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MRI for evaluation of gastric physiology

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Chapter 2

Review of MRI for evaluation of gastric physiology

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Introduction

The function of the stomach comprises storage of ingested food, production of gastric secretion and mixing food with gastric secretion, grinding the ingested food (motility) and emptying of the stomach to the duodenum. This function can roughly be summed up by two main processes: gastric emptying and gastric motility.

Disorders of gastric function such as diabetic gastroparesis, functional dyspepsia and disorders after gastrointestinal surgery are characterized by a variety of changes of gastric motility and emptying: hyper- or hypomotility, disturbed gastric accommodation and delayed emptying, all in the absence of pathology found at endoscopy or abnormal laboratory results (1-3). Patients with disorders of gastric motility and gastric emptying experience a wide variety of complaints that are meal-related, such as nausea, bloating, gastric pain and/or gastric tension after meal consumption. Assessment of these disorders plays an important role in differential diagnosis and subsequent treatment of these patients.

Several techniques are currently applied to study normal and pathological gastric motility and gastric emptying but they measure or evaluate only few of the various aspects. For example, the barostat technique is considered the gold standard for evaluation of proximal gastric motor function, including gastric accommodation (20, 27). Accommodation of the stomach wall is considered to be a vagally mediated reflex that causes the stomach wall to relax in response to a meal that has been consumed and acts as both a chemical and a mechanical stimulus.

Gastric accommodation results in a reduction of gastric wall tone, which gives the stomach the opportunity to distend, providing a reservoir for the meal (7).

Disadvantages of the barostat technique are the invasive nature requiring oral intubation with intragastric positioning of a polyethylene bag (27). Moreover, questions have been raised about possible interference of the barostat with gastric physiology (11, 14, 18), since it could act as a mechanical stimulus itself. Recognition of these characteristics may contribute to the diagnosis of motility disorders.

Since the early 1990's, magnetic resonance imaging (MRI) has been employed experimentally to investigate gastric motility and emptying non-invasively (4-7).

Feinle *et al* validated MRI as a tool for the analysis of gastric emptying (8).

And since that time, MRI has been used more often to study gastric pathophysiology (1,2,9-13).

This review summarizes the literature from the validation studies to the clinical studies that used MRI as a method for evaluation of gastric physiology.

Methods

A search for relevant original publications was conducted in Medline from 1990 to 2008, using the following search keys: functional tests, gastric physiology, gastric emptying, gastric motility, MRI. The articles were primarily selected on the basis of the title and the abstract, no specific exclusion criteria were used. Additional references were obtained from the bibliographies of the original articles. The full text of 15 relevant articles was retrieved.

Table 2.1 summary of the studies mentioned in the article

Author	Year of publication	Goal of the study	MR-technique
Feinle	1999	Scintigraphic validation of MRI for evaluation of gastric emptying	3D TSE (28 x 0.75mm slices) Supine body position
Kunz	1999	Evaluation of gastric emptying and motility of solid and mixed solid/fluid meals	3D TSE (28 x 0.75mm slices) Supine body position
Boulby	1999	Evaluation of forward and backward antral flow in gastric emptying that is delayed by a fat containing meal	Echo Planar Imaging (3 volumes of 8 x 1cm slices) Supine body position
Wright	1999	Validation of antroduodenal motility measurements	Echo Planar Imaging (3 volumes of 8 x 1cm slices) Supine body position
Borovicka	1999	Evaluation of gastric emptying and motility in diabetic gastroparesis	Volume: 3D TSE (28 x 0.75cm slices) Motility: 2D TSE 60 x 1cm slice, 1 image/second Supine body position

