Optimising the performance and interpretation of Small Bowel Capsule Endoscopy

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Abstract

Small bowel capsule endoscopy has become a commonly used tool in the investigation of gastrointestinal symptoms and is now widely available in clinical practice. In contrast to conventional endoscopy, there is a lack of clear consensus on when competency is achieved or the way in which capsule endoscopy should be performed in order to maintain quality and clinical accuracy. Here we explore the evidence on the key factors that influence the quality of small bowel capsule endoscopy services.

Key words:

Capsule endoscopy

Quality

Bowel Preparation

Rapid reading software

Reading Modes

Introduction

Since its introduction at the turn of the millennium, small bowel capsule endoscopy (SBCE) has offered a non-invasive, acceptable and well tolerated means of examining the entirety of the small bowel [1]. A patient is simply required to swallow the capsule, which then passively passes through the gastrointestinal tract whilst acquiring images. These images are then later reviewed and interpreted. SBCE has become an established investigative modality for occult gastrointestinal bleeding and recurrent iron deficiency anaemia where bi-directional endoscopy has failed to reveal a cause, suspected small bowel Crohn's disease and in the surveillance of polyposis syndromes [2-4]. The availability of device assisted enteroscopy means that identified lesions can be investigated further and potentially treated endoscopically. As a result there has been an expansion of SBCE services globally. Despite this there still remains ambiguity on the optimal way in which SBCE should be read in order to ensure quality. In contrast to conventional endoscopy, at present there is no clear consensus on factors that lead to competence or how to monitor performance in SBCE. Here we review the evidence in order to answer the key questions that affect the performance and interpretation of SBCE.

What is the most effective way to prepare the small bowel prior to capsule endoscopy?

In common with conventional endoscopy, adequate mucosal views are required to make an accurate diagnosis. Complete cleansing of the small bowel is challenging due to the constant secretion of gastric, biliary and pancreatic fluids. This is further compounded by the passive nature of SBCE, which does not allow for the flushing or suctioning of bubbles and debris.

There are numerous studies examining the impact of purgatives on mucosal cleansing, with conflicting results. Several meta-analyses have pooled the results of these studies and suggest that the use of polyethylene glycol (PEG) is superior to a clear liquid diet alone [5-7]. A PEG preparation lends itself as an ideal candidate for intestinal lavage, as this is a transparent solution, the mucosa can be visualised through any residual fluid. Further, it has been proven to be more effective than available alternatives such as sodium phosphate regimes [6]. When volume was evaluated, there was no benefit in terms of cleansing or diagnostic yield with the use of a 4 litre PEG regime over 2 litres, with the latter being more patient friendly [8, 9].

One study examines the effect of the timing of bowel preparation, concluding that there was improved mucosal visibility when using a split dose regime with the last litre of PEG given 4 hours pre-procedure rather than 10 hours [10]. A pilot study aimed to overcome the common problem of poor distal views, by using a 'booster' consisting of a single sachet of Picolax administered one hour after the capsule is swallowed, following the consumption of clear fluids without purgatives during the previous day. Although a statistically significant difference in the number of lesions was not demonstrated when compared to a 2L PEG regime, distal views were improved, with the potential to offer a cheaper and more tolerable preparation regime [11].

In selected cases, it may be appropriate to forgo bowel preparation. Where patients are admitted with acute suspected small bowel bleeding it is known that a positive diagnosis is more likely to be made if this test is performed within a short period of the bleeding episode [12-14]. As the location of bleeding is the primary point of interest, rather than subtle mucosal pathology, the administration of preparation may result in a delay without a clear clinical benefit.

Antifoaming agents such as Simethicone have been proposed as a premedication to disperse bubbles, commonly encountered in the duodenum. This has been trialled with good effect, having been found to provide superior views of the proximal small bowel compared to a clear liquid diet alone [15]. Where antifoaming agents were combined with bowel preparation an improvement in visualisation was observed [3, 16-18].

