Radiology

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Published online before print
10.1148/radiol.2342031002
Radiology 2005; 234:569–575

Abbreviations:
SNR = signal-to-noise ratio
3D = three-dimensional

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Authors stated no financial relationship to disclose.

Author contributions:
Guarantors of integrity of entire study, all authors; study concepts and design, T.C.L., S.C.G., K.K., J.F.D., S.G.R.; literature research, B.N., W.A.; clinical studies, T.C.L., B.N., W.A., K.K., S.G.R.; data acquisition, T.C.L., B.N., W.A.; data analysis/interpretation, T.C.L., S.G.R., W.A.; statistical analysis, S.C.G.; manuscript preparation and editing, T.C.L., S.G.R.; manuscript definition of intellectual content, revision/review, and final version approval, all authors

MR Imaging of Apparent Small-Bowel Perfusion for Diagnosing Mesenteric Ischemia: Feasibility Study[1]

The purpose of this study, which was approved by the institutional review board, was to assess the differentiation of individuals with from those without mesenteric ischemia. All subjects provided written informed consent. Six healthy volunteers and six patients with documented chronic mesenteric ischemia underwent magnetic resonance (MR) imaging with and without oral caloric stimulation. After intravenous administration of paramagnetic contrast material, signal intensity values of the small-bowel wall were measured up to 130 seconds after contrast material injection. Volunteers and patients, respectively, had maximum enhancement of the bowel wall between 70 and 85 seconds after contrast material administration that amounted to 269% and 267% without and 425% and 333% with caloric stimulation. MR imaging assessment of small-bowel perfusion is possible and seems feasible for differentiating individuals with from those without mesenteric ischemia.

The symptoms associated with chronic mesenteric ischemia are well defined and include abdominal pain, weight loss, and food aversion (1–3). Arteriosclerotic changes of the splanchnic arteries have been implicated as the pathophysiologic mechanism underlying chronic mesenteric ischemia (4,5). The demonstration of significant stenoses in two of the three main mesenteric vessels in conjunction with appropriate clinical symptoms confirms the diagnosis of mesenteric ischemia (2). Unfortunately, arteriosclerotic changes are not limited to the proximal supplying arteries; rather, they often affect the level of the arterioles and therefore cannot be visualized with angiography (6). Furthermore, the mesenteric circulation is frequently supported by arterial collateral vessels, rendering the functional interpretation of high-grade stenosis affecting the origins of the celiac trunk and mesenteric arteries most difficult (7,8).

In view of the above outlined difficulties, it seems that the diagnosis of chronic mesenteric ischemia could be made more easily if it were based on a functional evaluation of mesenteric blood flow. It is well established that the postprandial augmentation of mesenteric blood flow is profound and peaks at 30 minutes after food intake (9–11) in healthy subjects. Patients with chronic mesenteric ischemia have a markedly reduced and delayed augmentation of blood flow (10). Magnetic resonance (MR) imaging offers several possibilities for assessing these meal-associated functional alterations: Phase-contrast MR imaging–based flow quantification (12–14) and/or oximetry (15) have been proposed. Technical challenges have limited the clinical utility of these techniques. A simpler approach involves the assessment of bowel wall perfusion after the intravenous administration of paramagnetic contrast material.

The aim of this study was to assess the feasibility of using enhancement values of the small-bowel wall determined before and after caloric stimulation as a measure of the apparent small-bowel perfusion in individuals with and those without mesenteric ischemia.

Materials and Methods

Subjects

Six healthy volunteers (two women and four men; age range, 19–35 years)

