The Current Main Types of Capsule Endoscopy

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2.1 The Given Imaging Capsule Endoscopy Platform: Clinical Use in the Investigation of Small Bowel, Esophageal and Colonic Diseases

2.1.1 Introduction

The first video capsule endoscope was introduced in 2001 by Iddan as a new tool for the investigation of the small bowel [1]. Initially called mouth to anus (M2A), its goal was small bowel visualization. Since then, various studies have shown the potential of this minimally invasive technique to improve diagnostic outcomes among a variety of gastrointestinal (GI) conditions. Later on, the esophageal and colonic capsules [2, 3] were launched into the market, and the patency capsule was introduced as well. The introduction of the second or even third generation of capsules enabled broadening the horizon for its possible medical use (Fig. 2.1, Table 2.1). To date, multiple capsule endoscopy (CE) systems are available (Fig. 2.2), mostly for the small bowel. As mentioned, the first capsule endoscopy system was manufactured by Given Imaging (Yokneam, Israel). To date, the Given Imaging platform of capsule endoscopes includes the PillCam SB2 and SB3 for the small intestine, the PillCam ESO2 for esophageal imaging, PillCam Colon2 for the large

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Fig. 2.1 PillCam small bowel 3 capsule endoscope system

bowel, as well as the Agile Patency capsule (second generation) (Fig. 2.3). Additional small bowel capsule systems include the Olympus EndoCapsule (Olympus, Japan) [4], the Chinese OMOM pill (Jinshan science and technology, Chongqing, China) [5], the Korean Miro pill [6], and the American CapsoCam SV-1. Comparative studies between the PillCam SB1 and the Olympus EndoCapsule or the Korean Miro Capsule did not show significant differences. Currently, only the Given PillCam SB system and the Olympus EndoCapsule are FDA- and CE-approved.

Table 2.1 Indications for the use of capsule endoscopy according to anatomic site

Esophagus
Gastroesophageal reflux disease
Barrett's esophagus
Esophageal varices
Small Bowel
Obscure gastrointestinal bleeding
Suspected Crohn's disease
Suspected small bowel tumor
Evaluation of any abnormal small bowel imaging
Evaluation of partially responsive celiac disease
Surveillance of inherited polyposis syndromes
Evaluation of drug-induced small bowel injury
Evaluation of mucosal response to medications
Colon
Polyp screening

Fig. 2.3 The Agile patency capsule system

The PillCam SB3 video capsule endoscopy system consists of (a) a 2 × 11 mm capsule containing the video camera, illumination, and batteries; (b) a sensing system comprising an array of sensor pads, a data recorder, and a battery pack; and (c) a workstation, based on a commercially available personal computer (Fig. 2.1). The new data recorders (DR3) also contain a portable real-time viewer that allows direct monitoring of the images received during

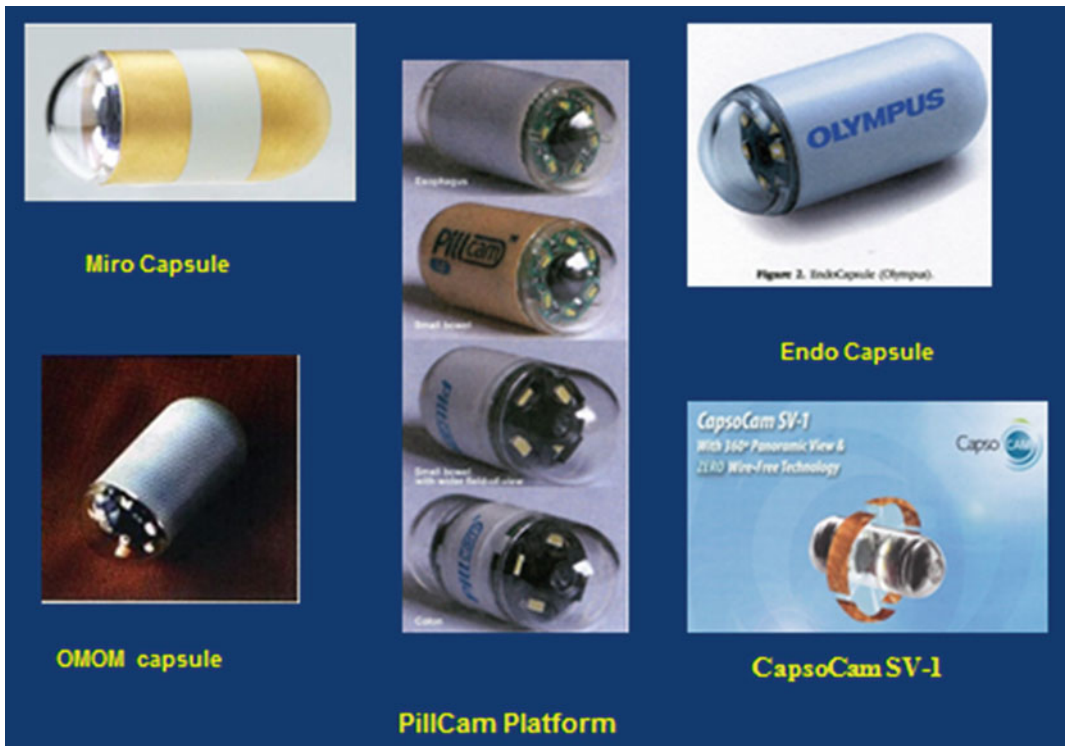


Fig. 2.2 Various systems of capsule endoscopes available for the small bowel

the examination. While the PillCam captures images using a complementary metal-oxide semiconductor (CMOS) sensor, the EndoCapsule, MiroCam, and OMOM capsule use a charge-coupled device camera (CCD). The four capsules also differ with regard to dimensions, image acquisition frame rate, field of view, and recording duration.

Almost all of the information provided in the literature is regarding the Given Imaging PillCam SB, as it dominated the market for a few years by itself, later on joined by the other small bowel capsules, and thus is the one on which most of the literature is written.

2.1.2 Small Bowel Video Capsule Endoscopy

Until the introduction of the small bowel video capsule endoscopy (SBCE), the small bowel was an organ that was very difficult to explore with the available techniques. Since its development, SBCE provided a reliable, noninvasive, and well-accepted and well-tolerated procedure, which has revolutionized the study of the small bowel.

PillCam SB3 video capsule endoscope is a wireless capsule (11 × 26 mm) comprised of a light source, lens, CMOS imager, battery, and a wireless transmitter. A slippery coating allows easy ingestion and prevents adhesion of bowel contents, as it moves via peristalsis from the mouth to the anus (Figs. 2.1, 2.4). The battery provides >11 h of work in which the capsule photographs using an adaptive frame rate technique two to six images per second (>80,000 images all together), in a 156° field of view and 8:1 magnification. The pictures are transmitted via a newly developed 'no attachments' sensor belt, to a small data recorder (DR3) which also allows real-time imaging. The recorder is downloaded into a Reporting and Processing of Images and Data computer workstation (RAPID 8) and seen as a continuous video film. Support systems have been added since the first prototype of the RAPID system, including a localization system, a blood detector, a double and quadric

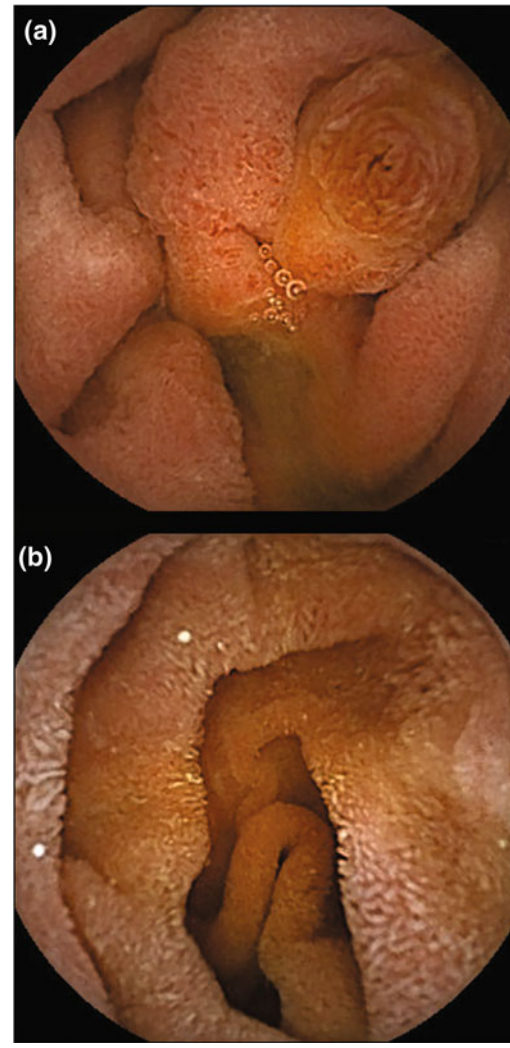


Fig. 2.4 Small bowel pictures taken with PillCam SB3: **a** Ampulla of Vater. **b** Small bowel normal mucosa

picture viewer, a 'quick viewer,' single picture adjustment mode, incorporation of the Fuji Intelligent Color Enhancement (FICE) system, an inflammation (Lewis) scoring system, and an atlas, all meant to assist the interpreter.

The procedure: The patient is on clear liquids the day prior to the procedure and swallows the capsule with water after a 12-h fast. Drinking clear fluids is allowed 2 h after ingestion as is a light lunch after 4 h. During the procedure, he is free to do his daily activities.

A few grading scales have been developed to assess the quality of bowel preparation in video capsule endoscopy, the most recent being a computer-assisted cleansing score (CAC) [7]. The impact of bowel preparation on the image quality and transit time was assessed in two meta-analyses. Preparation was found to improve the quality of visualization, but had no effect on transit times or percentage of capsules reaching the cecum, and no consensus was reached as to the effects on the diagnostic yield of the study [8, 9]. Another attempt to improve the small bowel diagnostic yield was attempted by using a capsule with two cameras (one on each side), which resulted in diagnosis of more lesions [10].

The main indications for SBCE include the following:

1. Obscure gastrointestinal bleeding
2. Crohn's disease (suspected/known)
3. Suspected small bowel tumor
4. Evaluation of abnormal small bowel imaging
5. Partially/non-responsive celiac disease
6. Surveillance of inherited polyposis syndromes
7. Evaluation of drug-induced small bowel injury and response to medications

Contraindications include the following:

1. History of or suspected small bowel obstruction
2. Swallowing disorders
3. Pregnancy
4. Non-compliance

Relative contraindications are as follows:

1. Major abdominal surgery in the previous 6 months.
2. Cardiac devices—pacemaker/defibrillator.

Although the capsule is easily ingested and swallowed by most individuals, patients with severe dysphagia, large Zenker's diverticulum, pill phobia, significant gastroparesis, and small children may have problems ingesting the device. For these situations, a capsule-loading device (AdvanCE, US Endoscopy, Mentor, Ohio, USA) is available to directly deliver the capsule into the stomach or duodenum.