The battery life of the first generation of capsules were limited to 8 hours, leading to a proportion of studies where the caecum was not reached. In order to overcome this potential limitation the concept of increasing the transit speed through the gastrointestinal tract with pro-kinetics was introduced. This appears to have a positive effect on completion rates with no deleterious effect on diagnostic yield [19]. However, in the current era of capsules with minimum recording times of 12 hours, routine use of pro-kinetics is rarely required and is usually limited to cases where the capsule has failed to exit the stomach after one hour [20].

Which capsule endoscopy system should be used?

At present there are five commercially available SBCE systems; PillCam (Given Imaging), EndoCapsule (Olympus), MiroCam (Medtronic), CapsoCam (CapsoVision) and OMOM (Chongqing Jinshan Science & Technology). Each of these share the same core components, which include; an imaging device, a lens, a light source and a battery, all of which are encased within a non-biodegradable toughened plastic casing. In all but one system (CapsoCam), images acquired from the capsule are transmitted wirelessly to a receiving device, before being uploaded and read at a workstation using proprietary software. Differences in the design and technical capabilities of these components leads to subtle differences in capsule specification, as summarised in the Table 1.

As first to the market the PillCam is the most widely used in clinical practice and studied in the literature. This system is now in its third generation (PillCam SB3), boasting improved image resolution and an adaptive frame rate, which increases from 2fps to 6 fps when the capsule is sensed to be moving at a high velocity. The EndoCapsule system followed shortly afterwards in 2004, offering a 3D tracking function to enable the localisation of detected lesions in order to guide therapeutic approach where this is required.

The MiroCam capsule uses electric field propagation, which exploits the patients' body as a conductor for data transmission. This reduces energy consumption compared to radio-frequency based systems, enabling a long battery life in spite of its smaller dimensions [21]. MiroCam offer also magnetically steerable capsule (Mirocam Navi) designed for examination of the upper gastro-intestinal tract is available, but at present its use is limited to the research setting.[22, 23]

CapsoCam is able to offer a 360 degree ‘panoramic’ view, owing to four laterally placed cameras. This may have the potential to result in a greater diagnostic yield through an increased number of images, although this needs to be offset against longer reading times [24-26]. The images acquired are stored within the capsule and so a receiving device is not required. Retrieval of the capsule following expulsion from the body is necessary, with a magnetic wand provided to aid recovery. This could be advantageous in rural settings, where patients may not be able to attend a hospital but could send and receive equipment through the post. However, this is clearly not suitable for all patients, with a proportion unable to retrieve the capsule in an observational study [27].

The OMOM capsule has been in used for many years and is well established in China and Asia, but has only been recently available in the USA and Europe. This capsule boasts duplex data communication, where the endoscopic view can be evaluated, allowing for real time adjustments of parameters such as frame rate, brightness and exposure in order to optimise the quality of the examination.

There are few head to head trials comparing the clinical implications of using one capsule versus another (Table 2) [3]. Where these exist, no significant differences have been demonstrated. Which capsule endoscopy system is used, is therefore determined by user preference, with cost and procurement undoubtedly influencing these decisions.

Table 1: Specifications of the commercially available capsule endoscopy systems

Model	Company	Dimensions (mm)	Weight (grams)	Field of view (degrees)	Frames per second	Image sensor	Transmission	Battery life (hours)
PillCam (SB3)	Given Imaging	26x11	1.9	156	2-6	CMOS	Radio-frequency	11
MiroCam	Intromedic	24x11	3.25	170	3	CMOS	Electrical field propagation	12
Endocapsule (EC-10)	Olympus	26x11	3.3	160	2	CMOS	Radio-frequency	12
OMOM (2)	Jianshan	28x13	4.5	140	2	CMOS	Radio-frequency	10
CapsoCam (SV2)	Capsovision	31x11	4	360 (laterally)	20	CMOS	Images stored	15

Table 2: Head to head trial comparing different capsule endoscopy systems

Study	Country	Systems compared	No of cases	Study Design	End points	Summary of results