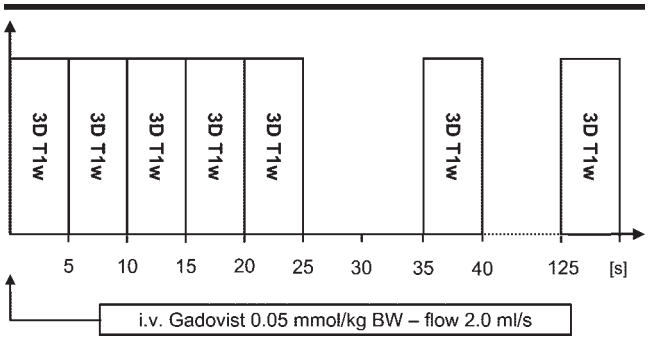
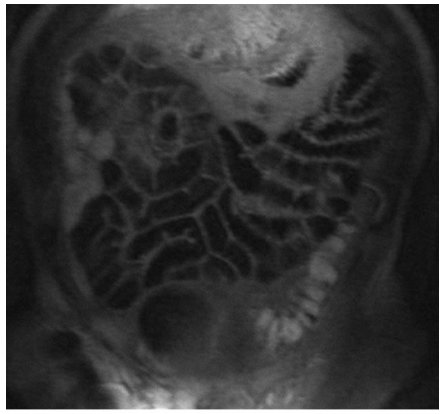
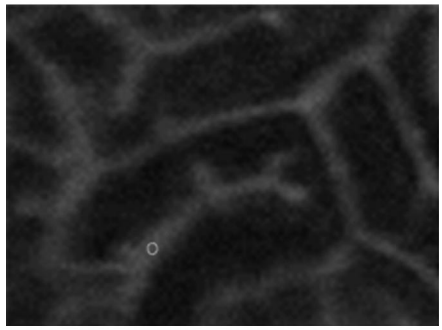


Figure 1. Examination protocol for perfusion MR imaging. After intravenous *(i.v.)* administration of 0.05 mmol per kilogram of body weight *(BW)* of a paramagnetic contrast agent *(Gadovist)* at a flow rate of 2.0 mL/sec, 3D T1-weighted *(T1w)* data sets are acquired in blocks of five data sets each. The last acquisition was performed 125 seconds after intravenous contrast agent administration.



a.



b.

Figure 2. **(a)** Coronal source image from T1-weighted gradient-echo 3D MR imaging data set (3.1/1.2; flip angle, 15°). Owing to the oral ingestion of contrast agent before MR imaging, good bowel distention is achieved. **(b)** Enlargement of **a**. Signal-to-noise ratios (SNRs) in the small-bowel wall can be easily determined (circle).

with no history of gastrointestinal disease, previous abdominal surgery, or even vague symptoms (eg, nausea, early satiety) of gastrointestinal disorders were included in this study. In addition, six patients (two women and four men; age range, 49–73 years) with symptoms of mesenteric ischemia (postprandial pain) and angiographically proved high-grade stenosis (reduction of the luminal diameter exceeding 50%) of the superior mesenteric artery were evaluated. Exclusion criteria were based on contraindications to MR imaging such as the presence of metallic implants or known claustrophobia. Written informed consent was obtained from all subjects, as set forth by the approving institutional review board. There was a statistically significant difference in age between the patient and volunteer groups ($P < .05$, unpaired Student *t* test).

MR Imaging

To ensure homogenization of bowel activity, all examinations were performed after the subjects had fasted for 8 hours. The subjects ingested 1000 mL of water mixed with locust bean gum (0.2% solution) (Roeper, Hamburg, Germany) starting 30 minutes before the MR imaging examination. Locust bean gum has been found to be a suitable oral contrast compound that provides homogeneous distention throughout the small bowel (16). In addition, locust bean gum does not impart any caloric content. To ensure consistent ingestion, all subjects were asked to drink 150 mL every 5 minutes. To enhance gastric emptying and achieve better small-bowel distention, 50 mg of erythromycin (Abbott Pharmaceutics, Wiesbaden, Germany) was administered intravenously (17).

MR imaging examinations were performed with subjects placed prone in a 1.5-T MR imaging unit (Magnetom Sonata; Siemens Medical Systems, Erlangen, Germany) equipped with high-performance gradient systems characterized by a maximum gradient amplitude of 40 mT/m and a slew rate of 200 mT/m/msec. For signal reception, a large "flex surface coil" (size, 31 × 45 cm; covered field of view in z direction, 45 cm), which was wrapped around the patient, was used.

To minimize bowel peristalsis, 20 mg of scopolamine (Buscopan; Boehringer Ingelheim, Germany) was administered intravenously directly before data acquisition. MR imaging was performed by using a three-dimensional (3D) T1-weighted gradient-echo sequence in the coronal plane with the following parameters: repetition time msec/echo time msec, 3.1/1.2; flip angle, 15°; section thickness, 3 mm; 16 sections per slab; and acquisition time, 5 seconds. A 390 × 292-mm^2 field of view combined with an interpolated matrix of 512 × 374 yielded an in-plane resolution of 0.8 × 0.8.

