REVIEW

Small bowel endoluminal imaging (capsule and enteroscopy)

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Received 30 October 2016

Accepted 11 December 2016

ABSTRACT

Over the last 16 years, the disruptive technologies of small bowel capsule endoscopy and device-assisted enteroscopy have revolutionised endoluminal imaging and minimally invasive therapy of the small bowel. Further technological developments continue to expand their indications and use. This brief review highlights the state-of-the-art in this arena and aims to summarise the current and potential future role of these technologies in clinical practice.

BACKGROUND

The introduction of small bowel capsule endoscopy (SBCE) in 2000¹ and double-balloon enteroscopy (DBE) in 2001² has dramatically revolutionised endoscopic investigation and management of small bowel (SB) disease. This 16-year paradigm shift in SB endoscopy, fuelled by these disruptive technologies, has enhanced our overall understanding of SB pathology and its natural history, and our ability to apply definitive, minimally invasive care. As an offshoot of these two groundbreaking technologies, several other platforms of SBCE and device-assisted enteroscopy (DAE) have become commercially available; this is an overview of developments in SB endoluminal imaging and current and potential future roles.

SMALL BOWEL CAPSULE ENDOSCOPY

The first SB capsule platform to gain food and drug administration (FDA) approval was introduced by Given Imaging, Israel, through the collaboration of Iddan and Swain in 2000.¹ Over the following years, two significantly improved versions were developed by the same company.³ The latest model (PillCam SB3, 2013) is the highest spec model to date and provides a dramatically enhanced resolution (340×340) and automatically adapts its image-capture

frame rate to SB transit (from two to six frames per second (fps)).³ Four more SBCE devices have now been commercialised by other companies, namely, Endocapsule (Olympus, Japan), Mirocam capsule (IntroMedic, South Korea), OMOM capsule (Jinshan Science and Technology, China) and the CapsoCam capsule (CapsoVision, USA), respectively. The Endocapsule (Olympus, Japan) was introduced in 2007, and no significant difference in diagnostic yield (DY) was found when this was compared with the PillCam SB platform.⁴ The Mirocam capsule (IntroMedic, South Korea) was approved by the FDA in 2013; in contrast to previous SB capsules, this platform uses 'electrical field propagation' to acquire an image-capture frame rate of 3 fps.⁵ No significant differences in DY were found in comparison with the PillCam SB2.⁶ The OMOM capsule (Jinshan Science and Technology, China) provides a bidirectional transmission, allowing real-time modification of frame rate acquisition and light intensity.⁷ The CapsoCam capsule (CapsoVision, USA) has four centralised rotating cameras that allow for a 360° field of view and provides the longest battery life (15 hours).⁷ Since the images captured by this capsule are stored onto an onboard flash memory drive, it has to be retrieved by the patient using a dedicated 'stool retrieval tool' (CapsoRetrieve, CapsoVision, USA). Although a recent prospective comparative study of the PillCam SB2 and CapsoCam showed these to have a similar overall DY ($p=0.791$),⁸ the CapsoCam capsule detected more lesions overall (108 vs 85 lesions; $p=0.001$). In another prospective clinical trial, however, despite its 360° field of view, the CapsoCam platform was only able to identify the duodenal ampulla in 71% of the 33 patients enrolled.⁹

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To cite: Murino A,
Despott EJ. *Frontline
Gastroenterology*
2017;**8**:148–151.