Bilecen	2000	Visualization of gastric wall motility	T2-w RARE Supine body position
De Zwart	2002	Influence of pharmacological stimuli on gastric emptying and motility	Volume: 3D TFE (20 x 1cm slices) Motility: 2D TFE (300 x 1cm slices, 1 image/second) Supine body position
Lauenstein	2003	Influence of pharmacological stimuli on gastric emptying	3D GE (64 slices 3.14mm thickness) Supine body position
Ajaj	2004	Influence of pharmacological stimuli on gastric motility	2D True FISP Supine body position
Ajaj	2004	Study of gastric motility disorders	T1 True FISP (0.5 mm slice thickness) Supine body position
De Zwart	2005	Influence of barostat device on gastric accommodation and motility	Volume: 3D TFE (20 x 1cm slices) Motility: 2D TFE (300 x 1cm slices, 1 image/second) Supine body position
Kunz	2005	Evaluation of ingestion order of fat in meal on intragastric fat distribution and gastric emptying	3D TSE (28 slices, 0.75mm thickness) Supine body position
Treier	2006	Influence of body position on gastric motor function and emptying	3D and 2D T1 SENSE (slice thickness 1cm) Upright body position
Fruehauf	2007	Study of variability of gastric volumes to liquid meals in healthy subjects and in FD	T1-w, 20 slices, slice thickness 1cm Upright body position
Treier	2008	Quantification of gastric secretion	Fast t1-mapping with variable flip angles Supine body position

Technical aspects of gastric MRI

The evaluation of gastric physiology requires the use of appropriate techniques to evaluate the various aspects of changes in volume and contraction. Based on the literature we summarize how investigators perform MRI studies to assess gastric physiology. First, the preparation of the meal is reviewed; second, the preparation of the patient and MRI acquisition techniques used; thirdly, the analysis of the data to assess both gastric emptying and gastric motility.

1) Preparation of the meal

To evaluate gastric emptying, positive labeling of a meal is necessary to obtain reliable results (4,8). Since the experimental studies of Schwizer and Kunz in the 90's, most authors use Gadolinium tetraazacyclododecane tetraacetic acid (Gd-DOTA) to label the meal, since it is shown that Gd-DOTA is the most stable contrast agent in the acidic gastric environment. Moreover, Gd-DOTA adheres well to both fluids and solids and is not easily absorbed by the gastrointestinal tract and thereby provides excellent positive contrast (14).

2) Patient positioning and MRI technique.

In most studies, each experiment starts after a period of fasting. Then, the subjects are positioned in a conventional MRI scanner (mostly 1.5 tesla fieldstrength) in a right sided semi-supine position (30-45°) (Figure 2.1)(4,5,8,15-18). Most studies use this semi-supine position, since MRI in the sitting position is not widely available (19).



Fig. 2.1 Illustration of patient positioning for gastric MRI study . Patient is positioned in right-sided semi-supine position to enhance gastric emptying. Surface-coil is positioned anterior to the patient for improved image quality at 1.5 tesla

For the evaluation of gastric emptying, a 3-dimensional (3-D) volume scan is applied (4,5,8,15-19). In this sequence, the entire stomach is included in the volume acquisition; from the volume data multiple slices with a slice thickness of 0.5 to 1 cm are reconstructed for further evaluation. To evaluate momentary gastric volume, the use of a multi receive parallel body-synergy-coil has been advocated at 1.5 T. Sequence parameters include, for example, a Turbo Field Echo (TFE) sequence, TE = 3.5 ms, TR = 10 ms, field of view 450 mm, rectangular field of view 55%, symmetric reduction 50%, flip angle 25°, 256x256 pixels, slice thickness 10 mm, with a total scan duration 25 seconds, without breath hold (16).

To assess gastric motility, a fast 2-dimensional (2-D) dynamic scan (such as Turbo Field Echo, Turbo Spin Echo, Echo Planar Imaging, True FISP, Balanced FFE, RARE) has been advocated (4,5,7,16,20,21). There is no particular preference for a specific acquisition technique, as the only goal of the technique is to be sufficiently fast to reach a temporal resolution that is high enough to analyse gastric motility with MRI. Some authors have advocated a single slice approach at the level of the stomach to assess dynamic gastric volume changes in a semi-coronal image orientation in which both part of the antrum and part of the fundus along the longitudinal stomach axis is included (see figure 2.2) (4,5,16).