After intravenous administration of paramagnetic contrast material (gadobutrol, Gadovist; Schering, Germany) at a dosage of 0.05 mmol per kilogram of body weight and a flow rate of 2.0 mL/sec, the 3D acquisition was continuously repeated five times within a single breath hold. Total acquisition time amounted to 25 seconds. Subsequently, the subjects were instructed to breathe for 10 seconds. Hereafter, the procedure of data collection was repeated three times. Hence, the total data acquisition time for all data sets amounted to 130 seconds (Fig 1). Owing to higher gadolinium concentrations per volume, gadobutrol was chosen as the intravenous contrast agent; this allowed the administration of smaller volumes per time point than would be possible with 0.5-mol/L contrast agent compounds. The small volume was used so that we could potentially repeat the perfusion examination after different forms of stimulation.

The examination was performed in an identical manner on the next day in conjunction with a caloric stimulation: 30 minutes before the MR examination the subjects ingested first 250 mL of a high-caloric nutrient (Fresubin; Fresenius, Germany; 1 kcal/mL) followed by 750 mL of a 0.2% locust bean gum solution.

Data Analysis

All images were transferred to a post-processing workstation (Virtuoso; Siemens Medical Systems), where they were analyzed in a consensus mode by two radiologists (T.C.L., W.A.) who remained blinded to the type of the MR imaging examination (with or without caloric stim-

