Dynamic Contrast Enhanced MRI Evaluation of Small Bowel Crohn's Disease: A Correlation with Histopathologically quantified Microvascular Density

S. Punwani[1,2], M. Rodriguez-Justo[3], A. Bainbridge[4], E. De Vita[4,5], R. Greenhalgh[2], S. Halligan[1,2], and S. Taylor[1,2]

[1]Department of Medicine, University College London, London, United Kingdom, [2]Department of Radiology, University College London Hospital, London, United Kingdom, [3]Department of Histopathology, University College London Hospital, London, United Kingdom, [4]Medical Physics and Bioengineering Department, University College London, London, United Kingdom, [5]Medical Physics and Bioengineering Department, University College London Hospital, London, United Kingdom

Aim: Assessment of quantitative and semi-quantitative in-vivo DCE-MRI in predicting histopathologically quantified small bowel wall microvascular density in resection specimens from patients with known ileal Crohn's disease.

Introduction: In common with neoplastic disease [1,2], angiogenesis is increasingly recognised as a fundamental feature of Crohn's disease [3]. For example, increased microvascular density has been demonstrated in histopathological specimens taken from patients with Crohn's disease affecting the colon [4]. Imaging assessment of angiogenesis in tumours has been useful in the assessing tumour grade and treatment response [5]. Accurate in-vivo assessment of angiogenesis in Crohn's disease may therefore also prove useful in assessing disease activity and monitoring treatment. This study examines the relationship between histopathologically quantified microvessel density (MVD) and semi-quantitative (enhancement ratio (ERdyn) and slope of enhancement (SoE) [6]) and quantitative (volume transfer constant K^{trans} and the fractional volume of extracellular extravascular space, v_e) DCE-MRI parameters in patients with known ileal Crohn's disease, undergoing elective surgery for small bowel related complications.

Methods: Ethical permission was obtained. Nine consecutive patients (>16 yrs age) with a known previous histopathological diagnosis of small bowel Crohn's disease undergoing elective surgery for related complications were recruited. Patients were 'nil by mouth' for four hours prior to the study. Oral contrast (1200 mls of 0.2% locust bean gum + 2% mannitol) was administered 40 minutes prior to image acquisition. Intravenous spasmolytic (20mg Buscopan, Boehringer Ingelheim, Germany) was injected immediately prior to examination. MRI data were acquired on a 1.5T Siemens Avanto (Erlangen, Germany) using the manufacturer's body and spine array coils. HASTE and TrueFISP images were reviewed by a consultant radiologist and the diseased small bowel segment destined for surgical resection identified. For DCE MRI a 2D spoiled gradient echo sequence in the coronal orientation (TR/TE: 11/3.2 ms; flip angle 35°; field of view 360mm x 270 mm, in-plane resolution 1.45 x1.45 mm , slice thickness 6mm) was used. Data for T1 estimation was collected during a single breath-hold (flip angles of 5°, 10°, 35°). A further breath-hold allowed baseline data collection. A single dose (10ml) of Magnevist (Berlex Laboratories, NJ, USA) and saline chaser (10ml) was injected at 3ml/s immediately followed by the acquisition of single-slice DCE MRI data every 3 seconds during a 30s breath-hold. Further data was acquired during gentle breathing in 3-slice data sets (every 6 seconds) collected for 5 minutes. Regions of interest (ROIs) were manually placed in the abnormal bowel wall and shifted to keep the anatomical position constant during the free breathing time course. Signal enhancement curves corrected for contrast agent dose were used to extract SoE and ERdyn. The data was also modelled using the Kety equations [7] by assuming a population averaged arterial input function [8] to yield estimates of K^{trans} and v_e. Post surgical small bowel resection specimens were scanned to enable detailed imaging-histopatholgy matching, and histological sections were taken through the area of bowel corresponding to the MRI ROI placement site. Quantitation of mural microvascular density (MVD) was performed with CD34 (Fig 1) staining using the Chalkley point method [9]. Correlation between histopathological and MRI data was assessed using Kendalls rank correlation coefficient.

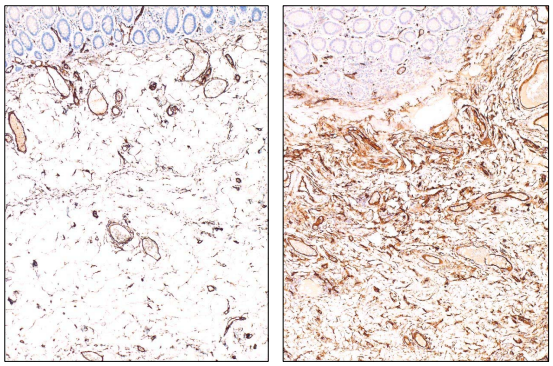
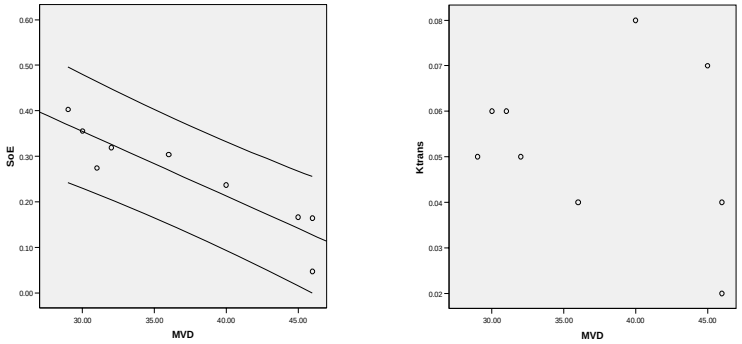


Fig 1: *Left* – Normal vessels (MVD=14); *Right* – Complex vascular architecture in Crohn's (MVD=44).

Results: The MVD ranged from 31 to 46 vessels/HPF, SoE from 0.05 to 0.40 kg/ml/s, ERdyn from 7.1 to 14.9 kg/ml, K^{trans} from 0.02 to 0.07 min^{-1} and V_e from 0.04 to 0.11. SoE was strongly negatively correlated with MVD (p=0.002) but there was no significant correlation between MVD and ERdyn (p=0.18) or quantitative MR parameters (K^{trans} and V_e, p=0.36 and 0.6 respectively).

Fig 2: *Left* – SoE vs MVD (95% CI illustrated); *Right* – Ktrans vs MVD



Conclusion: A strong negative relationship between slope of enhancement (SoE) and microvessel density (MVD) has been demonstrated. Increasing MVD in Crohn's disease may therefore be a response to reduced blood flow to the affected bowel segment. No significant relationship between K^{trans}/V_e and MVD was found, likely due to the dependence of these parameters on a complex set of physiological factors. Preliminary data presented in this paper suggest that SoE measurements maybe useful in assessing disease and monitoring anti-angiogenic therapy in patients with Crohn's disease.

References:. [1] Folkman J. Semin Oncol 2002; (6 Suppl16):15-18. [2] Folkman J. Eur J Cancer 1996; 32A:2534-2539. [3] Thornton M, Solomon MJ. Int J Colorectal Dis 2002; 17:287-297 [4] Danese S, Miquel S et al. Gastroenterology 2006; 130:2060-2073. [5] Goon PK, Lip GY et al. Neoplasia 2006; 8:79-88. [6] Florie J, Wasser MN et al. Am J Roentgenol. 2006 May;186(5):1384-92. [7] Kety S. Meth Med Res 1960; 8:223–227. [8] Parker GJM et al. Magn Reson Med 2006; 56:993-1000. [9] Salvato G.Thorax 2001; 56(12):902-906.