Hartmann D et al (2007) [28]	Germany (single centre)	EndoCapsule vs PillCam	40	Sequential capsules (randomly assigned order)	Diagnostic yield and completion rate	• Higher diagnostic yield in EndoCapsule- not statically significant. • Higher completion in EndoCapsule system (100% vs 82.5%)
Cave DR et el (2008) [29]	USA (multicentre)	EndoCapsule vs PillCam	51	Sequential capsules (randomly assigned order)	Diagnostic yield, completion rate and quality of view	• No significant difference in diagnostic yield • Subjective judgement in image quality favouring EndoCapsule
Kim HM et al (2010) [30]	Korea (single centre)	MiroCam vs PillCam	24	Sequential capsules (randomly assigned order)	Diagnostic yield and completion rate	• No significant difference in diagnostic yield • Higher completion in MiroCam system (83.3% vs 58.3%)
Pioche M (2011) [31]	France (Multicentre)	MiroCam vs PillCam SB2	73	Sequential capsules (randomly assigned order)	Diagnostic yield, transit time and capsule reading time.	• Statistically non-significant higher yield using MiroCam system • (95.2% vs 78.6% accuracy in detecting lesions)
Koulaouzidis et al (2012) [32]	UK (single centre)	MiroCam vs PillCam SB1/2	619	Retrospective analysis (209 MiroCam, 262 SB1, 148 SB2)	Identification of the Ampula	• Ampulla was identified in 9.5% cases • No difference in ampulla detection or number of frames in which this was visualised between systems
Hong SP et al (2012) [33]	Korea (Single centre)	MiroCam vs PillCam	141	Retrospective analysis (57 studies using MiroCam and 84 using PillCam)	Visualisation of the papillae	• Higher frequency of papillae detection using MiroCam (13.1% vs 29.8%)
Dolak W et al (2012)[34]	Austria (single centre)	MiroCam vs EndoCapsule	50	Sequential capsules (randomly assigned order)	Diagnostic yield and completion rate	• No significant difference in diagnostic yield • No significant difference in completion rate
Choi EH et al (2013) [35]	USA (multicentre)	MiroCam vs PillCam	105	Sequential capsules (randomly assigned order)	Diagnostic yield and completion rate	• No significant difference in diagnostic yield • Higher completion in MiroCam system (93.3% vs 84.3%)
Pioche M (2014) [36]	France (Multicentre)	CapsoCam vs PillCam SB2	73	Sequential capsules (randomly assigned order)	Diagnostic yield	• Technical issues with the CapsoCam system in 11 patients and with PillCam in 2 patients. • No significant difference in diagnostic yield.

Who should read and interpret capsule endoscopy cases?

SBCE does not form a part of the mandatory endoscopy training for gastroenterologists in most countries. Those that read capsule are therefore self-selecting, with this skill self-taught by interested physicians in a situation where the need for capsule endoscopy services has arisen. Studies in assessing accuracy and competence in SBCE are hampered by the fact that there is a known significant intra-observer variability, even between experts [37-39]. Further in clinical practice it is not always necessary to identify all lesions present in order to arrive at the same clinical conclusion.

In the UK, the British Society of gastroenterology (BSG) does not mandate a minimum experience prior to undertaking capsule reading and at present there is no formal accreditation process as for other endoscopic procedures. International guidance suggests an experience of 10- 25 supervised cases should be performed prior to independent practice. These recommendations are largely inferred from secondary findings from studies on training in SBCE. A Korean study of 12 gastroenterology trainees specifically set out to determine the learning curve in SBCE. By reading one capsule per week, it was shown that it required 11 weeks to reach kappa coefficients of 0.80 between the trainees and an expert reader [40].

The Mayo Clinic have developed the only SBCE competence test (CapCT), consisting of three elements; a multiple choice quiz on topics pertaining to the use of SBCE, video clips and images of pathological findings and finally a formal review of a full capsule case, with interpretation of findings and formulation of a management plan. Scores from each component are summed, with a requirement to reach at least 82% of the total available score of 100 prior to independent practice. When this tool was trialled in a group of gastroenterology fellows, who had no prior teaching in capsule endoscopy but were

experienced in flexible endoscopy, it was found that only those with a prior experience of 21-35 cases read were able to reach a mean score of 85% after a 4 hour teaching intervention. Experienced readers had a mean score of 91% [41].