DEVICE-ASSISTED ENTEROSCOPY

DBE was developed and introduced into clinical practice by Yamamoto *et al*² and was the first technology to allow direct flexible endoscopic investigation and therapy to be applied to the whole of the SB without the need for surgery. DBE uses a 200 cm long enteroscope (Fujifilm, Japan) and a flexible overtube with two inflatable balloons, attached to the tip of the enteroscope and to the distal end of a dedicated overtube, respectively. The balloons allow gentle anchoring of the SB, and the overtube provides stability for progressive 'push-and-pull' insertions deep into the SB.² In 2007, Olympus (Japan) introduced the alternative DAE platform of single-balloon enteroscopy (SBE), also using a 200 cm long enteroscope equipped with a latex-free flexible overtube with integrated inflatable balloon. To overcome the lack of an enteroscope balloon, distal anchoring is achieved by suction of the mucosa or angulation of the tip of the enteroscope to maintain position. Overall DBE appeared superior to SBE in terms of insertion depth and panenteroscopy rates, although this has not translated into a significant difference in DY to date.¹⁰ Manual spiral enteroscopy (SE), introduced by Akerman *et al*,¹¹ uses a proprietary overtube (Endo-Ease Discovery, Spirus Medical, USA) which has a raised soft plastic helix at its distal end; the SE overtube may be used with any type of therapeutic 200 cm long enteroscope. Manual clockwise rotation of the overtube allows engagement of the SB mucosa and advancement of the enteroscope and overtube into the SB, while counterclockwise rotation allows withdrawal.¹¹ Although rapid insertion and stability have been described, several studies have shown that SB insertion depths and panenteroscopy rates may be inferior to those provided by DBE.^{12,13} The NaviAid AB device (Smart Medical Systems, Israel) is a through-the-scope balloon device which is advanced ahead of the tip of a colonoscope. Inflation of the balloon provides some anchorage of the SB to facilitate scope advancement. Although a recent multicentre, retrospective study has suggested that this novel approach may allow overtube-free deep enteroscopy,¹⁴ further prospective, comparative studies are required to confirm this finding.¹⁵

MAIN CLINICAL INDICATIONS FOR SBCE AND DAE

(In accordance with the European Society of Gastrointestinal Endoscopy Guidelines (ESGE), 2015¹⁶).

Midgut bleeding

Approximately 5% of patients presenting with gastrointestinal (GI) bleeding have a negative upper GI endoscopy and colonoscopy.¹⁶ A SB (midgut) lesion is the cause of obscure GI bleeding (OGIB) in 75% of these cases.¹⁶ SBCE is superior to cross-sectional imaging and push enteroscopy for the identification

of the source of OGIB;¹⁶ when compared with DBE, several studies showed that both procedures have similar DY.¹⁶ SBCE is now the recommended first-line investigation for suspected midgut bleeding and should ideally be performed within 14 days of the episode.¹⁶ The application and route of DAE are usually guided by SBCE and/or cross-sectional imaging findings.¹⁶ DAE is useful for endotherapy of small intestinal vascular lesions, although the evidence suggests that repeat endotherapy may be required to reduce rebleeding frequency and transfusion requirements in the longer run.¹⁷

Crohn's disease

Although ileocolonoscopy (IC) remains the first-line investigation in patients with suspected Crohn's disease (CD), SBCE has the potential to identify SB inflammation in patients with a negative IC in whom a high index of suspicion remains.¹⁶ SBCE may also provide added information about the extent and severity of any ongoing SB mucosal inflammation.¹⁶ In the context of established CD, assessment of disease activity should be done with dedicated SB cross-sectional imaging in the first instance, since this modality also allows for assessment of any stricture and/or mural/extramural disease.¹⁶ In cases of established CD where SBCE is still required for further assessment of the mucosa, prior assessment of SB functional patency is required to mitigate the risk of capsule retention.¹⁶ The use of DAE in the context of suspected or established CD should be guided by clinical indication where histopathological confirmation is required and where endoscopic balloon dilation of short (<5 cm), non-angulated, fibrotic strictures is being considered for non-surgical minimally invasive management. In this setting, DAE may also be useful for retrieval of retained SB capsules.¹⁶

SB tumours and polyposis syndromes

SB tumours represent 5%–7% of all GI tumours, and usually present with midgut bleeding or iron deficiency anaemia. The role of SBCE in the detection of SB tumours is complementary to that of CT and MR enterography.¹⁶ In familial adenomatous polyposis syndrome, surveillance of the perianapillary region should be performed with standard endoscopy (forward and side-viewing upper GI endoscopes).¹⁶ In Peutz-Jeghers syndrome (PJS), the role of SBCE and dedicated SB cross-sectional imaging also appear complementary, and both may be used for surveillance purposes.¹⁶ DAE should be considered for tattoo localisation of SB tumours and resection of PJS SB polyps >1.5 cm.¹⁶

Coeliac disease

Although serology and upper GI endoscopy remain the gold standard for the diagnosis of coeliac

disease,¹⁶ SBCE is recommended in patients with refractory coeliac disease in order to rule out ulcerative jejunitis or enteropathy-associated T cell lymphoma. DAE may be critical for the confirmation of these diagnoses by the provision of histopathology through biopsy.¹⁶

