

GUIDELINES CLINICAL PRACTICE

Asbjørn Mohr Drewes, Professor, MD, PhD, DMSc, Series Editor

Imaging of the gastrointestinal tract-novel technologies

Jens Brøndum Frøkjær, Asbjørn Mohr Drewes, Hans Gregersen

Jens Brøndum Frøkjær, Asbjørn Mohr Drewes, Hans Gregersen, Mech-Sence, Aalborg Hospital, DK-9000 Aalborg, Denmark

Jens Brøndum Frøkjær, Department of Radiology, Aalborg Hospital, DK-9000 Aalborg, Denmark

Asbjørn Mohr Drewes, Mech-Sence, Department of Medical Gastroenterology, Aalborg University Hospital, DK-9000 Aalborg, Denmark

Hans Gregersen, National Center for Ultrasound in Gastroenterology, Haukeland University Hospital, Bergen, Norway; Center for Sensory-Motor Interaction (SMI), Department of Health Science and Technology, Aalborg University, Denmark; Center for Sensory-Motor Interaction (SMI), Department of Health Science and Technology, Aalborg University, DK-9000 Aalborg, Denmark

Author contributions: Frøkjær JB wrote the review, Gregersen H and Drewes AM contributed equally to the overall guidelines and inspiration.

Correspondence to: Jens Brøndum Frøkjær, MD, PhD, Mech-Sence, Department of Radiology, Aalborg Hospital, DK-9100 Aalborg, Denmark. jf@mech-sence.com

Telephone: +45-99326825 Fax: +45-99326407

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Peer reviewers: Marko Duvnjak, MD, Department of Gastroenterology and Hepatology, Sestre milosrdnice University Hospital, Vinogradska cesta 29, 10000 Zagreb, Croatia; Rami Eliakim, Professor, Department of Gastroenterology, Rambam Medical Center Institution, Haifa, Israel

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Abstract

Imaging of the gastrointestinal tract is very useful for research and clinical studies of patients with symptoms arising from the gastrointestinal tract and in visualising anatomy and pathology. Traditional radiological techniques played a leading role in such studies for a long time. However, advances in non-invasive modalities including ultrasound (US), computed tomography (CT), positron emission tomography (PET), magnetic resonance imaging (MRI), *etc*, have in the last decades revolutionised the way in which the gastrointestinal tract is studied. The resolution of imaging data is constantly being improved and 3D acquisition, tools for filtering, enhancement, segmentation and tissue classification are continually being developed. Additional co-registration techniques allow multimodal data acquisition with improved classification of tissue pathology. Furthermore, new functional imaging techniques have become available. Altogether, the future of gastrointestinal imaging looks very promising which will be of great benefit in clinical and research studies of gastrointestinal diseases. The purpose of this review is to highlight the capabilities of the newest techniques to explore the detailed morphology, biomechanical properties, function and pathology of the gastrointestinal tract.

INTRODUCTION

Examinations with visualisation of the anatomy and pathology of the gastrointestinal (GI) tract are often mandatory in the diagnosis of GI diseases. For this purpose, traditional radiological techniques played a leading role for a long time. However, improvements in endoscopic examinations, the latest including wireless capsule endoscopy, have radically changed the possibilities for direct visualisation and intervention in the GI tract. The introduction and advances in non-invasive imaging modalities including ultrasound (US), computed tomography (CT), positron emission tomography (PET) and magnetic resonance imaging (MRI) have in the last decades revolutionised the way in which the GI tract is studied^[1]. The resolution of imaging data is constantly being improved and 3D acquisition, tools for filtering, enhancement, segmentation and tissue classification are continually being developed. Additional co-registration techniques allow multimodal data acquisition (PET-CT, MR-PET, CT-US, *etc*) with improved classification of tissue pathology. Each modality is characterised by a distinct profile of favourable and unfavourable features, and the technique used depends upon availability, accuracy, usefulness, safety and costs. The diagnostic performance in terms of sensitivity, specificity and accuracy depends on several factors: the specific method and equipment used, the part of the GI tract investigated, patient constitution and preparation, most importantly the sort

of pathology being studied, and not least which “gold standard” the method is being compared to.

The purpose of this review is to highlight the capabilities of the newest imaging techniques to explore the detailed morphology, biomechanical properties, function and pathology of the GI tract. Table 1 provides an overview of the advantages and shortcomings of the most frequently used modalities in the study of the GI tract.

CONVENTIONAL RADIOLOGICAL EXAMINATIONS

Using non-contrast radiography, normal GI segments with no or little gas content cannot be separately visualised; but normal and abnormal gas accumulations, air-fluid levels, calcifications and motility of air contained in the intestines can be visualised^[2].

