

# Part 1

## Investigating IBD in the 21st Century

### 1

## Capsule endoscopy: do we need it?

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### LEARNING POINTS

#### Capsule endoscopy

- Capsule endoscopy (CE) has a diagnostic yield of 40–70% in patients with suspected small bowel Crohn's disease where other investigations have been normal
- It is not yet clear whether CE provides additional information about the small bowel in patients with known Crohn's disease
- There is an emerging role for CE in differentiating Crohn's disease from indeterminate colitis
- Small bowel follow through (SBFT) is not reliable in predicting capsule retention and the role of the patency capsule is evolving
- SBFT before CE may in due course prove unnecessary in suspected small bowel Crohn's disease

#### Introduction

In addition to being the section of the gastrointestinal (GI) tract most commonly affected by Crohn's disease, the small bowel (SB) is also the most difficult region to visualize endoscopically. Wireless video capsule endoscopy (CE) is a new technology which, at least in part, overcomes this problem, by allowing complete non-invasive endoscopic imaging of the small bowel.

However, for CE to have a role in the diagnosis and management of small bowel Crohn's disease, it should fulfill several criteria: it should be safe, provide additional diagnostic information and its use should lead to clinically meaningful changes in patient management. In this chapter we discuss the limitations of other small bowel imaging

techniques, the potential uses of CE in relation to Crohn's disease and the evidence to support its use in each scenario.

#### Limitations of other techniques for imaging small bowel

Imaging of the SB has been previously limited to the radiologic techniques of small bowel follow through (SBFT), enteroclysis (double contrast small bowel examination) and computed tomography (CT) enteroclysis, and the endoscopic techniques of push enteroscopy, double balloon enteroscopy and colonoscopy with ileal intubation.

SBFT is the most common technique used to assess small bowel Crohn's but it is relatively insensitive for subtle mucosal lesions. Enteroclysis and CT enteroclysis are more invasive than SBFT, requiring the passage of a catheter into the duodenum under sedation, and several investigators have found these techniques to be no more sensitive [1]. All three techniques result in significant radiation exposure, limiting the frequency with which they should be performed.

Push enteroscopy can only view the proximal small bowel 15–160 cm beyond the ligament of Treitz and is more invasive and technically difficult than CE. Double balloon enteroscopy is an exciting new technology which has the potential to biopsy and perform therapeutic endoscopy throughout the small bowel. However, the examination is invasive, time consuming and may not examine the entire small bowel even when the procedures are performed per orally and per anally. Visualization of the terminal ileum at colonoscopy is limited both to the distal 10–15 cm of SB and to those patients in whom the terminal ileum can be successfully intubated.

**TABLE 1.1** Trials assessing the role of capsule endoscopy in the diagnosis and assessment of Crohn's disease.

Reference	N	Preceding investigation	Yield (%)	Comparator	Yield (%)
<i>Diagnosis of small bowel Crohn's</i>					
Fireman [5]	17	SBFT, EGD, colonoscopy (ileoscopy 6/17)	71	N/A	N/A
Ge [6]	20	SBFT, EGD, colonoscopy	65	N/A	N/A
Herrerias [7]	21	SBFT, EGD, colonoscopy (ileoscopy 17/21)	43	N/A	N/A
Arguelles-Arias [8]	12	SBFT, EGD, colonoscopy	75	N/A	N/A
Liangpunsakul [9]	40	SBFT, EGD, colonoscopy	7.5	CT enteroclysis	0
Eliakim [10]	35	N/A	73	SBFT CT enteroclysis	23 20
Voderholzer [11]	5	SBFT, EGD, colonoscopy	40	CT enteroclysis	40
<i>Assessing disease activity/recurrence</i>					
Buchman [12]	30	N/A	70	SBFT	67
Voderholzer [11]	8	N/A	75	CT enteroclysis	75
De Palma [15]	8	SBFT, OGD, colonoscopy, push enteroscopy	75	N/A	
Debinski [14]	10	N/A	N/A	CDAI, IBDQ, CRP	N/A
<i>Differentiating SB Crohn's from indeterminate colitis</i>					
Mow [13]	22	N/A	59	Ileoscopy	23
Whitaker [16]	7	Colonoscopy and ileoscopy	29	N/A	

CDAI, Crohn's Disease Activity Index; CRP, C-reactive protein; CT, computed tomography; IBDQ, Inflammatory Bowel Disease Questionnaire; N/A, not available; EGD, esophagogastroduodenoscopy; SBFT, small bowel follow through.

## Capsule endoscopy

The Pillcam® capsule endoscope from Given Imaging® was first used in clinical trials in 2000 and was granted Food and Drug Administration (FDA) approval in 2001 (Table 1.1). Since then it has been used in over 200 000 individuals.

Capsule endoscopy images are different from standard endoscopic images. The images are seen through intestinal content without air insufflation. Minimum standard terminology is being developed to allow consistent image description, but more validation with histology is required [2]. In a recent large randomized placebo-controlled trial looking at intestinal inflammation in patients on non-steroidal anti-inflammatory drugs, 7% of those on placebo had small bowel abnormalities [3]; these data raises the question of what constitutes a normal small bowel appearance.

The appearance of Crohn's disease at CE ranges from gross mucosal ulceration and stricturing to subtle mucosal breaks and denuded villi. A CE scoring index has been proposed along the lines of the endoscopic ones, but has not been fully validated [4].