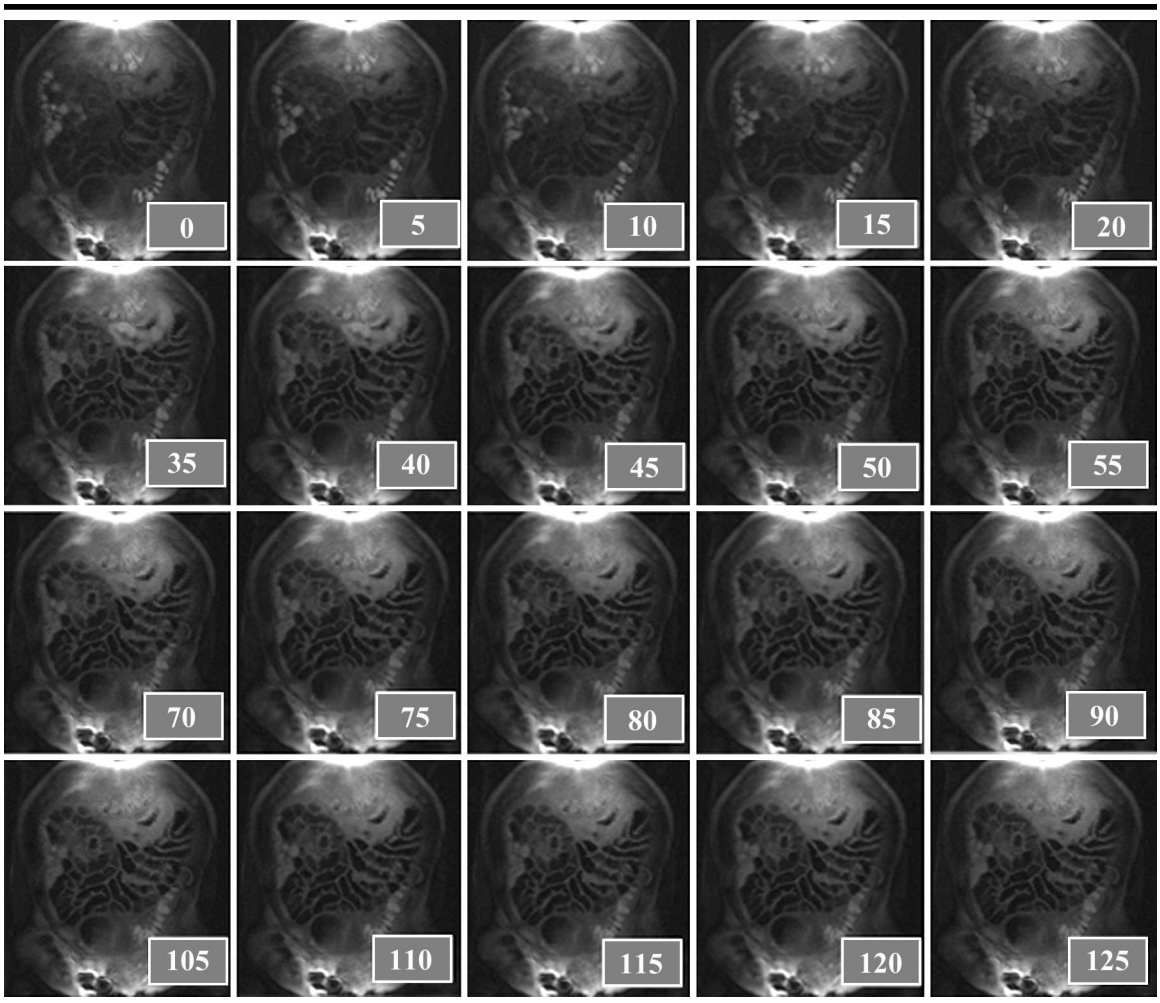


Figure 3. Selected coronal source images from T1-weighted gradient-echo 3D MR imaging data set (3.1/1.2; flip angle, 15°) obtained at all 20 acquisition times in one healthy volunteer, a 24-year-old man. Increasing bowel wall enhancement can be observed within the first 70 seconds. Thereafter, the SNR values in the bowel wall are seen to be in a plateau phase. The numbers in the lower right hand corners of the images represent the time (in seconds) after contrast agent injection at which each image was obtained.

ulation). To assess small-bowel perfusion, signal intensity measurements were performed in small (mean diameter, 1.5 mm) elliptic regions of interest in the small-bowel wall at five separate, predefined locations: the descending part of the duodenum; the proximal, middle, and distal thirds of the jejunum; and the ileum (Fig 2). SNRs were calculated in the usual manner: $SNR = SI_{cw}/N$, where SI_{cw} is the signal intensity of the colonic wall and N is noise. Noise was defined as the standard deviation determined in a signal intensity measurement outside the body. To this end, an elliptic region of interest (mean diameter, 20 mm) was placed in the recorded field of view either on the left or the right side outside the abdomen.

On the basis of the five small-bowel wall measurements, the mean SNR was calculated for each 3D data set. Furthermore, the "reserve capacity" was calculated for each subject and each acquisition by subtracting the respective SNR value obtained before caloric stimulation from that obtained after caloric stimulation. Reserve capacity is a measure for the additional perfusion induced by caloric stimulation.

Statistical Analysis

The effect of caloric stimulation on bowel wall enhancement was determined by using a Wilcoxon test for both the volunteer and patient groups. Subsequently, the reserve capacities determined in the patient group were compared with those determined in the volunteers by using the Mann-Whitney test. In both cases, a P value of less than .05 was considered to indicate a statistically significant difference. To account for repeated measurements, an additional analysis of variance in which time, stimulation, experimental group, and day of examination were used as factors was performed.

Results

All 24 examinations (two per subject) were considered diagnostic, and their results were thus entered into the analysis (Fig 3). On the initial images obtained without contrast enhancement, signal intensity measurements in the small-bowel wall were not significantly different between examinations performed before and those performed after caloric stimulation or between volunteers and patients ($P >$ .05). The bowel wall of healthy volun-

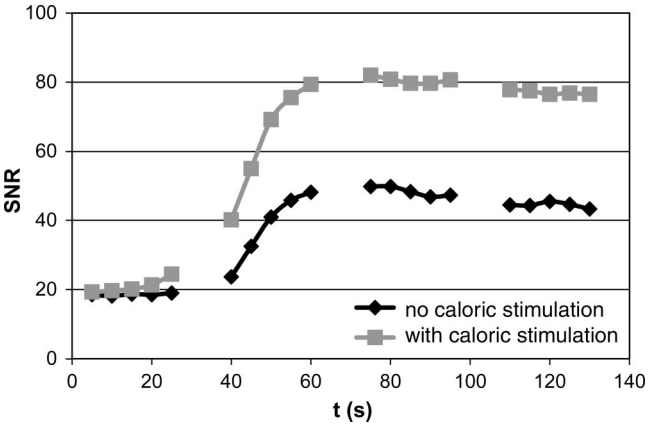


Figure 4. Graph shows mean SNR values for the volunteer examinations performed with and those performed without caloric stimulation. The caloric stimulation leads to a significantly higher bowel wall perfusion compared with the baseline examination without caloric stimulation.

