Title: WILL MRI OF GASTROINTESTINAL FUNCTION PARALLEL THE CLINICAL SUCCESS OF CINE CARDIAC MRI?

Short title: MRI of gastrointestinal function

Abstract:

Cine cardiac MRI is generally accepted as the 'gold-standard' for functional myocardial assessment. It only took a few years after the development of commercial MRI systems for functional cardiac imaging to be developed, with ECG gated cine imaging first reported in 1988. The function of the GI tract is more complex to study compared to the heart. However, the idea of having a non-invasive tool to study the GI function that also allows the concurrent assessment of different aspects of this function has become more and more attractive in the gastroenterological field. This review summaries key literature of the last 5 years to describe the current status of MRI in respect to the evaluation of GI function, highlighting the gaps and challenges and the future prospects. As the clinical application of a new technique requires that its clinical utility is confirmed by demonstration of its ability to enable clinicians to make a diagnosis and/or predict the treatment response, this review also considers whether or not this has been achieved, and how MRI has been validated against techniques currently recognised as the gold standard in clinical practice.

(186 words)

INTRODUCTION

How cine MRI entered clinical practice in the cardiac field:

MRI has always been an attractive imaging modality for the evaluation of cardiac morphology and function¹. Cardiac MRI has the advantage that both cardiac and respiratory motion are generally periodic and relatively easily monitored, albeit indirectly, through synchronisation to the subjects' electrocardiogram (ECG) and the use of respiratory bellows. However, it only took a few years after the development of commercial MRI systems for functional cardiac imaging to be developed, with ECG gated cine imaging first reported in 1988².

In this context, "cine" imaging refers to the ability to acquire multiple, temporally-resolved, images throughout the cardiac cycle. The acquisition only allowed a single phase-encode for each temporal phase to be performed in each heartbeat, so images with an acceptable spatial resolution took several minutes to acquire. Artefacts due to respiratory motion during the acquisition were initially addressed using simple signal averaging techniques³ or using complicated schemes that adjusted the acquired phase-encoding step dependent upon the point in the respiratory cycle⁴. A step change in image quality came with the development of the necessary hardware and software to allow segmented *k*-space acquisition methods⁵ allowing the cine cardiac acquisitions to be performed in a single breath-hold.

Whilst this method worked reasonably well, image contrast was dependent upon the dynamics of the blood flow and contrast was impaired when the imaging plane was parallel to the direction of flow, particularly in diastole when flow was relatively stationary. It was the emergence of what is now known generically as the balanced steady state free precession (bSSFP) gradient echo sequence that led to further improvements in image quality. The initial implementation of this sequence by Oppelt working for Siemens was given the name "Fast Imaging with Steady Precession" (FISP)⁶. However, FISP necessitated a static magnetic field uniformity that was not practically achievable, and the sequence was subtly modified to reduce its sensitivity to field uniformity, albeit at the expense of reduced contrast. Around the year 2000 field uniformity had improved to the point that the original implementation could be deployed, however since the name FISP has already been used, this original implementation was renamed by Siemens as True-FISP.

The contrast in a bSSFP sequence (variously known as True-FISP, bFFE and FIESTA by the major manufacturers) is proportional to the ratio of the $T_2:T_1$ of tissues. Fluids, like blood, with long T_1 and T_2 relaxation times therefore yield high signals in comparison to muscle for example. Combining True-FISP with a cine segmented *k*-space acquisition provides high quality functional cardiac images with excellent blood pool/myocardial contrast⁷. This is now the standard method for global and regional functional cardiac imaging and analysis (Figure 1). Whilst it is possible to use advanced acquisitions and reconstruction methods to acquire dynamic images without either cardiac or respiratory gating⁸, standard cine imaging involves data acquisition over a small number of consecutive heartbeats within a single breath-hold.

Contemporaneous with the development of improved MRI system hardware and software for cardiac imaging was the involvement and interest of not only radiologists but also cardiologists. Market forces drove the manufacturers to improve their product offerings whilst the clinical end users established the high accuracy and reproducibility of cine MRI. These contributions led to the development of both European and US consensus panel reports^{9, 10} with bSSFP-based cine cardiac MRI becoming accepted as the 'gold-standard' for functional myocardial assessment.

Is MRI following the same approach in the gastrointestinal (GI) field?

The function of the GI tract is more complex to study compared to the heart. The GI tract occupies a larger area of the body and the function comprises motility, secretion and transit, which all interact with each other. Moreover, the motion is not periodic. The relevance of studying GI function (motility, secretion and transit) have been demonstrated to impact on many clinical conditions encompassing functional and organic diseases. Alterations of gut motility have been reported to play a role in the pathophysiology of functional bowel disorders such as irritable bowel syndrome (IBS) and functional dyspepsia $(FD)^{11, 12}$, and also play a role in the pathophysiology of symptoms of organic diseases like scleroderma and inflammatory bowel disease (IBD)^{13, 14}. Until recently, the study of GI motility, secretion and transit have relied on techniques with varying degrees of invasiveness. The study of gut motility has been based on intraluminal catheters measuring the pressure generated by gut wall¹⁵. This has been obtained by passing a manometry catheter through the nose to reach the oesophagus, stomach and proximal small bowel or inserted through the anus, after bowel preparation, to reach the colon. Similarly, the study of gut secretion has involved the insertion of intraluminal catheters able to collect fluids in the small bowel¹⁶. With regard to gut transit, relatively less invasive techniques have been used ranging from radiopaque markers, scintigraphy, a wireless pH and pressure recording capsule (SmartPill), and a telemetric capsule system (3D-Transit)¹⁵. The major limitation of all these techniques has been the difficulty to simultaneously evaluate different aspects of GI function.

Therefore, the idea of having a non-invasive imaging tool that allows the concurrent assessment of different aspects of GI function has become more attractive in gastroenterology. This review summaries the last 5 years key literature describing the current status of MRI in respect to the evaluation of GI function, highlighting the gaps and challenges and future prospects. The clinical application of a new technique requires that its clinical utility is confirmed by demonstration of its ability to enable clinicians to make a diagnosis and/or predict the treatment response¹⁷. This review will discuss whether this has been achieved, and how MRI has been validated against techniques recognised as the gold standard in clinical practice.

Evaluation of GI motility and movement of chyme by MRI

The clinical indications to evaluate gut motility are to investigate patients with suspected small bowel and colonic motor disorders¹⁸, such as diagnosis of chronic intestinal pseudo-obstruction or motor dysfunction in patients with chronic constipation refractory to pharmacological treatments, when a surgical operation is considered¹⁸. The current gold standard techniques to evaluate gut motility are antro-duodenal manometry and colonic manometry¹⁸.

Many advances have been made using MRI in the observation and quantification of GI motility in recent years mainly in the image processing and analysis domain. In terms of imaging, cine (or dynamic) techniques used to observe the motion of the heart, as discussed above, have been adapted for use in the GI tract. Whereas segmented k-space acquisitions are used to acquire images across the cardiac cycle during a breath-hold, in GI imaging single shot techniques are used to rapidly generate images which are then repeated; either during a breath hold or during free breathing to capture the irregular motion in the GI tract. The most widely used sequence performed to assess GI motility is the bSSFP acquisition¹⁹⁻²¹. Like cardiac MRI, this sequence is particularly attractive for GI motility due to its capability for rapid imaging with a high signal-to-noise-ratio (SNR) and excellent image contrast between gut wall and fluid-filled lumen, resulting in excellent quality dynamic images acquired with a high temporal resolution.

