Original Research

Real-Time High-Resolution MRI for the Assessment of Gastric Motility: Pre- and Postpharmacological Stimuli

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Purpose: To determine the practicality of MRI using a new real-time sequence for the assessment of gastric motion, and quantify the effects of motility-modifying substances.

Materials and Methods: Six healthy volunteers ingested 400 mL of a high-calorie liquid nutrient. Two-dimensional real-time TrueFISP sequences were acquired for up to 30 minutes following the ingestion. The acquisition plane was chosen parallel to the axis of the gastric antrum. The examination was performed on three separate days with and without i.v. administration of 10 mg metoclopramide or 20 mg scopolamine. A motility index was calculated for each real-time data set.

Results: Delineation of the gastric lumen proved easy and robust. The intravenous application of motility-modifying agents resulted in significant changes in the motility index. The administration of metoclopramide resulted in an average increase of the index by a factor of 1.5, whereas the application of scopolamine led to a decrease of the index by a factor of 3.0.

Conclusion: TrueFISP MRI performed well in depicting the gastric lumen and assessing gastric motility. Furthermore, we were able to evaluate and quantify the effect of motility-modifying agents. The noninvasive nature of MRI makes this imaging modality an attractive alternative to conventional invasive diagnostic tools for gastric motility disorders and monitoring of therapy.

Key Words: MRI of the stomach; real-time TrueFISP; motility-modifying drugs; metoclopramide; butylscopolamine
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GASTRIC PERISTALSIS originates in the corpus, which functions as a spacious reservoir. From the corpus the peristaltic wave spreads via the antrum to the pylorus at a speed of up to 40 mm/second (1). Gastric motility is affected by a variety of different diseases, such as functional dyspepsia or diabetic gastroparesis. Associated disturbances of gastric motor function are believed to play a dominant role in the development of many gastrointestinal symptoms. These can be ameliorated by pharmacologic therapies that permit the isolated relaxation or tonic contraction of the cardia, antrum, or pylorus (2–4). However, the choice of an effective therapeutic strategy is predicated upon a comprehensive diagnostic assessment of gastric motility—preferably with quantification of peristaltic wave velocities (5).

Despite the high prevalence of functional gastrointestinal pathologies (6), no single diagnostic test has emerged as generally recommended in a clinical environment. This observation reflects the different drawbacks that affect each of the many tests in clinical practice. For example, gastric barostat studies that assess proximal motor function with an intragastric balloon provide accurate results (7), but they are hampered by their intrinsic invasiveness, which translates into poor patient acceptance. On the other hand, electrogastrography, which is based on the recording of gastric electrical activity from the body surface, is well accepted but fails to provide an acceptable correlation with gastric contractions (8). Finally, nuclear medicine studies are capable of quantifying gastric emptying but lack the spatial and temporal resolution necessary to provide detailed data on gastric contraction and peristalsis. Furthermore, they are associated with considerable exposure to ionizing radiation.

Recently, MRI has been proposed for the evaluation of gastric function (9). The technique is noninvasive and is not associated with ionizing radiation. To date, MR-based imaging strategies have focused on evaluating changes in gastric volume over longer time intervals (10,11). New real-time sequences, which were primarily developed for cardiac imaging, now provide the temporal resolution required to resolve gastric motion. The goal of this study was to determine the practicability of a real-time fast imaging with steady precession (TrueFISP) sequence for assessing gastric motion. Furthermore, the known effects of motility-modifying sub-

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stances (metoclopramide and butylscopolamide) were quantified with the new real-time technique (12,13).

MATERIALS AND METHODS

Six healthy volunteers (three males and three females, mean age = 29 years) with no history of gastrointestinal disorders or contraindications to the administration of metoclopramide or scopolamine were each studied on three different occasions on three successive days. The study was approved by the local institutional review board, and written informed consent was obtained from each subject prior to the examination.

All imaging was performed on a 1.5 T scanner equipped with high-performance gradients characterized by an amplitude of 40 mT/m and a slew rate of 200 mT/m/msec (Magnetom Sonata®; Siemens Medical Systems, Erlangen, Germany). The examinations were always performed at the same time of day after the subjects fasted for eight hours. The environmental temperature in the examination room was held constant at 20°C for all examinations. The patients sat on the exam table just prior to commencing the exam and ingested 400 mL of a high-calorie, widely available vanilla pudding (Ravensberger®, Everswinkel, Germany, 100 kcal/100 g). In previous in vitro experiments, we found that we could increase the signal intensity of the pudding on two-dimensional TrueFISP images by adding a small amount of paramagnetic contrast in the form of gadopentetate dimeglumine (Gd-DTPA, Magnevist®; Schering AG, Berlin, Germany) in a concentration of 1:200. Accordingly, the pudding (400 mL) was spiked with 2 mL of Gd-DTPA prior to ingestion.

