DCE-MRI evaluation of microvascular abnormalities in the female pelvis

G. J. Parker[1], P. S. Murphy[2], B. Whitnall[1], C. E. Hutchinson[1]

[1]Imaging Science & Biomedical Engineering, University of Manchester, Manchester, United Kingdom, [2]Global Clinical Sciences, Pfizer GLobal Research & Development, Sandwich, Kent, United Kingdom

Introduction There is a need to characterise inflammatory conditions of the female pelvis, such as endometriosis, non-invasively in the clinical trial setting. Such a technique would permit serial analyses of disease for monitoring drug efficacy. Investigating symptoms of conditions such as endometriosis is currently undertaken with laparoscopy where a small laparoscope is inserted through the lower abdomen under general anaesthesia, a technique that is not readily compatible with a clinical trial. An alternative could potentially provide greater patient compliance whilst also providing improved objectivity. Dynamic contrast-enhanced MRI (DCE-MRI) offers a potential non-invasive window on assessment of treatment efficacy. Owing to the neo-vascularisation of endometriotic lesions (>3mm^3), monitoring with DCE-MRI may provide a sensitive index for assessing progression or regression of the disease. This is particularly true if early stage endometriosis (rAFS stage 1,2) is studied where small peritoneal lesions are beginning to express angiogenesis. Potentially, the temporal characteristics of contrast agent transfer between the blood pool and tissue could be modelled to estimate physiological parameters such as the endothelial volume transfer constant (k^{trans})[1]. Such measures could provide information related to the angiogenic status of a lesion.

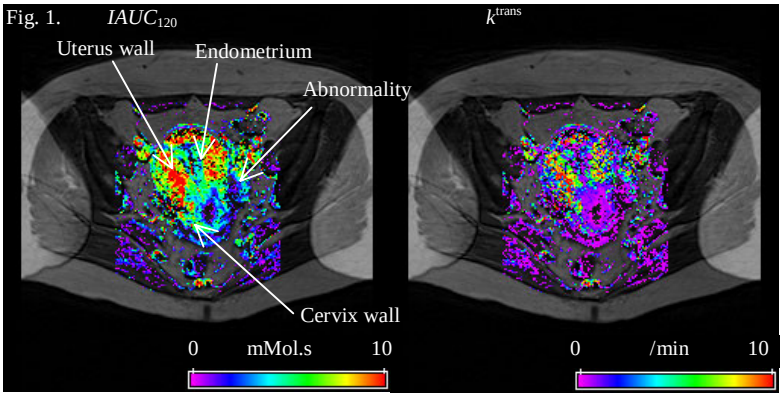
Patients 8 female patients of child bearing age and with a history of severe menstrual pain were enrolled in the study. All patients had peritoneal lesions with microvascular abnormalities indicative of endometriosis or other inflammatory processes, as demonstrated laparoscopically. Laparoscopic images were used to guide the placement of the MRI imaging volume. All MR imaging was performed during the proliferative phase of the menstrual cycle. The study was approved by the Local Research Ethics Committee.

DCE-MRI Protocol A strategy of volume coverage of the general region indicated by laparoscopy was followed to screen for possible microvascular abnormalities. This required a relatively large field of view and volume extent, leading to a trade-off of with temporal and spatial resolution to allow dynamic information content and signal to noise ratio to be maintained within the DCE-MRI acquisition. All data were acquired on a 1.5T Philips Intera system using the whole body coil (Q body coil) for transmission and reception. A baseline T_1 measurement consisted of 3 axial spoiled Fast Field Echo (gradient echo) volumes with flip angles 2, 15, 25 degrees, respectively and 8 NSA. The dynamic series consisted of 35 consecutively-acquired axial Fast Field Echo volumes with a flip angle of 25 degrees, 1 NSA, and a temporal resolution of ~9 s. Typical imaging parameters: FOV 305 mm × 267 mm; depth of coverage 56 mm; acquisition matrix approx 256 × 224 × 13, reconstructed matrix 256 × 256 × 25; reconstructed voxel resolution 1.19 mm × 1.19 mm × 2.25 mm; 6 pre-injection images; 0.1 mmol/kg Omniscan (Amersham Health) injected as a bolus (0.1 mmol/kg) using a power injector to deliver the bolus at 4 ml/s followed by a flush of saline at the same rate. Elliptical k-space sampling, partial Fourier encoding, and partial echo acquisition were used to improve temporal resolution. Hyoscine N-butylbromide was administered prior to DCE-MRI to minimise involuntary motion of the pelvic tissues. Signal intensity changes were converted to contrast agent concentration using previously described methods[2].