In mono-contrast examinations, the intestinal lumen is filled with a positive contrast material in order to visualise peristalsis, emptying and pathological changes such as stenosis, dilatation, luminal filling defects and external compression. In double contrast examinations, the inner surface is coated with contrast material and the lumen is distended with air. This allows detailed visualisation of the mucosa which is especially useful in the detection of inflammatory and neoplastic changes of the small and large intestine^[2]. However, the methods do not allow direct description of the deeper wall layers and extraintestinal lesions.

ANGIOGRAPHY

Conventional angiography of the GI tract has a clear role in the visualisation and treatment of GI bleeding. However, oesophago-gastroduodenoscopy and colonoscopy are the primary methods for identifying GI bleeding; but, sometimes these approaches cannot identify the source of bleeding^[3]. In these cases, the leakage may be visualised using scintigraphy with tagged red blood cells, capsule endoscopy, double balloon endoscopy and increasingly multi-detector CT (MDCT)^[3,4].

ULTRASONOGRAPHY

Transabdominal US is a safe procedure without any radiation exposure and allows visualisation of the intestinal wall, fluid-filled intestinal segments and the surrounding environment. US has excellent soft tissue imaging capabilities which make it ideal for both clinical and research studies of the GI tract. This is especially valuable in the detection of GI tract inflammation, where wall thickening, disturbed wall morphology, surrounding oedema and lymphadenopathy can be visualised^[5]. In cases of extraintestinal fluid collections and abscess formation, mini-invasive drainage of these collections can be performed guided by US. Endosonography using intraluminal probes allow high-resolution imaging of the wall layers^[6-8]. By applying special techniques (see below), additional information can be obtained.

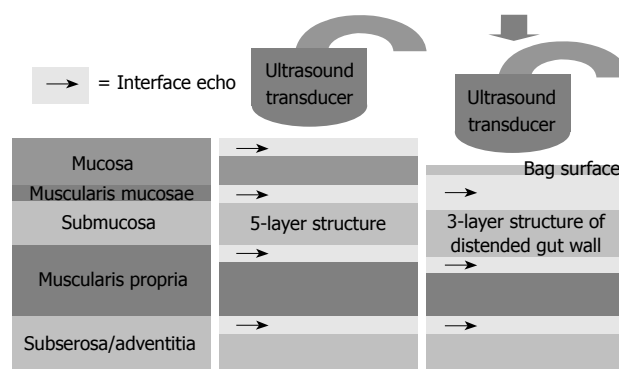


Figure 1 The principles of endosonography. The histological gastrointestinal wall layers (left) are correlated to the typical layered ultrasound appearance of the gastrointestinal wall (middle). The 5-layered appearance is due to the addition of several interface echoes at the tissue interfaces. During compression or distension the wall is further stretched (including mucosal unfolding) which together usually obscures the second echo-rich mucosal layer. Hence, the wall appears 3-layered (see Figure 2).

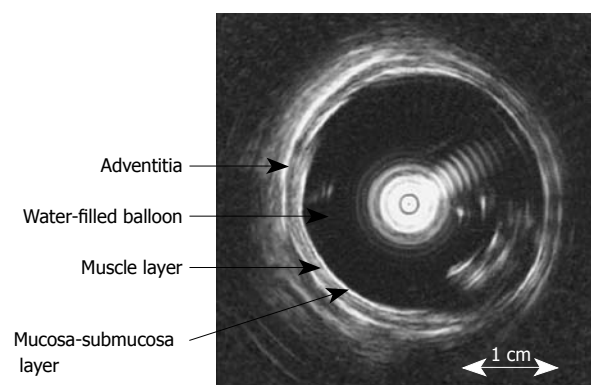


Figure 2 Cross-sectional endosonographic image of the distended distal oesophagus allows identification of three oesophageal sub-layers, i.e. mucosa-submucosa, muscle and adventitia. The white shadows inside the water-filled bag (4-5 o'clock) represent artefacts due to convulsions of the water-filled balloon, which results in reduced image quality at low degrees of distension. Modified from [17].

Perfusion of the intestinal wall and surrounding tissues can be assessed using Doppler imaging. Recently, the application of intravenous US contrast agents has improved the detection of hypervascularisation and hyperemia, especially in inflammatory bowel diseases^[9,10].

Qualitative and quantitative information of intestinal motility and gastric filling/emptying can be obtained using transabdominal US^[11,12]. 3D position and orientation systems allow real-time 3D visualisation with reconstructions and volumetry of the GI tract^[13,14]. Intraluminal flow can be assessed using Doppler flow imaging^[15]. This is especially useful in studying flow through the pylorus.