Immediately after the subjects ingested the pudding, they were injected intravenously with normal saline, 10 mg metoclopramide (mean halflife = 3.6 hours) (14), or 20 mg scopolamine (mean halflife = 5.1 hours) (15). The volunteers were blinded to the order in which the substances were administered. Since each subject was imaged three times, each subject received each substance once. The subjects were imaged in the supine position, and a standard phased-array body coil was used for signal reception. Imaging was performed at 0, 15, 20, 25, and 30 minutes following a 60-second break after the intravenous injection. To that end, a two-dimensional real-time TrueFISP sequence (TR/TE = 3.9/1.9 msec, flip angle = 69°) was used with and without tagging lines. The acquisition plane of the single 5-mm section was chosen interactively to be parallel to the axis of the gastric antrum. The entire stomach was displayed. A 33 × 40 cm field of view (FOV) in conjunction with an acquisition matrix of 166 × 256 interpolated to 332 × 512 was chosen. Real-time TrueFISP provided one image per second. Imaging was performed under breath-hold conditions over 20 seconds. To assess gastric motion, dark parallel tagging lines were applied in the cranio-caudal direction in a manner similar to that described for cardiac MRI (16). The gap between two tagging lines amounted to 6 mm. Hence, we could simply quantify the distance that a peristaltic wave had passed by counting the number of tagging lines.

All images were transferred onto a workstation (Leonardo; Siemens Medical Systems, Erlangen, Germany) for subsequent qualitative and quantitative analysis.

A motility index was calculated for each real-time data set. The frequency and propagation speed of the gastric contractions were calculated by use of the tagging lines. Thus, the distance (ΔX) the peristaltic wave traveled within 10 seconds (Δt) was calculated. The gastric peristaltic wave velocity (V) was defined as follows:

$$\frac{\Delta X}{\Delta t}\frac{mm}{s} = V mm/s. \qquad (1)$$

Subsequently, the gastric motility index (GMI) was determined. To that end, we calculated the minimal diameter of the antrum (Δd) by drawing a line parallel to the antral axis. The distance between the parallel line and the deepest antral contraction was then calculated. To determine the GMI, the velocity (ΔV) was multiplied with the minimal diameter of the antrum (Δd) (Figs. 1 and 2):

$$\mathrm{GMI} = \Delta V \times \Delta d = \frac{mm}{s} \times mm = mm^2/sec \qquad (2)$$

Finally, the data from all 18 examinations performed on the six subjects were statistically analyzed. The McNemar test for matched-pairs proportions was used to determine the statistical significance of the differences between gastric peristaltic wave velocities and GMIs for each of the three administered substances. A Bonferroni correction for multiple comparisons was applied. A test value of $P < 0.05$ was considered to be statistically significant.

RESULTS

All of the MR examinations were completed without complications. The mean exam time, including the pudding ingestion, amounted to 40 minutes (range = 38–43 minutes).

The high-calorie nutrient spiked with paramagnetic contrast was homogeneously bright on the real-time two-dimensional TrueFISP images. Thus, delineation of the gastric lumen proved easy and robust. The mean antral wave propagation speed and GMIs determined over time following the intravenous administration of normal saline, butylscopolamide, or metoclopramide are summarized in Figs. 3 and 4.

