High Spatiotemporal Resolution Dynamic Contrast-Enhanced MR Enterography in Crohn Disease Terminal Ileitis Using Continuous Golden-Angle Radial Sampling, Compressed Sensing, and Parallel Imaging

OBJECTIVE. The purpose of this article was to assess the feasibility of golden-angle radial acquisition with compress sensing reconstruction (Golden-angle RAdial Sparse Parallel [GRASP]) for acquiring high temporal resolution data for pharmacokinetic modeling while maintaining high image quality in patients with Crohn disease terminal ileitis.

MATERIALS AND METHODS. Fourteen patients with biopsy-proven Crohn terminal ileitis were scanned using both contrast-enhanced GRASP and Cartesian breath-hold (volume-interpolated breath-hold examination [VIBE]) acquisitions. GRASP data were reconstructed with 2.4-second temporal resolution and fitted to the generalized kinetic model using an individualized arterial input function to derive the volume transfer coefficient ($K_{\text{trans}}$) and interstitial volume ($v_e$). Reconstructions, including data from the entire GRASP acquisition and Cartesian VIBE acquisitions, were rated for image quality, artifact, and detection of typical Crohn ileitis features.

RESULTS. Inflamed loops of ileum had significantly higher $K_{\text{trans}}$ (3.36 ± 2.49 vs 0.86 ± 0.49 min$^{-1}$, $p < 0.005$) and $v_e$ (0.53 ± 0.15 vs 0.20 ± 0.11, $p < 0.005$) compared with normal bowel loops. There were no significant differences between GRASP and Cartesian VIBE for overall image quality ($p = 0.180$) or detection of Crohn ileitis features, although streak artifact was worse with the GRASP acquisition ($p = 0.001$).

CONCLUSION. High temporal resolution data for pharmacokinetic modeling and high spatial resolution data for morphologic image analysis can be achieved in the same acquisition using GRASP.

Crohn disease is a chronic inflammatory condition affecting the gastrointestinal tract, marked by transmural inflammation of discontinuous loops of bowel. Contrast-enhanced MR enterography has an established role in the diagnosis and surveillance of Crohn disease. Findings on standard contrast-enhanced MR enterography have been shown to be useful in differentiating actively inflamed loops of bowel from noninflamed bowel [1–3] as well as in evaluating complications of Crohn disease, such as perianal fistulizing disease [4] and enterointeretic fistulas [5]. Additionally, qualitative features seen on contrast-enhanced MR enterography are key components in several measures of global disease activity in Crohn disease [6, 7].

The lack of ionizing radiation during MR enterography affords the opportunity to routinely acquire multiple time points at high temporal resolution after the IV administration of gadolinium-containing contrast material. The use of dynamic contrast-enhanced MRI (DCE-MRI) enables pharmacokinetic modeling of biophysical properties of local tissue microenvironments. For example, the most widely used pharmacokinetic model, the generalized kinetic model, uses tissue gadolinium concentrations derived from DCE-MRI to model such physiologic parameters as the transfer constant describing gadolinium exchange between blood plasma and tissue interstitium ($K_{\text{trans}}$) and local tissue extravascular-extracellular volume fraction ($v_e$) [8–10].

Studies [2, 11, 12] have shown the possibility of quantitative DCE-MRI in accurately differentiating actively inflamed loops of bowel from normal loops of bowel in patients with Crohn disease. However, routine DCE-MRI obtained using Cartesian reconstruction involves a trade-off between spatial and temporal resolution [13]. This is of critical importance in Crohn disease, in which potential involvement along the entire gastrointestinal tract requires both a large FOV.
and volumetric coverage, including the entire abdomen and pelvis, as well as high spatial resolution to detect subtle bowel wall involvement and, in doing so, necessitating the sacrifice of temporal resolution. Studies using animal models have shown that decreasing temporal resolution causes systematic underestimation of $K_{\text{trans}}$ [14], possibly related to inaccurate sampling of the arterial input function. Thus, simultaneous high spatiotemporal resolution bowel wall imaging to assess perfusion remains challenging. Given the increasingly accepted role of pharmacokinetic modeling in assessing and predicting treatment response in cancer [15], it is possible that achieving high spatial and temporal resolution in MR enterography imaging of Crohn disease may offer a means for similar assessment and prediction of response to the widely used anti-inflammatory medications that have become the mainstays of treatment of inflammatory bowel disease [16].

