

# Capsule endoscopy: Beyond small bowel

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## Abstract

In this article the brief and dramatic history of capsule endoscopy of the digestive tract is reviewed. Capsule endoscopy offers a non invasive method to diagnose diseases that affect the esophagus, small bowel and colon. Technological improvements relating to optics, software, data recorders with two way communication have revolutionized this field. These advancements have produced better diagnostic performance.

## Key words

Capsule Endoscopy, Second generation colon capsule, Esophageal capsule

Wireless capsule endoscopy (CE) was invented by Gabriel Iddan and Paul Swain simultaneously and independently in 1997. Within 4 years, the first controlled clinical prospective trial in occult gastrointestinal bleeding (OGIB) was completed. CE was twice as effective as enteroscopy in diagnosing the source of OGIB and the same year, it received approval by the FDA. CE of the small bowel has proven its clinical relevance in diagnosing nonsteroidal anti-inflammatory drug (NSAID)-induced small bowel disease, Crohn's disease, neoplastic disease, and others. Since then, the use of CE in the daily practice of gastroenterologists has become routine and the number of publications using CE has experienced a meteoric rise [Figure 1].

Direct viewing of the gastrointestinal (GI) mucosa is superior to traditional barium studies of the GI tract. This is the reason why the gastroscope has replaced the upper GI series and the colonoscope has replaced barium enemas. The same is true for CE. The diagnostic superiority of CE over small barium series is documented.

Picture quality of CE has been improved by the introduction of devices with wider angle of view, better lenses, and automatic control of light exposure, with superior performance of small bowel survey by the capsule.<sup>[1,2]</sup> The software contains more

sophisticated algorithms as well as image modifiers (Blue and FICE mode). Further improvements can be expected in the near future.


The concept of CE should not stop with the small bowel. The trend in modern medicine is to avoid invasive diagnostic procedures and replace them with noninvasive methods. Therefore, the esophagus, stomach, and colon were included for the potential use of CE.

CE has been extended to examine the esophagus. Capsule transit time via the esophagus is significantly faster than the transit time in the small bowel. For this reason, two cameras transmitting images at a high rate (14 frames per second) have been placed at each end of the esophageal capsule camera. These cameras with high transmission screen the esophagus well. The esophageal capsule has a very high diagnostic sensitivity for diseases such as reflux esophagitis, Barrett's esophagus, and esophageal varices. The advantages of using CE are the lack of need for sedation, noninvasiveness, and the possibility of performing the procedure at the first office visit. The disadvantage is that the esophageal capsule is competing with a very good, albeit invasive device, the gastroscop, which is in most places cheaper.<sup>[3]</sup>

The colon offers serious challenges to CE for the following reasons.

1. The small bowel is narrow (hence its name). As the capsule camera enters the small bowel, it remains by and large oriented in the same direction, either camera first or transmitter first. The capsule will not flip around its own axis. The capsule will remain oriented in the given position as it entered the small bowel along its journey through the small bowel. For this reason, the single camera will screen the entire small bowel mucosa. This is not true for the colon. In the large bowel,

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with its wide diameter, the capsule can tumble backward and forward. A capsule with a single camera would film certain areas twice and other areas not at all. The solution to this challenge is a colon capsule that has two cameras, one camera at each end [Figure 2]. The colonic mucosa is visualized from both directions simultaneously, and thus complete visual coverage of the entire colon is guaranteed.

2. The capsule transit time to reach the end of the colon is much longer than the time required for the capsule to reach the cecum, and the colon capsule consumes more energy than the small bowel capsule since it transmits images from two cameras. To reduce the energy requirements, the colon capsule is put to sleep for an hour and a half, 5 min after ingestion.

3. The third hurdle is bowel cleansing. In standard colonoscopy, some minimal amount of liquid debris can be aspirated, yet minimal amount of debris may compromise the capsule's ability to identify pathological changes. A more vigorous bowel preparation had to be offered to patients to assure proper cleansing for colon capsule examinations.

The first colon capsule was tested in the years 2005 and 2006.<sup>[4]</sup> The results of three studies were encouraging. Firstly, the bowels could be adequately cleansed in 80% of patients. Secondly, the capsule could pass the GI tract and transmit images from the entire colon. Finally, the capsule did identify pathologies such as polyps, tumors, colitis, diverticulosis, and internal hemorrhoids. The suboptimal identification of patients with colonic polyps as compared to standard colonoscopy fell short of expectations.

After analysis of the shortcomings of this first colon capsule, a second-generation colon capsule was created. The angle of view of the second-generation colon capsule camera was extended to 172° for each camera [Figure 3]. This change provides a near-full panorama view. The Data Recorder 3 (DR3) is a true revolution in CE. This device has been endowed with smart features. The DR3 communicates with the capsule and the capsule is programmed to carry out the instructions received by the DR3. Furthermore, DR3 also communicates with the patient undergoing the colon capsule examination and instructs the patient if and when to take a prokinetic agent, when to ingest the first booster laxative which accelerates the small bowel transit time of the capsule and keeps the colon clean, if and when to ingest a second booster laxative, and finally when the patient may eat and when the procedure is over. This is how the second-generation colon capsule system works. Three minutes after capsule ingestion, the rate of transmission is reduced to 16 images per minute to conserve energy. The received images are constantly analyzed by DR3. If after 1 h DR3 notices that the colon capsule has not left the stomach, it will instruct the subject by activating an alarm ring tone, a vibrating device attached to the antenna, to look at the LCD screen where the number 0 is displayed. The instruction sheet indicates that the number 0 requires the subject to take a prokinetic agent such as domperidone or metoclopramide.