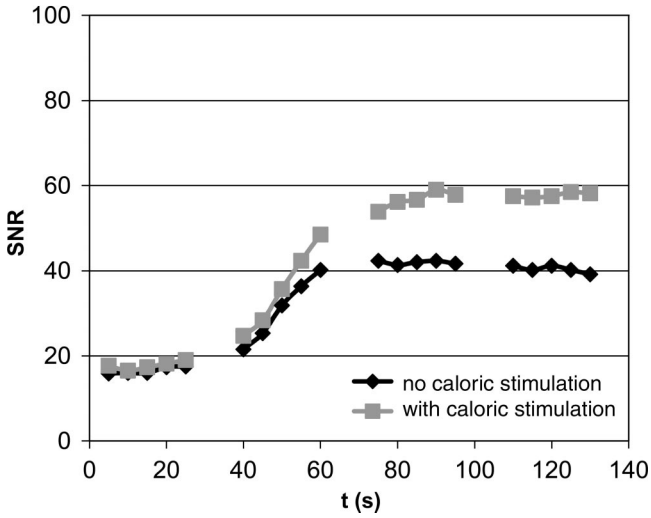


Figure 5. Graph shows mean SNR values for the patient examinations performed with and those performed without caloric stimulation. As in the volunteer group, in the patient group, caloric stimulation leads to increased bowel wall perfusion. However, the increase is less compared with that in the volunteer group (Fig 4).

teers showed maximum contrast enhancement 70 seconds after intravenous administration of contrast material that, as compared with the baseline value, amounted to a mean of 269% ± 44 (standard deviation) without caloric stimulation (ie, 49.8/18.5) and 425% ± 58 with caloric stimulation (ie, 82.0/19.3) (Fig 4, Table 1). At the examinations performed in patients with mesenteric ischemia, however, mean maximum enhancement values amounted to merely 267% ± 43 without caloric stimulation (ie, 42.3/15.8) and 333% ± 46 with caloric stimulation (ie, 59.0/17.7) (Fig 5, Table 1). All SNR values at the volunteer and patient examinations, as well as the respective results of the reserve capacity evaluations, are shown in Table 1. Differences between SNR values determined in image sets obtained with and those determined in image sets obtained without caloric stimulation were statistically significant after 20 seconds for the volunteers and after 55 seconds for the patients (Table 2).

TABLE 1
Dynamic Bowel Wall Perfusion Measurements in Healthy Volunteers and Patients

	Volunteers			Patients		
Time (sec)	No Caloric Stimulation	Caloric Stimulation	Reserve Capacity	No Caloric Stimulation	Caloric Stimulation	Reserve Capacity
0	18.5	19.3	0.8	15.8	17.7	1.9
5	18.2	19.7	1.5	16.0	16.5	0.5
10	18.7	20.2	1.5	16.0	17.3	1.3
15	18.5	21.3	2.8	17.3	18.2	0.9
20	19.0	24.5	5.5	17.5	19.0	1.5
35	23.7	40.2	16.5	21.5	24.7	3.2
40	32.5	55.0	22.5	25.3	28.3	3.0
45	41.0	69.2	28.2	31.8	35.7	3.9
50	45.8	75.5	29.7	36.3	42.3	6.0
55	48.2	79.3	31.1	40.2	48.5	8.3
70	49.8	82.0	32.2	42.3	53.8	11.5
75	49.8	80.8	31.0	41.3	56.2	14.9
80	48.3	79.7	31.4	42.0	56.7	14.7
85	46.8	79.7	32.9	42.3	59.0	16.7
90	47.3	80.7	33.4	41.7	57.8	16.1
105	44.5	77.8	33.3	41.2	57.5	16.3
110	44.3	77.5	33.2	40.2	57.2	17.0
115	45.5	76.5	31.0	41.2	57.5	16.3
120	44.7	76.8	32.1	40.2	58.5	18.3
125	43.3	76.5	33.2	39.2	58.2	19.0

Note.—Data are mean SNR values.

As for the comparison between the volunteer and patient examinations, there was little difference in terms of enhancement values before caloric stimulation (Fig 6). However, differences in SNR values of images obtained after caloric stimulation proved significant between volunteers and patients (Fig 7, Table 2). The greatest differences were identified in the time window between 35 and 75 seconds ($P = .002$). When we compared the reserve capacities of the volunteers and the patients, a statistically significant difference was determined for all 3D data sets obtained later than 35 seconds after the administration of paramagnetic contrast material ($P \leq .004$) (Fig 8). Results of analysis of variance underlined these findings (Table 2): When we compared volunteers and patients with regard to the examination performed with caloric stimulation, dedicated statistical significance (5% level) was found for the acquisition time points between 35 and 125 seconds. A dedicated statistical significance for comparison of reserve capacities was determined even for the time points between 15 and 125 seconds.