Recently, a novel method for rapid acquisition of data using compressed sensing [17],

Fig. 1—16-year-old girl with biopsy-proven Crohn disease and active terminal ileitis. A–F, Axial images through inflamed terminal ileum before (A) and after (B, red) placement of ROI, axial images through normal segment of ileum before (C) and after (D, blue) placement of ROI, and conventional axial volumetric-interpolated breath-hold examination (VIBE) images at same levels (E and F). (Fig. 1 continues on next page)
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Fig. 1 (continued)—16-year-old girl with biopsy-proven Crohn disease and active terminal ileitis. G, Graph shows time-normalized signal intensity curve through ROIs. Note that ROIs used in this study were 3D, involving voxels on multiple slices, and images here are representative single axial images depicting portion of 3D ROI.

parallel imaging [18], and a golden-angle acquisition scheme has been introduced. This acquisition method, known as GRASP (Golden-angle RAdial Sparse Parallel), involves continuous acquisition of data during free-breathing [19, 20]. By retrospectively varying the number of radial spokes per frame, this method enables flexible temporal reconstructions. Thus, with GRASP, both high temporal resolution perfusion data for quantitative pharmacokinetic modeling and high spatial resolution morphologic data for qualitative assessment of disease involvement can be derived from the same acquisition without additional acquisition time or contrast injection. Additionally, the radial volume-interpolated breath-hold examination (VIBE) acquisition on which GRASP is based has been shown to be motion robust. Thus, it offers benefits in patient populations in which standard breath-hold acquisitions may be difficult [21, 22].

The study had two purposes: to show the feasibility of GRASP acquisition with high temporal resolution reconstruction for perfusion imaging of the bowel in patients with Crohn disease terminal ileitis undergoing clinically indicated MR enterography without the need for additional acquisition time or contrast injection [1] and to compare image quality of the morphologic GRASP reconstruction with a standard Cartesian acquisition scheme [2].

**Materials and Methods**

**Patients**

This HIPAA-compliant retrospective study was approved by our institutional review board with a waiver of consent. On the basis of promising preliminary data previously presented by our group [23], GRASP acquisition had been introduced into our routine clinical MR enterography protocol [24]. All MR enterography studies performed between June 2013 and March 2014 on a scanner capable of performing GRASP acquisition were identified. Studies were included if the reports mentioned findings of active inflammation in the terminal ileum and if the patient had biopsy-proven Crohn disease terminal ileitis. Patients with prior bowel resection were excluded from the study. A total of 17 clinical MR enterography examinations meeting these criteria were identified; three examinations were excluded because of nonstandard imaging parameters, leaving a total of 14 examinations. Patients included nine men and five women (mean age ± SD, 25.5 ± 8.0 years; age range, 14.3–39.5 years). Eleven of 14 patients had a known diagnosis of Crohn disease before MR enterography. The remaining three patients had no prior known history of Crohn disease, but all three underwent a subsequent biopsy showing active Crohn terminal ileitis after the positive MR enterography (mean time between study and biopsy was 35 days; range, 34–36 days).

**MRI Technique**

All patients were imaged on a 1.5-T system (Magnetom Avanto, Siemens Healthcare). Sequences included in the routine MR enterography protocol but not directly evaluated in this study include multiplanar HASTE, axial T2-weighted imaging both with and without fat saturation, coronal diffusion-weighted imaging with generation of apparent diffusion coefficient (ADC) maps, and dynamic steady-state free precession coronal imaging through the terminal ileum.

All subjects underwent axial DCE-MRI of the abdomen and pelvis using an axial 3D gradient-
Performing using in-house software. For each subject, multiple 3D ROIs were drawn by a board-certified radiologist with 4 years of experience reading MR enterography studies. One ROI was drawn on the aorta in the region of the origin of the superior mesenteric artery to derive an individual arterial input function. Two additional ROIs were drawn, one on the segment of the terminal ileum that qualitatively appeared to have the most severe involvement using traditional MR enterography parameters of hyperenhancement and increased T2 signal intensity and one on a normal-appearing segment of more proximal ileum (Fig. 1). Bowel segment ROI locations were determined by the radiologist on the basis of findings on conventional MRI analysis using T2-weighted and delayed contrast-enhanced sequences. ROIs for both the inflamed and normal loops of ileum were then drawn on the basis of the time point that showed maximal enhancement of the target bowel loop. Finally, each ROI was propagated through the entire time series to generate tissue signal intensity–time curves. Dynamic depictions of the ROI superimposed on the target bowel loops were examined to ensure minimal confounding bowel wall peristalsis over the course of acquisition.