Much of the research in recent years has looked to move away from time consuming observer analysis of data to a more automated approach using the advances in image processing and, in particular, image co-registration techniques to provide faster more robust analysis that are more observer independent²⁰⁻²⁴. Registration of the cine data allows for regions of bowel wall to be tracked over time using information of the deformation parameters generated during the registration process^{24, 25}. From this concept there have been two main approaches to the subsequent analysis, the first looks at luminal diameter changes across the region of interest of the GI tract with this information used to look at frequency and depth of contractions^{19, 22}. The second approach takes the motility information inferred from the registration parameters to create a metric which is a surrogate of the underlying motion^{20, 21}.

The major area where these techniques have been explored in detail is the small bowel²⁶⁻³¹. Crohn's disease has been the main focus assessing motility following oral contrast agent administration and prior to administering hyoscine butylbromide for the traditional anatomical MRE scan. Reduced motility in the terminal ileum region has been a feature of several studies^{26, 30}. Motility was found to be reduced in inflamed regions of the small bowel²⁹ and researchers have also shown that there is a correlation between small bowel motility measurements with inflammatory markers such as C-reactive protein and calprotectin²⁷, histopathology of the terminal ileum²⁸, and response to medical therapy²¹. Differences in small bowel motility have also been shown in stricturing disease where both the stricture site and pre-strictured bowel showed reduced motility compared with normal bowel³². In addition, recent papers applying cine MRI to chronic intestinal pseudo-obstruction³³⁻³⁵ demonstrated that motility in these patients was reduced compared to healthy controls.

The role of MRI in studying oesophageal motility has been looked at and compared with high resolution manometry to diagnose achalasia³⁶ and observe functional and anatomical information in Nissen fundoplication³⁷. Both studies had subjects swallowing liquids whilst undergoing MRI, acquiring images using fast spin-echo and cine bSSFP sequences. Studying eleven suspected achalasia patients and three control subjects, the authors concluded that MRI was safe and feasible for the diagnosis of achalasia³⁶. MRI in three planes of the oesophagus and gastro-oesophageal junction at 1.5 T of 29 Nissen fundoplication patients offered simultaneous morphological and functional imaging in one diagnostic method concluded the authors³⁷ and that MR 'fluoroscopy' offers the possibility to identify the wrap position, providing detailed information for the surgeon.

Although gastric motility was the first to utilise cine MRI^{38, 39}, it has not thus far been taken up in the clinical setting. This may be because of time consuming data analysis. More recently there have been several papers looking at gastric motility^{23, 40-42} using more automated software for analysis and these improvements could offer MRI as a potential alternative to manometry and gamma scintigraphy by combining motility and emptying in a single examination.

Colonic motility is the most recent area of the GI tract that cine MRI has been applied to. Unlike small bowel motility which can be assessed over a short breath-hold scan, motility of the colon is much more erratic with large time gaps between consecutive contractions. This problem has led to the development of further post-processing advances allowing for data collection during free breathing and hence longer acquisition times are possible^{43, 44}. Despite the longer acquisition time fasting or fed state colon motility is still very unpredictable and therefore to provoke contractions in the colon, laxatives have been used to induce movement⁴⁵, (Figure 2 A-B). Metrics to characterise the motility induced in the colon have looked at both luminal diameter changes and the same deformation metric used in the small bowel⁴⁶. Using the luminal diameter change metric applied in constipation, researchers have found that different types of constipation evoke different responses to this strong stimulus⁴⁷.

Another technique that was originally developed for cardiac MRI is tissue tagging⁴⁸. This method was originally developed to assess transmural motion and allow the calculation of myocardial strain⁴⁹ (Figure 3). It has now been adapted to look at motility in the small bowel and colon^{50, 51}. The bending or smearing of the tag lines have been used to assess motion in the small bowel⁵¹ and shown to differ pre and post administration of an anti-spasmodic agent. Mixing and movement of the colonic contents following a laxative stimulus (Figure 2 C-D) has also shown different responses between healthy and constipated subjects⁵⁰.

In terms of limitations of these techniques, the majority need a stimulus to provide both contrast between the GI lumen and walls, and to provoke reliable motility. As there are currently no recommended guidelines on which oral contrast media should be used, and the number and timing of scans, further research is necessary to refine protocols for wider clinical implementation. Limited coverage of the area can also be an issue as there is generally a trade-off between temporal resolution, coverage and spatial resolution. Good spatial resolution is normally needed to obtain good quality registration information, particularly if wall tracking analysis is required. As has happened in cardiac MRI, the use of multi-channel receiver coils has allowed the development of parallel imaging techniques⁵² that can be used to allow greater coverage with adequate temporal resolution to fully cover the small bowel. Further improvements will aid coverage in the gastric and colonic regions to provide a more comprehensive measurement. Work has started on developing some of the protocol requirements⁵³ in terms of assessing the duration and temporal resolution needed for accurate small bowel motility measurements. As with cardiac MRI, the radiographer plays a key role in the quality of data acquired from GI motility measurements, particularly for single slice or reduced coverage imaging of the segment of interest, where the angulation of the slices through the GI tract segment can dramatically change the images acquired.

The lack of validation of MRI as a measure of GI motility against the recognised gold standard techniques is also perceived as a limitation. There are some ongoing studies which are validating the use of MRI against conventional antro-duodenal manometry (NCT03191045, clinicaltrials.gov) and high-resolution colonic manometry (NCT03226145, clinicaltrials.gov). One of these studies (NCT03226145, clinicaltrials.gov) and another ongoing one (ISRCTN14481560, isrctn.com) are evaluating the possible predictive value of motility as measured by MRI on the response to treatment in patients with chronic constipation and patients with Crohn's disease.

The evaluation of GI transit by MRI

MRI has been used to study gastric and colonic transit time. The clinical indication for gastric emptying studies is to investigate patients with suspected gastroparesis and for colonic transit time is to investigate patients with constipation refractory to treatment¹⁸. In the first case MRI has been validated against scintigraphy⁵⁴, while in the second case against radiopaque markers⁵⁵.

The MRI technique for gastric emptying involves is based on collecting a number of slices across the entire stomach postprandially. Multislice, bSSFP, half-fourier acquisition single shot turbo spin-echo (HASTE) or echo-planar (EPI) sequences can be acquired rapidly and provide adequate contrast (Figure 4). During a breath-hold scan (to reduce motion artefacts) the volume of the entire stomach including test meal (positive contrast) and gas (negative contrast) are imaged. Using paramagnetic agents mixed into the test meal, gastric volume (defined manually or semi-automatically) can be corrected for gastric secretions by reference to the signal intensity of an external standard.^{56, 57} Plotting the changes in gastric volume with time allows a calculation of the time to half empty the stomach contents (t50%)

and also the time delay after which the stomach starts emptying (also called the lag time or tlag). MRI correlated well against gamma scintigraphy for both liquid and mixed liquid and solid test meals, with the advantage of the lack of radiation dose. Other advantages of MRI include multi-slice high spatial resolution acquisition with no gaps between slices, providing images covering the 3D volume. From the images one can also investigate the intragastric distribution of components of the test meal (e.g. sedimentation and layering).

