SHORT COMMUNICATION

Quantitative MRI of colonic mural enhancement: segmental differences exist in endoscopically proven normal colon

^{1,2}S PUNWANI, FRCR, PhD, ³R HAFEEZ, MRCS, ⁴A BAINBRIDGE, PhD, ³P BOULOS, FRCS,
^{1,2}S HALLIGAN, FRCR, MD, ⁵S BLOOM, MRCP, and ^{1,2}S A TAYLOR, FRCR, MD

¹Centre for Medical Imaging, University College London Hospitals, London, UK, ²Department of Radiology, University College London Hospitals, London, UK, ³Department of Surgery, University College London Hospitals, London, UK, ⁴Department of Medical Physics, University College London Hospitals, London, UK, and ⁵Department of Gastroenterology, University College London Hospitals, London, UK

Objectives: Abnormal contrast enhancement on MRI is advocated as a biomarker for inflammation in colitis, although the enhancement kinetics of normal colon are poorly described. Our purpose was to quantitatively assess mural enhancement in normal colon and test for intersegmental differences.

Methods: Eight patients without prior history of inflammatory bowel disease underwent standard MRI colonography followed by normal same-day colonoscopy. Acquired sequences included a volumetric interpolated breath-hold examination (VIBE) to encompass the whole colonic volume, performed at 5°, 10° and 35° flip angles for T_1 quantitation and then at a fixed 35° flip angle three times prior to and every 30 s following intravenous gadoterate meglumine for 220 s. Ascending colon, descending colon and rectal R_1 ($1/T_1$) was plotted against time. Mean pre-contrast R_1 , initial change of R_1 (ΔR_1), early and late “plateau phase” enhancement and the area under the R_1 –time (AUC– R_1) curve were compared between segments using the Student’s paired t -test.

Results: There was no significant difference of pre-contrast R_1 between segments ($p=0.49$ to 0.62). ΔR_1 was higher for ascending colon compared with descending colon ($0.0023 \pm 0.0012 \text{ ms}^{-1}$ vs $0.0010 \pm 0.0011 \text{ ms}^{-1}$, $p=0.03$). There was no significant difference for early or late plateau phase R_1 between colonic segments ($p=0.08$ to 1.00). AUC– R_1 was greater for ascending than descending colon (0.54 ± 0.19 vs 0.30 ± 0.14 , $p=0.03$).

Conclusions: Intersegmental differences in colonic enhancement are present and should be considered when interpreting differential segmental enhancement.

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MRI has shown considerable promise in quantifying inflammatory activity in Crohn’s disease and ulcerative colitis [1–3]. When applied to the colon, most workers have used the technique of MR colonography (MRC, *i.e.* distension of the colon usually via water enema) [1]. Various MRI parameters have been shown to correlate with disease activity, notably bowel wall thickness, T_2 signal and contrast enhancement pattern [2]. Absolute post-gadolinium enhancement remains more controversial, with some workers finding high

correlation [4], while others have found no relationship [5]. The reasons for this variability probably include differences in studied patient cohorts, applied standards of reference for disease activity (histological, biochemical, endoscopic or clinical) and methods of enhancement measurement (simple relative change in signal intensity at one time point, or more complex quantitative dynamic contrast enhancement techniques). However, the baseline post-contrast enhancement of normal (*i.e.* non-inflamed) colon has received little attention. There are good reasons why enhancement may differ among bowel segments. Anatomical differences exist in segmental blood supply; the right colon is supplied via the superior mesenteric artery, the left predominantly by the inferior mesenteric artery and the lower rectum via the iliac vessels [6]. Colonic function also differs with proximal colon providing much of the water absorptive capability of the colon [7].

In 15 normal volunteers, Ajaj et al [1] have shown that at a single time point post contrast (75 s), relative

Address correspondence to: Professor Stuart Andrew Taylor, Centre for Medical Imaging, Level 3 East, 250 Euston Road, University College London, London NW1 2PG, UK. E-mail: csytaylor@yahoo.co.uk

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enhancement differs according to colonic segment (being highest in the rectum and sigmoid, and lowest in the right colon and descending).

Clearly intersegmental differences of normal colonic enhancement will influence the interpretation of MRI in inflammatory bowel disease, in particular when assessing potentially inflamed bowel. The purpose of this short communication is to present and discuss the quantitative MRI changes that occur following enhancement of endoscopically proven normal colon and to assess intersegmental differences.

Methods and materials

The local research ethics committee approved the study and informed consent was obtained from all patients.

Eight patients (four female; mean age 45 years, range 25–57 years) with no known history of inflammatory bowel disease and undergoing conventional colonoscopy were recruited to undergo additional MRC on the day of their conventional examination.