GI wall layers can be visualised endoscopically using high-frequency endosonography. This is normally used in tumour diagnosis, but has also been used experimentally to study e.g. the biomechanical properties of the GI tract^[16,17]. Usually 3-7 layers of the wall can be visualised (Figures 1 and 2)^[7]. The separate layers are bound together and possess dissimilar active and passive biomechanical (i.e. anisotropic) properties

Table 1 Most frequently used imaging modalities in the study of the gastrointestinal tract: Overview of main advantages and shortcomings

Modality	Advantages	Shortcomings
Multidetector computed tomography (MDCT)	High temporal and spatial resolution Fast image acquisition without motion artefacts Total evaluation of entire intestine and its surroundings 3D reconstructions and virtual endoscopy Possibility for image guided intervention	High radiation exposure Less suitable for research in healthy subjects No direct functional information Low risk of nephropathy due to intravenous iodised contrast media
Ultrasound (US)	High soft tissue resolution No radiation exposure Ideal for repeated examination and research Evaluation of intestinal wall and surroundings Information on motility, function and flow directly available using special techniques Possibility for intraluminal imaging Ideal for image guided intervention	Relatively high interobserver variability Intestinal gas lowers image quality Artifacts may be difficult to interpret Total visualisation of the entire intestine is difficult
Magnetic resonance imaging (MRI)	Good soft tissue imaging capabilities No radiation exposure Ideal for repeated examinations and research Total evaluation of entire intestine and its surroundings Functional and motility information directly available using special techniques	Motion artifacts due to intestinal motility Long image acquisition Image resolution less than CT making 3D reconstructions and virtual endoscopy cumbersome Potential long term effects of gadolinium-based contrast media (nephrogenic systemic fibrosis)
Conventional radiography	High temporal and spatial resolution Fast image acquisition Motility and function easily studied using intraluminal contrast	Only direct visualisation of luminal/mucosal properties Radiation exposure No 3D image data
Endoscopy	Direct visualisation of the mucosa Possibility for intervention (biopsies, polypectomy and endoscopic surgery)	Invasive procedure Discomfort and potential intestinal perforation No visualisation of deeper wall layers and surroundings

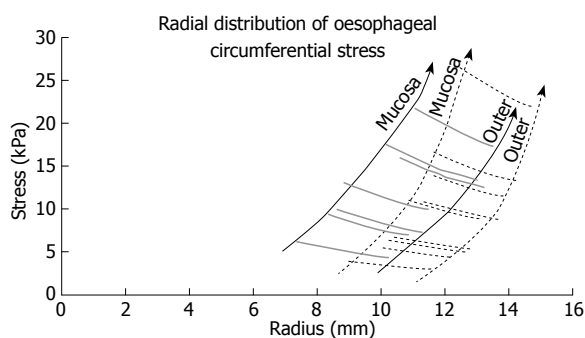


Figure 3 The oesophageal stress is calculated based on endosonography images and manometry. The alignment of solid curves represents the oesophageal stress profiles during oesophageal distension in a healthy volunteer. The alignment of dashed curves represents distension during butylscopolamine smooth muscle relaxation. As the oesophagus distends the inner radius and stress increases, i.e. the left end of the curves shift to the right and upwards. At high degrees of distension the steepness of the stress profile increases. Oesophageal relaxation shifts the alignment of the stress profiles to the right. Modified from [17].

which make a detailed analysis complex^[16]. To assess the biomechanical properties, the intestine can be distended with fluid-filled balloons containing pressure measurement and US mini-probes providing cross-sectional images of the intestine^[17,18]. The applied load on the wall can be controlled and accurately quantified. This allows calculation of passive and active biomechanical properties of the distended segment with parameters such as strain (relative deformation), tension, stress (force per cross sectional area) and stiffness of the wall layers^[16,17,19]. The radial distribution of the circumferential wall stress has been assessed in the oesophagus^[17]. Both the circumferential strain and

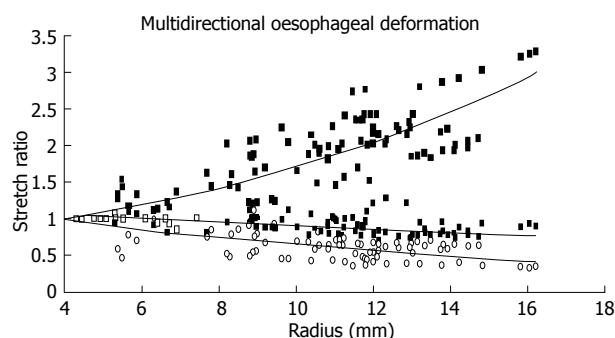


Figure 4 The circumferential, radial and longitudinal deformation of the oesophageal muscle layer is here described as the stretch ratio and as a function of the radius. The stretch ratio and radius are calculated based on endosonography. Data are from 12 healthy volunteers and shows a tensile circumferential stretch, radial compression and longitudinal shortening. Modified from [17].