Discussion

The results of the present study show that determination of small-bowel contrast enhancement at MR imaging is feasible, that the analysis of enhancement in 3D data sets obtained before and after

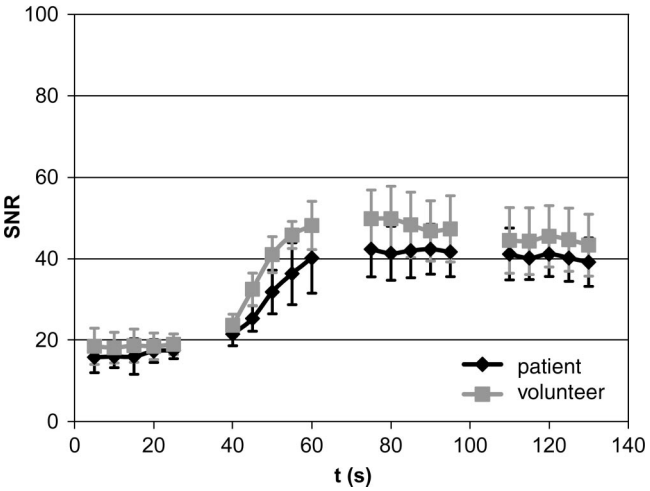


Figure 6. Graph shows results of comparison between SNR values without caloric stimulation in the patient group and those in the volunteer group. Error bars indicate single standard deviations. In baseline conditions with no caloric stimulation, mean bowel wall perfusion is only slightly higher in the volunteer group than in the patient group.

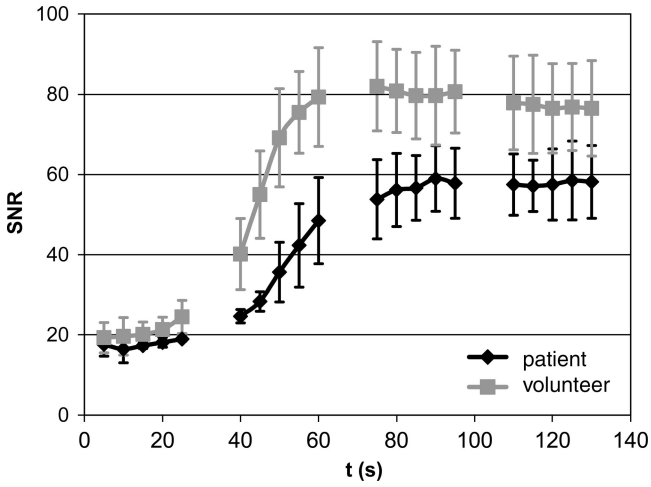


Figure 7. Graph shows results of comparison between SNR values with caloric stimulation in the patient group and those in the volunteer group. Error bars indicate single standard deviations. Bowel wall perfusion is significantly higher in the volunteer group than in the patient group when caloric stimulation is applied.

TABLE 2
***P* Values for Examinations Involving versus Those Not Involving Caloric Stimulation and for Examinations in the Volunteer Group versus Those in the Patient Group**

Time (sec)	Without Stimulation versus with Stimulation*		Volunteers versus Patients‡		
	Volunteers	Patients	Without Stimulation	With Stimulation	Reserve Capacity
0	.915	.216	.310	.310	.937
5	.496	.750	.394	.240	.699
10	.102	.400	.394	.093	.818
15	.144	.399	.699	.026‡	.699§
20	.043‡	.246	.394	.009‡	.180§
35	.028‡	.063	.310	.002§	.015‡§
40	.028‡	.172	.009‡§	.002§	.004‡§
45	.028‡	.248	.009‡§	.002§	.002‡§
50	.028‡	.116	.009‡§	.002§	.002‡§
55	.027‡	.027‡	.093	.002§	.002‡§
70	.027‡	.028‡	.132	.002§	.002‡§
75	.028‡	.028‡	.065	.002§	.004‡§
80	.027‡	.028‡	.180	.004§	.002‡§
85	.028‡	.028‡	.310	.009§	.002‡§
90	.028‡	.027‡	.240	.004§	.002‡§
105	.027‡	.027‡	.394	.009§	.002‡§
110	.027‡	.028‡	.394	.009§	.002‡§
115	.028‡	.028‡	.310	.015§	.004‡§
120	.028‡	.027‡	.310	.015§	.002‡§
125	.028‡	.027‡	.394	.015§	.002‡§

