The importance of video capsule endoscopy

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Synopsis
Capsule endoscopy is an important new tool in the diagnosis of small-bowel diseases. Routine diagnosis of small-bowel abnormalities was previously difficult with all of the imaging methods available – endoscopy, conventional radiography, arteriography, scintigraphy, and even enteroclysis. Capsule endoscopy is based on an image sensor – a charge-coupled device (CCD) or complementary metal-oxide semiconductor (CMOS) – that is incorporated into a tiny, swallowable device, which includes a light source, an optical lens, a battery, and a transmitter. The procedure is easy to perform, has few contraindications, and is well accepted by patients.

The main clinical indications are obscure gastrointestinal bleeding, suspected inflammatory bowel diseases such as Crohn's disease, and drug-induced disorders. The examination method also for the first time makes it possible to diagnose small-bowel tumors.

Capsule endoscopy has a bright future, with further areas of diagnosis being envisaged in the esophagus and perhaps the colon. It is expected that a steerable capsule or even a drug delivery device may become possible in the near future.

Introduction
The European Society of Gastrointestinal Endoscopy (www.esge.com) has recently reviewed the current indications for the important new technique of capsule endoscopy, in order to assess its clinical benefits and potential future applications [1]. Video capsule endoscopy (CE) has already become a very important tool for diagnosing gastrointestinal disorders. It can be used for the primary investigation of many small-bowel disorders, and clinical use of the technique to investigate disorders in the esophagus, stomach, and colon also appears to be promising.

Description of the procedure
The procedure can be conducted on an outpatient basis. Standard patient preparation includes a 12-hour fast before the procedure. It is debatable whether bowel preparation is necessary. Some experts recommend that partial or complete bowel preparation should be administered with polyethylene glycol, in the same way as is done for colonoscopy.
Patients are allowed to drink clear liquids 2 h after ingesting the capsule and to eat a light meal 4 h after ingestion.

Two models of video capsule are currently available. The Given Imaging capsule (PillCam SB, initially marketed as the M2A capsule) was the pioneering device for this technique, and it uses complementary metal-oxide semiconductor (CMOS) technology. More than 300,000 PillCam capsules have been used throughout the world since the development of the technology.

The Olympus capsule endoscope (EndoCapsule), with technology based on a charge-coupled device (CCD) and an enhancement system for electronic image processing in order to improve the imaging quality, was recently launched (limited data on the device have been presented at only a few meetings to date) [2]. The system also includes an external control system (the “Real Time Viewer”) with a monitor that allows real-time checking of the images from the capsule, which provides better monitoring of the capsule examination.

Reading the recorded images

- Localization
  The Given Imaging workstation software used to process the capsule images incorporates a localization feature. The system attempts to estimate the location of the capsule in the abdomen by triangulating signals from the three closest sensors, selected according to the strength of the signals received from the capsule by the eight sensors attached to the abdominal wall. The Olympus EndoCapsule system includes a system of eight antennas attached to the recorder unit. The antenna receiving the strongest signal is highlighted, providing an idea of the capsule’s position. However, in clinical practice, localization is often considered imprecise, and the location of the capsule is usually established on the basis of the distinct mucosal patterns visualized in the jejunum and ileum and in relation to the length of the examination time up to a given point.

- Software
  Multiple viewing. The software used for reading the videos recorded from the capsule has also recently had a multiple-viewing feature added. This allows the simultaneous display of two (consecutive) images or even four (consecutive) images from the recording in adjacent windows on the computer monitor. The new RAPID 4 software provided by Given provides a faster “QuickView” browsing facility, a “RAPID Atlas” for comparing pathological images, a “Circumference Scale” for estimating the circumferential involvement of a finding such as a varix or an ulcer, and a new automatic viewing mode.

  Suspected bleeding indicator. The newer capsule endoscopy systems include software that detects the color red, which may help identify bleeding in
the small intestine. Both the PillCam and the EndoCapsule include this feature.