The examinations after i.v. administration of saline yielded the following results: After the ingestion of 400 mL of pudding, the propagation speed of the antral contraction increased only slightly from a mean of 1.8 mm/second to a mean of 2.4 mm/second, and this remained unchanged for 15–30 minutes. The differences in the propagation speed at 0 and 15 minutes were statistically significant ($P < 0.05$). The GMI, which is more sensitive to changes in gastric contraction, almost doubled from a mean of 1.3 to 2.5 mm^2/second over the first 15 minutes, and continued to increase to 2.9 mm^2/second at 25 and 30 minutes. The differences

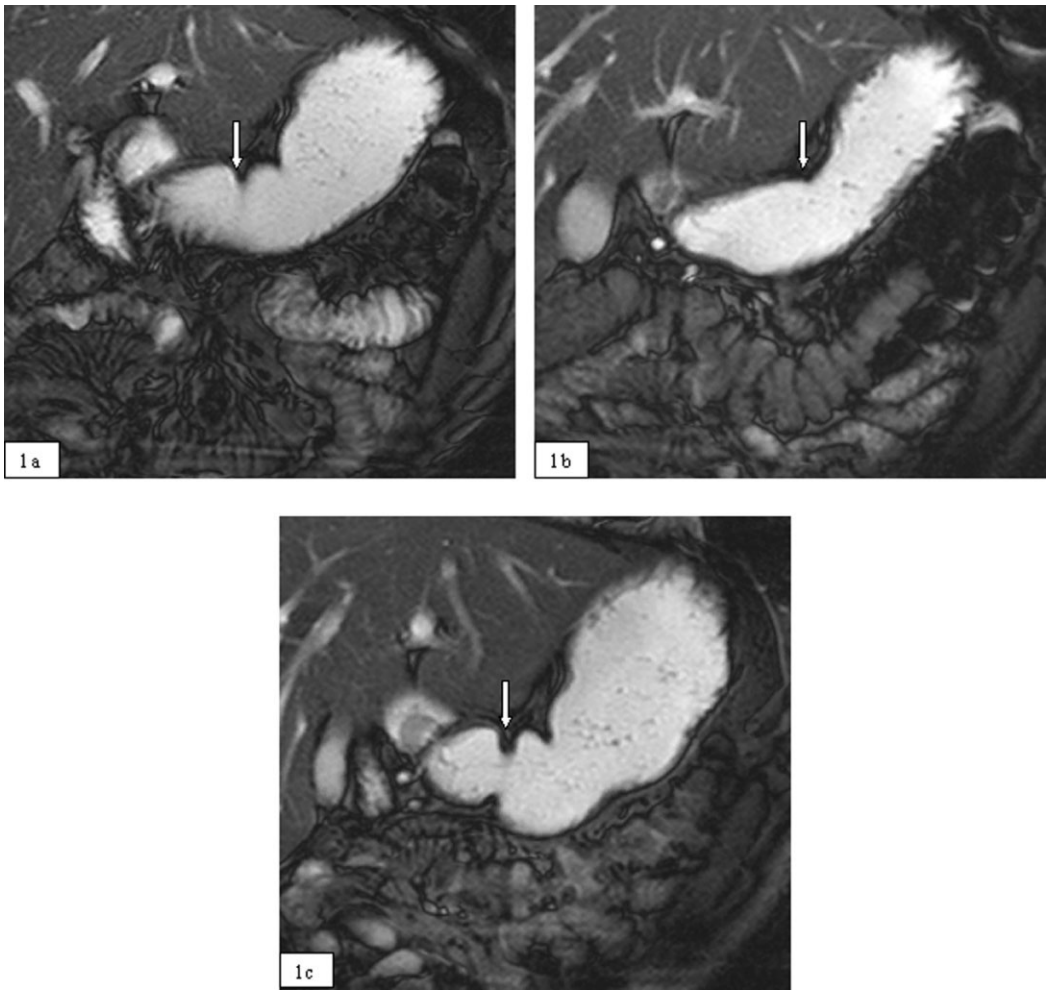

Figure 1. Two-dimensional real-time TrueFISP in an oblique plane displaying the antral axis. Images **a–c** show the peristaltic wave toward the pylorus (arrow) in the same volunteer. Image a with normal saline shows a low antral contraction. Image b was acquired after i.v. injection of butylscopolamine, with only a distinct contraction. Image c, acquired after i.v. injection of metoclopramide, shows an increased antral contraction.

between the 0- and 15-minute measurements proved statistically significant ($P < 0.05$).

The intravenous administration of butylscopolamine dramatically reduced both the measured antral wave propagation speed and the GMI. While the antral wave propagation speed doubled from 0.6 to 1.2 mm/second ($P < 0.05$), the GMI increased from a very low mean of 0.2 to 0.8 mm^2/second at 15 minutes ($P < 0.05$). As the pharmacological action of butylscopolamine wore off, both the propagation speed and the motility indices increased to the levels seen following the injection of normal saline. The differences between the 0- and 15-minute measurements, and the 15- and 30-minute measurements were statistically significant ($P < 0.05$).