stress were highest at the mucosal surface and decreased throughout the wall (Figure 3). The stiffness increased throughout the wall and was highest at the outer surface. The high stiffness of the muscle layers (compared to the mucosa) may limit the total oesophageal deformation (i.e. further distension) and protect the vulnerable and less stiff mucosa from damage when overstretched. This method has also been used to assess the multidirectional deformation and wall layer thicknesses of the oesophagus. Distension induces tensile circumferential stretch, radial compression and longitudinal shortening (Figure 4), which is not taken into account when using conventional barostat methods. This has shown to be valuable in the description of structural remodelling in organic GI disorders. Patients with longstanding diabetes

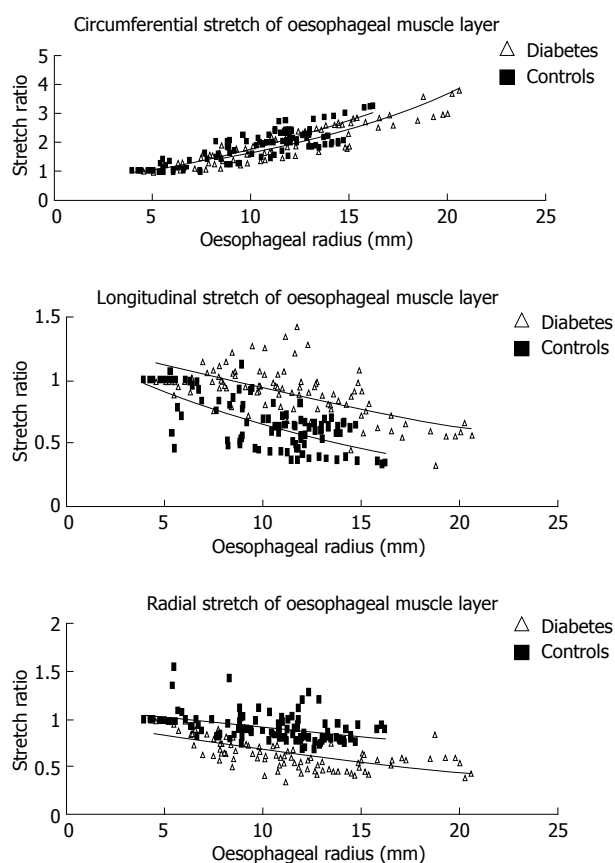


Figure 5 The graphs show the effect of diabetes on deformation of the oesophagus. The distension-induced change in oesophageal circumferential, longitudinal and radial deformation (stretch ratio) are calculated based on endosonography and illustrated as a function of the oesophageal radius. The curves were obtained during smooth muscle relaxation with butylscopolamine. The data points represent multiple measuring points during distension in diabetic patients and controls. Exponential trend lines (solid lines) of the diabetic patients and controls are shown. Oesophageal shortening during distension was clearly reduced in the diabetic patients while the radial stretch was decreased. Modified from [20].

mellitus have increased thickness of the oesophageal wall layers^[20]. Also, longitudinal shortening was decreased in the diabetic oesophagus combined with a decreased radial stretch (Figure 5)^[20]. Together with these structural changes indicating remodelling of the GI tract, diabetic patients also have an increased reactivity to oesophageal distensions and impaired coordination of the contractions which may reflect neuronal abnormalities due to autonomic neuropathy^[20].

Further developments in the Doppler imaging technique can, when applied on the wall tissue itself, give information about movements inside the wall structure. This technique is known as strain rate imaging (SRI) and allows detailed mapping of the deformation of the wall layers with description of local tissue velocities^[21]. Hence, the different contractile activity of the circular and longitudinal muscle layers can be visualised^[12]. Elastography is a new US method which allows assessment of tissue stiffness. The tissue is compressed and the deformation pattern is visualised as colours (from soft to stiff) on the US image. The stiffness depends on the biomechanical properties, allowing differentiation between normal and abnormal tissues^[12,22].

Cross-sectional endosonography of oesophageal contractions has shown that the cross-sectional area of the outer longitudinal muscle layer increases during contractions^[23]. This indicates a contraction of the longitudinal muscle and shortening of the oesophagus which is thought to support the peristaltic force generated by the inner circular muscle^[23]. Endosonographic studies have revealed that episodes of oesophageal chest pain and heartburn are associated with sustained contraction of the longitudinal muscle layer^[24].