MRI uses a similar approach to radiopaque markers to study the transit in the colon. Subjects swallow five MRI marker capsules, doped with a gadolinium-based contrast agent, before undergoing an MRI scan. From the MRI images, a transit score is calculated by sub-dividing the bowel into eight sections and each capsule is scored according to its position⁵⁵. A weighted average score is then calculated to allow for the spread of the marker capsule positions along the gut. The transit marker technique requires a single appointment and a very quick MRI scanning session (about 5 minutes). The result are simple to analyse because of the good anatomical detail available in the images and good agreement between different observers has been assessed. Moreover the imaging sequences needed for the transit test are generally implemented on most manufacturers' platforms. The calculation yielding the gut transit time in hours provides an objective measure of gut transit which is easy to interpret for the medical practitioners. Using these MRI marker pills, differences in transit times were observed between different constipated patients, with those suffering from IBS-C having a lower transit score compared to those with functional constipation.⁴⁷ Given that a substantial proportion of patients in whom such tests are indicated are females of child-bearing age, MRI can overcome some of the limitations of scintigraphy and radiopaque markers, potentially offering a test which could be widely adopted and benefit from being non-invasive and avoiding ionizing radiation.

The case of MRI defecography

In clinical practice, defecography (evacuation proctography) can be conducted with fluoroscopy or MRI and is used to diagnose defecatory and pelvic floor dysfunction. The current gold standard for diagnosis of prolapse of the posterior pelvic compartment is video-fluoroscopy, in which thick barium paste is introduced into the rectum and cine images are obtained during straining, squeezing and evacuation. MRI defecography is generally conducted in the supine position, avoids radiation exposure, and visualizes the pelvic floor muscles, the urinary bladder, small bowel and vagina/uterus without adding additional contrast to these organs. MRI utilises bSSFP imaging in the sagittal plane and similarly to the fluoroscopic procedure, images are acquired during straining, squeezing and evacuation. Generally, ultrasound gel is used per-rectum as it is easily visualised on cine images.

It has been recognised that with MRI alone, rectoceles, intussusception and perineal descent may be missed⁵⁸ and it can be difficult to demonstrate complete emptying of the rectal ampulla, hence some centres perform both fluoroscopic and MRI examinations to evaluate the anatomy and function in a complementary fashion. It is likely that these limitations of MRI could be overcome by imaging the patient in a more physiological sitting position, and although there have been promising studies of sitting patients in open-magnet MR units⁵⁹⁻⁶¹, the patient numbers are low and further studies are required.

Until recently a robust characterization of anorectal motion in asymptomatic people with MRI was lacking. As MRI defecography is useful for diagnosing defecatory disorders, particularly when other tests are normal, a comparison with healthy people is necessary to determine the utility of the technique for diagnosing defecatory disorders. The recent publication of a large study of 113

asymptomatic healthy women which provides normal values for anal sphincter and pelvic floor anatomy and function (Figure 5)⁶², and of a validated semi-automated program to measure anorectal parameters to reduce observer errors⁶³ are likely to facilitate the future application of this technique in clinical practice. Similar data are needed for healthy males and for patients in the sitting position.

Additional insights in gastrointestinal pathophysiology

The advances in rapid imaging and range of image contrast available have in turn opened the possibility to investigate with MRI, parameters of gastrointestinal pathophysiology that were not previously available. These are unprecedented insights including gastrointestinal fluid distribution, colonic volumes and bowel gas volumes. The following paragraphs review these new developments.

The evaluation of GI water content by means of MRI

The evaluation of GI water content is normally not considered in clinical practice. The bowel handles many litres of fluid per day. Physiological responses to food and pathological differences with disease and treatment can cause marked differences, however quantifying bowel fluid volumes has always been difficult. MRI provides a novel application in this field. Freely mobile water is seen particularly well in heavily T2 weighted, 'cholangiopancreatography-like' sequences; as the long T2 of the free water maintains a high signal whereas less mobile/bound water decays away. Previous work has validated thresholding methods to quantify the fluid volumes⁶⁴. The MRI images provide a 'snapshot' of the fluid volume which is a combination of transit, secretion and absorption.

The effect of different foods has been studied, showing large changes in small bowel water content induced by different carbohydrates in healthy volunteers⁶⁵ and patients⁶⁶, and also the effect of changing the physical characteristics of fat emulsions⁶⁷ or rates of nasogastric feeding⁶⁸. It has been shown that oral laxatives can dramatically increase small bowel fluid volumes⁶⁹ as well as secretin stimulated pancreatic secretion in chronic pancreatitis^{70, 71} and cystic fibrosis⁷². The effect of stress on small bowel water has been studied^{73, 74} and some initial applications to peritoneal dialysis and chronic kidney disorder have been reported^{75, 76}. The MRI measurements of bowel fluids have also caught the attention of the pharmaceutical sciences concerned with drug dissolution. Recent publications looked at the distribution of fluid in the small bowel (Figure 6) quantifying the volumes and distribution of water pockets⁷⁷ and also assessing the response to ingestion of different fluids⁷⁸. Similar methods have been extended to freely mobile colonic water pockets⁷⁹.

The evaluation of colon volumes using MRI

The evaluation of gut volumes is not something that is normally required in clinical practice. Noninvasive assessment of the volume of the undisturbed colon is a more recent application of MRI, aiming to investigate the effect of feeding and disease on organ volumes and symptoms. This is another unique advantage of MRI with previous reports based only on post-mortem or abdominal computed tomography scan which provide the subjects a considerable radiation dose. The methods used vary between different groups. From laborious, manual segmentation of moderately T1 weighted dual-echo fast field echo sequences⁸⁰ to semi-automated segmentation methods using T2 weighted single shot fast spin echo sequences⁸¹. The latter method is used to propagate the colon segmentation to a corresponding set of water only images; it has low variability between operators and changes in the sigmoid/rectum segment correlated well with true faecal volume after defecation⁸². Others have also used semi-automated, region-growing algorithms to segment the colon using T2 and T1 weighted MRI sequences⁸³. Colonic volume measures were elegantly validated by measuring colon volume decreases against corresponding volume of stool defecated, and also volume increases against a corresponding volume of air infused intrarectally⁸³. Colorectal length has also been estimated from the segmentation⁸⁴.

The study of colonic volumes has provided novel insights on the effect of feeding poorly absorbed carbohydrates in healthy volunteers⁶⁵ and patients⁶⁶. Colon volumes in healthy volunteers were also shown to increase unexpectedly by 27% upon 2 days of feeding gluten free bread compared to bread with a normal gluten content⁸⁵. The effect of gastrointestinal formulation such as polyethylene glycol (PEG) ingestion has been studied too, showing that a single large dose of PEG can double the volume of the colon^{47, 69}. Opioid induced constipation significantly increases in colonic volume of healthy volunteers after treatment with oxycodone⁸⁶.