Following the intravenous administration of metoclopramide, both the propagation speed and the GMIs were considerably increased. Thus, the mean antral contraction speed amounted to 3 mm/second at the outset and increased only mildly over time to reach a maximum at 25 and 30 minutes, with a mean of 3.5 mm/second. The differences between the 0- and 25-minute measurements failed to prove statistical significance ($P > 0.05$). In analogy to the propagation speed, the motility indices were also considerably higher compared to measurements following the intravenous injection of normal saline. They increased on average from 2.1 mm^2/second at the outset to 3.6 mm^2/second at 15 minutes. The maximal motility index was reached after 25 minutes (mean = 4.2 mm^2/second). The average value of the motility index amounted to 3.62 mm^2/second (SD = $\pm$0.2) (Figs. 3 and 4).

A comparative analysis revealed changes in both the antral wave propagation speed and the GMI induced by the gastric motility-modulating drugs. While metoclopramide increased gastric motility on average by a factor of 1.5 relative to the data collected following the injection of normal saline, the application of butylscopolamine led to a decrease of the motility index by a factor of 3. These differences were all statistically significant ($P < 0.05$) (Figs. 3 and 4).

DISCUSSION

Gastric motility disorders are common and represent the symptomatic hallmark of many gastrointestinal disorders (17,18). Due to the lack of a technique with