Signal intensity versus time curves were generated in each patient for the diseased and normal-appearing bowel wall as well as the aorta. Tissue curves were analyzed using a standard two-compartment model [8, 9, 25, 26]:

\[
\frac{dC_t}{dt} = K_{\text{trans}} \times (C_p - C_v) / v_e
\]

where \(K_{\text{trans}}\) is the rate transfer constant of gadolinium between plasma and tissue interstitium, \(C_v\) is the extracellular-extravascular volume, \(C_p\) is the gadolinium concentration in the arterial blood plasma, and \(C_v\) is the tissue gadolinium concentration. \(C_p\) and \(C_v\) were derived from the signal intensity–time curves, with hematocrit held constant at 0.45. Signal intensity values were converted to gadolinium concentration assuming a linear relationship [27].

**Image Quality Evaluation**

Two board-certified radiologists independently scored both the morphologic contrast-enhanced series derived from the GRASP DCE-MRI acquisition (obtained by collapsing time points over the entire 2-minute acquisition) and the standard Cartesian VIBE contrast-enhanced acquisition, which had been acquired immediately after the GRASP acquisition. Both sequences were given an overall image quality score from 1 (unreadable) to 5 (excellent quality). Images were also scored on the basis of the presence of streak artifact and motion artifact on a scale from 1 (artifact renders the series unreadable) to 5 (absent). Both sequences were also used to evaluate the presence of multiple widely accepted contrast-enhanced findings typical of active Crohn disease [28–30], including wall thickening, mucosal hyperenhancement, and mesenteric hypervascularity. A 3-point scale was used for each measure (0 = absent, 1 = possibly present, and 2 = definitely present).

**Statistical Analysis**

Mean values and SDs for both \(K_{\text{trans}}\) and \(v_e\) were calculated, and these generalized kinetic model parameters derived from normal and inflamed loops of ileum were compared using a paired two-sample t test. Image quality scores of both the GRASP DCE-MRI and standard Cartesian contrast-enhanced acquisition were recorded and compared using the Wilcoxon rank sum test. For detection of features of active Crohn disease, scores of the two readers were averaged and weighted kappa scores were calculated to assess for agreement of feature detection between the two different acquisition schemes. Analysis was performed using SPSS Statistics for Windows, version 21.0 (IBM). Statistical significance was defined as a \(p\) value less than 0.05.

**Results**

Quantitative DCE-MRI

Table 1 shows the summary of data derived from pharmacokinetic modeling of the high temporal resolution GRASP reconstruction using the generalized kinetic model for analysis of inflamed loops of terminal ileum and normal loop of proximal ileum. The \(K_{\text{trans}}\) was significantly higher (\(p = 0.004\)) in inflamed terminal ileum (3.36 ± 2.49 min⁻¹) compared to normal ileum (0.86 ± 0.49 min⁻¹).

**TABLE 1: Pharmacokinetic Parameters of Inflamed Terminal Ileum and Normal Ileum Using Generalized Kinetic Model**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Actively Inflamed Segment of Terminal Ileum</th>
<th>Segment of Normal Ileum</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume transfer coefficient, (K_{\text{trans}}) (min⁻¹)</td>
<td>3.36 ± 2.49</td>
<td>0.86 ± 0.49</td>
<td>0.004*</td>
</tr>
<tr>
<td>Extravascular-extracellular space volume fraction, (v_e)</td>
<td>0.53 ± 0.15</td>
<td>0.20 ± 0.11</td>
<td>0.00001*</td>
</tr>
</tbody>
</table>

Note—Data are mean ± SD.

