Location matched histological validation of MRI parameters relating to mural Crohn's disease activity.

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Aim: To validate proposed magnetic resonance imaging markers of Crohn's disease activity against a robust histopathological reference standard.

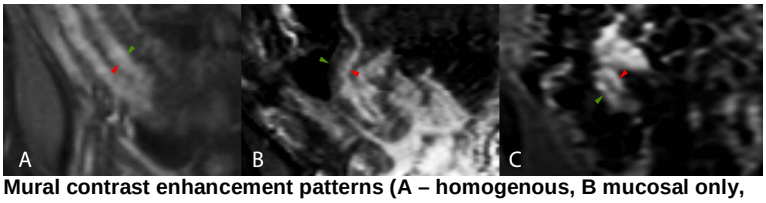
Introduction: Therapeutic strategy in Crohn's disease relies upon accurate characterisation of disease extent and activity. Whilst active inflammation may respond to medical therapy, established fibrotic disease often will not. Furthermore, potentially toxic immuno-modulatory medication requires regular intensive monitoring of treatment efficacy [1,2]. Currently, disease activity is largely based on a combination of clinically derived scores, biochemical markers and imaging via endoscopy and radiology [3,4]. In particular, symptom based scoring systems remain the current standard but the limitations of these scoring systems are widely acknowledged; patients with quiescent disease sometimes attract high scores and, conversely, disease activity may be underestimated in other patients [5]. Similarly, biochemical tests such as C-reactive protein are a useful adjunct but are not only non-specific, but may also fail to rise in the presence of active disease [6]. Specific findings on MRI have been proposed as accurate markers of disease activity, for example mural signal characteristics and contrast enhancement patterns [7]. The purpose of this study was to validate proposed MR imaging feaures of Crohn's disease activity against a robust precision matched histopathological reference standard.

Method:

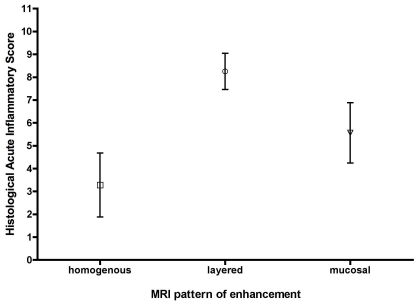
	Coronal / Axial HASTE	Coronal / Axial TrueFISP	Baseline VIBE	30s and 70s VIBE	Specimen HASTE
FOV (mm)	Variable	Variable	Variable	Variable	Variable
No. Slices	20 / 26	25 / 34	48	48	15
Stacks	1 / 4	1 / 2	1	1	1
TR (ms)	1200 / 800	4 / 4.2	7.2	7.2	1200
TE (ms)	86 / 86	1.7 / 2.1	2.4	2.4	84
Matrix	256x195	256x205	256 x 135	256 x 135	256x195
Slice Thickness (mm)	4 / 4	4 / 4	3	3	2
Slice Gap (mm)	5.2 / 4.2	5.2 / 5.4	0	0	0
Averages	1	1	1	1	1
Turbo Factor	195	-	-	-	195
iPAT	Grappa x 2	Not applied	Not applied	Not applied	Grappa x 2
Flip Angle	50° refocusing	46° refocusing	10°	10°	150° refocusing

Local ethics committee permission was obtained for this prospective study. Eighteen consecutive patients (mean age 34.6 yrs, 9 men) with endoscopically and histologically proven Crohn's disease who were scheduled for elective small bowel resection for related enteric complications were recruited. All patients underwent MRI enterography within 2 weeks of their surgery (mean time to surgery = 4 days, range 1 to 13 days) using a standard small bowel protocol. Images were acquired in the prone position using a 1.5T Siemens Avanto (Erlangen, Germany) magnet with the manufacturer's body and spine array coils. Axial and coronal Half Fourier Acquisition Single Shot Turbo Spin Echo (HASTE) and True Fast Imaging with Steady Precession (TrueFISP) images of the small bowel were acquired, together with coronal Fat saturated HASTE images (see table). Prior to intravenous contrast injection, breath hold coronal T1 weighted 3D fast low angle shot with a fat selective (VIBE – Volume Interpolated Breath hold Examination) images were acquired through the abdomen and pelvis. A single dose (10ml) of gadopentetate dimeglumine (Magnevist, Berlex Laboratories, NJ, USA) was injected into an arm vein at 3ml/s, followed by a saline chaser (10ml). Two further post contrast breath hold coronal VIBE acquisition were performed at 30 and 70 seconds post contrast. Within 24 hours of excision the unopened ex-vivo bowel specimen was scanned to allow precise anatomical matching of histopathology sections and in-vivo MR images. Using the specimen scan the study radiologist selected between 1 to 5 (median 3) sites within the abnormal bowel on the pre-operative MRI for detailed image analysis and subsequent histopathological matching. Wall thickness, mural and lymph node T2 signal (expressed as a ratio with CSF signal), gadolinium contrast uptake, enhancement pattern and mesenteric T2 signal were recorded at these sites from the pre-operative MRI. Histopathological grading of acute inflammation (AIS) (based on mucosal ulceration, oedema and quantity and depth of neutrophilic infiltration) and degree of fibrostenosis was obtained at each site and compared with MRI features using Spearmen, Pearson, student and Mann Whitney, linear regression and ANOVA testing.

Results: Histological AIS was positively correlated with mural thickness and T2 fat saturated mural / CSF signal intensity ratio ($p = 0.003$ and 0.006 respectively), but not mural enhancement at 30 and 70 seconds ($p = 0.650$ and 0.678 respectively). AIS was significantly higher at sites of layered mural enhancement (see figure below, $p = 0.003$), and also commonly present at fibrostenotic sites (75%). T2 fat saturated mural / CSF signal intensity ratio was significantly higher in histologically oedematous bowel versus non-oedematous bowel wall ($p = 0.009$). There was no correlation between any lymph node characteristics and AIS.



Mural contrast enhancement patterns (A – homogenous, B mucosal only, C – layered)



Conclusion: Increasing mural thickness, mural T2 signal intensity and layered pattern of enhancement reflect histological features of acute small bowel inflammation.

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