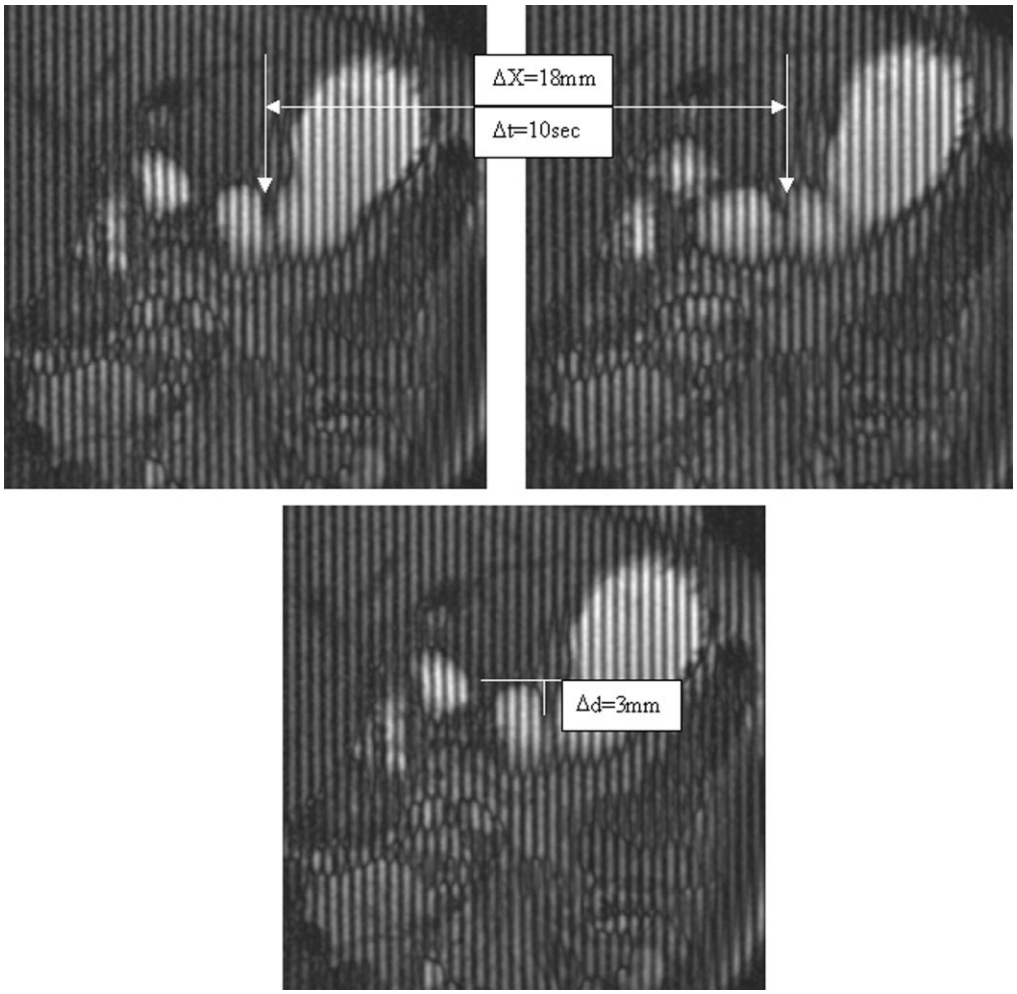

Figure 2. Two-dimensional real-time TrueFISP sequence with tagging lines in an oblique plane displaying the antral axis. Images **a** (t = 0) and **b** (t = 10 s) show the motion of the peristaltic wave toward the pylorus (arrow). In image **c**, the highest amplitude of the according peristaltic wave is shown. A motility index was calculated based on the distance that one wave passes within 10 seconds, and its maximal diameter.

sufficient diagnostic accuracy and patient acceptance, these conditions frequently remain undiagnosed (7,19). In view of the increasing availability of affordable and effective therapeutic strategies (20,21), it is high time to

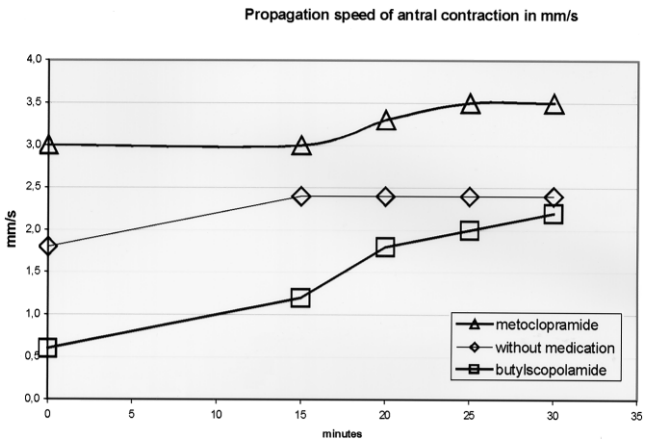

Figure 3. Propagation speed of antral contractions (mm/second) depending on different pharmacological stimuli.

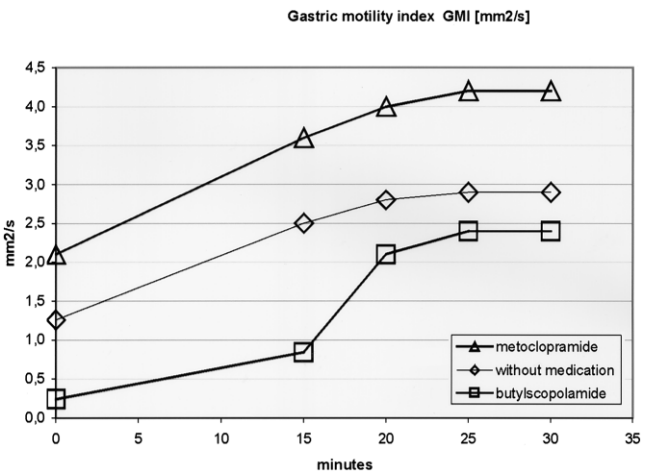

Figure 4. The GMI (mm^2/second) under different medications shows a statistically significant difference 15 min after i.v. injection of normal saline, butylscopolamide, and metoclopramide, and remained unchanged after 25 minutes.

overcome this diagnostic void. This initial technical report suggests that real-time TrueFISP MRI can provide a noninvasive alternative that offers good diagnostic accuracy and patient acceptance. Real-time TrueFISP MRI is capable of depicting gastric motility with sufficient temporal and spatial resolution for both qualitative and quantitative assessments. With the use of tagging techniques, gastric peristaltic motion can be objectively quantified and hence characterized. Three easily measurable parameters permit the determination of both the peristaltic wave velocity and the GMI. By employing these parameters in the current study, the pharmacologic effects of the motility-modifying substances metoclopramide and butylscopolamide on gastric peristalsis were successfully illustrated.