Training has been proven to be beneficial in the interpretation of SBCE examinations. An 8-hour hands on training course delivered to 268 participants throughout 4 European countries has be evaluated. This demonstrated that 10 twenty-second videos with a range of findings were read more accurately following the training course. Where readers had previous capsule experience the baseline score was higher compared to novices, however an improvement in detection and interpretation was still observed following the intervention [42].

A background in conventional endoscopy appears to correlate with a better ability to interpret SBCE. When 10 gastroenterology trainees with experience in flexible endoscopy were compared with 5 medical students, it was seen that they were more likely to pick up pathology, and less likely to produce false positives [43]. This is corroborated by the findings of the European training study, which found prior experience in conventional endoscopy was a predictor of better baseline score, independent of the degree of prior capsule experience [42].

There is increasing interest in employing nurses as physician extenders in the provision of endoscopy services. The relatively short learning curve and low risk profile makes SBCE particularly appropriate for non-physician reading. Several studies have demonstrated that nurses are able to detect lesions accurately in a ‘pre-reading’ capacity [24, 44-50].

One study estimated adopting this approach would enable a cost saving of as much as $324 per case read [51]. Observational studies highlight some differences in the way in which nurses read, with a greater tendency to mark up more lesions of doubtful significance [46].

At present there is insufficient evidence to support the ability of nurses in independent SBCE interpretation, including the formulation of a management plan and recommendations.

Which reading settings should be used to interpret capsule endoscopy cases?

A SBCE study typically results in the acquisition of tens of thousands of images. A clinically significant lesion may be present on just a single frame and could therefore be easily missed. The likelihood of missing lesions can be influenced by the way in which the capsule study in read. Within the various interpretation software programs there is an option to read one (Single View: SV), two (Dual View: DV) or four frames (Quad View: QV) as either sequentially or overlapping images. Use of QV overlap mode means that any one image is viewed four times, as it is seen moving across the screen there is a longer exposure to the image compared to SV. The display of the images does however occupy the whole screen, requiring greater use of peripheral vision compared to a single central image. In addition the speed at which the images are presented (expressed as frames per second) can be adjusted across a numerical scale.

In a recent study evaluation of a single 15 minute video clip containing 60 frames during which there was a pathological lesion was performed in 9 different viewing modes; SV at 10 fps, 15 fps and 25 fps, DV at 10 fps, 15 fps and 25 fps, or QV at 10 fps, 15 fps and 25 fps. This confirmed that increased speed was associated with an increased chance of missing lesions. The optimal setting was found to be QV overlapping at 10 fps (detecting 51 of the 60 lesions), compared

to the One image setting at 25fps which detected just 14 [52]. This is supported by a study examining the most commonly used reading combinations, which found SV at 25fps had a mean diagnostic yield of 26%, compared to 45% when reading SV at 15fps. When four images were displayed in the overlap view there was no reduction in accuracy compared to SV at 15fps, even when increasing the speed to QV 20 fps and even QV 30 fps [53].

In daily clinical practice a range of speeds should be used. It is appreciated that the passage of a capsule through the duodenum and the proximal jejunum is faster than that through the ileum. It is this phenomenon that results in the ampulla, the only landmark within the small bowel, to be visualised during just 10% of SBCE examinations [32]. It would therefore be prudent to significantly reduce reading speeds during such areas of the small bowel in order to increase pathology detection.

Are software enhancements helpful in capsule endoscopy interpretation?

There has been attempt to exploit advances in information technology to aid the interpretation of SBCE, by both enhancing the detection of lesions and by reducing the number of normal images reviewed [3, 54]. Given that the movement of a capsule through the bowel is non-liner, multiple duplicate images are captured. Removal of such images from the reading stream offers the possibility of dramatically reducing reading times. Several software algorithms have been developed to remove redundant images and only present clinically relevant frames. In clinical practice however the success of this approach has been mixed. Whilst reading time is undoubtedly reduced, some studies quote an unacceptably high lesion miss rate. This is likely to be due to the capsule software being unable to differentiate between subtle mucosal pathology and normal mucosa. The rapid presentation of non-

sequential images may also be harder to for the viewer to visually process causing relevant images to be overlooked.