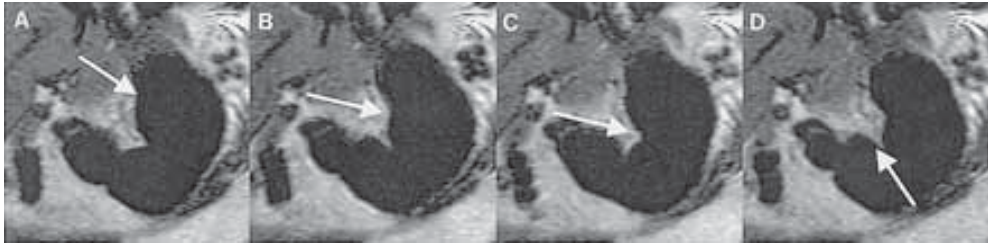


Fig. 2.2 An example of a peristaltic contraction beginning at the level of the gastric fundus and propagating towards the antrum

For following parameters have been proposed for a Turbo Field Echo acquisition, including 300 images per scan over a time period of, for example 5 minutes, a temporal resolution of 1 image per second, TE = 3.6 ms, TR = 10 ms, field of view 450 mm, rectangular field of view 55%, symmetric reduction 50%, flip angle 25°, 256/128 pixels, slice thickness 10 mm, without breath hold.

3) *Data-analysis*

a) gastric emptying

As part of the post-processing, in most studies, the outline of the stomach is drawn manually and special software (such as MASS© (22)) is used. Slices encompassing the entire stomach are then summed up to measure momentary gastric volume. As a function in time, the percentage in decrease of the gastric volume represents gastric emptying. As gastric secretion mixes with the meal and hereby influences gastric volume, Kunz et al. designed a robust method to correct gastric meal volume for progressive dilution due to gastric secretion (4). First, the relationship between dilution of gastric content by gastric secretions and signal intensity for meals was experimentally determined by filling small bottles with defined quantities of the meal and mixing them with increasing quantities of hydrochloric acid. Then, the bottles were imaged simultaneously in a single plane. With liquid meals, an exponential correlation was found between the concentration of hydrochloric acid and the signal intensity. During gastric emptying studies, an external standard (containing both the same meal that the subject had just ingested consisting of a mixture of fluid or solid food mixed with contrast medium) was placed in a

polyethylene tube beside the subject and imaged simultaneously. The image intensity of the tube content served as a reference to correct for gastric secretion. An increase in gastric secretion resulted in a decrease in signal intensity of gastric contents (8).

b) gastric motility

When gastric motility is studied, most attention is given to gastric peristalsis. In most studies, gastric diameters were measured at equally distributed points perpendicular to the stomach axis. On the basis of this diameter calculation, peristaltic contractions are detected and their frequency is calculated (4,16). Other authors advocate the use of dark parallel tagging lines that can be applied in the images in the cranio-caudal direction in a manner similar to that described for cardiac MRI. The gap between two tagging lines can be measured and the distance that a peristaltic wave had passed by counting the number of tagging lines, can be quantified (figure 2.3) (9,23).

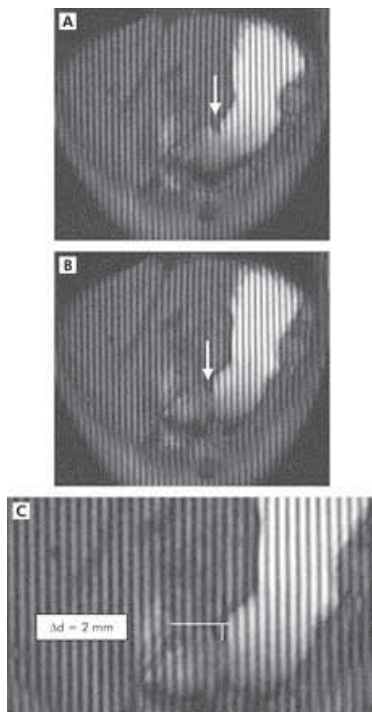


Fig.2.3 Two dimensional real time fast imaging with steady state precession sequence (TrueFISP) with tagging lines in an oblique plane displaying the antral axis. Images (A) ($t=0$) and (B) ($t=20$ s) show the motion of the peristaltic wave towards the pylorus (arrow). In (C), the lowest amplitude of the according peristaltic wave is shown. Based on the distance that one wave passes within 20 seconds and its lowest amplitude, a motility index could be calculated.

Basic research for validation of MRI

Several initial studies have validated MRI techniques for studying gastric physiology.