The evaluation of intestinal gas by MRI

Gas is present in various sections of the GI tract and some studies have suggested its possible role in the induction of symptoms in functional bowel disorders⁸⁷. As in the case of water content, the evaluation of gas content of the gut is not used in clinical practice, even though physiological responses to food and diseases can cause marked differences, which are difficult to quantify in a non-invasive way. On proton MR images GI gas pockets appear black as they provide no signal, which allows measurement of their volumes against the boundaries of the bowel wall and chyme. Gas presence in the stomach, particularly after feeding, has long been recognised and its volume quantified. Recently however attempts have been made to measure bowel gas volumes. One report quantified small bowel gas volumes to be of the order of median 49 mL (IQR 44-52mL), the measurements carried out by using region growing techniques in each slice with a semi-automatic method⁸⁸. Others have used subtraction of T1 weighted from T2 weighted images to determine colonic gaseous content⁸³. Histogram analysis can also be used to integrate the signal distribution of the chyme from black to a manually determined threshold based on signal from visible gas⁶⁵. Recent applications demonstrated an increase of over 100mL of gas following an inulin drink in healthy volunteers⁶⁵ and patients⁶⁶.

Conclusion

The development and clinical use of cardiac cine MRI has been driven by both improvements in scanner hardware and its adoption by the wider cardiac imaging community. Technical developments have resulted in better magnetic field uniformity, and improved gradient performance that allows shorter sequence repetition times. These features have allowed the development of sequences such as bSSFP that provide the capability for dynamic imaging with a high SNR and excellent image contrast. The development of (semi-) automated commercially-available analysis tools allowing quantitative measurements of both global and regional myocardial function has also increased the diagnostic efficacy of the technique. Clinically the contribution of both radiologists and cardiologists in the validation of the technique has driven it to become the 'gold-standard'. The emerging application of MRI to Gl imaging leverages many of these developments.

MRI enables the concurrent evaluation of the different functions of the gut as summarised in Table 1. This is particularly relevant to the evaluation of food or drugs expecting to simultaneously modify gut secretion, physical characteristics of intraluminal content, motility, volume and transit. Studies conducted so far have just explored, in an inconsistent way, the potential application of this technique

in different fields and diseases of gastroenterology. It is now necessary to validate the techniques against gold standard measurements and to standardise the protocols across different centres in a similar way in which cardiac MRI has evolved over recent years. As reported above, there are many studies currently ongoing with the aim of achieving these goals in IBD, functional bowel disorders and pharmaceutical applications. In particular the application of MRI to the defecation process in patients with defecatory and pelvic floor disorders seem to be the techniques closer to wide clinical applications. It has indeed been already endorsed by the American College of Gastroenterology⁸⁹. Recognising the gaps in current literature will help refine the technique and when possible overcome its limitations. This currently includes a lack of commercially available software to analyse the data, although this is now starting to be addressed for motility data. It is quite clear that the potential of MRI in gastroenterology is huge and we have just started to follow in many of the footsteps of cardiac MRI.

However it is clear that if MRI of GI function is to follow the route of cardiac MRI, gastroenterologists need to start working more closely with radiologists and validate the technique to measure what is clinically relevant. At the moment the community of functional gastroenterology has shown interest in this but it is probably waiting for the results of the ongoing studies to appraise whether they will demonstrate the clinical utility of MRI in this field.

Future developments

The next step for the development of cine cardiac imaging is the extension to 4D, i.e. three spatial plus one temporal dimension. This effectively means the acquisition of multiple, temporally-resolved, 3D volumes throughout the cardiac cycle. This obviates the current need for multiple breath-hold acquisitions in different scan planes. However, the challenge is the extended acquisition periods required to acquire volumetric data covering the whole heart. Initial studies used both spatial and temporal parallel-imaging based acquisition and reconstruction techniques to acquire 3D cine imaging in a breath-hold albeit with anisotropic spatial resolution.⁹⁰ Other methods have utilised the concept of "self-gating" where the respiratory-induced cardiac motion is directly estimated from the acquired data.⁹¹ Recently advanced acceleration techniques such as compressed sensing have allowed further reductions in acquisition time to a single breath-hold with near-isotropic coverage of the left ventricle in approximately 19s.⁹² A good review of the various methods used to accelerate MRI for the assessment of cardiac function can be found in the article by Axel and Otazo.⁹³ These 4D advances would also be of utility to the motility applications of GI MRI allowing full coverage of stomach and colon whilst maintaining good temporal resolution and in the small bowel allowing for a reduction in the number of breath-holds needed to cover the abdomen.

References

- Lanzer P, Barta C, Botvinick EH, Wiesendanger HU, Modin G, Higgins CB. ECG-synchronized cardiac MR imaging: method and evaluation. *Radiology* 1985; 155: 681-6. doi: <u>https://doi.org/10.1148/radiology.155.3.4001369</u>
- 2. Glover GH, Pelc NJ. A rapid gated cine MRI technique. In: Kressel HY, editor. Magnetic Resonance Annual. New York: Raven Press; 1988. p. 299-333.
- 3. Haacke EM, Patrick JL. Reducing motion artifacts in two-dimensional Fourier transform imaging. *Magn Reson Imaging* 1986; **4**: 359-76. doi: <u>https://doi.org/10.1016/0730-725X(86)91046-5</u>
- Bailes DR, Gilderdale DJ, Bydder GM, Collins AG, Firmin DN. Respiratory ordered phase encoding (ROPE): a method for reducing respiratory motion artefacts in MR imaging. *J Comput Assist Tomogr* 1985; **9**: 835-8. doi: <u>https://doi.org/10.1097/00004728-198507010-00039</u>
- Atkinson DJ, Edelman RR. Cineangiography of the heart in a single breath hold with a segmented turboFLASH sequence. *Radiology* 1991; **178**: 357-60. doi: <u>https://doi.org/10.1148/radiology.178.2.1987592</u>
- 6. Oppelt A, Graumann R, Barfuss H, Fischer H, Hartl W, Scahajor W. FISP: a new fast MRI sequence. *Electromedica* 1986; **54**: 15-8.
- Carr JC, Simonetti O, Bundy J, Li D, Pereles S, Finn JP. Cine MR angiography of the heart with segmented true fast imaging with steady-state precession. *Radiology* 2001; 219: 828-34. doi: <u>https://doi.org/10.1148/radiology.219.3.r01jn44828</u>
- Xue H, Kellman P, Larocca G, Arai AE, Hansen MS. High spatial and temporal resolution retrospective cine cardiovascular magnetic resonance from shortened free breathing real-time acquisitions. *J Cardiovasc Magn Reson* 2013; **15**: 102. doi: <u>https://doi.org/10.1186/1532-429X-15-102</u>
- Fratz S, Chung T, Greil GF, Samyn MM, Taylor AM, Buechel ERV, et al. Guidelines and protocols for cardiovascular magnetic resonance in children and adults with congenital heart disease: SCMR expert consensus group on congenital heart disease. *J Cardiovasc Magn Reson* 2013; 15; 51. doi: <u>https://doi.org/10.1186/1532-429x-15-51</u>
- von Knobelsdorff-Brenkenhoff F, Schulz-Menger J. Role of cardiovascular magnetic resonance in the guidelines of the European Society of Cardiology. J Cardiovasc Magn Reson 2016; 18; 6. doi: <u>https://doi.org/10.1186/s12968-016-0225-6</u>
- 11. Lacy BE, Mearin F, Chang L, Chey WD, Lembo AJ, Simren M, et al. Bowel Disorders. *Gastroenterology* 2016; **150**: 1393-+. doi: <u>https://doi.org/10.1053/j.gastro.2016.02.031</u>
- Stanghellini V, Chan FKL, Hasler WL, Malagelada JR, Suzuki H, Tack J, et al. Gastroduodenal Disorders. *Gastroenterology* 2016; **150**: 1380-92. doi: <u>https://doi.org/10.1053/j.gastro.2016.02.011</u>
- Bassotti G, Antonelli E, Villanacci V, Baldoni M, Dore MP. Colonic motility in ulcerative colitis. United European Gastroenterol J 2014; 2: 457-62. doi: <u>https://doi.org/10.1177/2050640614548096</u>
- 14. Savarino E, Mei F, Parodi A, Ghio M, Furnari M, Gentile A, et al. Gastrointestinal motility disorder assessment in systemic sclerosis. *Rheumatology* 2013; **52**: 1095-100. doi: <u>https://doi.org/10.1093/rheumatology/kes429</u>
- 15. Corsetti M, M. C, Bassotti G, Bharucha AE, Borrelli O, Dinning P, et al. First "translational" consensus on terminology and definition of colonic motility as studied in humans and animals by mekans of manometric and non-manometric techniques. *Nature Reviews* in press 2018.
- 16. Hens B, Corsetti M, Spiller R, Marciani L, Vanuytsel T, Tack J, et al. Exploring gastrointestinal variables affecting drug and formulation behavior: Methodologies, challenges and opportunities. *Int J Pharm* 2017; **519**: 79-97. doi: https://doi.org/10.1016/j.ijpharm.2016.11.063
- Sackett DL, Haynes RB. Evidence base of clinical diagnosis The architecture of diagnostic research. *BMJ* 2002; **324**: 539-41. doi: <u>https://doi.org/10.1136/bmj.324.7336.539</u>
- 18. Camilleri M, Bharucha AE, Di Lorenzo C, Hasler WL, Prather CM, Rao SS, et al. American Neurogastroenterology and Motility Society consensus statement on intraluminal measurement