Motivated by MRI's inherent noninvasiveness, operator-independence, and lack of ionizing radiation, many researchers have proposed its use for evaluation of the stomach. However, despite initial enthusiasm, the clinical utility of MRI for the detection and staging of gastric malignancies (22–24) has remained rather limited. This reflects the lack of sufficient spatial resolution to depict the gastric mucosal surfaces. MR-based analyses of functional gastric disorders, on the other hand, appear to have considerably more potential (11,25–27). The first approaches, proposed by Schwizer et al (28), were handicapped by long acquisition times that rendered breath-held data acquisitions impossible. As a result, image quality was poor, which translated into an imperfect correlation with nuclear scintigraphy (28). Despite consistent advances in MR technology, examination protocols remained cumbersome for some time. Thus, Kunz et al (10,11) proposed the assessment of gastric motor function based on an MR acquisition lasting 60 seconds. To avoid respiratory motion artifacts, data collection was divided into four packages, during which the volunteers were instructed to hold their breath. However, differences in inspiratory depths limited the volumetric accuracy.

More recent hard- and software developments have enabled the acquisition of three-dimensional data sets within the confines of a single breath-hold (29). These data are of sufficient quality to permit the accurate delineation of gastric contours for volume measurements. In a previous study (30), repeated breath-held three-dimensional imaging to determine gastric volumes permitted the quantitative documentation of the prokinetic effect resulting from intravenously applied erythromycin. In that volunteer study, the agent resulted in a substantial acceleration of gastric emptying. The present study also demonstrated the ability of time-resolved three-dimensional MRI to identify patients with gastric dyspepsia: three of six patients revealed much reduced gastric-emptying rates in comparison to the mean determined in healthy volunteers (30). The real-time imaging technique proposed in this study complements the aforementioned efforts by providing a real-time analysis of gastric motion. The peristaltic wave itself can be resolved with sufficient temporal and spatial resolution to permit both qualitative and quantitative assessments. Accordingly, both the peristaltic wave velocity and the GMI could be readily determined. Based on these findings, we determined that the intravenous application of metoclopramide led to a significant acceleration of antral peristaltic waves, whereas scopolamine decreased gastric motility.

Real-time imaging of gastric peristalsis was achieved with a TrueFISP sequence that offers high temporal and spatial resolution (31). Primarily designed for cardiac imaging, FISP is based on a steady-state buildup in both the longitudinal and transverse directions. Whereas in FISP only one or two of the gradients are balanced, TrueFISP is characterized by balanced gradients in all three directions, which ensures maximum recovery of the transverse magnetization. In a direct comparison with two-dimensional-fast low-angle shot (FLASH) Cine MRI, TrueFISP was characterized by shorter acquisition times and superior image quality in a volunteer study examining the quantification of ventricular motion (32). Although a relatively high frame rate with one image per second was achieved, the signal-to-noise ratio (SNR) for anatomic display was not a limiting factor. Because of the unique signal characteristics of TrueFISP, it is conceivable that even higher frame rates can be achieved without running into SNR limitations. Echo-sharing techniques or radial projection TrueFISP imaging may be alternative means of maintaining the TrueFISP contrast mechanisms while enhancing the temporal resolution even further; however, these approaches remain to be evaluated (32). Real-time sequences are not appropriate for the assessment of gastric emptying. For such assessments, the applied protocol could be amplified with three-dimensional sequences, which have been shown to sufficiently display gastric volumes and enable the calculation of gastric-emptying rates (30).

The assessment of gastric motility is predicated upon the delineation of the gastric contours. For this purpose, the stomach has to be distended and filled with a contrast agent. The agent should on the one hand simulate the prokinetic effects of food (to stimulate gastric motility) and on the other hand have signal characteristics that permit easy differentiation between gastric content and the surrounding gastric wall. Since the gastric wall is inherently dark on TrueFISP images, a contrast agent is needed to render the gastric lumen bright. In this study, we chose a pudding as the high-calorie base for the oral contrast agent. In vitro experiments had revealed the pudding to be brightest following the addition of paramagnetic contrast in a concentration of 1:200. This resulted in vivid contrast between the bright gastric lumen and the surrounding dark gastric wall. Since the use of a semiliquid nutrient only partly mimics the situation in real life (29), it would be preferable to use a similar model with solid food. However, the distribution within the stomach would not be as homogenous as in our trial, and it would be far more difficult to delineate the peristaltic waves.

We conclude that real-time TrueFISP imaging is feasible for the assessment of gastric motility. The acquired two-dimensional real-time TrueFISP data are robust and characterized by sufficient temporal and spatial resolution. Clearly, this technical note represents merely the beginning of a long road to proving the clinical utility of real-time TrueFISP MRI for the assess-

ment of gastric motility disorders. Future clinical studies are planned.

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