In 1999, the applicability of MRI to assess gastric emptying and motility of liquid and solid meals, was studied by Kunz et al. (5). Gastric emptying and motility of a liquid and a solid meal were studied in eight volunteers. Gastric emptying of the liquid meal was faster than emptying of the solid meal when considering half-times of emptying. Hereby, this study showed that with MR it was possible to evaluate gastric motility and gastric emptying and at the same time it provided an important new insight in the physiology of gastric emptying of different gastric contents.

In 2002, MRI was validated for evaluation of gastric accommodation with the barostat method, which is considered the gold standard for evaluation of postprandial accommodation of the gastric wall. In the barostat method, the subject ingests an intragastric balloon that is connected to a device that maintains the pressure in the barostat balloon on a certain level. When by postprandial relaxation the stomach wall relaxes, the system starts to sufflate air into the balloon to maintain the pressure inside the balloon to the preselected level.

Measurements of gastric volume and motility with MRI were compared with simultaneously performed measurements with a barostat. MR images and barostat measurements were obtained both at rest and after infusion of glucagon and erythromycin that alter gastric volume and motility. Volume measurements with MRI followed volume changes of the barostat balloon. That study showed that MRI is as accurate as barostat measurement in determining changes in gastric volume (16).

The same study raised questions about the influence of the barostat balloon on gastric physiology. To address this issue, gastric accommodation, motility, and emptying have been studied twice in 14 healthy subjects with MRI once in the presence of a barostat bag and once when the barostat bag was not present. Fasting and postprandial intragastric volumes were significantly higher in the experiment with barostat vs. without barostat. No significant differences were found in gastric emptying and contraction frequency between both experiments.

The accommodation response observed in the presence of the barostat bag was not observed in the absence of the barostat bag. The presence of an intragastric barostat bag did not interfere with gastric emptying or motility, but the accommodation response measured with the barostat in situ is not observed without the barostat bag

in situ (24). Postprandial gastric accommodation shown as gastric wall distension is solely an effect caused by the barostat device. The intragastric meal alone does not cause the stomach to distend to the same proportions as the barostat balloon, which distends the stomach more pronounced than the intragastric meal volume.

Demonstrating that MRI is able to detect changes in gastric physiology is the basis of the validation of MRI for evaluation of gastric motility and emptying disorders. These changes in emptying and motility can, of course, be caused by the most natural way i.e. food that acts as both a mechanical and a chemical stimulus to gastric function, but also more artificially by infusion of pharmacological substances. The evaluation of the effect of these pharmacological stimuli in itself forms the basis of development and evaluation of future pharmacological therapy for disturbances of gastric function disorders.

Lauenstein et al. assessed the effect of intravenously administered erythromycin on gastric emptying and subsequent small-bowel filling using three-dimensional (3D) MR imaging in both healthy subjects and patients with functional dyspepsia (18). Six healthy volunteers and 6 patients with symptoms of functional dyspepsia ingested 500 ml of a gadolinium labeled, fluid meal. In healthy volunteers, gastric volumes decreased significantly more after the administration of erythromycin. In three patients with functional dyspepsia, MR imaging revealed reduced rates of gastric emptying. The administration of erythromycin resulted in a significantly faster rate of gastric emptying in two of those three patients, indicating the possible therapeutic effect of this drug.

Ajaj et al. determined the practicality of MRI for the assessment of gastric motion, and tried to quantify the effects of metoclopramide and scopolamine (23). The intravenous application these substances 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 (23).

One could criticise MRI because in most MR scanners, subjects are studied in a non-physiological body position, i.e. supine instead of upright or seated, which might cause different meal distribution inside the stomach which might influence gastric physiology (figure 2.4).