of gastrointestinal and colonic motility in clinical practice. *Neurogastroenterol Motil* 2008; **20**: 1269-82. doi: <u>https://doi.org/10.1111/j.1365-2982.2008.01230.x</u>

- Bickelhaupt S, Froehlich JM, Cattin R, Raible S, Bouquet H, Bill U, et al. Software-assisted small bowel motility analysis using free-breathing MRI: feasibility study. *J Magn Reson Imaging* 2014; 39: 17-23. doi: <u>https://doi.org/10.1002/jmri.24099</u>
- 20. Menys A, Plumb A, Atkinson D, Taylor SA. The challenge of segmental small bowel motility quantitation using MR enterography. *Br J Radiol* 2014; **87**: 20140330. doi: https://doi.org/10.1259/bjr.20140330
- 21. Menys A, Taylor SA, Emmanuel A, Ahmed A, Plumb AA, Odille F, et al. Global small bowel motility: assessment with dynamic MR imaging. *Radiology* 2013; **269**: 443-50. doi: <u>https://doi.org/10.1148/radiol.13130151</u>
- Bickelhaupt S, Cattin R, Froehlich JM, Raible S, Bouquet H, Bill U, et al. Automatic detection of small bowel contraction frequencies in motility plots using lomb-scargle periodogram and sinusfitting method--initial experience. *Magn Reson Med* 2014; **71**: 628-34. doi: https://doi.org/10.1002/mrm.24708
- 23. Bickelhaupt S, Froehlich JM, Cattin R, Raible S, Bouquet H, Bill U, et al. Software-supported evaluation of gastric motility in MRI: a feasibility study. *J Med Imaging Radiat Oncol* 2014; **58**: 11-7. doi: <u>https://doi.org/10.1111/1754-9485.12097</u>
- 24. Hahnemann ML, Nensa F, Kinner S, Gerken G, Lauenstein TC. Motility mapping as evaluation tool for bowel motility: initial results on the development of an automated color-coding algorithm in cine MRI. *J Magn Reson Imaging* 2015; **41**: 354-60. doi: https://doi.org/10.1002/jmri.24557
- Odille F, Menys A, Ahmed A, Punwani S, Taylor SA, Atkinson D. Quantitative assessment of small bowel motility by nonrigid registration of dynamic MR images. *Magn Reson Med* 2012; 68: 783-93. doi: <u>https://doi.org/10.1002/mrm.23298</u>
- 26. Akerman A, Mansson S, Fork FT, Leander P, Ekberg O, Taylor S, et al. Computational postprocessing quantification of small bowel motility using magnetic resonance images in clinical practice: An initial experience. *J Magn Reson Imaging* 2016; **44**: 277-87. doi: https://doi.org/10.1002/jmri.25166
- 27. Bickelhaupt S, Pazahr S, Chuck N, Blume I, Froehlich JM, Cattin R, et al. Crohn's disease: small bowel motility impairment correlates with inflammatory-related markers C-reactive protein and calprotectin. *Neurogastroenterol Motil* 2013; **25**: 467-73. doi: https://doi.org/10.1111/nmo.12088
- 28. Cullmann JL, Bickelhaupt S, Froehlich JM, Szucs-Farkas Z, Tutuian R, Patuto N, et al. MR imaging in Crohn's disease: correlation of MR motility measurement with histopathology in the terminal ileum. *Neurogastroenterol Motil* 2013; **25**: 749-e577. doi: <u>https://doi.org/10.1111/nmo.12162</u>
- 29. Hahnemann ML, Nensa F, Kinner S, Kohler J, Gerken G, Umutlu L, et al. Quantitative assessment of small bowel motility in patients with Crohn's disease using dynamic MRI. *Neurogastroenterol Motil* 2015; **27**: 841-8. doi: <u>https://doi.org/10.1111/nmo.12558</u>
- Menys A, Atkinson D, Odille F, Ahmed A, Novelli M, Rodriguez-Justo M, et al. Quantified terminal ileal motility during MR enterography as a potential biomarker of Crohn's disease activity: a preliminary study. *Eur Radiol* 2012; 22: 2494-501. doi: <u>https://doi.org/10.1007/s00330-012-2514-2</u>
- 31. Plumb AA, Menys A, Russo E, Prezzi D, Bhatnagar G, Vega R, et al. Magnetic resonance imagingquantified small bowel motility is a sensitive marker of response to medical therapy in Crohn's disease. *Aliment Pharmacol Ther* 2015; **42**: 343-55. doi: <u>https://doi.org/10.1111/apt.13275</u>
- Menys A, Helbren E, Makanyanga J, Emmanuel A, Forbes A, Windsor A, et al. Small bowel strictures in Crohn's disease: a quantitative investigation of intestinal motility using MR enterography. *Neurogastroenterol Motil* 2013; 25: 967-e775. doi: <u>https://doi.org/10.1111/nmo.12229</u>
- 33. Fuyuki A, Ohkubo H, Higurashi T, Iida H, Inoh Y, Inamori M, et al. Clinical importance of cine-MRI assessment of small bowel motility in patients with chronic intestinal pseudo-obstruction: a

retrospective study of 33 patients. *J Gastroenterol* 2017; **52**: 577-84. doi: <u>https://doi.org/10.1007/s00535-016-1251-8</u>

