Is this the end of an era for conventional diagnostic endoscopy?

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Introduction

Since the inception of flexible fibre-optic instruments 50 years ago, endoscopy has become a mainstay of gastrointestinal (GI) investigation and method of delivering therapeutic intervention.[1] It remains, however, an intrusive and uncomfortable test. It is difficult to perform in a manner that preserves privacy and dignity and can be unpopular with patients. It is also not without risk. A UK audit performed in 2004 showed a major complication (perforation or bleed) rate of 1:769 patients undergoing colonoscopy.[2] Yet nearly half of patients undergoing colonoscopy to investigate symptoms have no relevant findings.[2] For some time, the hunt has been on for an accurate and non-invasive test which has the ability to predict the need for endoscopic biopsy or therapy.

In 1999, Iddan and colleagues described a technology so fantastic that it seemed to have been lifted from the script of a science fiction movie.[3] They developed a novel pill camera that could be swallowed and subsequently propelled through the GI tract by the action of peristalsis while acquiring images.[4] The first model, for the small bowel (Pillcam SB™, Given Imaging, Yoqneum, Israel), is 26 × 11 mm, contains a battery powered complementary metal oxide silicon imager (technology required to capture images digitally), a transmitter, antenna and six light-emitting diodes (LEDs) in a rounded cylindrical plastic container.[3] The clear optical dome-shaped window of the capsule allows the intestine to be illuminated by the LEDs. The imager is activated by removal of the capsule from its magnetic holder. As peristalsis propels it through the gut, images taken twice per second are transmitted via sensors attached to the abdominal wall to a data recorder.[5] The raw data is subsequently downloaded to a workstation after completion of the procedure. The software produces a video of these images that can be reviewed anytime.[5]

Small bowel capsule endoscopy

Historically, radiology has been the mainstay investigation of the small bowel. Barium follow-through and enteroclysis (double contrast small-bowel follow-through) permit indirect examination of the small bowel but have a low diagnostic yield (particularly failing to detect subtle mucosal abnormalities, for example, angiodysplasia).[6] It is estimated that approximately 5% of small bowel follow-through examinations detect an intestinal bleeding site while, enteroclysis may have a positive yield in up to 25% of patients with GI bleeding.[6–8] Push enteroscopy (PE), a longer instrument than a gastroscope, allows endoscopic access to the small bowel but examination is limited to the proximal intestine.

Capsule endoscopy (CE), which allows the physician access to the entire small bowel, is often considered 'the final frontier of gastroenterology'. Over 40 studies comparing the diagnostic yield of CE with other investigative modalities have been published to date.[9,10] The two most common indications for CE are obscure GI bleeding (OGB), where a small bowel source is suspected (anaemia or overt blood loss), and suspected Crohn's disease, in which conventional investigation has failed to make a diagnosis.[11] A recent meta-analysis has shown that the diagnostic yield of CE in OGB was 63%, compared to 28% for PE. The yield of CE has also been shown to be superior to barium follow through and computed tomographic (CT) enteroclysis in the context of OGB.[10,12–14] When other investigative modalities were pooled together, a second meta-analysis of 17 studies (526 patients) showed that the rate difference between CE and other investigative modalities for OGB was 37% (95% confidence interval (CI) 29.6 to 44.1).[10]

The yield of CE in Crohn's disease has been equally encouraging. Meta-analysis of studies of suspected cases demonstrates a rate difference of 45% (95% CI 30.9 to 58) between CE and conventional modalities (such as radiology and PE).[10] The Food and Drug Agency recognises CE as a first line small bowel investigation and the National Institute for Health and Clinical Excellence (NICE) recommend its use for both of the indications discussed. Guidelines on the use of CE have already been produced in the USA, mainland Europe and, more recently, in the UK.[15–18]

Oesophageal capsule

As the technology was developed further, it became possible to incorporate two viewing heads, with

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images taken from both ends of the capsule at an increased rate of 14 frames per second.[19] This meant that with improved and longer image acquisition by asking patients to swallow the capsule in the recumbent position, it became feasible to examine the oesophagus with the Pillcam ESO™. Initial studies found that oesophageal CE diagnosed Barrett's oesophagus with a sensitivity of 67% and a specificity of 84% while the sensitivity and specificity for oesophageal varices has been 100% and 89% respectively.[20,21] However, screening for these conditions and the sales of the oesophageal capsule in the UK represent a relatively small market compared to that of the small bowel capsule.