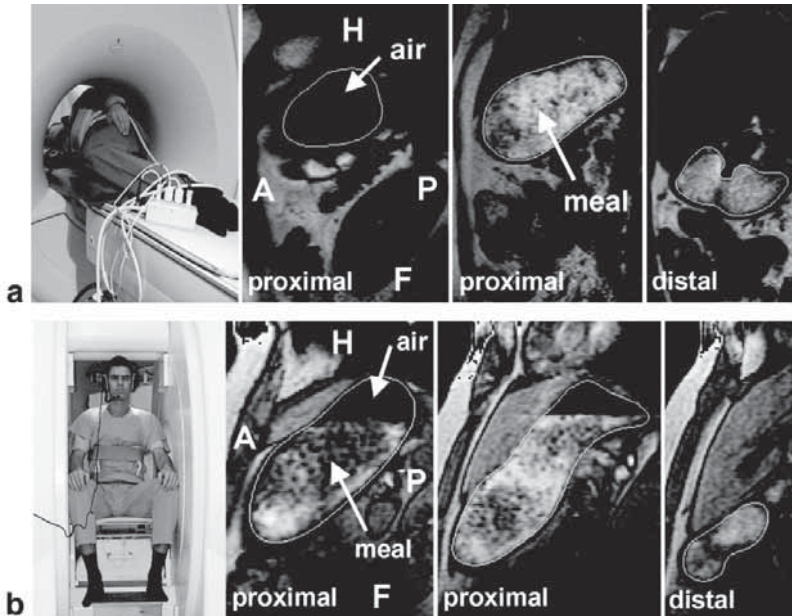


Fig. 2.4 **A** Left: Volunteer in RP inside the 1.5 T whole-body MRI system. Rectangular surface coils were fixed around the abdomen. Right: Three sagittal MR image slices (two proximal and one distal) of a volume scan in RP with outlined stomach wall. Air and meal are indicated in the MR images by arrows (F: feet, H: head, A: anterior, P: posterior) **B** Left: Volunteer sitting inside the 0.5 T open-configuration MRI system. A send-receive coil was fixed around the abdomen. Right: Three sagittal MR image slices (two proximal and one distal) of a volume scan in SP with outlined stomach wall. Air and meal are indicated in the MR images by arrows (F: feet, H: head, A: anterior, P: posterior)

Several studies were aimed at evaluation of these possible disadvantages of MRI as compared to other validated examination methods. Treier et al. determined the effect of the right decubitus lying body position on relevant parameters of human gastric motor function in healthy volunteers (see figure 2.5) (19).

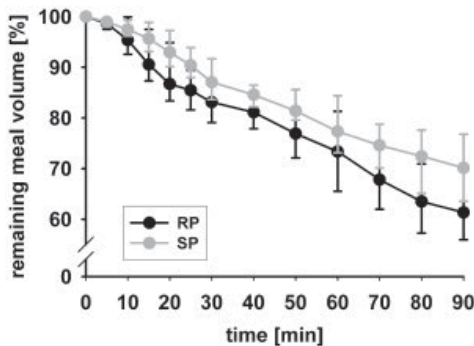


Fig. 2.5 Normalized gastric emptying curves (percentage of remaining meal volume in the stomach) for RP (black) and SP (gray). Data are expressed as the median (interquartile range). A divergence of the emptying curves is observed, especially during the first 30 minutes after meal ingestion

In this study, postprandial gastric function after ingestion of a solid/liquid meal was assessed in volunteers in the right decubitus position and seated position. Stomach and intragastric air volume, intragastric meal distribution, gastric emptying, and gastric peristalsis were compared between the right decubitus position and seated position. It was shown, that body position did not affect gastric relaxation and initial gastric volumes. Postprandial stomach volume and gastric activity were also similar. Meal emptying showed different characteristics, resulting in a significant but small difference in meal volume (see figure 2.5) that could have been induced by posture-dependent vagal activity. This study is valuable, because it confirmed that MRI in the right decubitus position is a reliable imaging technique for assessing gastrointestinal physiology and that results from MRI studies in the right decubitus position can be compared to studies performed in the sitting position. This is a solution to the fact that MRI in the sitting position is not widely possible to perform.

Study of patients with functional dyspepsia

After validation of MRI for evaluation of gastric function, MRI was employed as a method for research and study of several gastropathological disorders, such as functional dyspepsia.

Ajaj et al. evaluated whether patients with increased or decreased gastric motility can be differentiated from healthy volunteers by means of real time MRI (9). In this study, 10 healthy volunteers, 10 patients with gastroparesis, and 10 patients with functional pylorospasm/peptic pyloric stenosis underwent real time MRI. All patients were examined on two separate days; once prior to therapy and once after adequate therapy. Antral motility was quantified by calculating the gastric motility index. Patients with gastroparesis showed a lower motility index compared with the healthy volunteer group while the mean motility index of the patient group with pylorospasm was more than three times higher than that of the reference value of the volunteer group (figure 2.6). However, the gastric motility index in the patient group with gastroparesis increased, and in the group with functional pylorospasm/peptic pyloric stenosis it decreased significantly after therapy. This study shows, that MRI can clinically assess patients with suspected gastric pathophysiology as it is able to differentiate healthy subjects from patients with gastroparesis.