- 34. Menys A, Butt S, Emmanuel A, Plumb AA, Fikree A, Knowles C, et al. Comparative quantitative assessment of global small bowel motility using magnetic resonance imaging in chronic intestinal pseudo-obstruction and healthy controls. *Neurogastroenterol Motil* 2016; **28**: 376-83. doi: <u>https://doi.org/10.1111/nmo.12735</u>
- 35. Ohkubo H, Kessoku T, Fuyuki A, Iida H, Inamori M, Fujii T, et al. Assessment of small bowel motility in patients with chronic intestinal pseudo-obstruction using cine-MRI. *Am J Gastroenterol* 2013; **108**: 1130-9. doi: <u>https://doi.org/10.1038/ajg.2013.57</u>
- Miyazaki Y, Nakajima K, Sumikawa M, Yamasaki M, Takahashi T, Miyata H, et al. Magnetic resonance imaging for simultaneous morphological and functional evaluation of esophageal motility disorders. *Surg Today* 2014; 44: 668-76. doi: <u>https://doi.org/10.1007/s00595-013-0617-2</u>
- Kulinna-Cosentini C, Schima W, Ba-Ssalamah A, Cosentini EP. MRI patterns of Nissen fundoplication: normal appearance and mechanisms of failure. *Eur Radiol* 2014; 24: 2137-45. doi: <u>https://doi.org/10.1007/s00330-014-3267-x</u>
- Stehling MK, Evans DF, Lamont G, Ordidge RJ, Howseman AM, Chapman B, et al. Gastrointestinal tract: dynamic MR studies with echo-planar imaging. *Radiology* 1989; 171: 41-6. doi: <u>https://doi.org/10.1148/radiology.171.1.2928545</u>
- 39. Kunz P, Crelier GR, Schwizer W, Borovicka J, Kreiss C, Fried M, et al. Gastric emptying and motility: assessment with MR imaging: preliminary observations. *Radiology* 1998; **207**: 33-40. doi: <u>https://doi.org/10.1148/radiology.207.1.9530296</u>
- Hayakawa N, Nakamoto Y, Chen-Yoshikawa TF, Kido A, Ishimori T, Fujimoto K, et al. Gastric motility and emptying assessment by magnetic resonance imaging after lung transplantation: correlation with gastric emptying scintigraphy. *Abdom Radiol* 2017; **42**: 818-24. doi: <u>https://doi.org/10.1007/s00261-016-0959-5</u>
- Menys A, Keszthelyi D, Fitzke H, Fikree A, Atkinson D, Aziz Q, et al. A magnetic resonance imaging study of gastric motor function in patients with dyspepsia associated with Ehlers-Danlos Syndrome-Hypermobility Type: A feasibility study. *Neurogastroenterol Motil* 2017; 29. doi: <u>https://doi.org/10.1111/nmo.13090</u>
- 42. Bharucha AE, Karwoski RA, Fidler J, Holmes DR, Robb RA, Riederer SJ, et al. Comparison of manual and semiautomated techniques for analyzing gastric volumes with MRI in humans. *Am J Physiol Gastrointest Liver Physiol* 2014; **307**: G582-G7. doi: https://doi.org/10.1152/ajpgi.00048.2014
- 43. Hamy V, Menys A, Helbren E, Odille F, Punwani S, Taylor S, et al. Respiratory motion correction in dynamic-MRI: application to small bowel motility quantification during free breathing. *Med Image Comput Comput Assist Interv* 2013; **16**: 132-40.
- Menys A, Hamy V, Makanyanga J, Hoad C, Gowland P, Odille F, et al. Dual registration of abdominal motion for motility assessment in free-breathing data sets acquired using dynamic MRI. *Phys Med Biol* 2014; **59**: 4603-19. doi: <u>https://doi.org/10.1088/0031-9155/59/16/4603</u>
- 45. Marciani L, Garsed KC, Hoad CL, Fields A, Fordham I, Pritchard SE, et al. Stimulation of colonic motility by oral PEG electrolyte bowel preparation assessed by MRI: comparison of split vs single dose. *Neurogastroenterol Motil* 2014; **26**: 1426-36. doi: https://doi.org/10.1111/nmo.12403
- 46. Hoad CL, Menys A, Garsed K, Marciani L, Hamy V, Murray K, et al. Colon wall motility: comparison of novel quantitative semi-automatic measurements using cine MRI. *Neurogastroenterol Motil* 2016; **28**: 327-35. doi: <u>https://doi.org/10.1111/nmo.12727</u>
- 47. Lam C, Chaddock G, Marciani L, Costigan C, Paul J, Cox E, et al. Colonic response to laxative ingestion as assessed by MRI differs in constipated irritable bowel syndrome compared to functional constipation. *Neurogastroenterol Motil* 2016; **28**: 861-70. doi: https://doi.org/10.1111/nmo.12784

- 48. Zerhouni EA, Parish DM, Rogers WJ, Yang A, Shapiro EP. Human heart: tagging with MR imaging--a method for noninvasive assessment of myocardial motion. *Radiology* 1988; **169**: 59-63. doi: <u>https://doi.org/10.1148/radiology.169.1.3420283</u>
- 49. Osman NF, Kerwin WS, McVeigh ER, Prince JL. Cardiac motion tracking using CINE harmonic phase (HARP) magnetic resonance imaging. *Magn Reson Med* 1999; **42**: 1048-60.
- Pritchard SE, Paul J, Major G, Marciani L, Gowland PA, Spiller RC, et al. Assessment of motion of colonic contents in the human colon using MRI tagging. *Neurogastroenterol Motil* 2017; 29. doi: <u>https://doi.org/10.1111/nmo.13091</u>
- 51. van der Paardt MP, Sprengers AM, Zijta FM, Lamerichs R, Nederveen AJ, Stoker J. Noninvasive automated motion assessment of intestinal motility by continuously tagged MR imaging. *J Magn Reson Imaging* 2014; **39**: 9-16. doi: <u>https://doi.org/10.1002/jmri.24094</u>
- 52. Niendorf T, Sodickson DK. Parallel imaging in cardiovascular MRI: methods and applications. *NMR Biomed* 2006; **19**: 325-41. doi: https://doi.org/10.1002/nbm.1051
- 53. de Jonge CS, Gollifer RM, Nederveen AJ, Atkinson D, Taylor SA, Stoker J, et al. Dynamic MRI for bowel motility imaging-how fast and how long? *Br J Radiol* 2018: 20170845. doi: <u>https://doi.org/10.1259/bjr.20170845</u>
- 54. Feinle C, Kunz P, Boesiger P, Fried M, Schwizer W. Scintigraphic validation of a magnetic resonance imaging method to study gastric emptying of a solid meal in humans. *Gut* 1999; **44**: 106-11. doi: <u>http://dx.doi.org/10.1136/gut.44.1.106</u>
- 55. Chaddock G, Lam C, Hoad CL, Costigan C, Cox EF, Placidi E, et al. Novel MRI tests of orocecal transit time and whole gut transit time: studies in normal subjects. *Neurogastroenterol Motil* 2014; **26**: 205-14. doi: <u>https://doi.org/10.1111/nmo.12249</u>
- Curcic J, Sauter M, Schwizer W, Fried M, Boesiger P, Steingoetter A. Validation of a golden angle radial sequence (GOLD) for abdominal T1 mapping during free breathing: demonstrating clinical feasibility for quantifying gastric secretion and emptying. *J Magn Reson Imaging* 2015; **41**: 157-64. doi: <u>https://doi.org/10.1002/jmri.24530</u>
- Hoad CL, Parker H, Hudders N, Costigan C, Cox EF, Perkins AC, et al. Measurement of gastric meal and secretion volumes using magnetic resonance imaging. *Phys Med Biol* 2015; **60**: 1367-83. doi: <u>https://doi.org/10.1088/0031-9155/60/3/1367</u>
- Ramage L, Simillis C, Yen C, Lutterodt C, Qiu S, Tan E, et al. Magnetic resonance defecography versus clinical examination and fluoroscopy: a systematic review and meta-analysis. *Tech Coloproctol* 2017; 21: 915-27. doi: <u>https://doi.org/10.1007/s10151-017-1704-y</u>
- 59. Bertschinger KM, Hetzer FH, Roos JE, Treiber K, Marincek B, Hilfiker PR. Dynamic MR imaging of the pelvic floor performed with patient sitting in an open-magnet unit versus with patient supine in a closed-magnet unit. *Radiology* 2002; **223**: 501-8. doi: <u>https://doi.org/10.1148/radiol.2232010665</u>
- Fielding JR, Griffiths DJ, Versi E, Mulkern RV, Lee MLT, Jolesz FA. MR imaging of pelvic floor continence mechanisms in the supine and sitting positions. *Am J Roentgenol* 1998; **171**: 1607-10. doi: <u>https://doi.org/10.2214/ajr.171.6.9843296</u>
- 61. Schoenenberger AW, Debatin JF, Guldenschuh I, Hany TF, Steiner P, Krestin GP. Dynamic MR defecography with a superconducting, open-configuration MR system. *Radiology* 1998; **206**: 641-6. doi: <u>https://doi.org/10.1148/radiology.206.3.9494480</u>
- 62. Tirumanisetty P, Prichard D, Fletcher JG, Chakraborty S, Zinsmeister AR, Bharucha AE. Normal values for assessment of anal sphincter morphology, anorectal motion, and pelvic organ prolapse with MRI in healthy women. *Neurogastroenterol Motil* in press 2018. doi: https://doi.org/10.1111/nmo.13314
- 63. Noelting J, Bharucha AE, Lake DS, Manduca A, Fletcher JG, Riederer SJ, et al. Semi-automated vectorial analysis of anorectal motion by magnetic resonance defecography in healthy subjects and fecal incontinence. *Neurogastroenterology and Motility* 2012; **24**: e467-e75. doi: https://doi.org/10.1111/j.1365-2982.2012.01962.x