CT

The introduction of multidetector CT (MDCT) scanners with typically 64 detectors or more allows fast acquisition of thin slices and allows multi-planar reconstructions in any direction. This is a valuable tool in the study of intestinal loops^[25]. Non-contrast enhanced CT scanning is increasingly replacing plain radiography in the evaluation of free intraabdominal air and intestinal obstruction. Intravenous contrast enhancement and filling of the intestinal lumen with water or positive contrast agents are performed in order to optimise imaging of the bowel wall. This is particularly valuable in the detection of inflammatory and neoplastic intestinal lesions, and allows accurate detection of extra-intestinal findings^[26].

MDCT colonography is a relative new way of studying the large intestine. After proper colonic preparation, the large intestine is distended with air and the patient is scanned in the prone and supine positions^[27]. The examination is reviewed in multiplanar views and as virtual endoscopy allowing flight-through of the intestine in both directions. This allows detection of smaller (> 6 mm) colonic polyps with a similar high accuracy to that of conventional colonography, while the accuracy for even smaller polyps is poor^[27-29]. New generations of software with virtual dissection and unfolding of the colon will, together with computer-aided detection (CAD), probably improve the diagnostic accuracy and reduce the imaging time^[30,31]. In addition, the detection of any incidental extra-colonic pathology is possible^[32,33]. This technique may replace the traditional double contrast examinations in the case of incomplete colonoscopy and may also play a central role as a non-invasive screening examination.

MAGNETIC RESONANCE IMAGING (MRI)

MRI has no known short- or long-term hazards, and, therefore, provides excellent soft tissue imaging capabilities for studying the GI tract. This makes MRI favourable compared with CT which has considerable radiation exposure. However, intestinal MRI is limited by long acquisition times and a high risk of motion artefacts. Since the early days of MRI, the technology has advanced significantly and recent developments in MRI techniques such as parallel imaging, allow much faster and higher quality image acquisition.

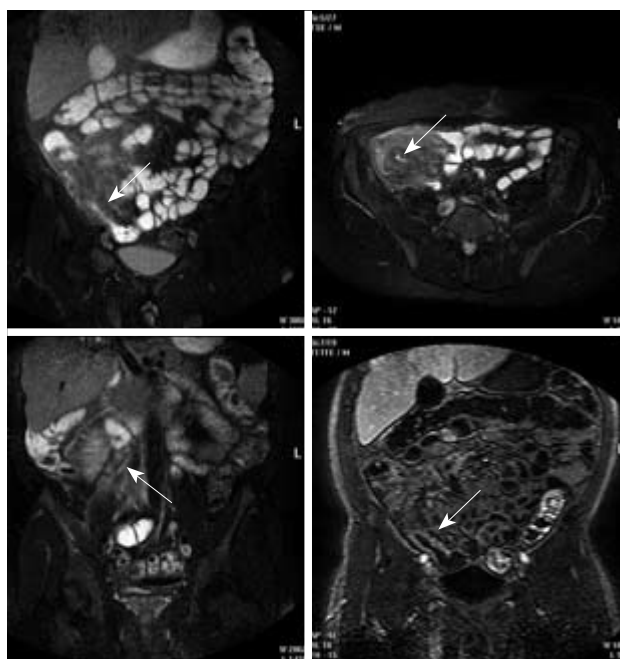


Figure 6 MRI of Crohn's disease. The coronal and axial (upper panel) fat-saturated T2-weighted MRI display marked wall thickening, mucosal irregularity and stenosis of the terminal ileum (arrows). Advanced mesenteric inflammation with hypervascularity and enlarged lymph nodes (arrow) are visualised on coronal fat-saturated T2-weighted MRI (lower left). Coronal T1-weighted MRI (lower right) shows clear wall enhancement (arrow). Modified from [36].

MRI is generally accepted as the gold standard examination in the staging of rectal cancers and inflammatory bowel diseases. Pelvic MRI, especially with endorectal coils, gives exact visualisation of infiltration of the rectal wall and perirectal fat allowing reliable TNM staging^[34]. MRI of the small intestine has several advantages compared with conventional enteroclysis. It provides cross-sectional images without radiation hazards, and the entire small bowel can be visualised including other relevant abdominal pathology not directly related to the small bowel^[26,35]. Luminal (stenosis, cobble stoning, and fissures), mural (wall thickening, and wall enhancement upon iv gadolinium) and exoenteric (mesenteric inflammation, fibrofatty proliferation, lymphadenopathy, hypervascularity, abscesses and fistulas) pathologies are visualised with high sensitivity and specificity (Figure 6)^[35-38]. In particular, MRI is superior in the evaluation of fistulas in the anorectal region^[39]. The optimal protocol for small intestinal MRI is not yet developed, since many different methods of preparation and imaging sequences exist. The intestine can be filled both orally or by intubation of the small intestine. Various positive and negative intestinal contrast materials exist. The use of water-based positive contrast agents are generally accepted with the addition of hyperosmotic substances (polyethylene glycol, methyl cellulose, bulk fibre laxative, mannitol, locust bean gum, *etc*) securing optimal distension of the entire small intestine^[36,40-42]. Spasmolytics such as butylscopolamine and glucagon are usually administered to avoid motion-induced artefacts. The administration of intravenous contrast permits enhancement of hypervascular and