Patient preparation

All patients underwent solid food restriction from lunchtime the day before colonoscopy followed by full bowel purgation—10 senna tablets and two sachets of magnesium citrate dissolved in 1 l of water. An experienced practitioner (RH) performed MRC 2 h before colonoscopy in all patients. Following rectal introduction of a 16 F Foley catheter, the colon was gently filled with 1.5 l of warm tap water from an enema bag held at shoulder height (*i.e.* filling by gravity). Bowel motility was abolished by intravenous (iv) spasmolytic (Buscopan®; Boehringer Ingelheim, Ingelheim, Germany) 0.3 mg kg⁻¹ (maximum 20 mg) immediately prior to abdominal imaging.

MRI protocol

Images were acquired in the prone position with a 1.5 T Siemens Avanto (Siemens, Erlangen, Germany) magnet using the body and spine array coils.

The pre-contrast T_1 relaxation time of colon was measured by using three breath-hold coronal fat-saturated three-dimensional (3D) fast low-angle shot (FLASH) images of the abdomen and pelvis with different excitation flip angles (flip angles 5°, 10° and 35°; Table 1) [8].

Prior to intravenous contrast administration, three 3D FLASH baseline sets of coronal images were acquired during suspended inspiration (Table 1). A single dose of (0.2 ml kg⁻¹) intravenous (iv) gadoterate meglumine (Dotarem®; Guerbet, Roissy, France) was then injected into an arm vein at 3 ml s⁻¹, followed by a saline chaser (10 ml). At injection the patient was asked to hold his/her breath for 20 s (during which a single 3D FLASH volume data set was acquired), followed by 10 s of gentle breathing, immediately followed by another 20 s breath-hold acquisition and 10 s of gentle breathing. The acquisition protocol was repeated to generate a total of eight post-contrast 3D FLASH data sets.

Colonoscopy

Indications for colonoscopy for recruited patients were change in bowel habits ($n=3$), previous history of colonic polyps ($n=3$) and rectal bleeding ($n=2$).

Patients remained nil by mouth for a further 1–2 h while awaiting colonoscopy performed by experienced (2–10 years) operators. Intravenous sedative (midazolam 50 µg kg⁻¹, max 10 mg and fentanyl 100 µg) was administered, together with nasal oxygen. Of the patients recruited for MRC, all had multiple ileocolonic biopsies taken to exclude microscopic colitis. None of the patients had any complications and all were discharged within few hours. None of the biopsies showed features of inflammation.

Table 1. MRI acquisition parameters

Parameter	FLASH 3D ^a (T_1 calculation)	FLASH 3D ^a (pre-contrast)	FLASH 3D ^a (post contrast)
TE (ms)	2.4	2.4	2.4
TR (ms)	5.15	5.15	5.15
FA (degrees)	5, 10, 35°	35°	35°
NEX	1	1	1
iPAT	2	2	2
FOV (mm)	500×500	500×500	500×500
STH	3	3	3
No. slices	48–60	48–60	48–60
BW (Hz)	300	300	300
Acquisition matrix	256×154	256×154	256×154
Reconstruction matrix	512×512	512×512	512×512
TA (s)	17	17	17
Number of acquisitions	1 ^b	3	8

3D, three-dimensional; BW, pixel bandwidth; FA, flip angle; FLASH, fast low-angle shot; FOV, field of view; iPAT, parallel imaging factor; NEX, number of signal averages; STH, slice thickness; TA, time for single 3D FLASH acquisition; TE, echo time; TR, repetition time.

^aBreath-held fat-saturated coronal T_1 weighted 3D FLASH.

^bSingle acquisition at each flip angle.

MRI data analysis

Region of interest (ROI) analysis was performed on 3D FLASH MR images using the open-source OsiriX medical imaging platform (www.osirix-viewer.com). Single freehand linear ROIs (mean size 5.4 cm; range 2.3–9.8 cm) were located in the colonic wall of the ascending colon, descending colon and the lower rectum by a radiologist (SP) and gastroenterologist (RH) in consensus (Figure 1). These segments were chosen as representative of the known differing vascular supply and functional properties of the colon over its length. To guide ROI placement, the observers first reviewed the whole MR contrast-enhanced data set and chose those parts of the bowel wall reliably identifiable throughout the time series. In order to maintain the ROI within the colonic wall between successive acquisitions, the shape of the linear ROI was altered (with the length ± 0.01 cm and anatomical position kept constant) to account for any colonic deformations.

The mean ROI signal intensity was recorded for each segment. The signals from the three pre-contrast baseline acquisitions for a given ROI were averaged, providing a single pre-contrast ROI signal intensity for each colonic segment. T_1 was calculated for each segment in Microsoft Excel for Mac (2011) (Microsoft Corporation, Redmond, WA) using the expression for the evolution of signal intensity in a spoiled gradient echo and solving for T_1 [8]. The T_1 relaxation rate (R_1) was derived by $1/T_1$.

