

Where do I see minimally invasive endoscopy in 2020: clock is ticking

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Abstract: Since it was introduced 17 years ago, capsule endoscopy has become an important diagnostic tool for the small bowel. Three generations of the original small bowel capsule have been developed since (PillCam SB3, Medtronic, USA), and four competitors were introduced for the small bowel. A non-video patency capsule (Agile patency capsule, Medtronic, USA) was also developed, in order to confirm patency and thus avoid retention in the GI tract. Moreover, capsules viewing other organs of the body (esophagus, colon) as well as three different magnetic guided capsules that visualize the stomach as good as optical endoscopy (OE) have been developed. Over 2,000 articles looking at the efficacy of the small bowel capsule in different clinical situations were published since then. Studies are comparing capsule endoscopy versus other modalities in various indications, looking at preparations aiming to improve the diagnostic yield and at technical aspects. The present paper, describes the available capsules in the market and my biased future expectations.

Keywords: Small bowel capsule endoscopy (SBCE); colon capsule endoscopy (CCE); magnetic capsule endoscopy (MCE); optical endoscopy (OE)

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Introduction

In late 1998 Gabriel Meron, the CEO of a small Israeli company named Given Imaging, travelled around the country introducing a concept a wireless capsule travelling along the small bowel and transmitting pictures of small bowel mucosa. Many of the listeners laughed within themselves, others were enthusiastic. The small bowel capsule endoscopy (SBCE) was introduced in 2000 by its inventor—Dr. Iddan (1), and the rest is history. SBCE became an important if not the most important investigational tool for the small bowel.

Over 2,000 studies have been published since it is in the market, looking at its efficacy versus other modalities in various indications.

The present article focuses on the Medtronic (Given Imaging) platform on which most of the literature exists.

SBCE

PillCam SB1 video capsule endoscope (CE), the original CE is wireless (11 mm × 26 mm) with its light source, lens, CMOS imager, a battery and a wireless transmitter. The capsule, easily ingested, moves from the mouth to the anus via the bowels peristaltic waves (M2A—was how it was originally called). PillCam SB1's battery provided 8 hours of work at the rate of two images per second. The capsule's angle of view was 140 degree and it had an 8:1 magnification. The second generation (PillCam SB2) is in the market a few years now. It has a broader angle of view, 156 degrees, better optics with ALC (automatic light control), altogether allowing much better small bowel mucosal coverage. The 3rd generation—PillCam SB3 released about 1 year ago, has an adaptive frame rate allowing it to transmit up to six frames per second according to its

Capsule endoscopy: “the device”



Capsule	PillCam® SB 3 Given Imaging	EndoCapsule® Olympus America	MiroCam® IntroMedic Company	OMOM® Jinshan Science and Technology
Size	Length: 26.2 mm Diameter: 11.4 mm	Length: 26 mm Diameter: 11 mm	Length: 24.5 mm Diameter: 10.8 mm	Length: 27.9 mm Diameter: 13 mm
Weight	3.00 g	3.50 g	3.25–4.70 g	6.00 g
Battery life	8 h or longer	8 h or longer	11 h or longer	6–8 h or longer
Resolution	340x340 30% better than SB2	512x512	320x320	640x480
Frames per second	2 fps or 2–6 fps	2 fps	3 fps	2 fps
Field of view	156°	145°	170°	140°
Communication	Radio frequency Communication	Radio frequency Communication	Human body Communication	Radio frequency Communication
FDA approval	Yes	Yes	Yes	No
Price per capsule	\$500	\$500	\$500	\$250

Figure 1 The most widely used video capsule endoscopes.

speed of movement and has even better optics. The new “no attachments” sensor belt, delivers the pictures to a small recorder. Most of the new generation capsules in the market provide about 12 hours or more of battery time, thus allowing full view of the small bowel in practically all patients. Upon completion of the study, downloading into a Reporting and Processing of Images and Data computer workstation (RAPID 9) is done, and the examination seen as a continuous film. Many supporting gadgets were developed and added in the past 15 years. Some examples are the localization system, blood detecting monitor, the ability to see simultaneously a double or quadric picture, the quick viewer mode, or the single picture adjustment mode. Other modalities included incorporation of the Fuji Intelligent Color Enhancement (FICE) system, the inflammation (Lewis) scoring system and an atlas.

Additional small bowel capsule systems have been developed and approved for use: the Olympus EndoCapsule (Olympus, Japan), found to be as good the old generation PillCam SB1 (2), the Chinese OMOM pill (Jinshan science & technology, Chongqing, China) (3), and the Korean Miro pill (4) (Figure 1). Now a day, most of the systems in the market have different color enhancement features in their software.