Colon capsule

The development of a double-headed capsule opened a further avenue for exploration: the large bowel. Image capture from a single head had proved successful in the small bowel lumen, but seemed likely to miss lesions behind haustral folds in the more capacious colon. The colon capsule, however, takes two images per second from forward and backward viewing heads and has a wider visual optic field of 156° with automatic light control. The Pillcam COLON™ is similar to the Pillcam SB™ in that it is activated following removal from a magnetic holder, but it goes into sleep mode after five minutes, once image acquisition is confirmed. Reactivation occurs one hour and 45 minutes later when image transmission resumes in the distal small bowel and colon.[22] Two published studies to date have shown this new modality to be promising for the evaluation of the colon.[22,23] In a blinded comparison with conventional colonoscopy, the Pillcam COLON™ had a sensitivity and specificity of 50% and 83% respectively for the detection of significant polyps (polyps greater than 6 mm or three or more polyps of any size) compared to colonoscopy.[23] However, this improved to values of 70% and 100% respectively when videos were reviewed by a panel of three investigators.[23] Thus yield may improve with greater reader experience. Furthermore, the optimal bowel preparation has the potential to improve the propulsion of the colon capsule thereby reducing the number of incomplete examinations (where the entire colon is not visualised). The reduced sensitivity of the colon capsule could thus be partly explained by the number of incomplete examinations, as occurred in both colon capsule studies.[23,24] In the study by Eliakim *et al* complete examinations, in the first group of subjects, occurred in 70% of patients.[23] In the same study, a second booster of laxatives given to the final group of subjects improved the capsule completion rate from 70% to 78%.[23] It is therefore possible that sensitivity may improve as the bowel preparation is optimised. Larger multi-centre trials are currently underway in the USA and Europe which aim to address these issues.[22]

Radiology

The colon capsule follows major advances in radiological imaging of the colon. A recent meta-analysis of CT colonography compared to conventional colonoscopy showed a sensitivity of 70% for polyps of 6–9 mm in size, 85% for polyps >9 mm and a specificity of 93% and 97% respectively for the polyp groups.[25] However earlier studies on CT colonography have reported to miss cancers and the accuracy between different centres has been reported to be variable depending on experience.[26] A large multicentre randomised trial is currently underway in the UK to evaluate CT colonography against colonoscopy or barium enema for colorectal neoplasia (the SIGGAR study) which may provide information about the relative roles of these modalities.[27]

Computed tomography is now, however, being marketed for colon cancer screening, as it can screen for cancers outside the GI tract. The demand for an accurate, non-invasive cancer screening tool has seen a sharp rise in the number of CT scans performed in the USA.[28] Concerns remain, however, about the relevance of the incidental pathology identified and the risk of radiation exposure. Incidental findings can cause anxiety and incur risk if they require invasive investigation. Furthermore, some experts suggest that between 1–2% of all cancers are related to ionising radiation from CT scans.[29,30] Magnetic resonance imaging (MRI) colonography does not have the problem of unnecessary radiation and has been shown to have a sensitivity and specificity of 95% in detecting colonic polyps >10 mm.[31,32] It has the advantage of simultaneous assessment of other organs particularly the liver in the context of neoplasia. The availability of this modality, however, remains limited.

The stomach is an important source of symptoms and pathology. While most small bowel capsules pass through it within 30 minutes, there are reports of delayed passage of the capsule when conducted in an inpatient setting.[33] Delayed passage can also occur in patients with gastroparesis or those taking medications which delay gastric emptying. It seems quite possible that a study in which the capsule acquires images of the stomach over several hours will provide a thorough examination. It could be conducted with the patient in a sequence of positions suited to examine each part of the stomach similar to the oesophageal capsule. Medications which delay gastric emptying might be considered. Such a capsule might supplant the current oesophageal capsule, thereby allowing a complete upper GI tract examination.

In the very near future, gastroenterologists will be able to visualise the whole of the gut mucosal surface using a remote technology, without recourse to the discomfort, indignity and risk of conventional endoscopy. As the technology improves with time, it seems likely that there will be a frame shift in the way we approach the investigation of GI symptoms. Much as diagnostic endoscopic retrograde cholangiopancreatography was supplanted by MRI, CE and/or radiology may become the diagnostic choice, with conventional endoscopy being used predominantly for targeted biopsy or therapy. As we move into the 21st century, fantasy is fast becoming reality.

Conflict of interest

ME McAlindon attended the 3rd International Conference for Capsule Endoscopy in Miami 2004 courtesy of Given Imaging. RS, DSS and MEM are all co-authors on the British Society of Gastroenterology guidelines on capsule endoscopy and enteroscopy.

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