In case of suspected small bowel obstruction, the use of a patency capsule (the AGILE capsule, Given Imaging, Yokneam, Israel) has been shown to provide evidence of the functional patency of the gastrointestinal tract [10] (Fig. 2.3). This system consists of a self-disintegrating capsule without a camera that contains radio frequency identification (RFID) tag and a RFID scanner. In a case of obstructive small bowel pathology, the AGILE capsule disintegrates within 30 h, and the remnants can pass through even small orifices [11]. The radiopaque capsule can be detected by plain abdominal X-ray.

2.1.3 Occult GI Bleeding

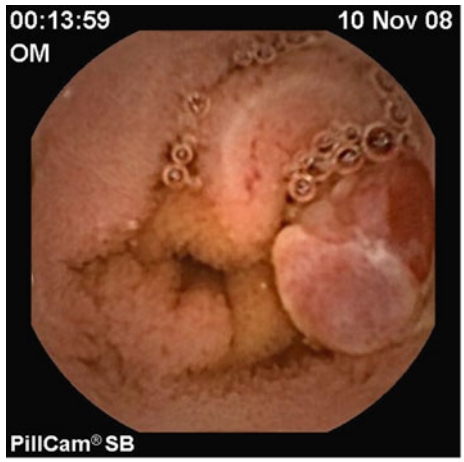
Occult GI bleeding accounts for up to two-thirds of SBCE studies performed [12]. It was shown that 20–38 % of patients with normal upper and lower endoscopy have significant intestinal lesions [13, 14] (Fig. 2.5). SBCE has been shown to be superior to push enteroscopy, abdominal computed tomography, abdominal magnetic resonance and angiographic studies [15–18], and as good as balloon-assisted small bowel enteroscopy [19], with diagnostic yield between 39 and 90 % [20]. Moreover, the rate of rebleeding in patients with occult GI bleeding and negative SBCE was found to be significantly lower (4.6 %) compared with those with a positive SBCE (48 %) [21].

This information will be covered in detail in the chapter on PillCam small bowel.

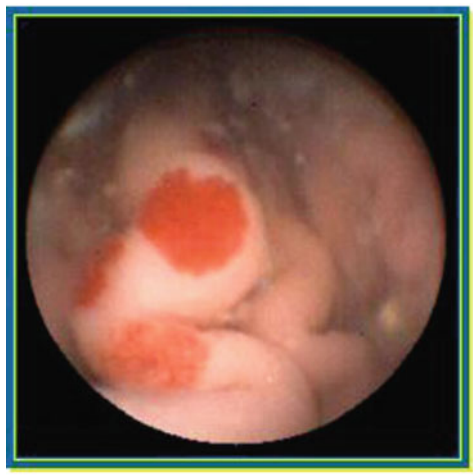
2.1.4 Crohn's Disease

SBCE is an important tool both in the diagnosis and in the follow-up of Crohn's disease. It is used to establish the diagnosis, to assess disease extent, severity, and disease activity, and to assess mucosal healing post-therapy (Fig. 2.6).

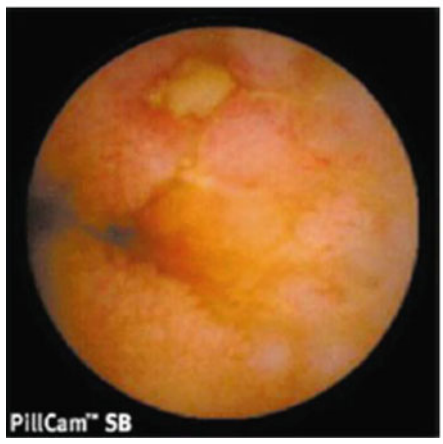
SBCE has a high diagnostic yield in suspected Crohn's disease. Moreover, for both known and suspected Crohn's disease, SBCE was found to



Panel A: Active bleeding



Panel B: Angioectasia



Panel C: Small bowel ulceration

Fig. 2.5 Causes for small bowel obscure bleeding

have a better incremental yield (ranging between 15 and 44 %) compared with other modalities, including small bowel follow-through, computed tomography, MRI, ileo-colonoscopy, and push enteroscopy [21]. Increase in the diagnostic yield of SBCE can be achieved by selecting patients with high pretest probability such as those with perianal disease and negative work-up, using the international conference on capsule endoscopy (ICCE) selection criteria and/or patients with high fecal calprotectin level.

SBCE may alter disease management of patients with known Crohn's, by assessing mucosal healing after medical therapy. SBCE is the only method, except for double-balloon enteroscopy, to accurately assess small bowel mucosal healing. SBCE was also found to be clinically useful for categorizing patients with indeterminate colitis, although negative SBCE study did not exclude further diagnosis of Crohn's.

The rate of SBCE retention in patients with suspected Crohn's disease is similar to the general population (1.4 %), but retention rates of more than 8 % were reported in patients with established Crohn's disease.

2.1.5 Small Bowel Tumors

The introduction of SBCE had resulted in doubling the rate of diagnosis of small bowel tumors to 6–9 % of patients undergoing SBCE for various indications, obscure GI bleeding being the most common indication. More than half of the tumors diagnosed were malignant. Adenocarcinoma is the most common malignant tumor, followed by carcinoids, lymphomas, sarcomas, and hamartomas [22]. Gastrointestinal stromal tumors are the most frequent benign neoplasm (32 % of all cases). Melanoma is the most common tumor metastasizing to the small bowel, although metastases derived from colorectal cancer and hepatocellular carcinoma have also been reported. Tumors are located most frequently in the jejunum (40–60 %), followed by the ileum (25–40 %), and the duodenum (15–20 %). Small bowel tumors can be easily missed due to the predominant submucosal and extraluminal

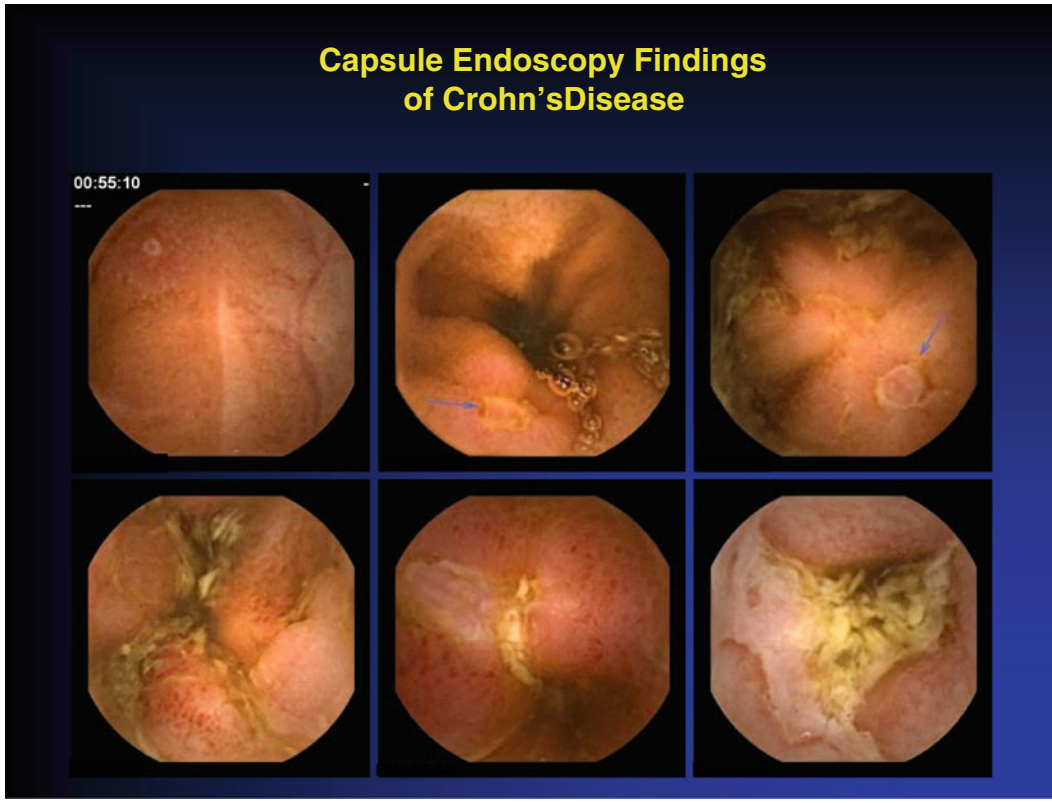


Fig. 2.6 Small bowel Crohn's disease

location of the tumors. Specific indexes and scales were developed for improving the detection rate of small bowel tumors, including the Smooth Protruding Index on Capsule Endoscopy (SPICE score) and an automated scale using multiscale wavelet-based analysis [23, 24].

More details will be provided in the chapter on PillCam SB.

2.1.6 Celiac Disease

SBCE has a role in both the diagnosis of celiac disease and in the evaluation of gluten refractory celiac disease (Fig. 2.7). SBCE provides high-resolution magnified view of the mucosa, easily identifying the endoscopic changes found in celiac such as scalloping, mosaic pattern, flat mucosa, loss of folds, and nodularity. In a recent published meta-analysis, SBCE had an overall pooled sensitivity of 89 % and specificity of 95 % for identifying celiac disease [25]. In gluten non-responsive celiac disease, SBCE can be used for investigating the small bowel for tumors (enteropathy-associated T-cell lymphoma and adenocarcinoma) and ulcerative jejuno-ileitis (Fig. 2.7).