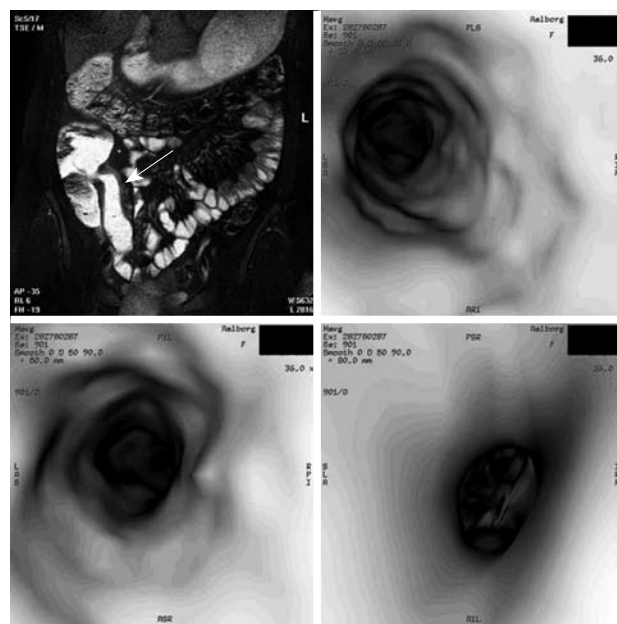


Figure 7 MRI of Crohn's disease. Virtual endoscopy views of the displayed diseased small bowel segment (arrow) shows mucosal nodularity, ileo-caecal narrowing and minor prestenotic dilatation. Modified from [36].

hyperperfused areas allowing distinction between active and inactive inflammatory lesions. Acquisition of 3D images allows the possibility of virtual endoscopy which contributes to the detailed evaluation of a diseased bowel segment and the intraluminal display is easily recognized by gastroenterologists^[36,43,44].

Our research group performed MRI and conventional enteroclysis in 36 patients with suspected Crohn's disease who underwent oral administration of plum juice and bulk fibre laxative^[36]. Virtual endoscopy was performed with excellent demonstration of the mucosal surface (Figure 7). The main limitation of virtual endoscopy is the long and cumbersome computer post-processing and a high image quality is needed for this technique. However, this technique ensured sufficient distension of the small bowel for detecting small bowel changes. Pathological abdominal changes were found in 70% more patients using MRI compared with conventional enteroclysis^[36]. MRI using this technique is preferable to conventional enteroclysis due to a superior demonstration of the entire small bowel pathology, low patient discomfort and absence of radiation exposure. In a study by Gourtsoyiannis *et al*^[45], MR enteroclysis (MRE) was compared with conventional enteroclysis (CE) as the gold standard in 52 patients with small intestinal Crohn's disease. The sensitivity of MRE in the detection of superficial ulcers, fold distortion and fold thickening was 40%, 30% and 62.5%, respectively. The sensitivity of MRE in the detection of deep ulcers, cobblestoning pattern, stenosis and prestenotic dilatation was 89.5%, 92.3% and 100%, respectively. Additional findings demonstrated on MRE images included fibrofatty proliferation in 15 cases and mesenteric lymphadenopathy in 19 cases. Hence, MRE strongly correlates with CE in the detection of individual lesions expressing small intestinal Crohn's disease, and provides