* Calculated with Wilcoxon test.
† Calculated with Mann-Whitney test.
‡ Statistically significant difference.
§ Statistically significant difference at 5% level according to results of analysis of variance.

caloric stimulation permits determination of an apparent small-bowel perfusion reserve capacity, and that analysis of this reserve capacity permitted the differentiation of patients with mesenteric ischemia from healthy volunteers in our small subject population of patients and volunteers.

Despite its inherent invasiveness and inability to depict arterial disease at an arteriolar level, selective angiography continues to be considered the standard of reference for establishing the diagnosis of chronic mesenteric ischemia (18). Owing to its noninvasive character, MR angiography has become an attractive alternative for the evaluation of the proximal mesenteric vessels (19,20). Its clinical impact in this setting, however, has remained limited; this reflects the poor spatial resolution that precludes the delineation of smaller mesenteric branch vessels (21,22). Thus, other parameters need to be defined if the diagnosis of chronic mesenteric ischemia is to be rendered on the basis of MR imaging findings.

MR flow quantification has been proposed as an indirect method for the evaluation of mesenteric ischemia (9–11). With the use of phase-contrast techniques, flow characteristics of the superior and inferior mesenteric arteries, as well as those of the celiac trunk, can be qualitatively and quantitatively assessed. Thus, a reciprocal correlation between the degree of stenosis in the superior mesenteric artery and the degree of flow augmentation after caloric stimulation was proved (11). Other authors have promoted flow quantification of the superior mesenteric vein: Since the superior mesenteric vein drains blood from the entire bowel except the rectum and stomach, flow quantification measurements in this vein reflect the combined bowel flow components of all three visceral arteries and therefore capture changes in the combined mesenteric blood supply (10,22). Technical difficulties and method imperfections have limited the utility of phase-contrast tech-

niques in a clinical setting. Furthermore, flow measurements represent merely an indirect means of characterizing the blood supply to the bowel. Direct assessment of bowel wall perfusion itself would be far more desirable.

In conjunction with commercially available extracellular paramagnetic contrast agents, MR imaging techniques are increasingly used to assess myocardial perfusion (23). Cardiac perfusion examinations are usually performed during baseline conditions, as well as during pharmacologically induced hyperemia (24,25). Thus, a "myocardial perfusion reserve," which has been shown to accurately reflect blood flow to the myocardium in patients with coronary artery disease (24), can be determined. We have adapted the underlying physiologic "stressing" principle and applied it to bowel wall perfusion. The stimulation required to augment organ activity and hence blood flow to the organ being considered is achieved with the oral administration of a high-caloric foodstuff. In fact, the reserve capacity of the apparent bowel wall perfusion proved comparable to that of the myocardium: It was reliable for differentiating between healthy volunteers and patients with mesenteric ischemia, although our subject groups were admittedly small. Similar to the situation with the myocardium, analysis of baseline apparent bowel perfusion alone did not enable reliable differentiation between ischemic and healthy subjects.

Reliable assessment of apparent bowel perfusion is predicated on the fulfillment of several requirements. Thus, the bowel itself needs to be sufficiently and homogeneously distended. This was achieved with the ingestion of a specially prepared oral contrast agent consisting of water and locust bean gum in which the locust bean gum bound the water into a distending gel. Furthermore, the contrast agent rendered the bowel lumen homogeneously dark on T1-weighted images, thereby fulfilling another important requirement. Thus, signal intensity alterations within the bowel wall could be appreciated against a dark background. Most important in this regard was the integrated fat saturation inherent to the 3D sequence used. It ensures dark signal in the mesenteric fat surrounding the bowel. Final requirements relate to the spatial and temporal resolution of the imaging sequence used. High spatial resolution is mandatory for resolving the often-thin bowel wall sufficiently to ensure accurate region-of-interest placement without too much signal modification induced by partial volume effects. Sufficient temporal resolution is required to ensure that the contrast agent bolus is caught during peak enhancement levels.