2.1.7 Inherited Polyposis Syndromes

SBCE was shown to be effective tool in detecting small bowel polyps in Peutz–Jegher syndrome. It is especially effective in demonstrating small- and medium-size polyps. However, large polyps are sometimes only demonstrated partially, and polyp location is not accurate [26]. The duodenum is a potential pitfall as the capsule passes it very fast and thus may give false-negative results. The new SB3 SBCE may improve that with its six frames per second mode. Coupling of SBCE with double-balloon

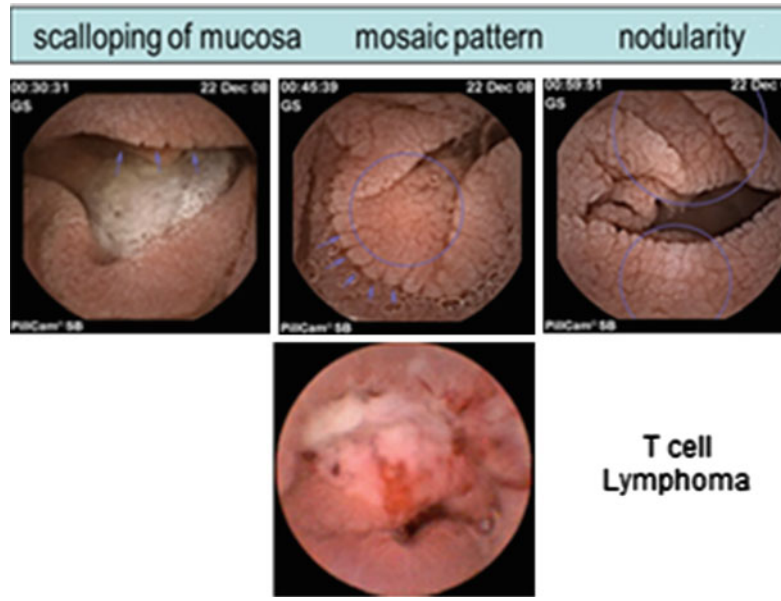


Fig. 2.7 Typical PillCam SB findings in celiac disease

enteroscopy and polypectomy may offer an ideal method of follow-up and treatment of these patients, possibly avoiding surgery.

Another indication for SBCE in this setting is familial adenomatosis polyposis (FAP) in which one may find patients with duodenal polyps, as well as small bowel polyps. However, the major papilla is not demonstrated effectively, and complementary examination with a side-view duodenoscope is mandatory.

2.1.8 Monitoring Effects and Side Effects of Drugs

SBCE can be used to monitor deleterious effects of drugs such as NSAIDs on small bowel mucosa. Lesions that can be found in these patients include erythema, erosions, small ulcerations, and weblike strictures. SBCE can be used to monitor the effect of drugs used to protect against NSAIDs-induced small bowel injury, to monitor the small bowel mucosal appearance in transplanted patients, to manage graft versus host disease, and, possibly, to monitor mucosal healing of small bowel Crohn's disease after various medical treatments.

2.1.9 Capsule Retention

Capsule retention is the major complication of SBCE. Very rarely this may end in bowel obstruction/perforation. High risk of retention occurs in patients on NSAIDs, with known Crohn's, with radiation enteritis, or with small bowel tumors. Normal prior radiological examination does not always protect from having capsule retention. Once retention is diagnosed (capsule not excreted 2 weeks after ingestion), endoscopic (balloon-assisted enteroscopy) or surgical removal was shown to be effective. The intervention not only allows removal of the capsule, but also allows the offending abnormality.

2.1.10 Esophageal Video Capsule Endoscopy

In 2004, Given Imaging developed an esophageal video capsule (PillCam ESO) as a noninvasive device for the examination of the esophagus. The second-generation esophageal capsule, the PillCam ESO2 (Given Imaging, Yokneam, Israel), was FDA-approved for marketing in 2007

Fig. 2.8 PillCam ESO capsule endoscope

(Fig. 2.8). The esophageal capsule endoscope (ECE) is a 26 × 11 mm capsule that differs from the SBCE in a few parameters: It has optical domes on both sides, the frame rate is much faster (9 frames from each side versus 2), a wider angle of view (169 vs. 156°), more advanced optics (3 lenses), and a shorter battery life of up to 30 min, all aimed to address the very short time (<2 s) of esophageal transit as well as the necessity to demonstrate the esophageal–gastric junction, where most of the esophageal pathology is located. It works for approximately 30 min and then shuts off and passed through the intestine via peristalsis and is naturally excreted. As in PillCam SB 3 system, or PillCam Colon2, real-time viewing is feasible.

Procedure: Prolongation of the transit time of the capsule has been achieved by an alteration of the capsule ingestion technique, using the simplified ingestion procedure (SIP) (Fig. 2.9), where the patient swallows the capsule after at least 3 h of fasting, lying in the right lateral position while sipping 15 mL of water every 30 s through a straw [27]. The procedure requires up to 5 min in an unsedated patient. Thus far, no other esophageal capsules are in the market. Competition includes attempts to attach a string to a Given Imaging small bowel capsule, the Given Imaging magnetic capsule, and the Olympus gastric capsule which are maneuvered with a joystick (Fig. 2.10).

Indications for ECE:

- Screening for Barrett's esophagus
- Surveillance of esophageal varices in patients with portal hypertension.

ECE is safe, well tolerated, and reported to be preferred by patients to unsedated EGD. ECE was found to have variable sensitivity and specificity for the detection of GERD-related complications. Few studies reported very high specificity and sensitivity for the detection of erosive esophagitis and Barrett's esophagus (Fig. 2.11) [28, 29], while others found much lower rates of sensitivity and specificity. A recent meta-analysis of seven studies involving 446 patients, ECE was found to have a sensitivity of 86 % and specificity 81 % in detecting esophageal varices (Fig. 2.12) [30].

Further details will be given in the chapter on Esophageal Capsule Endoscopy.

ECE may be used as an alternative to conventional upper GI endoscopy for the diagnosis of varices in complex patients with portal hypertension. It is most useful in certain patient groups: patients who poorly tolerate endoscopy or who have significant comorbidity, thus increasing the risks of repeated endoscopy, and patients with high risk of variant Creutzfeldt–Jakob disease.

Although the major innovations and technological advancement, at this point of time, ECE is not recommended as initial screening tool for the mentioned conditions, mainly due to the lower cost and higher availability of upper endoscopy.

2.1.11 Colon Capsule Endoscopy

Colon capsule endoscopy (CCE) (Given Imaging Ltd., Yokneam, Israel) was introduced in 2006 for the diagnosis of colonic pathologies, mainly polyps and tumors. In 2009, it went through major upgrading when the second generation of the capsule was introduced (Fig. 2.13). The second-generation capsule is slightly larger than the SBCE (31 × 11 mm) and has two camera domes with an adaptive frame rate of 4–35 frames per second, a 172° view angle for each camera, and longer life of up to 11 h due to the addition of a third battery and advanced engineering techniques. As mentioned, the frame rate can reach up to 35 frames

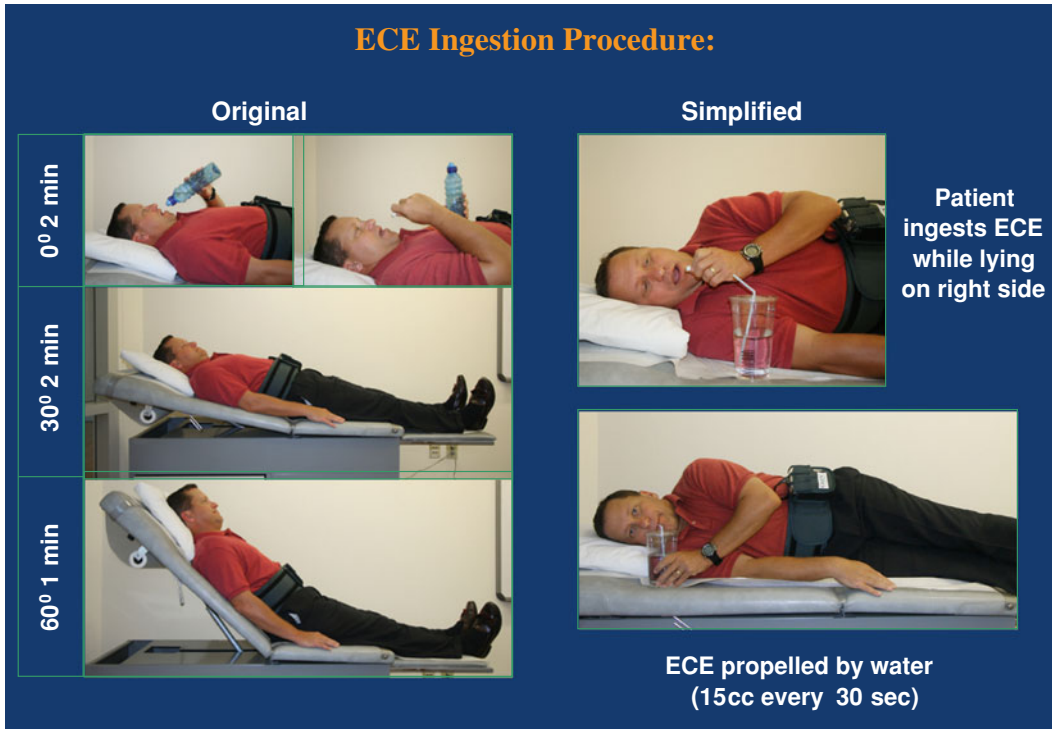


Fig. 2.9 Ingestion procedure for PillCam ESO capsule endoscope

Fig. 2.10 String capsule device. Reprint with permission from Ramirez et al. [32]

per second depending on the capsule movement speed in the colon and is determined using the revolutionized adaptive frame rate technique via a cross talk between the capsule and the data recorder (DR3). This new recorder is endowed with artificial intelligence that communicates with the capsule, as well as with the patient by beeping and vibrating when the capsule leaves the stomach and displaying on the LCD screen a message that informs the patient to ingest a booster laxative which will accelerate the passage of the capsule through the small bowel.

Procedure: As in colonoscopy, bowel preparation is compulsory in order to achieve adequate mucosal visualization. This is done using a strict preparation that includes liquid diet on the day prior to capsule ingestion, two doses of 2 l of PEG solution (on the evening prior to ingestion and on the morning of the capsule ingestion), as well as propulsive agents to enhance capsule movement in the small bowel and advance it to and through the colon, while the battery is still working.

