(t) = R_{10} + r_1 C(t) \quad \text{.....[1]}$$

θ is the FA, S_0 is the fully relaxed signal with θ=90°, $R_1=1/T_1$, $R_{10} = 1/T_{10}$, $T_{10} = T_1$ before injection

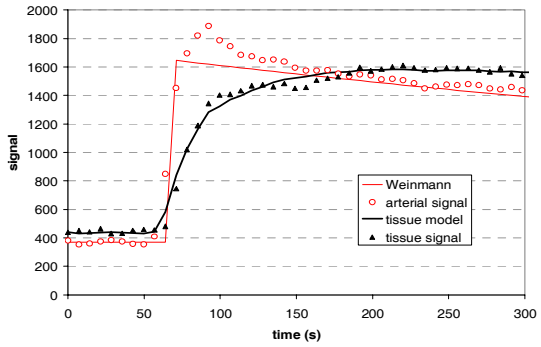
of Gd, r_1 is the relaxivity, C(t) is the Gd concentration. T_2* losses are ignored.

The plasma concentration C_p (i.e. the AIF) was estimated as follows: Eq [1] was fitted to the pre-Gd arterial signal by adjusting S_0., assuming T_{1blood}=1.4s. In a spreadsheet, numerical inversion of this eq then gives C_p, for any signal, using r_1=4.5 s^{-1} mM^{-1}; $C_{blood} = C_p$ (1-Hct/100), where Hct is the hematocrit (41%). The Weinmann expression for plasma concentration [4] was also plotted for comparison.

The tissue signal was then fitted using eq [1] and[5]

$$C_t(t) = v_p C_p(t) + K^{trans}\int_0^t C_p(T)\,e^{-k_{ep}(t-T)}\,dT$$

C_t = total tissue concentration; v_p = plasma volume; $k_{ep}=K^{trans}/v_e$; T_{10} was fixed at 1.0s [3]; S_0, v_p, K^{trans} and v_e were free parameters.



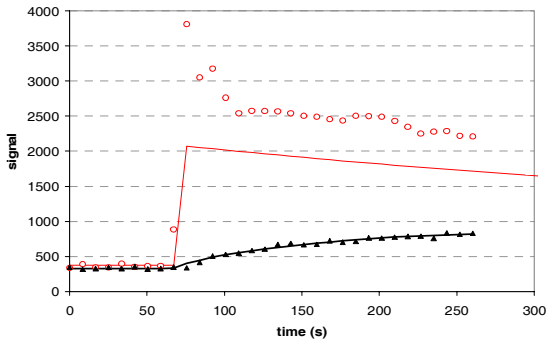


Fig 1: fits to nonlinear model, T_{10}=1.0s; left: fast enhancement, K^{trans}=0.51min^{-1}, v_e=65%; v_p=14%; right: slow enhancement, K^{trans}=0.11min^{-1}, v_e=28%; v_p=0%

Results: Typical slow and fast enhancement curves (from unregistered images) could be fitted by the model (fig 1), with no evidence of systematic error. Parameter estimates were very sensitive to the assumed value of T_{10}, as found previously[6]. Varying Gd injection times altered the shape of the AIF (fig 1 left: 33s, right: 7s). Images showed much detail (fig 2).

Discussion and Conclusions:
1. T_{10} measurement is essential to obtain absolute measurements of K^{trans} and v_e
2. Fixing T_{10}=1s gave a wide biological range of values of K^{trans} (0.1-0.8 min^{-1}) and v_e (25-95%)
3. Including IV tracer in the model improved the fit for the fast enhancer (fig 1 left part)
4. AIF partial volume error with this 3D sequence is small as judged by comparison with Weinmann values for C_p after initial bolus passage
5. Image registration improves image quality (data not shown)
6. Injection of Gd should be completed in 30s or less to capture rapid uptake (fig 1)
7. Cramer-Rao modelling will give the uncertainty in K^{trans} and v_e parameter estimates arising from image noise.
8. Scan-rescan reproducibility will give the minimum detectable difference in parameters

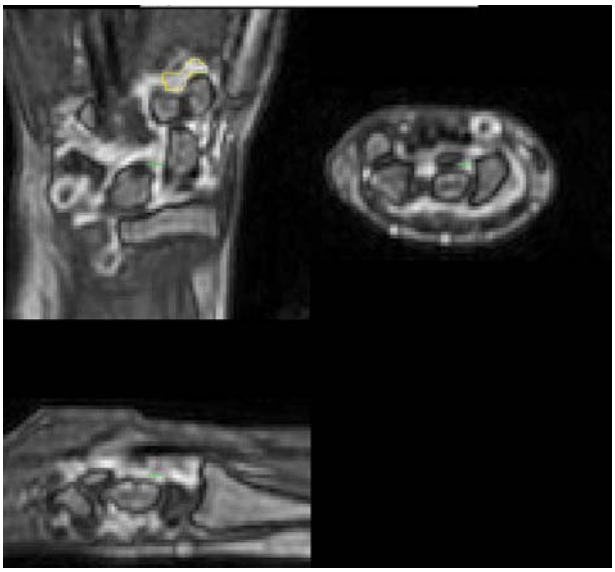


Fig 2: volume image dataset from the wrist

References:
1. Tofts JMRI 1999; 10:223
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3. Workie MRM 2005; 54:560
4. Tofts MRM 1991: 17:357
5. Tofts JMRI 1997; 7:91
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