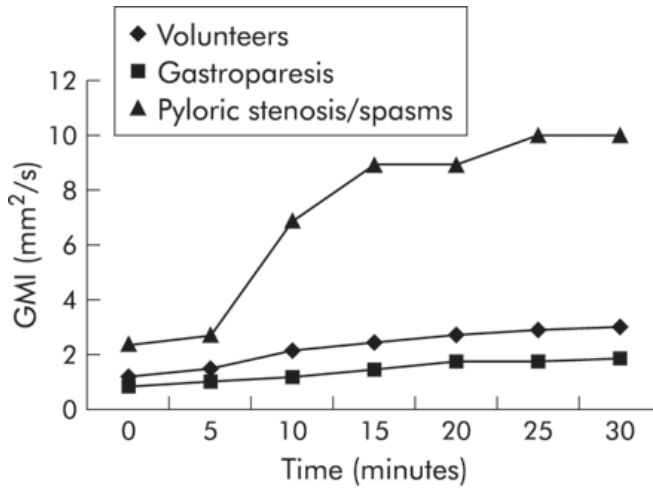


Fig. 2.6 Mean gastric motility index GMI for the volunteer group and both patient groups (gastroparesis / pyloric stenosis and/or spasms) prior to therapy. The motility index shows a significant difference 15 minutes after pudding ingestion

Borovicka et al. studied the effect of orally administered cisapride on gastric emptying and motility in eight diabetic patients with previously demonstrated delayed gastric emptying. MRI studies were also performed in seven diabetic patients with normal emptying who served as disease controls. Gastric emptying was slower in the gastroparetic patients compared to patients with normal emptying. Cisapride accelerated gastric emptying in patients with gastroparesis. The contraction amplitudes in the proximal stomach of gastroparetic patients were increased during cisapride treatment, whereas antral contraction frequency, amplitude, and velocity were unchanged. It was concluded that cisapride-induced acceleration of liquid gastric emptying in diabetic gastroparesis does not appear to result from changes in antral contractility, but may be related to changes in proximal gastric tone or gastric outlet resistance (10).

Discussion and conclusion

Prevalence of functional gastrointestinal disorders is high (12), but no single diagnostic test has been generally recommended for clinical use in patients with suspected functional dyspepsia. All available tests have certain disadvantages that withholds them from being used in the clinical environment. Barostat, for example,

is an invasive test that comprises the use of an intragastric balloon, and therefore has poor patient acceptance. Nuclear studies are associated with considerable exposure to ionizing radiation and lack spatial and temporal resolution (8), as does electro gastrography, which gives no details about gastric contractions (25). Therefore, since the early nineties, researchers have searched for a non-invasive, non-radiation technique that had sufficient diagnostic accuracy, as well as patient acceptance. As MRI becomes more and more widely available, lacks exposure to ionizing radiation and is accepted by patients in the clinical setting since it does not require any oral intubation, MRI has been proposed for evaluation of gastric functional disorders.

First approaches were hampered by long acquisition times that resulted in poor image quality and less robust results. But as experience with MRI grew longer and acquisition times were shortened, MRI proved to be a promising new technique for evaluation of gastric function. Standard fast MR techniques allow complete depiction of the stomach volume and gastric peristalsis in sufficient temporal and spatial resolution without exposure to ionizing radiation.

MRI has evolved from a technique that evaluates gastric function in healthy subjects to a technique that evaluates the effect of pharmaceutical products in patients with functional dyspepsia or other disorders of gastric function (16,18). MRI has shown in smaller research and clinical settings to be able to evaluate both gastric emptying and gastric motility, now the technique should be evaluated in a clinical setting on a larger scale

Footnote

Permission to use figures 2.3, 2.4, 2.5 and 2.6 was obtained at BMJ-Group and Wiley Liss Inc.

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