- 64. Hoad CL, Marciani L, Foley S, Totman JJ, Wright J, Bush D, et al. Non-invasive quantification of small bowel water content by MRI: a validation study. *Phys Med Biol* 2007; **52**: 6909-22. doi: https://doi.org/10.1088/0031-9155/52/23/009 issn 0031-9155
- 65. Murray K, Wilkinson-Smith V, Hoad C, Costigan C, Cox E, Lam C, et al. Differential effects of FODMAPs (Fermentable Oligo-, Di-, Mono-Saccharides and Polyols) on small and large intestinal contents in healthy subjects shown by MRI. *Am J Gastroenterol* 2014; **109**: 110-9. doi: <u>https://doi.org/10.1038/ajg.2013.386</u>
- 66. Major G, Pritchard S, Murray K, Alappadan JP, Hoad CL, Marciani L, et al. Colon hypersensitivity to distension, rather than excessive gas production, produces carbohydrate-related symptoms in individuals with Irritable Bowel Syndrome. *Gastroenterology* 2017; **152**: 124-33. doi: <u>https://doi.org/10.1053/j.gastro.2016.09.062</u>
- 67. Hussein MO, Hoad CL, Wright J, Singh G, Stephenson MC, Cox EF, et al. Fat emulsion intragastric stability and droplet size modulate gastrointestinal responses and subsequent food intake in young adults. *J Nutr* 2015; **145**: 1170-7. doi: <u>https://doi.org/10.3945/jn.114.204339</u>
- 68. Chowdhury AH, Murray K, Hoad CL, Costigan C, MArciani L, MAcdonald IA, et al. Effects of bolus and continuous nasogastric feeding on gastric emptying, small bowel water content, superior mesenteric artery blood flow, and plasma hormone concentrations in healthy adults: a randomized crossover study. *Ann Surg* 2016; **263**: 450-7. doi: <u>https://doi.org/10.1097/SLA.000000000001110</u>
- 69. Marciani L, Garsed KC, Hoad CL, Fields A, Fordham I, Pritchard SE, et al. Stimulation of colonic motility by oral PEG electrolyte bowel preparation assessed by MRI: comparison of split vs single dose. *Neurogastroenterol Motil* 2014; **26**: 1426-36. doi: https://doi.org/10.1111/nmo.12403
- Madzak A, Olesen SS, Haldorsen IS, Drewes AM, Frokjaer JB. Secretin-stimulated MRI characterization of pancreatic morphology and function in patients with chronic pancreatitis. *Pancreatology* 2017; 17: 228-36. doi: <u>https://doi.org/10.1016/j.pan.2017.01.009</u>
- Madzak A, Olesen SS, Poulsen JL, Mark EB, Drewes AM, Frokjaer JB. MRI assessed pancreatic morphology and exocrine function are associated with disease burden in chronic pancreatitis. *Eur J Gastroenterol Hepatol* 2017; 29: 1269-75. doi: <u>https://doi.org/10.1097/meg.00000000000955</u>
- 72. Madzak A, Engjom T, Wathle GK, Olesen SS, Tjora E, Njolstad PR, et al. Secretin-stimulated MRI assessment of exocrine pancreatic function in patients with cystic fibrosis and healthy controls. *Abdom Radiol* 2017; **42**: 890-9. doi: <u>https://doi.org/10.1007/s00261-016-0972-8</u>
- 73. Murray KA, Lam C, Rehman S, Marciani L, Costigan C, Hoad CL, et al. Corticotrophin releasing factor increases ascending colon volume after a fructose test meal in healthy humans: a randomised control trial. Am J Clin Nutr 2016; 103: 1318-26. doi: <u>https://doi.org/10.3945/ajcn.115.125047</u>
- 74. Pritchard SE, Garsed KC, Hoad CL, Lingaya M, Banwait R, Thongborisute W, et al. Effect of experimental stress on the small bowel and colon in healthy humans. *Neurogastroenterol Motil* 2015; **27**: 542-9. doi: <u>https://doi.org/10.1111/nmo.12529</u>
- 75. Grant C, Harrison L, Hoad C, Marciani L, Cox E, Buchanan C, et al. Endotoxemia in peritoneal dialysis patients: a pilot study to examine the role of intestinal perfusion and congestion. *Perit Dial Int* 2017; **37**: 111-U69. doi: <u>https://doi.org/10.3747/pdi.2016.00079</u>
- 76. Grant CJ, Harrison LE, Hoad CL, Marciani L, Gowland PA, McIntyre CW. Patients with chronic kidney disease have abnormal upper gastro-intestinal tract digestive function: A study of uremic enteropathy. *J Gastroenterol Hepatol* 2017; **32**: 372-7. doi: <u>https://doi.org/10.1111/jgh.13458</u>
- 77. Mudie DM, Murray K, Hoad CL, Pritchard SE, Garnett MC, Amidon GL, et al. Quantification of gastrointestinal liquid volumes and distribution following a 240 mL dose of water in the fasted state. *Mol Pharmaceut* 2014; **11**: 3039-47. doi: <u>https://doi.org/10.1021/mp500210c</u>
- 78. Grimm M, Koziolek M, Saleh M, Schneider F, Garbacz G, Kuhn JP, et al. Gastric emptying and small bowel water content after administration of grapefruit juice compared to water and isocaloric solutions of glucose and fructose: a four-way crossover MRI pilot study in healthy

subjects. *Molecular Pharmaceutics* 2018; **15**: 548-59. doi: <u>https://doi.org/10.1021/acs.molpharmaceut.7b00919</u>