*Statistically significant, \(p < 0.05\).
TABLE 3: Agreement Between GRASP and Cartesian VIBE Acquisitions for Detection of Classic Findings of Active Crohn Disease

<table>
<thead>
<tr>
<th>Parameter</th>
<th>GRASP</th>
<th>Cartesian VIBE</th>
<th>Kappa</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terminal ileum wall thickening</td>
<td>2.0</td>
<td>2.0</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Terminal ileum mucosal hyperenhancement</td>
<td>1.9</td>
<td>1.9</td>
<td>0.573</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Mesenteric hypervascularity</td>
<td>1.8</td>
<td>1.6</td>
<td>0.536</td>
<td>&lt; 0.001*</td>
</tr>
</tbody>
</table>

Note—GRASP = Golden-angle RAdial Sparse Parallel, VIBE = volumetric-interpolated breath-hold examination.
*Statistically significant, p < 0.05.

TABLE 2: Mean Image Quality Scores of GRASP and Cartesian VIBE Acquisitions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>GRASP</th>
<th>Cartesian VIBE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall image quality (1–5)</td>
<td>3.6</td>
<td>3.5</td>
<td>0.180</td>
</tr>
<tr>
<td>Absence of streak artifact (1–5)</td>
<td>3.9</td>
<td>5.0</td>
<td>0.001*</td>
</tr>
<tr>
<td>Absence of motion artifact(1–5)</td>
<td>4.5</td>
<td>4.3</td>
<td>0.476</td>
</tr>
</tbody>
</table>

Note—GRASP = Golden-angle RAdial Sparse Parallel, VIBE = volumetric-interpolated breath-hold examination.
*Statistically significant.

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Image quality results are presented in Tables 2 and 3 and Figure 3. There was no significant difference in overall image quality (p = 0.476) between morphologic GRASP and Cartesian VIBE acquisitions, although there was significantly more streak artifact perceived with the GRASP acquisition (p = 0.001). There was no significant difference in perceived motion artifact (p = 0.132).

There was moderate agreement of the averaged reader scores in detection of terminal ileum wall thickening (κ = 0.573) and mesenteric hypervascularity (κ = 0.536) between the two acquisition schemes (p < 0.001). There were identical score ratings of detection of wall thickening between the two readers; however, because both readers gave a maximum score of 2 in each case for both acquisitions, a kappa score could not be calculated.

Discussion

This is a proof of concept study that shows the feasibility of reconstructing high temporal resolution data from the same acquisition used for high spatial resolution morphologic imaging without the need for additional acquisition time, contrast injection, or compromise of volumetric coverage in patients with Crohn disease terminal ileitis undergoing clinically indicated MRI. It was feasible to achieve 2.4-second temporal resolution while maintaining diagnostic spatial resolution and large volumetric coverage that included the entire abdomen and pelvis. The rapid temporal resolution achieved in this study for the volumetric acquisition is not possible using standard Cartesian acquisition schemes. Pharmacokinetic modeling of regional concentration curves derived from this rapid acquisition showed higher Ktrans and ve in the inflamed segments of ileum compared with the normal-appearing segment. The overall image quality of the GRASP acquisition (acquired over 120 seconds) was equivalent to that of standard Cartesian breath-hold acquisitions.

Thus, obtaining morphologic and perfusion data from the same acquisition while maintaining high diagnostic image quality for assessing morphologic features of Crohn disease and enabling quantitative assessment of bowel perfusion may have a tremendous potential impact in management of patients with Crohn disease. Potential applications of this method include the assessment of treatment response to standard antiinflammatory treatments in Crohn disease (including possibly identifying quantitative imaging markers to predict which patients will respond to such medications); assessment of possible perfusion differences in predominantly fibrotic and predominantly inflammatory segments of Crohn disease; and application of quantitative perfusion metrics to other conditions, such as ischemic enteritis.