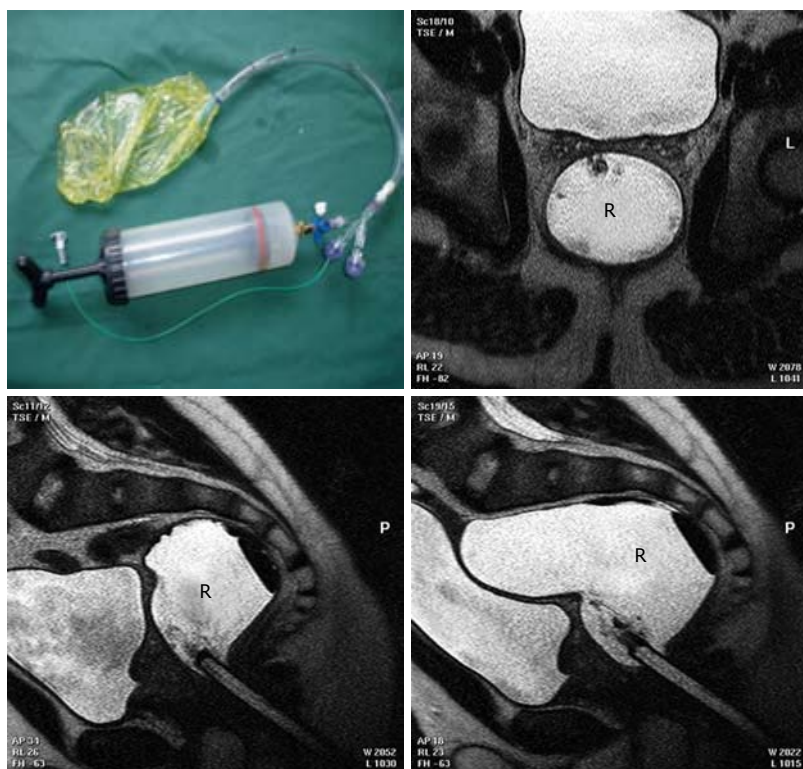


Figure 8 Stepwise distension of water filled balloon with simultaneous MRI and pressure recording. The rectal probe (upper left) allows rectal water distension and pressure measurement. MRI shows the distended water-filled bag in the rectum (R). The sagittal MRI (lower panel) shows the distension, elongation and relation to neighbouring structures at 100 mL and 300 mL inside the bag. Modified from [50].

additional information on the mesenteries. However, its capability in detecting subtle lesions is still inferior to CE. Additional functional cine-MRI will allow studies of intestinal motility with detection of intraabdominal adhesions due to surgery or inflammation^[46]. The technique is also relevant for research studies on GI function and motility.

The technique of MRI colonography is also still developing^[29,47,48]. Intestinal preparation is crucial in order to distinguish between polyps and intestinal residuals. Basically, the large intestine has to be cleaned and filled with water. New ways of faecal tracking with the oral application of negative contrast agents before the examination may allow less intestinal cleansing^[49]. However, the method of MR colonography is not yet as sensitive as CT colonography in detecting smaller polyps.

Since MRI provides excellent soft tissue imaging capabilities without the use of radiation, it is ideally suited for research studies of the GI tract. Using advanced image processing, the three-dimensional geometry and mechano-sensory properties can be studied. Stepwise distension of water filled rectal and sigmoid balloons with simultaneous MRI and bag pressure recording was performed by our group (Figure 8)^[50,51]. Based on the cross-sectional images, 3D models of curvatures, radii of curvature, tension and stress were generated and the circumferential and longitudinal strains were calculated (Figure 9). The distributions of the biomechanical parameters throughout the rectal and sigmoid surfaces were distinctly different between individuals and non-homogeneous throughout the colorectal wall due to its complex geometry. This complex geometry suggests that simple estimates of tension based on pressure and volume do not reflect the true 3D biomechanical properties of the intestine. This

tool may in the future be useful in the research and clinical setting for assessing the geometry and mechano-sensory properties of visceral wall structures in health and disease.

PET

¹⁸F-fluorodeoxyglucose positron emission tomography (FDG-PET) has high accuracy in the detection and follow-up of oesophageal, colorectal and stomal cancers^[52]. The advantage of PET is that metabolic changes often precede clear structural changes and, therefore, can be detected early in disease development. A combination of PET-CT is a powerful tool in the primary staging and assessment of any recurrent disease.

OTHER NOVEL TECHNIQUES

Other techniques such as impedance measurements and manometry which were initially not direct imaging modalities have developed more and more into techniques with imaging data display.

Impedance planimetry with assessment of multiple closely arranged cross-sectional areas can be displayed in 3D. This concept is known as the Functional Lumen Imaging Probe (FLIP) allowing direct on-line imaging of the luminal geometry of the GI tract^[53,54]. This is particularly suitable for visualisation of the complex physiology of the GI sphincters, especially in the evaluation of gastro-oesophageal reflux and sphincter incompetence.