Statistical analysis

The mean R_1 ($n=8$ patients) prior to contrast and at each of the 8 post-contrast time points was used to generate an enhancement (R_1 -time) curve for the three colonic segments.

The initial change in R_1 (ΔR_1) was calculated between the 10 s (first post-contrast) and 40 s (second post-contrast) time points.

Early "plateau-phase" post-contrast R_1 was derived as the average of the 40, 70 and 100 s measurements for each segment. Late "plateau phase" post-contrast R_1 was calculated as the average of the 130, 160, 190 and 210 measurements.

The area under the R_1 -time curve (AUC- R_1) was determined using Prism (GraphPad Prism v. 4.00 for Mac; GraphPad Software, San Diego, CA; www.graphpad.com).

A Student's paired t -test was used to compare R_1 at pre-contrast, ΔR_1 , early and late post-contrast plateau phase R_1 , and the AUC- R_1 between the individual colonic segments.

Results

All colonoscopies were complete to the terminal ileum and normal, with no evidence of inflammatory bowel disease on direct inspection or biopsy.

The mean pre-contrast T_1 of ascending colon, descending colon and rectum were 606 ± 244 ms, 661 ± 264 ms and 680 ± 300 ms, respectively.

R_1 -time curves for ascending colon, descending colon and rectum are illustrated in Figure 2. Mean curve parameters are given in Table 2. Pre-contrast, there was no significant difference of R_1 values among individual segments (Tables 2 and 3). ΔR_1 was greater for the ascending than descending colon (Tables 2 and 3; $p=0.03$). There was no significant difference in ΔR_1 for other colonic segments (Tables 2 and 3).

Early and late post-contrast plateau phase R_1 values were not significantly different between bowel segments (Tables 2 and 3).

Figure 1. Region of interest (ROI) placement was performed using OsiriX (www.osirix-viewer.com). (a) Pre-contrast coronal T_1 weighted fat-saturated three-dimensional fast low-angle shot examination image of the ascending colon with a linear mural ROI (length 4.4 cm, signal intensity 109). (b) Matched post-contrast 10, 40, 70, 100, 130, 160, 190 and 220 s (1–8, respectively) images demonstrating the linear ROI on successive acquisitions (length 4.4 cm for each ROI, signal intensity values of 116, 179, 188, 181, 192, 151, 156 and 134 for ROIs 1 to 8, respectively).

Figure 2. R_1 -time curve for the (a) ascending colon, (b) descending colon and (c) rectum. Error bars represent standard error of the mean. Pre-con., pre-contrast injection.

The AUC- R_1 of the ascending colon was significantly greater than the descending colon (Tables 2 and 3; $p=0.03$). There was no significant difference of AUC- R_1 between the rectum and other colonic segments (Tables 2 and 3).

Discussion

T_1 relaxation is a consequence of fluctuations in the magnetic field experienced by individual hydrogen nuclei, which in the body are predominantly bound

Table 2. Quantitative MRI colonic segmental parameters

Parameter	Ascending colon	Descending colon	Rectum
Pre-contrast T_1 (ms)	606 ± 244	661 ± 264	680 ± 300
Pre-contrast R_1 (ms ⁻¹)	0.0019 ± 0.0007	0.0023 ± 0.0021	0.0018 ± 0.0004
ΔR_1 (ms ⁻¹)	0.0021 ± 0.0011	0.0009 ± 0.0007	0.0029 ± 0.0027
Early post-contrast R_1 (ms ⁻¹)	0.0042 ± 0.0010	0.0033 ± 0.0015	0.0048 ± 0.0025
Late post-contrast R_1 (ms ⁻¹)	0.0049 ± 0.0021	0.0036 ± 0.0015	0.0049 ± 0.0024
AUC- R_1	0.54 ± 0.19	0.30 ± 0.14	0.60 ± 0.46

ΔR_1 is the change in R_1 between the 10 s (first post-contrast) and 40 s (second post-contrast) acquisitions.

AUC- R_1 is the area under the R_1 -time curve.

within water molecules. As each hydrogen nucleus has magnetic properties, the rotational and tumbling movements of water molecules themselves act as the main source of magnetic field fluctuations. For effective T_1 relaxation, the oscillations in magnetic field have to occur at a specific frequency called the Larmor frequency. The greater the number of hydrogen nuclei experiencing fluctuations at the Larmor frequency, the shorter the T_1 relaxation time and the brighter the signal. The number of oscillations at the Larmor frequency is greater for water contained within soft tissues than for pure water or solid structure [9]. We found the mean pre-contrast T_1 of normal colonic segments was 606–680 ms with a narrow range, and that there was no significant inter-segmental difference between R_1 ($1/T_1$), reflecting the nature of the T_1 relaxation mechanism.