The main indication for CCE is colonic polyp detection (Table 2.1, Fig. 2.14). Colonic screening programs in moderate- and high-risk groups reduced the incidence, morbidity, and mortality due to colorectal carcinoma. However,

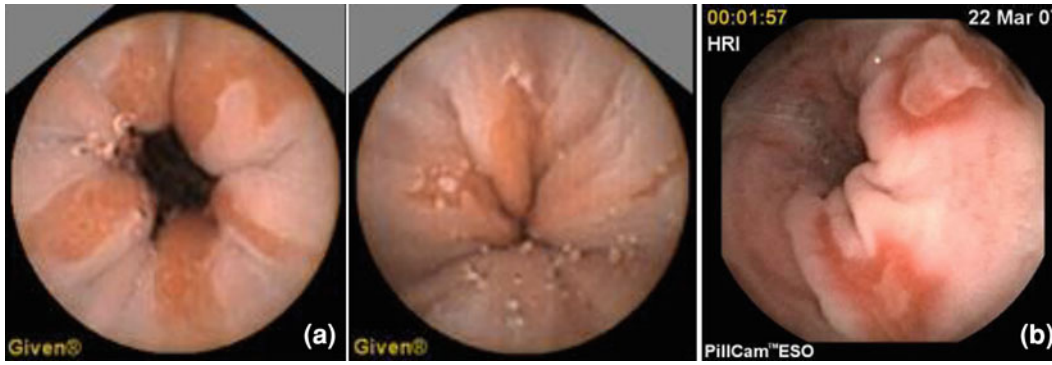


Fig. 2.11 PillCam ESO pictures of Barrett's (**a**) and esophagitis (**b**)

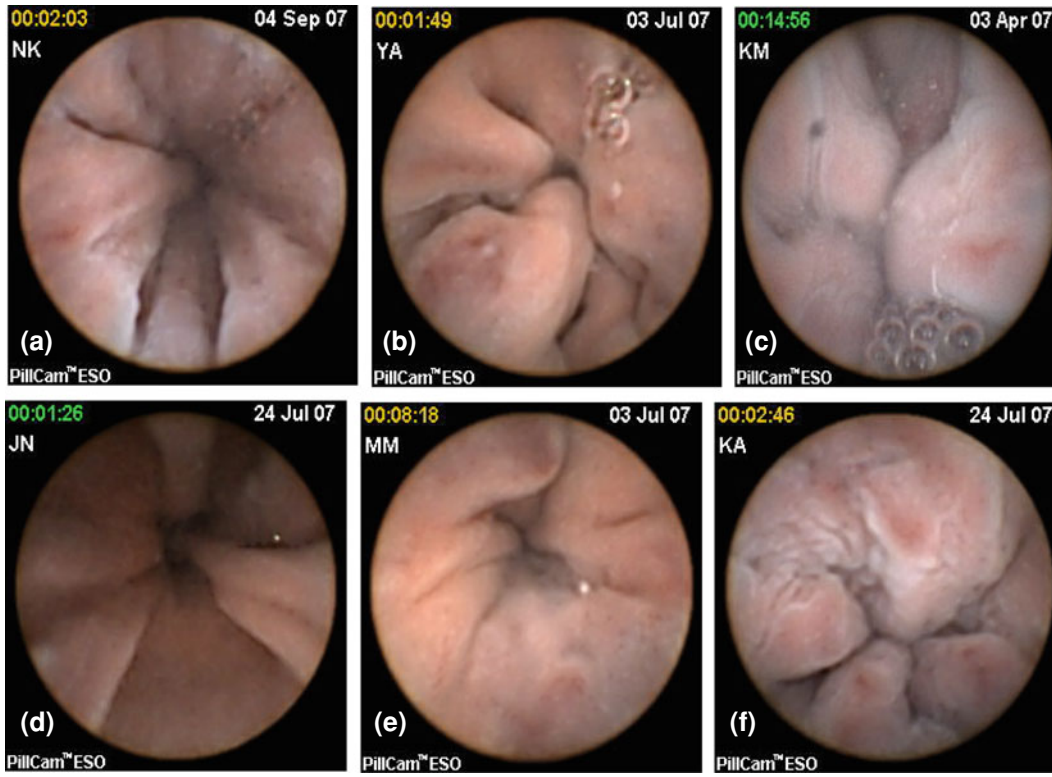


Fig. 2.12 **a–f** Images of Esophageal varices taken with Pillcom ESO

compliance rates to colonoscopy screening programs are hampered due to fear of the invasiveness and possible complications. CCE allows visualization of colonic mucosa with a minimally invasive procedure using no sedation, insufflation, or radiation and a practically complication-free method for colorectal screening. Because noninvasive colorectal imaging tests cannot provide a histological diagnosis, morphological criteria (i.e., polyp/mass ≥6 mm in size, or ≥3 polyps) are accepted as surrogate markers of advanced neoplasia. The average sensitivity of the first generation of CCE for significant findings (≥6 mm size, or ≥3 polyps

Fig. 2.13 PillCam Colon2 capsule endoscope

irrespective of size) was relatively low, but it significantly improved with the use of the second-generation CCE (49).

Indications: The latest guidelines published in 2012 by the European Society of Gastrointestinal Endoscopy (ESGE) [31] state that:

- CCE is feasible and safe and appears to be accurate when used in average-risk individuals.
- In patients with high risk for colorectal carcinoma in whom colonoscopy is not possible or not feasible, CCE could be a possible study.
- CCE is also a feasible and safe tool for visualization of the colonic mucosa in patients with incomplete colonoscopy and without stenosis.

Another possible indication for CCE is in the diagnostic work-up or in the surveillance of patients with suspected or known inflammatory bowel disease (IBD), especially ulcerative colitis. Further details can be found in the chapter on Colonic Capsule Endoscopy.

2.1.12 Summary

Since its introduction almost 13 years ago, the clinical indications for the use of capsule endoscopy have widened considerably. Capsule endoscopy has been proven to be a useful minimally invasive tool in the exploration of the entire gastrointestinal tract, allowing visualization of previously inaccessible parts and achieving worthy satisfaction from both physicians and patients. New indications and future possibility to control the capsule movement enabling new possibilities for diagnosis and targeted therapy will evolve with the future technologic advancement.

2.2 EndoCapsule

The EndoCapsule (Olympus, Tokyo, Japan) is a video capsule endoscopy for the small intestine using a charge-coupled device sensor instead of a CMOS to acquire images (Fig. 2.15). Launched in Europe in 2005, EndoCapsule obtained FDA clearance in 2007 [33]. The EndoCapsule consists of a camera, light source, transmitter, and batteries. Once the capsule is activated and swallowed by the patient, it begins transmitting images of the digestive system to a receiver worn by the patient. After the examination, the patient returns the receiver to the physician or a nurse who can download all images to a computer and find the abnormalities in small intestine (Fig. 2.16).

2.2.1 Special Characteristics [34]

1. High-resolution CCD
2. Smart Recorder: It combines a receiver and viewer in a compact and easy-to-handle unit, allowing the physician to playback and capture images any time during the procedure.
3. 3D Track Function: That function offers intuitive operation, showing capsule location to help you decide what approach should be taken for subsequent procedures.

2.2.2 Preparation

The bowel preparation of Endocapsule examination includes a 12-h fast prior to the procedure, the administration of 2 l of polyethylene glycol (PEG) solution in the evening and 1 l 30 min before the procedure.

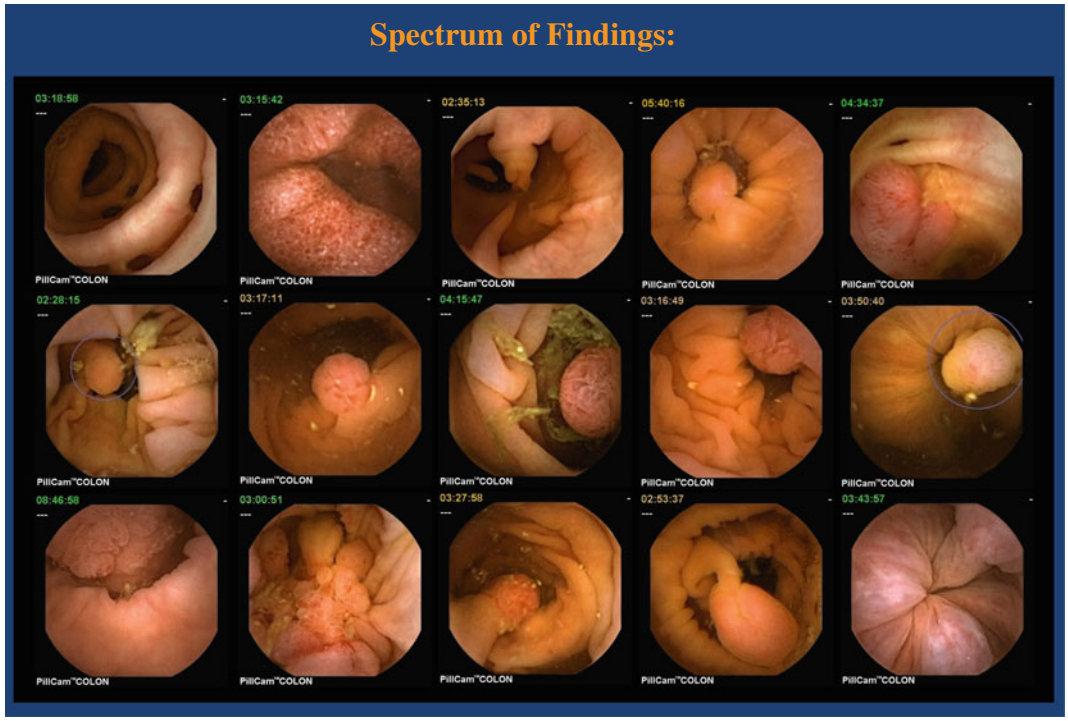


Fig. 2.14 Pathologies found with PillCam Colon2 capsule endoscope

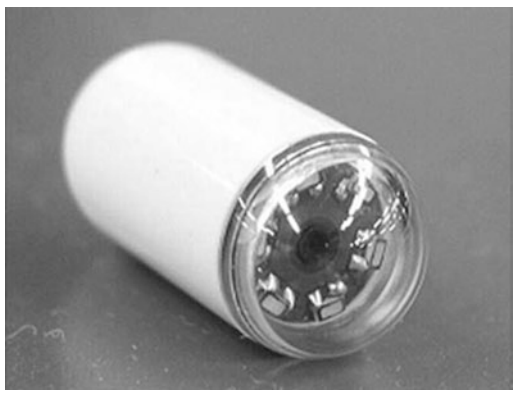


Fig. 2.15 The Endocapsule. Reprint with permission from Ogata et al. [38]

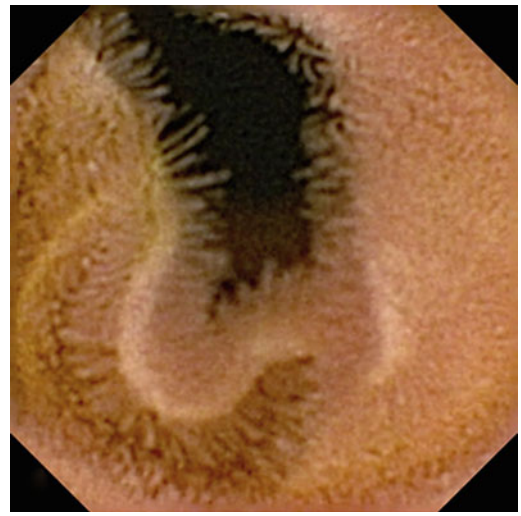


Fig. 2.16 Small intestinal villi detected by the Endocapsule. Reprint with permission from Cave et al. [36]

2.2.3 Clinical Studies

In a British retrospective cohort study, 70 patients performed Endocapsule examination using either overview with express-selected (ES) or overview with auto-speed-adjusted (ASA) modes. The ES-mode software eliminates images with no significant changes (compared with the previous frames) in the video. And the ASA-mode software speeds up the fps of the CE

video when detecting repetitive images. Among 40 (57 %) patients found with clinically significant findings, 32 (80 %) were recognized with overview function alone, while 39 (97.5 %) were recognized with overview function plus ES or ASA modes. The average reading time for overview with ES mode (19 ± 5 min) was significantly less than for overview with ASA mode (34 ± 10 min) ($p = 0.001$). These new playback systems can efficaciously reduce reading times of CE but need further evaluation in prospective multicenter studies [35].