However, if the capsule has left the stomach and entered the small bowel, the smart features of DR3 recognize that the capsule is now in the small bowel. DR3 orders the capsule to raise its transmission rate from 16 images per minute to 4 images per second and the patient to ingest the booster laxative. The purpose of this booster is to shorten small bowel transit time and to maintain adequate cleanliness of the bowel. Furthermore, the smart features of DR3 recognize if the capsule is stationary or in motion. Once DR3 recognizes that the capsule is in motion, it orders the capsule to raise its transmission rate to a staggering 35 images per second. The process of recognition to execution literally takes place in a split second. This rapid transmission rate (35 images per second) provides adequate number of colonic images while the capsule is in motion, especially while flying through the transverse colon.

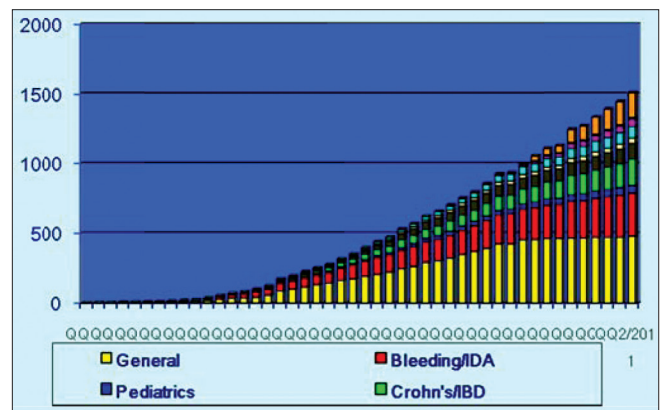


Figure 1: Number of peer reviewed publications per year



Figure 2: Colon capsule with two video cameras, one at each end of the capsule

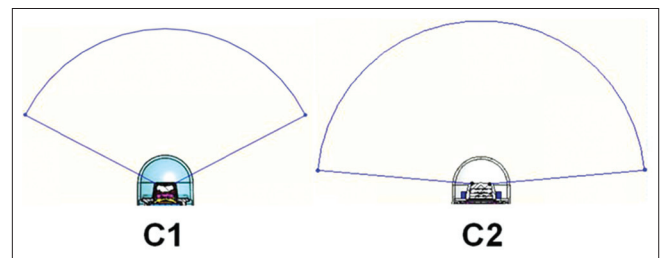


Figure 3: Extension of angle of view in second-generation colon capsule (C2) versus first-generation colon capsule (C1)

Polyp size is of clinical significance. The software program for colon capsule 2 has been equipped with a polyp size assessor. The cursor is drawn from one side of the polyp to the other and the algorithm spits out the size of the polyp in millimeters. The same polyp seen from a distance or from close up will have the same size.

While these technological achievements are very impressive (a data recorder talking to capsule and patient, analyzing images, determining location, position – stationary versus motion, altering transmission rate), the question remains. Is this a high-tech toy or a medically relevant tool?

We engaged in a five-center, prospective, double-blind feasibility study in Israel in which this second-generation colon capsule was compared to standard colonoscopy for the identification of patients with colonic polyps. One hundred and four patients were enrolled. Whereas in the European multicenter trial published in 2009 the sensitivity to identify patients with polyps was only 60%, the sensitivity in the multicenter Israel trial with the second-generation colon capsule rose to 89% and gave a negative predictive value of 97%.<sup>[5,6]</sup> This markedly improved diagnostic sensitivity was reproduced by a recent European study with the second-generation colon capsule.<sup>[7]</sup> This improvement (rise in diagnostic sensitivity from 60 to 89%) has to be attributed to the revolutionary new capsule platform of this second-generation colon capsule. The three previous studies with the first-generation colon capsule had a very similar design as our present study. Good bowel cleansing was obtained at similar rates as in this new study. The only factor which set this second-generation colon capsule study apart from the previous studies is the new technological platform. The negative predictive value of 97% is very high and clinically very meaningful. The physician offering his patient a colon capsule study can tell his patient that a negative study has 97% accuracy that he harbors no polyps.

The fact that the smart features of DR3 enable communication

with the patient has opened the door to offer colon capsule examination as an out-of-clinic procedure. Increasing compliance to participate in colon screening programs is essential to reduce colon cancer mortality in our society. Hassan *et al.*, using data from first-generation colon capsule studies with a relatively low sensitivity, have calculated that increasing compliance to participate in capsule colon cancer screening by 4% would save the same amount of lives as colonoscopy does today.<sup>[7]</sup> With the second-generation colon capsule, only a 2% increase in compliance will lead to an equal number of patients saved from colon cancer.

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