Oesophageal high-resolution manometry (HRM) with up to 36 pressure sensors allows on-line visual display with a spatio-temporal colour plot of oesophageal peristalsis^[55]. The technique is explained

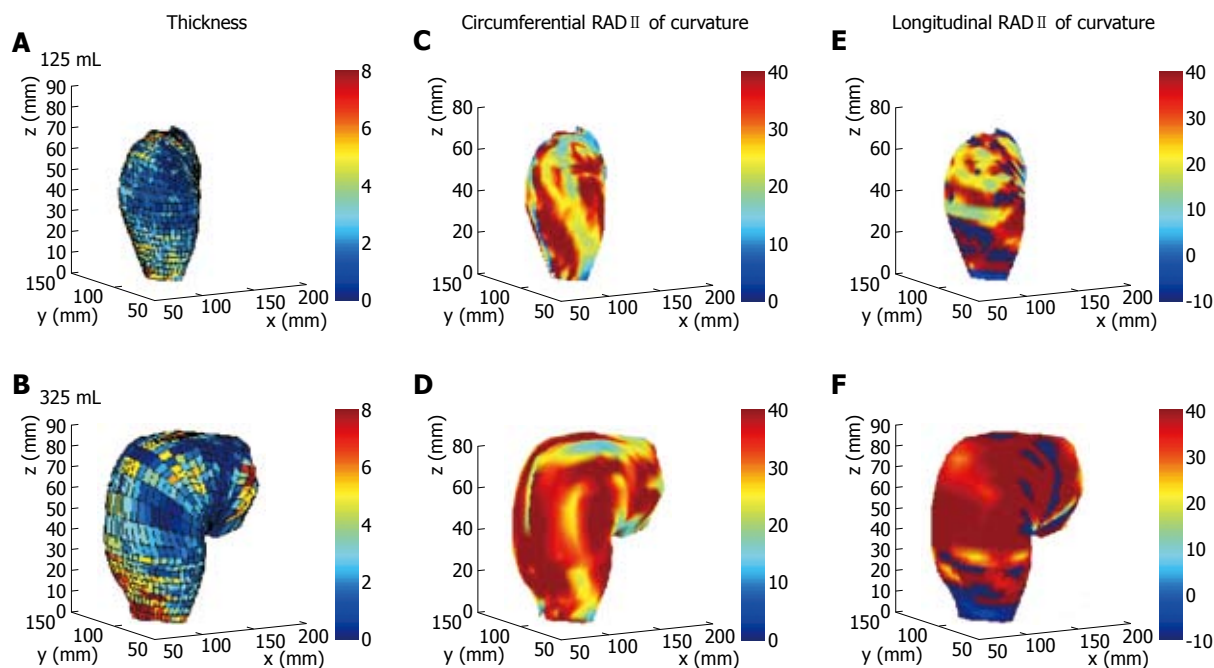


Figure 9 3D models of the rectum based on MRI and pressure recordings. The 3D distribution of the rectal wall thickness (A-B), circumferential (C-D) and longitudinal (E-F) principal radii of curvatures in one healthy volunteer at infused volumes of 125 mL (A, C, E) and 325 mL (B, D, F). The change in colour from blue to red during bag distension indicates an increase in rectal wall thickness or radius of curvature, i.e. increase in diameter. Modified from [50].

in detail in another paper in this issue. The recording reveals the complex motility of oesophageal bolus transport including sphincter function. Pathology related to oesophageal motor dysfunction is visualised with high accuracy^[56]. Manometry can be combined with intraluminal impedance and pH measurements allowing further characterisation of reflux episodes (fluid *vs* air, acid *vs* non-acid).

Scintigraphy and single photon emission computed tomography (SPECT) are applied for emptying and motility studies of the GI tract^[57,58]. Radionuclide transit/emptying scintigraphy is easy to perform, closely reflects physiology and provides quantitative data in the evaluation of several functional or motility disorders of the upper GI tract. However, scintigraphy has a low radiation burden. Like conventional radiography, dynamic scintigraphy with a radioactive liquid or semisolid bolus provides information on oesophageal motility useful in disorders such as nutcracker oesophagus, oesophageal spasm, non-cardiac chest pain, achalasia, oesophageal involvement in scleroderma, gastro-oesophageal reflux and monitoring response to therapy. Scintigraphy with a radiolabeled test meal represents the gold standard for evaluating gastric emptying in patients with dyspepsia, and evaluation of gastric function in various systemic diseases affecting gastric emptying. Similar scintigraphic methods are applied in the study of small intestinal and colonic transit. Recent radionuclide methods include dynamic antral scintigraphy and gastric SPECT for assessing gastric accommodation. However, US and MRI methods (see above) are still developing and the evaluation of functional GI diseases may in the future be subject to new and innovative techniques.

CONCLUSION

Imaging of the GI tract is essential in the diagnosis of GI diseases. This review highlights the capabilities of the newest techniques to explore the detailed morphology, biomechanical properties, function and pathology of the GI tract. The technological development is fast and the innovative potential enormous. Refinement of present modalities with faster image acquisition, higher resolution, increased computer power and improved software for post-processing are the main developing trends. Another trend is the development and refinement of “new sub-modalities” based on the traditional methods, and not least the fusion of different modalities into new multimodal concepts. Altogether, the future of GI imaging looks very promising, which will be of great benefit in clinical and research studies of GI diseases.

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