EMERGING INDICATIONS

In the emerging era of 'personalised medicine', particularly in the context of patients with CD, SBCE is increasingly recognised as a potentially useful instrument for the assessment of mucosal healing and response to medical therapy.¹⁸ The use of the latest generation colon capsule (PillCam Colon 2, Medtronic, Ireland), with its dual-headed cameras and enhanced variable frame rate (up to 35 fps), is also being studied for potential pan-GI assessment in patients with CD.¹⁹

Miniprobe-facilitated endoscopic ultrasound during DBE (DBE-EUS) is another emerging indication for the assessment of SB lesions and strictures.^{20 21} DBE-EUS has been shown to allow characterisation of SB submucosal lesions, facilitating appropriate management (endoscopic, surgical or conservative).^{20 21} DBE-EUS preassessment may inform the endoscopist of lesion depth and vascular involvement, potentially reducing the risk of endotherapy.^{20 21}

SBCE may complement the findings of dedicated SB cross-sectional imaging to identify and help localise SB varices.²² It has also recently been demonstrated that cyanoacrylate and polidocanol injection therapy of SB varices at DAE appears to be a safe and effective management strategy for this condition when other first-line options such as radiological intervention (TIPSS, stenting of occluded mesenteric veins ± embolisation of culprit varices) are not feasible.²³

In patients warranting long-term enteral feeding, direct percutaneous endoscopic jejunostomy (DPEJ) is a minimally invasive alternative to a surgical jejunostomy.²⁴ DPEJ also has advantages over percutaneous endoscopic gastrostomy with jejunal extension, in that it allows direct feeding into the jejunum through a wide-bore tube, circumventing issues such as retrograde migration of the jejunal extension and tube blockage. DPEJ has also been shown to reduce the risk of aspiration. The increasing use of DAE for DPEJ placement has been associated with good outcomes and a higher success rate as compared with push enteroscopy. In technically challenging cases, particularly in the setting of postsurgical adhesive disease, the employment of miniport laparoscopic assistance for DAE (Lap-DAE) has been associated with enhanced success rates for DPEJ placement.²⁵ Lap-DAE has also been shown to improve outcomes and safety for endotherapy of sizeable SB polyps in patients with PJS. DAE is also increasingly recognised as a useful instrument in patients with postsurgical altered SB anatomy to facilitate access for endoscopic

retrograde cholangio-pancreatography (ERCP) (DAE-ERCP) and excluded gastric remnants.²⁶ DAE is now also employed for completion of colonoscopy in patients with a technically challenging colon.²⁷

THE FUTURE

SBCE

Inability to control capsule motion and lack of capacity for tissue sampling are recognised as the major setbacks of SBCE. In an attempt to mitigate these limitations, SBCE prototypes controlled by mechanical 'legs' and paddles, propellers and gimbaled ducted-fan systems are being tested.^{28 29} The concept of magnet-controlled capsules is also being actively assessed with promising preliminary findings.^{28 29}

DAE

Motorised spiral enteroscopy (MSE) represents the second generation evolution of SE which is currently being studied in prototype form. First developed by Akerman *et al*,³⁰ MSE comprises the use of a single-operator 160 cm 'active enteroscope' incorporating a disposable spiral at its distal tip with integrated motorised foot-pedal control. Preliminary data from a small study of the original prototype³¹ and interim results of an ongoing study of an upgraded version in patients with no previous history of abdominopelvic surgery³² appear very promising.

SUMMARY

SBCE and DAE have revolutionised our approach to endoluminal imaging and therapy in the SB. Further technological advancements and expanding application of these disruptive technologies shall continue to fuel this paradigm shift. Clinical, technical, training and quality guidelines relating to their appropriate use in clinical practice shall continue to be updated by the ESGE and other societies to reflect this ongoing evolution.

Competing interests EJD: Research, education and travel grants received from Aquilant Endoscopy (UK), Fujifilm, Keymed-Olympus and Boston Scientific. Speaker honoraria received from Fujifilm and Keymed-Olympus.

Provenance and peer review Commissioned; externally peer reviewed.

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