Evaluation Of Activity In Crohn's Disease Using T1-Weighted Dynamic Contrast-Enhanced MRI.

K. V. Embleton[1], D. A. Nicholson[2], G. J. Parker[1], A. Jackson[1]

[1]Imaging Science and Biomedical Engineering, University Of Manchester, Manchester, United Kingdom, [2]Hope Hospital, Salford Royal Hospitals NHS Trust, Manchester, United Kingdom

Introduction

Crohn's disease is a chronic illness characterized by long periods of remission interspersed with new episodes of inflammatory activity Treatment of the disease requires monitoring of this inflammatory activity and drug effects upon it. The development of rapid MR acquisition sequences, combined with anti-peristaltic agents and bowel distension techniques, has allowed acquisition of high quality images of the small intestine. Although MRI without IV contrast is able to demonstrate bowel wall thickening, this may not give an accurate indication of current inflammatory activity due to fibrosis (1). Mural edema is assumed to be a more sensitive parameter for Crohn's activity and has been shown to be strongly associated with increased mural enhancement following IV administration of contrast agent. The highly vascularised nature of small bowel mucosa normally results in strong mural enhancement, however the additional enhancement in inflamed bowel may be explained by increased capillary leakage and accumulation of fluid in the interstitial space (2). Quantification of this contrast enhancement plays a central role in determining disease activity (1). The focus of this study is to apply T_1-weighted DCE MRI analysis using established kinetic models to Crohn's disease, in order to investigate their potential for use as surrogate markers for measurement of disease activity, essential in monitoring therapeutic effects.

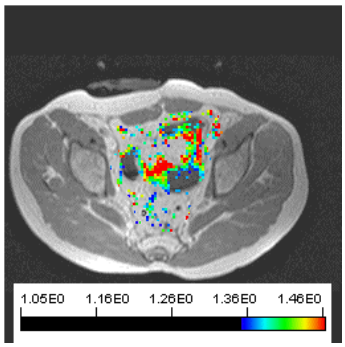
Method

Patients underwent a 4 hour fasting regime prior to examination (liquids were allowed up to 2 hours previously) followed by an oral bowel distension preparation consisting of 15ml Maxilon in syrup form 1 hour previous to the examination and 4 x 3.5g Ispaghula Husk (Fybogel, Reckitt Benckiser Healthcare, UK) in 250ml water, every 15 min, starting 1 hour previous to scan. Buscopan (20mg, IV) was administered immediately prior to acquisition of the dynamic series to reduce peristalsis. Patients were scanned in the prone position on a 1.5 T Philips MR system using a 3D T_1-weighted fast field echo (spoiled gradient echo) sequence (TR = 4.3 ms; TE = 1.21 ms). Images were acquired using flip angles of 2º, 10º and 35º with 4 averages to estimate baseline T_1. This was followed by a dynamic series in which 40 single average volumes (flip angle 35º) with a temporal resolution of 4.4 s. Image matrix for all scans was 128 x 128 in-plane, with 25 slices acquired using over-contiguous slicing. Early in the series 0.1 mmol/kg Magnevist (Gadopentatate, Schering) was administered as a bolus at 4 ml/s using a power injector. Custom-built software allowed analysis of the dynamic time series using the standard Tofts model(3), and the Tofts model extended to include vascular plasma volume (4). Arterial input function (AIF) was determined using an automated AIF identification algorithm (5).

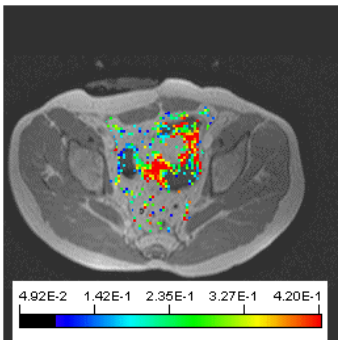
Results and Discussion

The sections covered by the dynamic sequence allowed AIFs to be measured from either the aorta or iliac arteries. The pharmacokinetic analysis allowed the production of maps of derived microvascular parameters. Figure 1 shows examples of these maps for the region of the abdominal cavity overlaid on morphological images.

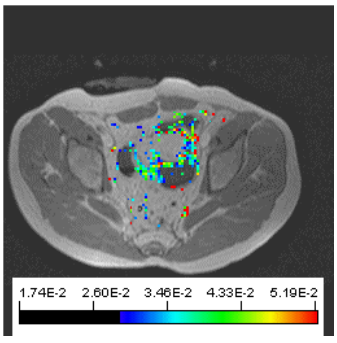
fig. 1a) Post-contrast WAVE SENSE image clearly demonstrating areas of inflammation



b) Parameter map of K^{trans} from extended Tofts model overlying FFE image of corresponding slice



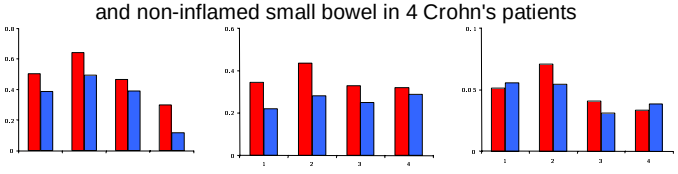
c) Parameter map of v_e from extended Tofts model (%)



d) Parameter map of v_p from extended Tofts model (%)

High values of K^{trans} (volume transfer constant) and v_e (fractional volume of extravascular extracellular space) corresponded with regions of inflamed bowel wall. Manual segmentation of higher resolution morphological images allowed derivation of separate regions of interest for inflamed and non-inflamed bowel wall. K^{trans} and v_e were both higher in inflamed tissue while the blood plasma volume (v_p) was not significantly different (fig. 2). This ability to quantify microvascular differences between Crohn's and healthy bowel indicates DCE-MRI as a potentially useful approach to generate markers of treatment efficacy.

Fig .2 Comparison of vascular parameters between inflamed (red) and non-inflamed small bowel in 4 Crohn's patients



k^{trans} v_e v_p

References

1. Schunk, KMD. *Topics in Magnetic Resonance Imaging* 13(6): 409–425, 2002.
2. Kettritz U, Isaacs K, Warshauer DM, et al. *J Clin Gastroenterol* 21:249–253, 1995.
3. Tofts PS, Kermode AG. *Mag Res Med* 17 357-367
4. Tofts, PS *J. Magn Reson. Imag*. 7, 91, 1997.
5. Parker, GJ, et al., *Proc. Int. Soc. Magn. Reson. Med.,* Toronto, 2003.

Acknowledgements

This work was supported by AstraZeneca Pharmaceuticals and a pump priming research grant form the Royal College of Radiologists.