Colonic CE

PillCam Colon2, the 2nd generation colonic capsule (Medtronic, USA) is available now for a few years all over the world. It is slightly larger (11 mm × 31 mm), has two cameras, and a wider 172 degrees angle of view. It also has the ability to adjust its frame rate between 2–35 frames per second from each head, based on the capsule’s speed of movement. The capsule’s battery allows >11 hours of transmission, and the new data recorder (DR3) allows the crosstalk that permits the different rates of transmission. The LCD panel on the recorder allows a real time view as well as the ability to transmit messages/instructions to the patient, depending on the capsule’s advancement. Important tools—polyp size estimator and the use of the FICE technique have also been added to the new software.

The preparation for the procedure takes into account (I) bowel cleanliness; (II) completion of the study within 11 hours (battery time). Similar preparation to that of optical colonoscopy is used up to the capsule’s swallow. This includes a clear liquid diet the day prior to the procedure. On that evening, 2 liters of PEG solution are given, and repeated early morning, of the day of the procedure. The capsule is ingested an hour later. Later on, when the capsule enters the small intestine, either Sodium Phosphate

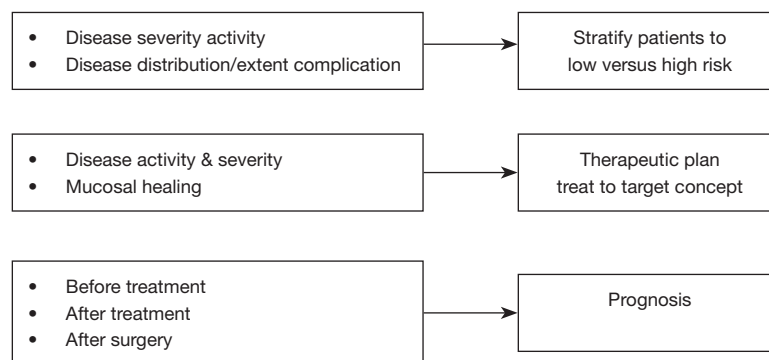


Figure 2 Possible new indications to use capsule endoscopy in established Crohn's disease.

(30 mL) boost, or a sachet of PicoLax followed by a liter of water is given, in order to move it to the colon and allow its exit through while photographing. Another smaller (15 mL) boost, or sachet of PicoLax might be needed depending on the capsule's location (5,6). Currently the percentage of capsules that are excreted while photographing from the anus exceeds 90%.

Current & future Indications for use wireless capsule endoscopy

SBCE-current

- (I) Occult gastrointestinal bleeding—the most commonly used;
- (II) Suspected Crohn's disease—second most common;
- (III) Suspected small bowel tumor;
- (IV) Surveillance of inherited polyposis syndromes—rare indication;
- (V) Partially responsive celiac disease—quite rarely used.

All these indications have been looked at quite intensively over the past 15 years. The two that are in daily practice and are reimbursed in many countries are obscure GI bleeding and suspected Crohn's (7-14).

Colon capsule endoscopy (CCE)-current

- (I) Incomplete colonoscopy—most commonly used;
- (II) Patients unwilling to undergo regular colonoscopy—second most common;
- (III) Individuals unwilling to undergo regular colonoscopy.

There have been two multicenter studies comparing, head to head, 2nd generation CCE to optical colonoscopy, latter being the “gold standard” (5,6), and also one big study comparing both modalities in average risk surveillance

population (15). A few studies comparing it to virtual colonoscopy in patients with incomplete colonoscopy were published with good results (16,17).

Future indications

Monitoring drug effects or side effects

CE can and has been used to evaluate drug induced damage on small bowel mucosa. SBCE can nicely demonstrate mucosal damage induced by either COX1 or COX2 antagonists in the small bowel. Characteristically, one may find erythema, erosions, minute ulcerations and classically web like strictures can be seen (18). Likewise, SBCE can monitor the effectiveness of drugs to protect against small bowel NSAIDS injury (19), to evaluate the mucosa of transplant patients, and in graft versus host disease (GVHD) (20,21).

Established Crohn's disease

Though recent guidelines are not enthusiastic regarding the use of CE in established Crohn's disease, there are more and more recent data showing its benefit in a few respects in this situation (*Figure 2*).

The use of SBCE in established CD patients has added new insights on disease phenotype (proximal distribution, stricturing disease), on disease activity in spite of normal inflammatory markers, and on data on small bowel mucosal healing and deep remission, as well as prediction of relapse (22-24).