### Current indications

#### Small bowel

**Obscure gastrointestinal bleeding.** The principal and most frequent indication for CE of the small bowel is the diagnosis of obscure gastrointestinal bleeding. Up to 5% of cases of gastrointestinal bleeding involve obscure gastrointestinal bleeding, defined as the absence of an identified source of (recurrent or persistent) gastrointestinal bleeding after standard evaluation using upper endoscopy and colonoscopy [3]. The purpose of this review is to update the previous set of European Society of Gastrointestinal Endoscopy guidelines (published in 2004). This update is based on our current knowledge of clinical practice and the published literature in the field.

In comparison with other diagnostic radiographic tests, including barium radiography, push enteroscopy, and cross-sectional imaging, CE has a significantly higher yield in patients with obscure gastrointestinal hemorrhage [4].

On the basis of a recent study [5], the optimal timing (higher yield) for a video capsule examination in patients with obscure gastrointestinal bleeding is within the first few days after bleeding, with the maximum wait being 2 weeks.

Capsule endoscopy using the Given Imaging PillCam device has been widely studied and is considered to be a very valuable tool for investigating obscure gastrointestinal bleeding. This can presumably translate into better management outcomes than are possible with other examination methods for patients with obscure gastrointestinal bleeding.

**Crohn’s disease.** Capsule endoscopy has proved valuable for diagnosing Crohn’s disease. CE was able to confirm the diagnosis of small-bowel Crohn’s disease both in patients known to have the condition and in those with suspected Crohn’s disease in whom diagnosis with other conventional examination methods was not possible.

These results clearly indicate that there is a role for CE in the context of early disease management, depending on the findings throughout the capsule examination. In some patients, the dosage of medication was either increased or reduced, with treatment with an immunomodulator or anti-tumor necrosis factor (anti-TNF) being started, while in other patients it was possible to avoid surgery [6]. CE will probably have a role in assessing the prognosis, disease activity, and tissue healing after therapy; however, prospective trials have not yet confirmed this. CE may also have a role in the management of Crohn’s disease patients by defining the extent and severity of the disease in the small bowel.
Celiac disease. Capsule endoscopy may be useful in diagnosing celiac disease. Since the small-bowel examination is carried out without air insufflation, the images are taken very close to the mucosa and clear pictures of the mucosa are obtained. With its eightfold magnification capacity, this technology can provide good-quality images of the small bowel, including the villi. The abnormalities detected include primary changes in the small-bowel mucosa – namely, villous atrophy [7] (scalloping, fissuring, mosaic pattern, flat mucosa, loss of the circular folds and nodularity) – and complications related to celiac disease, such as ulcerative jejunoileitis, enteropathy-associated T-cell lymphoma, and adenocarcinoma of the small bowel.

Hereditary polyposis syndromes. CE can be used to detect small-bowel polyps related to hereditary polyposis syndromes. The method was recently found to have a higher yield for detecting such polyps than barium studies [8]. There is increasing evidence from other studies to confirm the usefulness of this technique for detecting polyps in selected patients with familial adenomatous polyposis (FAP), who have an increased risk of developing polyps in the distal part of the small bowel, and as a first-line procedure in patients with Peutz–Jeghers syndrome. Capsule-endoscopic detection of polyps in patients with Peutz–Jeghers syndrome can lead to a change in management in a significant proportion of the patients affected. Capsule endoscopy therefore appears to be a promising alternative to enteroclysis, a classic radiographic examination method for surveillance in patients with hereditary polyposis syndromes.

Small-bowel tumors. The diagnosis of tumors in the small bowel is a new field for capsule endoscopy examinations. Before the advent of the video capsule, small-bowel tumors were considered to be rare (found with radiographic studies in about 1% of patients) [9]. Tumors were often diagnosed at a late stage of development, or incidentally at surgery. This may change with video capsule endoscopy. Some studies have reported small-bowel tumors in 6–9% of patients – many more than previously expected.