The following analyses were carried out in each patient: 1. T_1 assessment of normal and abnormal tissues; 2. IAUC analysis[3] of the change in contrast agent concentration over the first 60, 90, and 120 s post contrast agent arrival in the normal and abnormal tissues; 3. Kinetic modelling of contrast agent uptake using a two compartment model[4] to provide estimates of endothelial volume transfer coefficient, k^{trans}, and the extracellular extravascular volume, v_e. The T_1, IAUC, and modelling analyses were carried out using both parameter mapping and region of interest (ROI) analysis using locally-written software.

Results The data from 2 of the 8 patients were unsuitable for analysis due to a hardware or technical error during data acquisition. Microvascular abnormalities were identified on DCE-MRI in 4 of the remaining 6 patients; measurements were made in the uterine wall, endometrium, and cervix wall of all 6 successfully-scanned patients. Figure 1 shows maps of $IAUC_{120}$ and k^{trans} in one patient, clearly demonstrating the differing microvascular characterisitcs of the various tissues. No appreciable difference in native T_1 values was observable between *in situ* endometrium, uterine wall, cervix, and vascular abnormalities under ROI analysis. However, IAUC analysis and kinetic modelling both highlighted differences between *in situ* endometrium, uterine wall, cervix, and vascular abnormalities, with an indication that the abnormalities may be classified as either 'hypovascular' or 'hypervascular' types. The separation of tissue type was more pronounced with k^{trans} than with any of the IAUC analyses.

Fig. 1. $IAUC_{120}$ k^{trans}



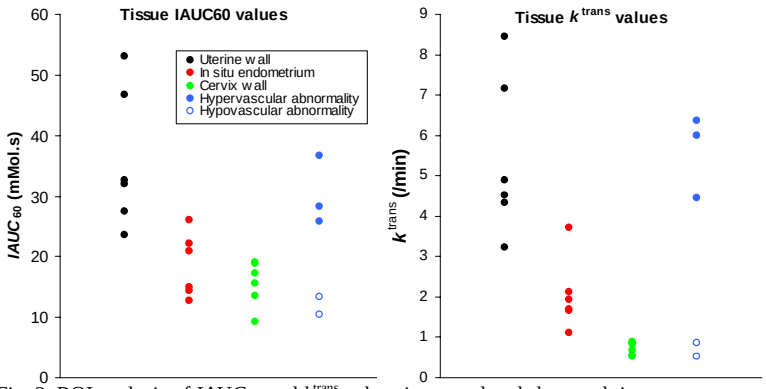


Fig. 2. ROI analysis of $IAUC_{60}$ and k^{trans} values in normal and abnormal tissues.

Discussion DCE-MRI is able to distinguish the microvascular characteristics of both normal tissues and inflammatory/vascular abnormalities in the female pelvis. The microvasacular characteristics of uterine muscle, endometrium and cervical tissue appear to be relatively consistent across the patient group, presumably partly due to the consistent timing of the data acquisition within the menstrual cycle. These findings demonstrate sensitivity of the technique to physiological differences (i.e. those between tissues), and, although it is not possible to infer reproducibility from these data, they do imply likely sensitivity to treatment-induced changes to microvascular characteristics in endometriotic and other tissues.

References

1. Tofts, P.S., *et al.*, *J. Magn. Reson. Imag.*, 10, 223, 1999.
2. Li, K.-L., *et al.*, *J. Magn. Reson. Imag.*, 12, 347, 2000.
3. Evelhoch, J.L., *J. Magn. Reson. Imag.*, 10, 254, 1999.
4. Tofts, P.S. and Kermode, A.G., *Magn. Reson. Med.*, 17, 357, 1991.

Acknowledgements

We are grateful to Martin Quinn for patient recruitment and for passing on details of the laparascopic evaluation. This work was funded by Pfizer.