- 79. Murray K, Hoad CL, Mudie DM, Wright J, Heissam K, Abrehart N, et al. Magnetic resonance imaging quantification of fasted state colonic liquid pockets in healthy humans. *Mol Pharmaceut* 2017; **14**: 2629-38. doi: <u>https://doi.org/10.1021/acs.molpharmaceut.7b00095</u>
- Pritchard SE, Marciani L, Garsed KC, Hoad CL, Thongborisute W, Roberts E, et al. Fasting and postprandial volumes of the undisturbed colon: normal values and changes in diarrheapredominant irritable bowel syndrome measured using serial MRI. *Neurogastroenterol Motil* 2014; 26: 124-30. doi: <u>https://doi.org/10.1111/nmo.12243</u>
- 81. Sandberg TH, Nilsson M, Poulsen JL, Gram M, Frøkjær JB, Østergaard LR, et al. A novel semiautomatic segmentation method for volumetric assessment of the colon based on magnetic resonance imaging. *Abdom Imaging* 2015. doi: <u>https://doi.org/10.1007/s00261-015-0475-z</u>
- 82. Nilsson M, Sandberg TH, Poulsen JL, Gram M, Frokjaer JB, Ostergaard LR, et al. Quantification and variability in colonic volume with anovel magnetic resonance imaging method. *Neurogastroenterol Motil* 2015; **27**: 1755-63. doi: https://doi.org/10.1111/nmo.12673
- Bendezu RA, Mego M, Monclus E, Merino X, Accarino A, Malagelada JR, et al. Colonic content: effect of diet, meals, and defecation. *Neurogastroenterol Motil* 2017; 29. doi: <u>https://doi.org/10.1111/nmo.12930</u>
- Mark EB, Poulsen JL, Haase AM, Frokjaer JB, Schlageter V, Scott SM, et al. Assessment of colorectal length using the electromagnetic capsule tracking system: a comparative validation study in healthy subjects. *Colorectal Dis* 2017; 19: O350-O7. doi: <u>https://doi.org/10.1111/codi.13810</u>
- Coletta M, Gates FK, Marciani L, Shiwani H, Major G, Hoad CL, et al. Effect of bread gluten content on gastrointestinal function: a crossover MRI study on healthy humans. *Br J Nutr* 2016; 115: 55-61. doi: <u>https://doi.org/10.1017/s0007114515004183</u>
- 86. Nilsson M, Poulsen JL, Brock C, Sandberg TH, Gram M, Frokjaer JB, et al. Opioid-induced bowel dysfunction in healthy volunteers assessed with questionnaires and MRI. *Eur J Gastroenterol Hepatol* 2016; **28**: 514-24. doi: <u>https://doi.org/10.1097/meg.00000000000574</u>
- Bendezu RA, Barba E, Burri E, Cisternas D, Malagelada C, Segui S, et al. Intestinal gas content and distribution in health and in patients with functional gut symptoms. *Neurogastroenterol Motil* 2015; 27: 1249-57. doi: <u>https://doi.org/10.1111/nmo.12618</u>
- Savarino E, Savarino V, Fox M, Di Leo G, Furnari M, Marabotto E, et al. Measurement of orocaecal transit time by magnetic resonance imaging. *Eur Radiol* 2015; 25: 1579-87. doi: <u>https://doi.org/10.1007/s00330-014-3575-1</u>
- Wald A, Bharucha AE, Cosman BC, Whitehead WE. ACG Clinical Guideline: Management of Benign Anorectal Disorders. *Am J Gastro* 2014; **109**: 1141-57. doi: <u>https://doi.org/10.1038/ajg.2014.190</u>
- 90. Xu J, Kim D, Otazo R, Srichai MB, Lim RP, Axel L, et al. Towards a five-minute comprehensive cardiac MR examination using highly accelerated parallel imaging with a 32-element coil array: Feasibility and initial comparative evaluation. J Magn Reson Imaging 2013; 38: 180-8. doi: https://doi.org/10.1002/jmri.23955
- 91. Usman M, Ruijsink B, Nazir MS, Cruz G, Prieto C. Free breathing whole-heart 3D CINE MRI with self-gated Cartesian trajectory. *Magn Reson Imaging* 2017; **38**: 129-37. doi: <u>https://doi.org/10.1016/j.mri.2016.12.021</u>
- Wetzl J, Schmidt M, Pontana F, Longere B, Lugauer F, Maier A, et al. Single-breath-hold 3-D CINE imaging of the left ventricle using Cartesian sampling. *Magn Reson Mater Phys* 2018; **31**: 19-31. doi: <u>https://doi.org/10.1007/s10334-017-0624-1</u>
- 93. Axel L, Otazo R. Accelerated MRI for the assessment of cardiac function. *Br J Radiol* 2016; **89**. doi: <u>https://doi.org/10.1259/bjr.20150655</u>

TABLE LEGEND

Table 1. Summary MRI measurements of the GI tract, detailing current standard and advantages and limitations of the MRI technique.

FIGURE LEGENDS

Figure 1. Example of functional cardiac analysis for the quantitative assessment of global left ventricular function.

Figure 2. Example bSSFP images of the ascending colon (AC) in a single healthy volunteer. (A, B) Different time frames from a cine acquisition following oral administration of a laxative. White arrows show the colonic contraction in the AC. (C, D) Single time frame from a tagged CINE acquisition. (C) No movement or distortion of the tag lines are seen for the scan acquired at baseline. (D) Smearing effects and tag line distortions are visible following oral administration of a laxative.

Figure 3. Ten phases from a myocardial tagging acquisition in the short axis. In the first image the regular tag lines are applied immediately following the cardiac trigger. The tag lines then deform with the cardiac motion clearly showing transmural motion. Note how the tag lines fade throughout the cardiac cycle due to T1 relaxation of the tagged magnetisation.

Figure 4. Two axial bSSFP images through the stomach at different times following a nutrient liquid meal. (A) Immediately after the meal has been ingested. (B) 75 minutes after the meal has been ingested, showing a reduction in the stomach volume. The thin white arrows highlight the negative contrast of gas in the stomach and the thick black lines the positive contrast of the meal, allowing for both meal, gas and total volume to be easily measured and hence gastric half emptying times to be calculated.

Figure 5. Examples of anorectal motion during rest, squeeze, and defecation in a younger women aged 34 years (upper panel) and an older women aged 63 years (lower panel). The pubococcygeal line and the perpendicular extending from this line to the anorectal junction are marked in black. The boundaries of the anorectal angle are shown in white. Compared to the younger woman, the anorectal junction at rest and during squeeze was lower in the older woman, in whom the angle change during squeeze was also more pronounced. Reprinted from ⁶².

Figure 6. (A) Axial, moderately T2 weighted image of a 240 mL water drink inside the stomach. (B) Coronal heavily T2 weighted image of the abdomen. (C) Individual small bowel water pockets coloured individually in this maximum intensity projection. Reprinted from ⁷⁷.