Cave et al. carried out a multicenter randomized comparison of the Endocapsule and the PillCam SB in the USA. Results showed the positive percent agreement of 70.6 % and a negative percent disagreement of 82.4 % with an overall agreement of 74.5 %. The overall agreement was 74.5 % (38/51) with a κ of 0.48 and $P = 0.008$. The study demonstrated that Endocapsule had a similar diagnostic yield and better image quality compared with PillCam SB [36].

In another randomized head-to-head comparison study in Austria, 50 patients were randomly assigned to swallow either the MiroCam first, followed by the EndoCapsule 2 h later, or vice versa. The MiroCam and EndoCapsule devices were not statistically different with regard to their rates of complete small bowel examinations (96 vs. 90 %) or diagnostic yield (50 vs. 48 %). However, the findings were concordant in 68 % only (kappa = 0.50). The combined diagnostic yield was 58 % [37].

2.3 OMOM Capsule Endoscopy Platform

2.3.1 Overview

The creation of capsule endoscopy provides a new method for the visualized diagnosis of digestive diseases. It fixes the deficiency of the visualized diagnosis of small bowel diseases and brings a development direction of noninvasive, convenient, safe, and comfort diagnosis.

OMOM capsule endoscopy system is developed by Chongqing Science and Technology (Group) Co. Ltd. Comparing with other similar products, the unique feature of duplex multichannel communication mode has largely increased the controllability and convenience in its clinical use. Through the verification of clinical application, the product has equal validity and yield rate comparing with other similar products from overseas in the diagnosis of small bowel diseases, such as obscure GI bleeding, Crohn's disease, small bowel tumor, and small bowel polyp [39–41].

Since the first generation of OMOM capsule endoscopy successfully created in 2004, Chongqing Jinshan Science and Technology has been dedicated to provide comprehensive solutions in the diagnosis of digestive diseases. Based on the first generation of capsule endoscopy, the company has developed various new capsule endoscopy products according to different clinical uses, such as controllable capsule endoscopy, storable capsule endoscopy, and CCE, in which it can provide safe, noninvasive, comfort, and convenient visualized diagnosis for the whole digestive tract.

After nearly 10 years of development, Chongqing Jinshan Science and Technology in the field of digestive medical area has launched a series of high-end products according to different clinical uses, in which they are able to provide accurate diagnosis of digestive tract disease with comprehensive and personalized solutions. The following article will describe in detail about the application range, product formation, functions, and features of the products.

2.3.2 Small Bowel Capsule Endoscopy

OMOM small bowel capsule endoscopy is mainly used for visualized diagnosis of small bowel diseases. It is a new diagnosis method which is noninvasive, painless, safe, and comfort. After swallowing the capsule, it will pass through esophagus, stomach, duodenum, jejunum, ileum, and colon and finally expel from human body naturally by digestive tract

Fig. 2.17 Small bowel capsule endoscopy system formation

peristalsis. The capsule will continuously capture images of the GI tract during its movement process and transmit real-time image data wirelessly to the external image recorder. After the monitoring process, doctors can replay and analyze the saved images through the image workstation and finally make diagnosis of the gastrointestinal illness.

Small bowel capsule endoscopy system is mainly comprised of three parts: capsule, image recorder, and image workstation (Fig. 2.17), and functions of each part are described below:

Capsule: Capturing real-time image of GI tract and transmitting image wirelessly to the external image recorder; meanwhile, it is able to receive control signal from the image recorder to adjust working parameter.

Image recorder: Receiving and saving digital images from the capsule; also, it is able to send control signal to adjust the working parameter of the capsule.

Image workstation: Man–machine interactive operation platform can monitor the working condition of the capsule in real time and adjusting its working status. It is able to download and replay image data from the image recorder, assisting doctors to make diagnosis.

Indications:

1. GI hemorrhage, with no positive finding in upper and lower GI tract endoscopic examination;
2. Small intestine imaging anomaly suggested by other examinations;
3. Any type of IBDs, excluding bowel obstruction;
4. Unexplained abdominal pain and diarrhea;
5. Small intestine tumor (benign, malignant, carcinoid, etc.);
6. Unexplained iron-deficient anemia.

Contradictions:

1. Patients who are confirmed (or suspected) to suffer from digestive tract malformation, gastrointestinal obstruction, gastrointestinal perforation, stenosis, or fistula;
2. Patients implanted with pacemaker or other electronic devices;
3. Patients suffering from severe dysphagia;
4. Patients suffering from acute enteritis or severe iron deficiency, for example, bacillary dysentery at active phase and ulcerative colitis at acute phase, particularly for patients suffering from fulminant diseases;
5. Patients allergic to polymer material;
6. Use with caution for patients below 18 and above 70 and for psychopath;
7. Pregnant woman.

2.3.2.1 Features

- Pioneer of duplex communication

It supports duplex data transmission between the capsule and the image recorder. The real-time monitoring function, which can check the captured images in real time during the

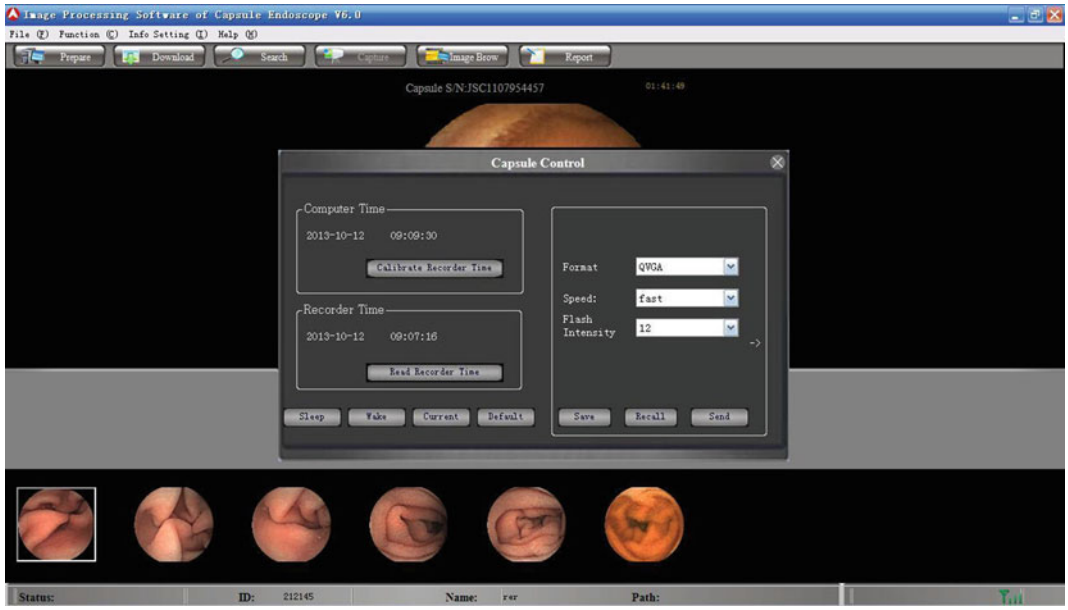


Fig. 2.18 Real-time monitoring and capsule working parameter adjustment

examination, can able to make intuitive judgment about the location of the capsule within the GI tract. At the same time, it can control the parameters of the capsule, such as capture frequency, brightness, and exposure, in order to extend the monitoring time (Fig. 2.18). This function has been widely spread in clinical use, and it can increase the completion rate of small bowel examination up to 100 % [42, 43].

- Unique multichannel mode

OMOM capsule endoscopy system supports simultaneous activation of multiple capsules at the same place, without interference between each of the capsules. Currently, OMOM capsule has 10 channels, which means it can undertake 10 patients simultaneously at the same location in the hospital without interference between each other. The image workstation can simultaneously monitor images from four capsules in real time (Fig. 2.19).

- Unique wireless USB monitoring

The wireless USB monitor is a convenient tool. It enables wireless communication, real-time monitoring, and capsule working parameter adjustment between the image recorder and the image workstation.

2.3.2.2 Clinical Application

Since 2005, OMOM capsule endoscopy has been used in clinic for over 8 years, and it has completed over 1 million samples. Clinical contrast study shows that OMOM capsule endoscope comparing with PillCam SB by Israeli company Given Imaging has no significant differences in the diagnosis of small bowel diseases, such as obscure GI bleeding, vascular malformation, small bowel tumor, small bowel polyp, and Crohn's disease [44]. In addition, during the clinical use of OMOM capsule, its special feature of duplex communication function that enables real-time adjustment of image capture frequency can achieve 100 % completion rate of small bowel examination [42].