Nonsteroidal anti-inflammatory drugs (NSAIDs). Considerable side effects and pathological lesions related to the gastrointestinal tract can be caused by NSAIDs. In a recent study, CE was found to be useful for detecting lesions caused mainly by NSAIDs [10]. This is a more common condition than previously thought, as many elderly patients are taking these drugs to relieve the pain of arthritis.

Pediatric patients. Capsule endoscopy has occasionally been used in pediatric patients to assess some of the indications mentioned above (e.g., obscure bleeding and Crohn's disease); the published data have mainly appeared in case reports and small series. In a small study including patients between the ages of 12 and 16, the video capsule was found to be superior to conventional studies (gastroscopy, colonoscopy with ileoscopy, and small-bowel follow-through examinations) in identifying lesions suggestive of Crohn's disease [11]. Safety issues may limit the use of CE in patients under the age of 10, as there may be difficulties in this group with passage of the capsule through the gastrointestinal tract, particularly the pylorus and ileocecal valve.
**Esophagus**
The PillCam ESO, specifically designed for investigating esophageal diseases, was recently released [12,13]. Due to the short transit time in the esophagus, the video capsule is equipped with miniature sensors at both ends to improve image quality. The main potential indication for the PillCam ESO is gastroesophageal reflux, a very common disorder, and Barrett’s esophagus, which is a premalignant condition. It will presumably also be possible to detect other esophageal diseases with the PillCam ESO as well. Small pilot studies have suggested that it is comparable with the well-accepted method of gastroscopy for detecting esophageal varices and assessing portal hypertension in patients with cirrhosis.

Whether the esophageal capsule is indicated should be decided on a case-by-case basis, depending on the patient’s presentation. The role of the esophageal capsule for other indications needs to be clarified further by larger prospective studies. The issue of whether the esophageal capsule or gastroscopy is more cost-effective for such indications also needs to be studied further for clarification.

**Limitations and risks**
CE is generally very well tolerated by patients. However, there are a few limitations and risks that need to be taken into consideration.

“Capsule retention” is defined as having a capsule endoscope remain in the digestive tract for more than 2 weeks. This problem has been reported particularly among patients with Crohn’s disease and those with a high risk for stricture formation, such as NSAID users and patients with ischemic colitis (due to small-bowel tumors, radiation enteritis, surgical anastomotic strictures). If CE is indicated in high-risk patients, careful assessment is therefore needed before CE. Capsule endoscopy should be preceded by imaging tests to exclude stenosis in patients with suspected Crohn’s disease. Patients with a history of abdominal obstruction, abdominal operations, and radiotherapy in the abdominal or pelvic area should be excluded.

Medical treatment with corticosteroids or infliximab may be able to release a trapped capsule, but endoscopic or surgical removal is required in some cases.

**Future capsule applications**
Further technological advances in capsule endoscopy are being made very rapidly, and there is no doubt that the method will have an increasing impact on many aspects of gastrointestinal disease. Ideas for therapeutic interventions with the capsule, such as the delivery of a drug to a specific disease site, and possibly the use of lasers, have already been discussed. Problems that would need to be overcome for such purposes would be finding a way of navigating with the capsule and providing facilities and staffing for real-time viewing of the examination, which might take several hours.
Capsule endoscopy is at an early stage of development in relation to the examination of the colon. Some clear images can be obtained in the ascending colon, but there are numerous technical pitfalls that make a complete examination difficult.

**Conclusion**

CE is an exciting new diagnostic modality in the gastrointestinal tract, which has been rapidly adopted by gastroenterologists and has already become part of routine clinical practice. Several promising new applications suggest that the role of the method in gastrointestinal disorders is likely to expand. It is a safe, noninvasive, and very well tolerated method in appropriate patients. CE is a valuable tool in the diagnosis of small-bowel diseases, particularly bleeding lesions and Crohn’s disease. Further research is likely to identify additional possible roles for the technique in the future.

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