A new video capsule—PillCam IBD has just been released to the market in Europe aimed to serve patients with suspected or known Crohn's disease. Similar in size and configuration to the colon capsule, this is a true mouth

Table 1 Future expectations from the video capsule endoscopy

Expectations	Action	Status
Patient & doctor-friendlier procedure	Home procedure	Ready for use
	Improve/minimize preparation	Long way to go
	Whole gut visualization	Ready—PillCam Crohn's
	Shorten reading time	Partially ready
Technical improvements	Maximize angle of view	Done
	External/internal maneuvering	Partly done
	Virtual biopsy	Not yet
	Therapeutic option	Not yet

to anus capsule that starts photographing once swallowed throughout the small and large bowel until excreted through the anus. The small bowel is divided to three parts according to length and the large bowel into two. The capsule is read looking at both cameras simultaneously in a relatively high speed and has a IBD programmed software in which one reports the most common lesion, the most severe one and the extent of disease in each of the parts giving a good clear estimation of the distribution and severity of the disease all over the gut and this is also exposed graphically. Feasibility study of this capsule without the new software has found it to be as good as ileocolonoscopy in patients with established Crohn's (25). With the use of the patency capsule, the safety of giving a regular small bowel or even PillCam IBD capsule to patients with known Crohn's has improved tremendously with practically no retentions. Thus, I foresee a change in the guidelines with more freedom of use of this important tool to monitor disease activity in response to different treatments.

Motility

Computer vision and machine-learning techniques allow reliable, non-invasive and automated diagnostic test of intestinal motor disorders using endoluminal image analysis (26). Unfortunately, this field has not been given enough attention and has not reached a step of routine use yet. The Smart-Pill—a “physiological” pill, has also been developed. Similar in length and diameter to the regular SBCE, the pill has pH, temperature and pressure sensors, but does not photograph. It was approved for gastric transit evaluation and characterization of constipation by the FDA.

What more can we look for? When I tried to anticipate this in 2011 I've created *Table 1*. So, let's see what was accomplished?

Home procedure

The system is ready for use at home. This is true for SBCE, CCE as for PillCam IBD. A package (“Kit”) containing the capsule, the sensors and data recorder, with simple instructions will allow the patient to actually perform the entire test at home, possibly on a weekend, without losing working days. The DR3 recorder with its LCD updates and guides the patient on each move of the capsule, giving actual instructions on boosts as needed. Wi-Fi may allow on demand, on-line visualization.

Preparation

In this respect, we have made no progress and to my mind even regressed. Instead of 12 hours fast for the small bowel procedure, many are giving some kind of bowel preparation prior to this procedure making it much less friendly with possibly a slight increase in the diagnostic yield. There's no doubt that cleansing is needed for a procedure involving the colon.

The preparation should be friendly, preferably using pills and not the large volume liquid solutions that are currently in use. For the colonic procedure, pill cleansers that are enteric coated, and start their effect in distal small bowel, should be the basic cleansing materials. Safer materials than the available ones, that will help propel the capsule faster to the colon should be developed.

Whole gut visualization

Just as the original capsule inventors dreamt, CE allows a comprehensive friendly examination and diagnosis of pathologies of the entire gut using a minimally invasive procedure. The new PillCam IBD complies with this

dream. It starts photographing in the mouth and in >90% of patients is expelled while photographing from the anus giving excellent visualization of the whole gut. In the future external maneuvering to control capsule movement can be used. Such a pill would be a perfect tool to evaluate patients with iron deficiency anemia or suspected IBD where the pathology can be in either small or large bowel or in both.

Short video reading time

CCE video reading time is way too long—>60 minutes. This should definitely be shortened significantly, possibly by using automated detection that alerts the interpreter of existing pathologies of any sort (i.e., “pathology detector”). This will lead to a shorter CCE procedure, possibly allowing continuation with optical colonoscopy if needed. The new specific software designed for IBD in the Rapid 9 of the PillCam IBD allows the reading time of the whole gut to be much shorter.

Technological improvements

External maneuvering of capsule

A proactive capsule that treats requires either external or internal maneuvering device that will propel it to its destination. Paul Swain, reported the 1st study where a CCE (Given Imaging) was transformed to contain neodymium-iron-boron magnets in one dome, there by manipulated by an externally held magnet (“joy stick”), for a few minutes in the upper GI (27,28). Olympus and Siemens have introduced a similar concept to the Japanese pill as well (29,30). Recently a big study (>300 patients) comparing the diagnostic yield in the stomach, of a new Chinese magnetic capsule was compared to optical gastroscopy with similar results (31). Another way of doing it is to add paddles or propellers to the pill, which will start operating upon demand at various parts of the digestive tract. Finally, one can combine both mentioned above techniques—a magnet for the upper tract and an internal device for the rest of the bowel. Such a device has been tested in pigs by an Italian group. It's easy to foresee the very thorough examination of the entire bowel done with such a device.

If these dreams come true by 2020, I think we'll have a great minimally invasive diagnostic tool for the entire gut.

Then, we can put all our energy on a therapeutic capsule, but that's a subject to another article.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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