In 2,400 patients who had OMOM capsule examination [45], the diagnostic yield of small bowel diseases was 47.7 %. In all findings of small bowel, 28.1 % was vascular malformation, 18.9 % small bowel tumor, 10.4 % polyp, 7.9 % Crohn's disease, 15 % mucosa injury and ulcers, 5.2 % bleeding, 11.3 % parasite, diverticulum, and so on. Comparing with traditional clinical methods such as GI radiography and CT, OMOM capsule endoscopy can provide more

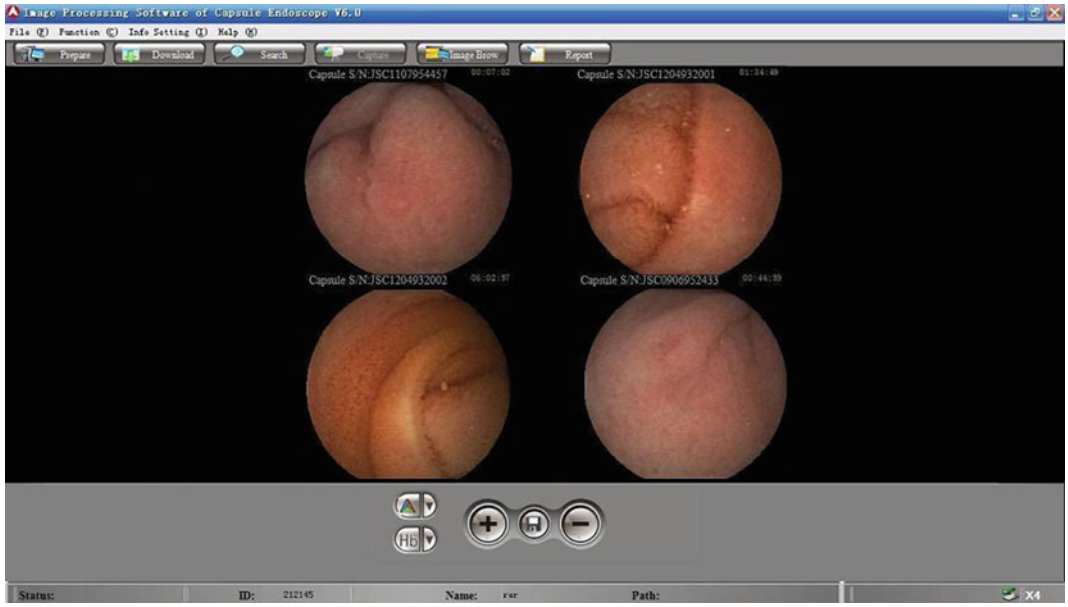


Fig. 2.19 Real-time monitoring of four capsules

intuitive and clear images of small bowel, which is able to significantly increase the complete small bowel examination rate (CSER) and yield rate, and also, it provides more safety and reliability [46, 47]. At the same time, OMOM capsule endoscopy can incorporate other diagnostic methods such as double-balloon endoscopy in clinical use. It can further improve the CSER and yield rate, and it can help to confirm the lesion position and features prior to the small bowel surgery which is efficient to lower the risk and difficulty of the surgery, thus improving the surgery succession rate [48, 49].

2.3.3 Controllable Capsule Endoscopy

OMOM controllable capsule endoscopy is developed based on the small bowel capsule endoscopy. It can not only be used for visual diagnosis of small bowel, but can also achieve movement and angle control within the stomach. After swallowing the controllable capsule into the stomach, an external controller can control the capsule movement, posture, and angle from outside the body, which makes stomach examination controllable and comprehensive. After the stomach examination, the capsule will enter duodenum, jejunum, and ileum through GI tract peristalsis, and after the complete visualized examination of small bowel, it will pass through colon and be expelled from the body naturally. The capsule will continuously capture images within the stomach and small bowel during the examination, and the images will be transmitted and stored into the external image recorder wirelessly. After the examination, doctors can analyze the images and make diagnosis through the image workstation. The controllable capsule endoscope has solved the problems of ordinary capsule when undertaking stomach examination, such as large blind spot, insufficient observation, and high misdiagnose rate. It provides a painless, noninvasive, safe, and comfort method for stomach examination. Clinical study shows that the controllable capsule can achieve comprehensive examination of stomach fundus, stomach antrum, stomach corner, and stomach body

Fig. 2.20 Controller

with high detection rate and low misdiagnose rate [50, 51].

Controllable capsule endoscopy system is comprised of four parts: capsule, image recorder, image workstation, and controller (Fig. 2.20).

2.3.4 Storable Capsule Endoscope

Storable capsule endoscope uses a large capacity storage module instead of traditional data transmission module. The captured images will be stored within the internal capsule memory module.

The advantages of storable capsule endoscopes are as follows: Patients do not need to wear an image recorder after swallowing the capsule, and they only need to be aware of the time of expelling the capsule from the body and collecting it. Then, a unique data reading and image viewing tool is used to process the images in order to make an analysis.

The storable capsule endoscope is disposable. The large capacity storage module contains 8 GB of memory which can store over 120,000 images. The working duration of the capsule reaches 15 h.

Storable capsule endoscope system is comprised of three parts: capsule, data reader, and image workstation.

Storable capsule endoscope is mainly used for the diagnosis of small bowel diseases such as unknown abdominal pain, GI hemorrhage, small bowel tumor, and Crohn's disease.

2.3.5 Colon Capsule Endoscope

Colon capsule endoscope is a painless, noninvasive, safe, and comfortable diagnose method specially designed for colon disease. According to the physiological structure of colon and based on traditional capsule endoscope, it augmented more features such as capsule controlling, position measurement, posture measurement, and adjustment. It can achieve to control the movement, posture, and position of the capsule within the whole colon. Colon capsule can be entered to the colon through swallowing or anus insertion. The movement of the capsule can be fully controlled by the external controlling device. The capture images will be transmitted to the control panel in real time wirelessly, and adjust the capsule posture and angle to ensure the comprehensiveness and reliability of the examination. Therefore, comprehensive diagnosis of the whole colon can be achieved.

Colon capsule endoscope system is comprised of three parts: colon capsule, controlling device, and control panel (Fig. 2.21).

Colon capsule endoscope system is mainly used for the diagnosis of various colon diseases such as colon inflammation, ulcer, diverticulum, polyp, and tumor.

2.3.6 pH Capsule Wireless Monitoring System

Gastroesophageal reflux disease (GERD) is a common digestive disease which affects 10–20 % of European and American population [52], and this ratio is relatively lower in Asia, but it has an increasing trend [53]. Clinical research shows that continuous pH monitoring within esophagus is the most effective way of diagnosing GERD [54]. OMOM pH capsule wireless monitoring system is mainly used to monitor the pH value inside the esophagus and make diagnosis of GERD through detecting the change in pH value.

Fig. 2.21 Colon capsule endoscope system formation

The pH capsule is sent and fixed on the mucosa of the esophagus through the catheter, and it will monitor the pH value within the esophagus with the sensor through 96 h of continuous examination. The monitored data will be transmitted to the external data recorder wirelessly, and the doctor can make diagnosis by analyzing the continuously monitored pH data parameter through the workstation after the examination is completed. The capsule will naturally drop off from the mucosa and finally expel from the body.

Clinical application research shows that OMOM pH capsule wireless monitoring system is safe and efficient for diagnosing GERD. Long continuous monitoring time can reflect the status of the gastroesophagus reflux, which leads to high GERD positive detection rate, and it can effectively evaluate the frequency and severity of the reflux [55]. Comparing with traditional pH monitoring method such as catheter-based monitoring and endoscopy, it has similar diagnosis effect, but with easier and more convenient clinical operation [56, 57]; also, long monitoring time of 96 h is not only effective for GERD diagnosis in the early stage, but also effective for assisting therapeutic decision in the later stage, and it evaluates the effectiveness of medical treatment.

pH capsule wireless monitoring system is mainly comprised of three parts: pH capsule (including the catheter), data recorder, and data analyzing software.

Indications:

1. Patients have classic symptoms of acid reflux or heartburn and are considered as GERD patients;
2. Patients suffer from unexplained chronic pharyngitis, hoarseness, trachitis, or asthma and are considered as those having extra-esophageal symptoms of GERD;
3. Patients who are considered as GERD patients and are positive in PPI therapeutic test;

Contradictions:

1. Patients who are confirmed (or suspected) to suffer from upper esophageal or nasopharyngeal obstruction;
2. Patients who are confirmed (or suspected) to suffer from esophageal varices according to gastroscopy, clinical radiology, or other examinations;
3. Patients who are confirmed to suffer from esophageal mucosa erosion according to gastroscopy or other examinations;
4. Patients who are confirmed (or suspected) to suffer from congenital digestive tract malformation, gastrointestinal obstruction, and perforation, stricture, or fistula of digestive tract according to clinical radiology or other examinations;
5. Patients who had bleeding tendency or gastrointestinal bleeding in the recent 6 months or have taken anticoagulant drugs for a long period of time;

6. Patients who suffer from heart disease and are not stable;
7. Patients implanted with pacemaker or other medical devices;
8. Patients who had history of allergy to polymer material.

2.3.7 Impedance–pH Monitoring System

Impedance–pH monitoring system is used for the diagnosis of GERD, which is an alternative method of pH capsule wireless monitoring system. The principle of this product is that it integrated both pH sensor and impedance sensor. The sensors are sent to the esophagus through nose by using a catheter, they will continuously monitor the patient's pH data and impedance data within the esophagus, and the data will be transmitted to the external data recorder. Doctors can analyze the changes of pH data and impedance data through the workstation, in order to make the final diagnosis. Through clinical study, the added impedance monitoring can not only increase the reliability of diagnosing GERD, but also detect alkaline reflux, which is valuable for comprehensive GERD monitoring and evaluation in clinical use [58, 59].

Impedance–pH monitoring system consists of three parts: catheter, data recorder, and data analyzing workstation.

2.3.8 Conclusion

Capsule endoscope has provided a new method of diagnosing GI diseases in clinical use. The medical field calls it as the development trend of GI endoscopy in twenty-first century, and it brings the third revolution in GI endoscopy development history. Its existence has made the development trend of GI disease diagnosis toward noninvasive, convenient, safe, and comfort.

OMOM capsule endoscope has entered for clinical use since 2005, and in 8 years of clinical use and research, it has verified this product as an effective method of visualized diagnosis for GI diseases. Comparing with similar products such as PillCam by Given Imaging, EndoCapsule by Olympus, and MiroCam by Intromedic, OMOM capsule endoscope has same diagnosis effect with lower price which is more acceptable and affordable for patients. Based on OMOM capsule endoscope, Chongqing Jinshan Science and Technology has developed a series of new products according to the clinical use of visualized diagnosis in GI diseases, such as controllable capsule endoscope and colon capsule endoscope. At the same time, it has developed products for diagnosing GI function disorders, such as pH capsule wireless monitoring system and impedance–pH monitoring system which is able to provide comprehensive solutions for GI disease diagnosis.

With the development of new technologies and applications in the field of medical application, the future research and application of the GI diagnostic technology will mainly carry out in three directions: (1) the application of multisensing and detection technology for more comprehensive diagnostic information; (2) the development direction from minimal invasive to noninvasive; and (3) the development direction from diagnosis to diagnosis–treatment combined. The capsule endoscope will eventually develop from a diagnostic tool to a diagnosis–treatment-combined intelligent robot.