We observed that the estimated generalized kinetic model parameters showed significant differences in the inflamed and normal segments of bowel, and this was achieved despite a relatively small number (14) of patients. However, the absolute values of Ktrans in our study were somewhat different than those previously published. For example, Oto et al. [11] reported a mean Ktrans of 0.81 min−1 in actively inflamed terminal ileitis and 0.49 min−1 in normal bowel, both of which are much lower than the Ktrans of 3.36 min−1 in actively inflamed terminal ileum and 0.89 min−1 in normal bowel seen in the current study. This may be at least partially explained by the differences in temporal resolution between the two studies: Oto et al. reported a variable temporal resolution of between 5 and 12 seconds, whereas in our GRASP acquisition, we achieved a temporal resolution of 2.4 seconds. Lower temporal resolution makes it difficult to derive accurate individual arterial input function [15], and this can decrease Ktrans as shown in animal models [14] and a human study in breast MRI [31]. The exact effects of acquisition protocol and temporal resolution on generalized kinetic model parameters needs to be further investigated, for which the GRASP acquisition is well suited for given its flexibility of temporal reconstruction. We also acquired GRASP data for only 120 seconds after contrast injection, a shorter duration than that of prior studies that variably imaged from 3 to 7 minutes after contrast administration [2, 11]. This may impact Ktrans estimation. However, to perform morphologic comparison of Crohn disease features between GRASP and conventional acquisition, it was necessary to terminate GRASP acquisition and perform conventional breath-hold acquisition approximately 120 seconds after contrast injection.

There are several limitations to this study. This study only included patients with known, histologically proven Crohn-related terminal ileitis. However, the goal of this study was to test the feasibility of this technique for performing bowel wall perfusion imaging from the same acquisition used for morphologic evaluation. The inflamed (histologically proven) and normal segments showed differences in pharmacokinetic parameters and provided an excellent way to assess these features in the same patients. We used a normal segment of proximal ileum as our control group. Histologic proof that the normal ileal segment was not affected by Crohn disease was not possible be-
cause typical colonoscopy can only directly assess the colon and terminal ileum and capsule endoscopy was not routinely performed on any of the patients in this study. However, all control segments were chosen on the basis of the lack of any of the classic findings of active Crohn disease, and, given the known high sensitivity and specificity of routine MR enterography for detection of actively inflamed bowel loops [32], there is a high degree of confidence that the control segments were in fact uninvolved. Additionally, the use of an uninvolved loop of bowel in patients with Crohn disease as control subjects rather than using a normal loop of ileum in different subjects without Crohn disease may provide a better comparison because it avoids the possible confounding effects of patient-specific factors (such as cardiac output) that can influence pharmacokinetic modeling parameters. We also acknowledge that due to the relatively thin wall in normal loops of bowel, the ROI in these normal loops may be more susceptible to partial volume averaging of tissue beyond the mucosa, which may artificially contribute to the differences between normal and abnormal loops of bowel. Finally, although this study achieved the goal of showing the feasibility of using GRASP for obtaining simultaneous high spatiotemporal resolution DCE-MRI to show higher perfusion metrics in the inflamed segment compared with the normal-appearing segment in patients with Crohn disease, further research is needed to determine whether pharmacokinetic parameters can play a role in early diagnosis, assessing disease severity, or assessing early treatment response in management of Crohn disease.

In summary, in this study we show the feasibility of using contrast-enhanced GRASP acquisition in routine clinical MR enterography to achieve simultaneous high temporal resolution perfusion data while maintaining large volumetric coverage and excellent image quality for morphologic assessment from the same single acquisition without additional acquisition time or contrast injection. The use of pharmacokinetic modeling to reliably separate inflamed from normal loops of bowel has previously been shown, although with lower temporal and spatial resolution or with limited volumetric coverage than we have shown here. These initial results are promising, especially in light of the increasing use of quantitative DCE-MRI modeling in clinical practice in both oncologic and nononcologic imaging [33, 34]. Although further research is needed, the use of high spatiotemporal resolution DCE-MRI with GRASP offers an excellent opportunity to assess the role of DCE-MRI in management of Crohn disease.

Fig. 3—Active Crohn disease terminal ileitis. A–D, 21-year-old man (A and B) and 28-year-old woman (C and D) with biopsy-proven disease, and active Crohn terminal ileitis (arrows). Both cases show classic findings of active Crohn disease, including wall thickening and mucosal hyperenhancement. Morphologic Golden-angle RAial Sparse Parallel (GRASP) images (A and C) were judged by readers to have equivalent diagnostic quality and there was equivalent detection of features of Crohn ileitis. High temporal resolution reconstructions (with resolution of 2.4 seconds) were generated from same acquisition for pharmacokinetic modeling. Axial Cartesian volumetric-interpolated breath-hold examination (VIBE) images (B and D) were acquired in same patients for comparison.
References