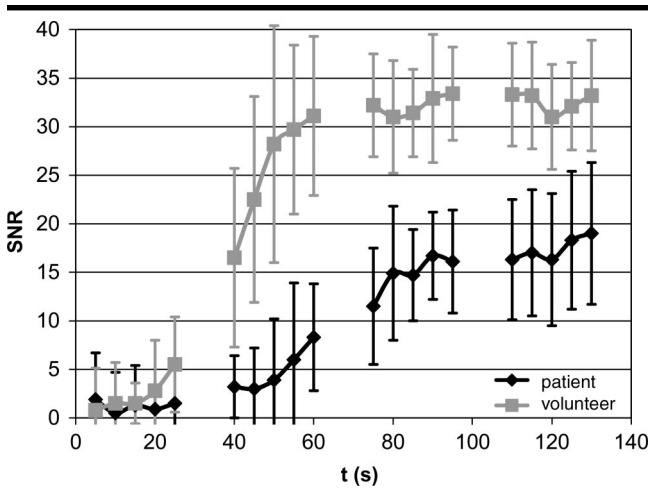


Figure 8. Graph shows results of comparison between reserve capacity values in the patient group and those in the volunteer group. Error bars indicate single standard deviations. Reserve capacity proves to be a reliable parameter for the detection of mesenteric ischemia. Especially during the first pass of the intravenous contrast agent, reserve capacity is significantly higher in healthy volunteers than in patients.

The chosen 3D T1-weighted imaging sequence fulfilled both requirements: An interpolated voxel size of $0.8 \times 0.8 \times 3$ mm^3 provided the basis for reproducible signal intensity measurements within the wall throughout the entire length of the small bowel. Further improvements would be possible by integrating parallel acquisition techniques (26). The data acquisition time of 5 seconds for each 3D data set ensured that we captured the peak of enhancement during the first pass of the contrast material bolus in each of the examined subjects. This proved important, because absolute contrast enhancement differences between patients with mesenteric ischemia and healthy volunteers were most significant during the first pass of the intravenous contrast agent. Hence, the evaluation of mesenteric ischemia should be focused on measurements obtained between 35 and 80 seconds after the intravenous administration of contrast agent. Subsequent measurements did not add further information and can therefore be eliminated from imaging protocols.

On the basis of our results with the described imaging technique, perfusion MR imaging of the bowel wall is feasible and permits the differentiation of apparent perfusion profiles associated with mesenteric ischemia from those associated with normal bowel. Beyond the noninvasiveness inherent with MR imaging, MR imaging–based analysis of apparent bowel perfusion in the setting of mesenteric ischemia enables direct measurement of bowel wall perfusion. In combination with a rectal water enema for wall distention, this technique could easily be extended to also encompass the inferior mesenteric artery perfusion territory in the colon.

Clearly, the proposed MR imaging protocol leaves room for optimization. First and foremost, it must be recognized that the extracellular nature of the contrast agents used precludes measurements of absolute perfusion to the bowel wall. This issue has also been comprehensively discussed in the context of myocardial perfusion (27). Similar to the situation with the myocardium, it seems that extracellular agents are also suitable for first-pass perfusion measurements in the bowel wall. It remains to be seen whether paramagnetic intravascular contrast agents currently undergoing clinical trials (28) will facilitate even better results.

Although no difficulties were seen in our study, the ingestion of 1000 mL of a contrast agent within a relatively short time range may be problematic for patients with abdominal symptoms. Therefore, it should be assessed whether sufficient distention of the small-bowel wall can be achieved with smaller volumes of oral contrast material. Furthermore, the use of a reserve capacity for the assessment of mesenteric ischemia requires two independent examinations: one with and one without caloric stimulation. To become clinically relevant, both components would need to be integrated into the same examination. In view of the small contrast

agent bolus of only 0.05 mmol/kg, only 15 minutes would be required between both examination components (23). Additionally, one should keep in mind that false-positive or false-negative results might occur in clinical conditions owing to nonconsistency in cardiac output and changes in bowel motility caused by several types of drugs.

In spite of the limited number of subjects who were examined and the differences between the volunteer and patient groups regarding age, we are convinced that MR imaging bowel perfusion measurements have the potential to enable individuals with mesenteric ischemia to be discriminated from individuals without mesenteric ischemia.

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