2.4 MiroCam

2.4.1 Background of Development

Since the first development of a wireless capsule endoscope, M2A, the prototype of PillCam (Given Imaging Yokneam, Israel) in 2000 [60], it has been widely applied in clinical practice for the investigation of small bowel disease. Capsule endoscopy is easily performed only by swallowing the pill-sized capsule and so overcomes the limitations of conventional endoscopy

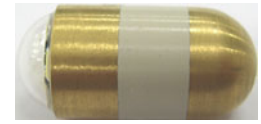
such as highly uncomfortable process, the necessity for skilled physician, and varied quality or outcome of examination depending on the physician's skill. Followed by M2A, other companies competitively released new capsule endoscopes in the market: Endocapsule EC type 1 (Olympus Ltd., Tokyo, Japan) in Japan [61] and OMOM (Jinshan Science and Technology Company, Chongqing) in China [62]. Even though there is a little difference in detail specs, these capsule endoscopes adopted the same transmission system, radio frequency (RF), for exporting imaging data to the receiver. RF system made wireless capsule endoscopes possible, but this system is energy-consuming, which limits the operation time of capsule endoscopes and complete examination up to cecum.

MiRo capsule endoscope, which was introduced in Korea in 2007 [63] and prototype of MiroCam, is the smallest and lightest capsule endoscope with the longest operation time up to 11 h by using distinctly different transmission system and human body communication. MiroCam was approved for general clinical use in Europe in August 2007 and by the US Food and Drug Administration (FDA) in June 2012.

2.4.1.1 Specifications of MiroCam

Generally, capsule endoscope systems have three components: a capsule endoscope body, an external receiving antenna with attached portable hard disk drive (data recorder), and a customized PC work station with dedicated software for review and interpretation of images [64]. MiroCam capsule is a pill-sized endoscopic body consisting of lens, imaging sensor, light source, power source, and telemetry device (Fig. 2.22).

Fig. 2.22 MiroCam (MC1000)



Characteristics of MiroCam

The MiroCam is 10.8 × 24 mm, smaller than PillCam at 11 × 24 mm and weighed 3.3 g [65]. It has an image field of 150° and resolution power of 320 × 320 pixels, which is a significant improvement over the 256 × 256 pixels in the PillCam. It includes a sensitive, low-power CMOS image sensor converting the optical rays to electrical voltages and a white-light-emitting diode (LED) as the illumination source. Two serial silver oxide batteries are used as a power source and operate for 9–11 h.

A Novel Transmission System and Human Body Communication with Electric Field Propagation

For imaging transmission, conventional endoscopes have a direct signal path, such as a conductive wire between the camera and data recorder. But capsule endoscope systems need wireless transmitter that delivers the imaging data to a receiver outside of the body. The basic telemetry system of capsule endoscope is composed of three elementary components [65]. The transmitter, at some location in space, converts the message signal produced by a source of information into a form suitable for transmission over a channel. The channel, in turn, transports the message signal and delivers it to a receiver at some other location in space [67].

For the wireless transmission, the standard capsule endoscope uses RF communication technology. But RF system has a drawback of severe power consumption as follows. A local oscillator makes a very-high frequency carrier, and an amplifier lets signal transport high power. In addition most energy generated from transmitter is lost because of radiation characteristics of RF energy [65]. Instead of this power-consuming technology, MiroCam adopted novel human body communication technology known as electric field propagation, which is patent in the USA [67]. This technology uses the human body as a semiconductor for data transmission, and an elective field can be induced and consequently generates drift current, even though the body has poor conductivity compared with a metal wire [65]. A space-occupying additional antenna or high-frequency circuit for remote communication is useless in MiroCam, and only

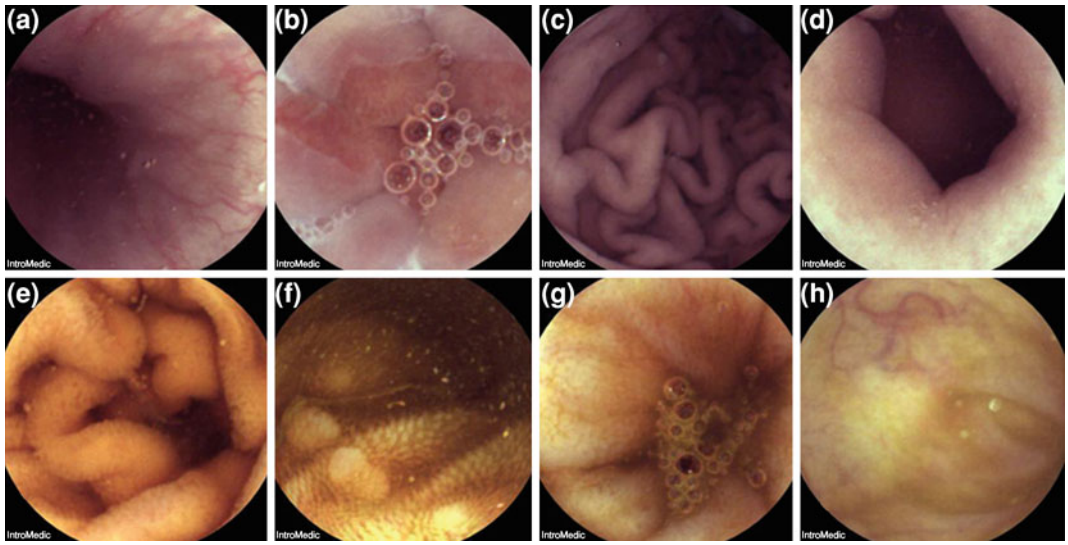


Fig. 2.23 Endoscopic images of normal lesions taken by MiroCam. **a** Esophagus. **b** Esophageal–gastric junction. **c** Body of stomach. **d** Pylorus of stomach. **e** Small bowel. **f** Lymphoid hyperplasia of terminal ileum. **g** Ileocecal valve. **h** Appendiceal orifice of Cecum

simple physical structure as a pair of gold plates coated on the surface of the capsule is enough for transmission.

Advantages of MiroCam

MiroCam overcomes inferior image quality of conventional capsule endoscopes that is inevitably caused by data compression for efficient data transmission under RF module. Blurring at edges of objects and of small or thin objects may hinder detection of mucosal lesion [64]. However, MiroCam with human body communication does not need data compression, which results in more precise images (Figs. 2.23, 2.24). In the first clinical trial, the fine structures of the bowel mucosal surface, including villi and vasculature of the entire small bowel lumen, could be observed without blurring or distortion in more than 90 % of cases [65].

MiroCam dramatically reduced power consumption in various ways. Firstly, human body communication consumes less power compared with RF by making the high-frequency modulation process unnecessary. Secondly, the CMOS image sensor was designed to minimize power consumption, and thirdly, the telemetry chip and image sensor were combined on one chip to reduce the current required for fan-out between chips. With this advantage, the capsule operation time prolonged up to 11 h only with two usual silver oxide batteries, and thereby, MiroCam improves the complete ratio to explore the entire small bowel [68].

Other functional equipments could be put in place where the additional antenna and high-frequency circuit of RF had been occupied, because these devices became unnecessary in human body communication. Capsule endoscope with the function of biopsies, drug delivery, or locomotive guidance will soon be realized.

2.4.1.2 Clinical Studies of MiroCam

Clinical Studies for the Diagnostic Feasibility and Safety

- **First clinical study of diagnostic feasibility and safety of the prototype of MiRo capsule**

The first clinical study for safety and diagnostic feasibility of MiRo capsule endoscope was reported in 2009 [65]. This study verified the safety of the MiRo capsule in human beings, especially with regard to the cardiac and neuromuscular systems, and evaluating the validity in the diagnosis of human small bowel. All 45

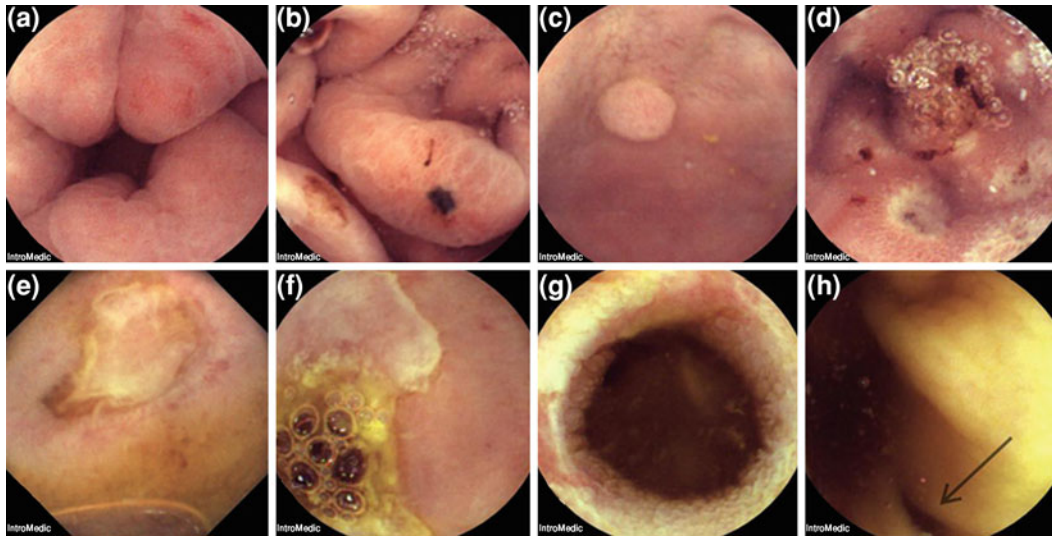


Fig. 2.24 Endoscopic images of abnormal lesions taken by MiroCam. **a** Gastritis. **b** Gastric erosion with adherent blood clot. **c** Duodenal polyp. **d** Duodenitis with erosions. **e** Small bowel ulcer. **f** and **g** Small bowel ulcer with stricture. **h**, Colonic diverticuli (*arrow*)

volunteers experienced no adverse effects, and there was no disturbance on one's daily life. All capsule endoscopes were expelled within 2 days, and the mean total duration of image transmission was 9 h 51 min (5 h 35 min–11 h). Complete exploration of the entire small bowel was achieved in all 45 volunteers. In 68.9 %, the images were fine and sophisticated and revealed microstructures over more than 75 % of the entire small bowel. The image quality was graded as good or better in 91 %.