The PillCam RapidView software offers Quickview, this allows the proportion of images excluded to be determined by the reader. Several studies have demonstrated reasonable accuracy in the detection of major lesions [55, 56]. When compared to alternate time saving strategies this software enhancement proves to be less promising. Reading in SV or DV at 20fps was more accurate than the use of Quickview, although not as rapid [57]. Further, it has been demonstrated that viewing alternate frames, by adopting the four image sequential view and covering half the screen with a piece of paper led to a lower lesion miss rate compared to the use of Quickview [58]. Implying that the selection of excluded frames was less accurate than random exclusion of half the images.

Similarly the OMOM similar picture elimination software has three modes, with increasing proportions of removed images. While each mode reduced reading times, only Mode 1, with the least images excluded had a sensitivity greater than 85%, saving a mean reading time of 9 minutes.

The equivalent EndoCapsule software has been evaluated in a single study comprising of 70 SBCE cases. This utilised two modes Express Selected, where repeat images are removed and Auto Adjust, where the repeated images are maintained within the viewing stream but are viewed at an increased speed. One lesion out of the 40 known lesions was missed in either

time saving mode, leading to an accuracy of 97.5%[59]. This software has been recently superseded by Omni-mode, which claims to be able to reduce the images displayed by 65% through the 'intelligent' removal of repeated as well as overlapping images. To date this has been studied in a Japanese multicentre trial, which showed the software was able to correctly remove images whilst maintaining all the pre-identified major lesions in 40 selected cases [60]. A larger multicentre European study is currently underway.

Table 3: A summary of the time saving software in the interpretation of small bowel capsule endoscopy

Study	Country	System	Study Design	Summary of results
Hosoe et al (2016) [60]	Japan (Multi centre)	EndoCapsule: Omni-Mode	• 40 pre-selected cases (based on the presence of lesions) • Each case read twice in Omni mode and twice in normal mode	• Reduction in average reading time from 75 minutes to 27 minutes. • 65% reduction in displayed images • Sensitivity of 87%
Subramanian et al (2012) [59]	UK (Single centre)	EndoCapsule: Express Selected/ Auto Adjust	• 70 capsule cases • Read in three mode, Normal (15 fps), Express selected + Overview, Adjusted mode + Overview • Each case read by two independent endoscopists	• Normal: sensitivity of 100%, taking an average of 45 mins • Express Selected: sensitivity of 97.5%, an average 19 mins • Auto Adjust sensitivity of 97.5%, an average 34mins
Kyriakos et al (2012) [57]	Greece (Single Centre)	Pill Cam: QuickView	• 100 capsule studies pre-selected cases (based on the presence of lesions) • Cases read in 5 different modes, Normal at 10 fps, Normal at 20 fps, Normal mode with two images at 20 fps, Automatic mode 10 fps, QuickView at 3 fps	• All time saving modes were faster than reading in Normal mode at 10 fps • Best compromise between speed and accuracy is Normal mode at 20 fps, with either a single or dual image.
Halling M et al (2014) [55]	Denmark (Single Centre)	Pill Cam: QuickView	• Analysis of 12 video clips with findings • 40 capsules of patients with suspected Crohn's disease	• Quickview missed 40% of ulcers seen in the normal viewing mode • This effect is pronounced for terminal ileal lesions
Saurin JC et al (2012) [24]	French (multi centre)	Pill Cam: QuickView	• 106 patients recruited across 12 centres • Quickview vs normal mode reading	• 94% of significant lesions were identified • Mean reading time of 11.6 mins using QuickView
Koulaouzidis A et al (2012)	UK (Single Centre)	Pill Cam: QuickView	• Retrospective review of 106 cases • Normal mode vs Quickview vs Quickview with BM	• Over 50% of ulcers missed in cases of suspect Crohn's using QuickView • 64% of potential/bleeding lesions were detected in the context of overt/occult bleeding
Shiotani A et al (2012) [61]	Japan (Single Centre)	Pill Cam: QuickView	• 100 capsule studies read in QuickView vs normal reading	• Unacceptable miss rate • Miss rate was greatest in the physicians with limited experience.