## Diagnosis of suspected small bowel Crohn's disease

The majority of trials examining the role of CE in the management of Crohn's disease have studied the diagnostic yield of CE in patients with symptoms and features suggestive of Crohn's who have undergone normal SBFT, esophagogastroduodenoscopy (EGD) and colonoscopy (with attempted ileal intubation in some).

In prospective analyses of this nature, CE appears to provide significant additional information, with a diagnostic

yield ranging between 43% and 71% [5–8]. Furthermore, in all of these studies the positive findings at CE led to a change in management with a resulting improvement in most patients (83–100%), although treatment outcomes are not well reported.

In a retrospective analysis, the diagnostic yield was lower at 7.5% [9]. However, CE compared favorably to enteroclysis and CT enteroclysis, which were reported as normal in all the patients with positive findings at CE. In addition, all the patients responded to instigation of medical therapy.

Other studies have compared the sensitivities of CE with other techniques for diagnosing SB Crohn's disease, by performing the tests in a sequential, blinded manner. In a study comparing sequential SBFT, CT enteroclysis and CE, Eliakim *et al.* [10] found the sensitivities for Crohn's to be 23%, 20%, and 73%, respectively. Volderholzer *et al.* [11] found CE made a new diagnosis of SB Crohn's in two of five patients with unexplained diarrhea, both of whom had normal prior CT enteroclysis.

In summary, current evidence suggests that CE has a diagnostic yield of 40–70% in patients with symptoms suggestive of Crohn's disease where SBFT, OGD and colonoscopy with attempted ileal intubation have been normal. Direct comparison of diagnostic yield with enteroclysis and CT enteroclysis favors CE. The new diagnosis of Crohn's by CE has led to the institution of a beneficial new treatment regimen in most patients.

### Assessment of disease activity and recurrence

Few trials have examined whether CE is useful in assessing the SB in patients with known Crohn's. Buchman *et al.* [12] found SBFT and CE to have similar diagnostic yields at 66% and 70% in patients with suspected disease recurrence while Voderholzer *et al.* [11] found CE and CT enteroclysis each to have a diagnostic yield of 75%. Mow *et al.* [13] suggested three or more ulcers were diagnostic of Crohn's; they found CE was diagnostic in 40% and suspicious for Crohn's in 30% of patients, but did not make additional diagnoses compared with ileoscopy.

In a study to assess its potential for detection of early postoperative recurrence of Crohn's, the diagnostic yield of CE was 75% in patients with previous SB resection and suspected recurrence who had had normal SBFT, OGD, colonoscopy, and push enteroscopy [14].

Only one study has examined the role of CE in assessing

response to therapy. In this, improvements in mucosal appearance at CE were seen in 8/10 patients given infliximab [15]; these correlated with changes in Crohn's Disease Activity Index (CDAI), Inflammatory Bowel Disease Questionnaire (IBDQ) scores and C-reactive protein (CRP).

In summary, CE appears to detect recurrent small bowel Crohn's disease with a diagnostic yield of approximately 70%. However, it is not clear whether CE adds usefully to the information provided by conventional imaging techniques in this setting, nor do we yet know whether findings at CE lead to beneficial changes in management. It is therefore too early to define the role for CE in the assessment of response to therapy and of postoperative disease recurrence.

### Differentiating Crohn's disease from indeterminate colitis

In a retrospective study, CE detected SB lesions suspicious of Crohn's in 13/22 patients with a previous diagnosis of indeterminate colitis and in five led to a change in management [13]. There was, however, no comparison made to other conventional imaging techniques or to the use of antibodies to *Saccharomyces cerevisiae*/antineutrophil cytoplasmic antibody (ASCA/ANCA) serology. In a second study, CE identified lesions characteristic of CD in 2/7 patients with a diagnosis of indeterminate colitis and ongoing pain and/or diarrhea, all of whom had already undergone non-diagnostic ileoscopy [16].

### Is capsule endoscopy safe in Crohn's disease?

In all of the studies discussed above, SBFT was performed prior to CE and patients with significant stricturing were excluded from CE. CE retention occurred in 1/71 (1.4%) patients with suspected Crohn's, and in 4/80 (5%) patients with known Crohn's disease. In the trials of suspected SB Crohn's, very few patients were excluded because of abnormal radiology and radiology did not reliably prevent retention; SBFT may not therefore be required prior to CE in this setting.

Concerns regarding capsule endoscope retention have led to the development of the Patency capsule. This has the same dimensions as the Pillcam® capsule but contains only a simple tracer and is designed to disintegrate in the GI tract 40–100 hours after ingestion. In a multicenter study, the Patency capsule was passed intact in 41/80 patients with

known small bowel strictures of whom 33 then underwent conventional CE. There were no cases of capsule retention although some patients did report abdominal pain [17].

### Tolerability and capsule failure

In all the studies discussed, with the exception of patients in whom it was retained, the capsule was easily swallowed and well tolerated. Although there are no comparative preference data in these studies, in a different analysis 49/50 patients preferred CE to push enteroscopy [18].

In those studies where the data were given, the capsule failed to reach the colon before the end of its 8 hour battery life in 25/132 cases (failure rate 19%). However, in most cases, an incomplete examination did not affect diagnostic efficacy.

### Conclusions

Although the number of studies is small, current evidence suggests that there is a role for CE in the diagnosis of suspected SB Crohn's disease. However, more work is required to determine the clinical significance of the more subtle mucosal lesions and whether CE can safely be performed without prior radiology. A role for CE in assessing patients with indeterminate colitis is slowly emerging but its role in assessing disease recurrence is less clear. The Patency capsule is likely to prove useful in patients with known or suspected small bowel strictures.

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