Gadolinium-based contrast agents work by producing additional magnetic field oscillations at the Larmor frequency, thereby further shortening the T_1 relaxation time and increasing signal within the image. For the effects of contrast agents to be realised they must be in close proximity to water molecules [9]. When confined within the vasculature, the number of water molecules affected is limited. With free leakage into the interstitium, more tissue water is exposed to the T_1 shortening effects.

We found significant differences between colonic segments in their behaviour following gadolinium administration. Notably, ΔR_1 and AUC- R_1 were greater for the ascending than the descending colon. By way of explanation, Skinner and O'Brien [10], using vascular casts of a normal human colon, showed a higher microvascular volume ($13.4 \pm 3\%$ and $7.7 \pm 2.2\%$, respectively) and microvascular surface area ($22.4 \pm 5\%$ and $17.5 \pm 6.9\%$, respectively) in the proximal colon than in the distal colon. A higher-percentage vascular volume in the proximal colon would mean that there is proportionally more intravascular water upon which intravascular gadolinium

can act. Furthermore, considering dynamic contrast-enhanced models, the volume transfer coefficient (K_{trans}) is the product of capillary permeability and surface area where blood flow is not limited [11]. As the microvascular surface area of the proximal colon is greater than that of the distal colon [10], it follows that K_{trans} should be higher (assuming the vascular permeability is equal or higher). A larger K_{trans} signifies that intravenous contrast will pass more freely into the interstitial space, exposing more tissue water to the gadolinium-induced T_1 relaxation effects, probably accounting for the greater increase in R_1 (larger ΔR_1) of ascending colon than of descending colon.

Ajaj et al [1] found that prior to iv contrast there was no difference between the contrast-to-noise ratio of different colonic segments, and at 75 s following iv contrast enhancement was highest in the rectum and sigmoid, and lowest in the ascending and descending colon. Our study partially supports their findings, as we found no difference in R_1 between segments prior to contrast and a lower enhancement within the descending colon. However, discrepant to Ajaj et al, we found no significant difference between rectum and ascending colonic R_1 changes, and we found R_1 change within the ascending colon to be higher than within the descending colon. By way of explanation, it is possible results were influenced by the differences in acquisition and analysis of the MRI data between the two studies. In contrast to Ajaj et al, we evaluated enhancement differences between segments based on quantitative R_1 change in order to avoid the effect of spatial signal intensity variation that can occur across images, and the potential difficulties with noise assessment within images where parallel imaging or image filters have been used [12].

The purpose of our study was to assess whether segmental variations are present in the enhancement of the normal colon. While our results present quantitative measurements performed on a total of eight normal

Table 3. Comparison of colonic segments

Parameter	Ascending vs descending colon t-test (p-value)	Ascending colon vs rectum t-test (p-value)	Descending colon vs rectum t-test (p-value)
Pre-contrast R_1 (ms ⁻¹)	0.50	0.62	0.49
ΔR_1 (ms ⁻¹)	0.03 ^a	0.48	0.07
Early post-contrast R_1 (ms ⁻¹)	0.21	0.60	0.24
Late post-contrast R_1 (ms ⁻¹)	0.08	1.00	0.30
AUC- R_1	0.03 ^a	0.14	0.75

ΔR_1 is the change in R_1 between the 10 s (first post-contrast) and 40 s (second post-contrast) acquisitions.

AUC- R_1 is the area under the R_1 -time curve.

^aSignificant difference at the $p < 0.05$ level.

patients at a single centre, they nevertheless illustrate statistically significant differences between colonic segments that support the anatomical and functional differences within the colon. While enhancement characteristics were consistent across patients for a given colonic segment, the range of pre-contrast T_1 values for individual colonic segments was large (wide standard deviation), which is probably representative of inherent intersubject differences. All patients in our study were scanned using a single MRI scanner and protocol; however, further variability in enhancement characteristics is likely to occur with diverse hardware and sequences found across multiple institutions. We have used a robust selection standard, ensuring all our patients had confirmed normal (non-inflamed) colonic appearances at endoscopy. We intentionally limited analysis to segments with clearly defined regional blood supplies and functional specialisations. We acknowledge that further recruitment is necessary to investigate the segmental differences that are "near statistical significance" in our results.

In conclusion, our results highlight that intersegmental differences in colonic enhancement are present. These should be considered when using enhancement as a biomarker for colonic inflammation as not all differential segmental enhancement is a result of inflammation.

Conflict of interest

The views expressed in this publication are those of the authors and not necessarily those of the UK Department of Health.

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