			• One nurse, two trainees and one experienced reader	
Hosoe N 2012	Japan (Single Centre)	Pill Cam: QuickView	• 45 capsule studies • Gold standard reading established by two experienced readers • Three trainees with no prior capsule experience read in Normal mode, Automatic mode and QuickView.	• Reduced reading time in automatic and QuickView compared to Normal mode • 179 missed lesions when using QuickView
Westerhof et al (2009) [58]	Netherlands (Single centre)	Pill Cam: QuickView	• 200 cases included • First 100 read in Normal mode and then only alternate images • Second 100 read in Normal mode then with QuickView	• Normal mode average reading time of 17 mins • Miss rate of 4% when viewing alternate images. Avreage reading time of 10 mins • Miss rate of 13% with QuickView. Average reading time of 4.4 mins
Xu Y et al (2014) [62]	China (single centre)	Omom: Similar Picture Elimination	• Retrospective study of 148 capsule studies. • Read in four modes Normal, Level I, Level II, Level III and Level IV • Each case read by four independent endoscopists	• Reading time reduction of 25.1-55.0% compared with normal mode. • Normal: sensitivity of 93.8% • Mode I: sensitivity of 87.7% • Mode II: sensitivity of 77.8% • Mode III: sensitivity of 70%

The Suspected Blood Indicator (SBI) is a rapid viewing tool available within the various capsule software programs. This highlights frames where an excess number of red pixels have been identified and may therefore represent a bleeding lesion. This function is activated by merely selecting the SBI mode within the reading software, this results in highlighted frames or regions along the scroll bar. In the context of gastrointestinal bleeding, this should obviate the need for a complete review of the capsule case, allowing the reader to quickly identify lesions and their location. Studies in clinical practice have however been disappointing, with reported sensitivities as low as 20% [63]

A meta-analysis of 16 studies comprising of 2049 patients, confirmed a high sensitivity of 98.8% in the detection of actively bleeding lesions. This fell to a sensitivity of just 55.3% and a specificity of 57.8% in the detection of lesions with bleeding potential that were not actively bleeding during the examination. It is noteworthy that the SBI has been trialled exclusively using the PillCam capsule software, its utility in in the alternate systems is unknown.

One study attempted to understand the limitations of the SBI with the passage of a capsule through an experimental small bowel model. Red lesions were displayed on backgrounds of varying colours, commonly encountered in clinical practice. This demonstrated a significantly improved likelihood of detecting lesions superimposed on a pale magenta or yellow background as compared to pale yellow or brown [64]. As this is a factor that cannot be influenced by the operator it remains a major limitation of this approach.

The accuracy of the SBI function is insufficient accurate to allow it use as a time saving technique in clinical practice [65]. Instead it could be considered as a useful adjunct to ensure no lesions have been missed following initial reading and interpretation.

The use of advanced imaging has become commonplace in the identification and characterisation of lesions during endoscopic procedures. This concept has been replicated within the PillCam capsule endoscope with the adoption of Flexible Spectral Colour Enhancement (FICE). FICE is a post processing visual enhancement technology, which by using proprietary software algorithms converts white light images to a restricted range of wavelengths in order to enhance mucosal surface pattern. Perhaps due to the lack of control and manoeuvrability afforded by flexible endoscopy, the results of SBCE FICE have been disappointing. Evaluation across studies showed there was no increase in the detection of lesions, although soe settings demonstrated improved lesion delineation [66]. The evidence for Blue Mode Imaging is still emerging [67, 68]

Conclusions

Clear standards in capsule endoscopy reporting are yet to be established. Maintaining the diagnostic potential of SBCE requires using this tool effectively. Before a SBCE is undertaken, bowel preparation with combined 2 litre PEG preparation and simethicone should be considered. Readers should ideally have previous experience of conventional endoscopy and undergo formal training and supervised reading of 10-20 cases prior to independent reading. Reading with up to 4 frames displayed concurrently at a rate no greater than 15 fps optimises

the chances of lesion detection. Software enhancements are not sufficiently accurate to be used on a routine basis, although remains an exciting area for future development and poses the possibility of automated reading.

Figures:

Table 1: Specifications of the commercially available capsule endoscopy systems

Table 2: Head to head trial comparing different capsule endoscopy systems

Table 3: A summary of the time saving software in the interpretation of small bowel capsule endoscopy

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