- **Safety of MiroCam in patients with cardiac devices**

Patients with cardiac pacemakers or implantable cardiac defibrillators always require their attention to environmental electromagnetic interference (EMI) which may cause serious cardiac device dysfunction. By the same reason, capsule endoscopy should be performed carefully in these patients due to EMI produced by electrical signals of capsule endoscope when the capsule wirelessly transmits endoscopic images to a receiver outside the patient's body. For this reason, the US FDA considers the presence of a cardiac pacemaker or ICD as a relative contraindication for CE.

When capsule endoscope operates, EMI with cardiac devices may occur by oversensing or undersensing the electric signal. Oversensing may be developed by the radio frequencies of 434 MHz pulsed with 2 or 4 Hz used in capsule endoscopy as a transmission method, because the frequency is equivalent to a heart rate of 120 or 420 beats/min that represents slow ventricular tachycardia to ventricular fibrillation [69]. Therefore, cardiac devices may recognize it as nonexisting heart signals and inhibit ventricular pacing, which may cause bradycardia and symptomatic dizziness or syncope. Moreover, inappropriate shock or antitachycardia pacing could occur if an ICD detects an electric signal originating from a capsule endoscope. On contrary, undersensing may result in competition with native QRS complexes. If cardiac device cannot recognize the actual heart signal, it fails to deliver an appropriate therapy with potential induction of asynchronous ventricular or noise-mode function and tachyarrhythmia will continue. However, these effects have not been observed to this time in vitro or clinical studies of conventional capsule endoscope [69–76]. Because, the vector of RF transmission with

capsule endoscope is mostly within the abdomen, where is far from the location of the cardiac devices [71].

MiroCam equipped other transmission systems instead of RF, and it may be affected by an additional source of interference. Because this method uses the human body as a conductive medium for transmission of endoscopic images, an actual electric current flows directly into the heart and skews the signals of cardiac devices. However, energy generated from MiroCam is only 0.0225 J, which is weaker than 0.5 $\sim$ 360 J of cardiac device. Power of mobile phone that caused significant disturbance of cardiac devices was 2 W, and it is 2×10^6 times stronger than 1uW of MiroCam. Moreover, frequency of cardiac devices, 0.5 $\sim$ 5 Hz, is quite different to 1.5 $\sim$ 3 MHz of MiroCam.

Based on these theories, clinical study was conducted in six patients with three pacemakers and three implantable cardiac defibrillators [77]. No disturbance in cardiac devices or arrhythmia was detected on telemetry monitoring during capsule endoscopy. No significant changes in the programmed parameters of the cardiac devices were noted after capsule endoscopy. There were no imaging disturbances from the cardiac devices on capsule endoscopy. Capsule endoscope with human body communication was safely completed in patients with cardiac devices in this study, however, in which, only small number of patients and limited types of cardiac devices were included. Therefore, it is recommended that capsule endoscope should be performed under continuous ECG monitoring in a hospital setting after cardiac assessment by cardiologists. And further study is in need of verifying the safety of capsule endoscopy in a large number of patients with various types of cardiac devices.

Comparative Studies with the Conventional Capsule Endoscopes

Several studies were conducted to compare the diagnostic yield and complete examination rate between MiroCam and other capsule endoscopes. While studies showed no statistical significance in difference of performance between MiroCam and other capsule endoscopes, a trend for the MiroCam to detect more small bowel lesions than with the other capsule endoscopes was observed.

The pilot study of sequential capsule endoscopies using MiroCam and PillCam showed complete examination rate 83.3 % in MiroCam and 58.3 % in PillCam ($p = 0.031$) [68]. Diagnostic yields for MiroCam and PillCam were 45.8 % and 41.7 % ($p > 0.05$), respectively. The agreement rate between the two capsules was 87.5 % with a κ value of 0.74.

In French multicenter study, 83 patients with obscure GI bleeding were enrolled and ingested the two capsules at a one-hour interval [78]. After analyzing 73 cases (10 technical issues), there were 30 concordant positive cases (41.1 %), and the diagnostic concordance between the two systems was satisfactory ($\kappa = 0.66$). The final diagnosis was different in 12 patients (16.4 %) with nine positive findings only on MiroCam, two positive findings only on PillCam, and one different diagnosis in one patient. MiroCam and PillCam identified 95.2 and 78.6 % of positive cases, respectively ($p = 0.02$). The significant difference may be explained in part by the longer transit time and the higher number of images produced. But there was no significant difference on image quality, field depth, and lightening between MiroCam and PillCam.

Another multicenter comparative study was performed in six academic hospitals in USA and enrolled 105 patients with obscure GI bleeding [79]. The result showed an overall agreement of 78.7 % (95 % CI, 68.7 $\sim$ 86.6 %), a positive agreement of 77.4 % (95 % CI, 58.9 $\sim$ 90.4 %), and negative agreement of 79.3 % (95 % CI, 66.7 $\sim$ 88.8 %). Twelve abnormal findings were observed only in MiroCam, and seven were observed only in PillCam. MiroCam had a 5.6 % higher rate of detecting small bowel lesions ($p = 0.54$). On average, MiroCam took 6.6 h to reach the cecum, which is longer than the time taken by PillCam, i.e., 5.2 h ($P < 0.0001$). This difference in small bowel transit time may be explained by the difference of the dimension of two capsules (10.8 vs. 11.0 mm). It was assumed that the smaller MiroCam may be sufficiently

large to ultimately be propelled through the small bowel; However, there may be some slippage with each peristalsis that causes the MiroCam to have a longer transit time in small bowel [79]. Despite longer transit time, the MiroCam achieved higher complete ratio than PillCam (93.3 vs. 84.3 %, $P = 0.1$)

To compare MiroCam and Endocapsule, a total of 50 patients with obscure GI bleeding, chronic diarrhea, and anemia of unknown origin participated in the clinical study in Austria [80]. Complete small bowel examination was achieved in 96 % patients using MiroCam and 90 % patients using EndoCapsule (odds ratio 2.67, 95 % CI, 0.49–14.45, $p = 0.38$). Diagnostic yield in the small bowel was 50 % in MiroCam and 48 % in EndoCapsule without statistical significance (OR 1.08, 95 % CI, 0.49–2.37, $P > 0.99$). The diagnostic concordance rate between the two different capsule endoscopes was 68 % ($\kappa = 0.50$).

Summarizing these comparative studies, MiroCam detects small bowel abnormalities at a rate that is at least comparable to that of other capsule endoscopes (Table 2.2). The longer operational time of the MiroCam resulted in a higher rate of complete small bowel examination. Although statistical insignificance, the larger numbers of images generated at three frames per second increased the detection rate of small bowel lesions [79].

2.4.1.3 Upgraded MiroCam and Advanced Capsule Endoscope

Upgraded model of the MiroCam (MC1000-W) has plans to market. The field of view of new model is improved to 170° compared with 150° of previous model (MC1000) (Table 2.3). The size is minimally changed from 10.8 × 24 mm to 10.8 × 24.5 mm, and the weight is reduced from 3.3 to 3.25 g. Resolution power of 320 × 320 pixels and frame rate of three frames per second are identical with previous model. Operating time over 11 h is maintained, and transmission method is same as human body communication using E-field propagation.

External receiver was upgraded to wire–wireless real-time viewer, and data transmission rate was two times higher. MiroView software was also upgraded from version 1.0 to 2.0 (Fig. 2.25). Rapid detection of bleeding focus by map view became available, and reading time could be markedly decreased by reading many images at a time using range view. Software system divided by sever, client, and operator makes reading easier anywhere and anytime via internal network of the hospital. Exporting program of the final report to the hospital image program such as PACS was also improved.

Capsule Endoscopes with Active Movement

The movement of capsule endoscopes entirely depends on the natural peristalsis of GI tract, which might be a main reason to prolong the gastrointestinal transit time. The uncontrollable movement of capsule endoscope might be obstacles to reach the cecum within capsule operating time and to make accurate diagnosis. Therefore, techniques for active control of the capsule movement have been being developed, such as a magnetic steering mechanism by external manipulation [81–87] and a locomotive mechanism by internal manipulation [88–91].

- **Magnetic steering capsule endoscope (MiroCam Navi)**

  MiroCam Navi (MC1000-WM) is one of the magnetic steering capsule endoscope, which was approved for clinical use in Europe. Observing the images on real-time viewer, magnetic capsule endoscope could be manipulated to move up and down by MiroCam Navi controller outside the body (Fig. 2.26). With MiroCam Navi, gastric transit time might be shortened, and the small bowel lesion could be observed in more detail. Moreover, targeted drug delivery will be realized with this ability to operate freely in the near future.

- **Paddling-based locomotive capsule endoscope**

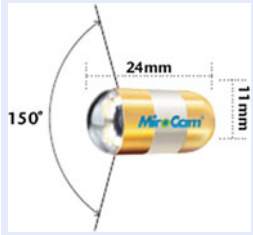
  For internal locomotive devices, paddling-based capsule endoscope has been developed. When a locomotive robot was suggested by Hirose [92], Pratt [93], and Ryu [94], it was

Table 2.2 Comparative studies of MiroCam to other capsule endoscopes

		Patients (n)	Diagnostic yield	Agreement rate	Rate of complete examination	Small bowel transit time	Operating time
Kim et al. [68]	MiroCam	24	45.8 %	87.5 %, $\kappa = 0.74$	83.3 %*	–	702 ± 60 min*
	PillCam		41.7 %		58.3 %*	–	446 ± 28 min*
Pioche et al. [78]	MiroCam	73	56.2 %	$\kappa = 0.66$	–	268.1 min (58 − 538)*	–
	PillCam		46.6 %		–	234.5 min (51 − 502)*	–
Choi et al. [79]	MiroCam	105	–	78.7 %, $\kappa = 0.547$	93.3 %	6.6 ± 2.2 h	11.1 ± 1.5 h*
	PillCam		–		84.3 %	5.2 ± 1.4 h	7.8 ± 0.8 h*
Dolak et al. [80]	MiroCam	50	50 %	68 %, $\kappa = 0.50$	96 %	319 ± 113 min	704 ± 56 min*
	EndoCapsule		48 %		90 %	316 ± 100 min	578 ± 53 min*

* $P < 0.05$

Table 2.3 Comparisons of MiroCam (MC1000) to upgraded MiroCam (MC1000-W)

	MC1000	MC1000-W
Image		
Size (mm)	10.8 × 24	10.8 × 24.5
Weight (g)	3.45	3.25
Pixels	320 × 320	320 × 320
Frames per second	3	3
Field of view (°)	150	170
Operation time (h)	Over 11	Over 11
Communication mechanism	Electric field propagation	Electric field propagation

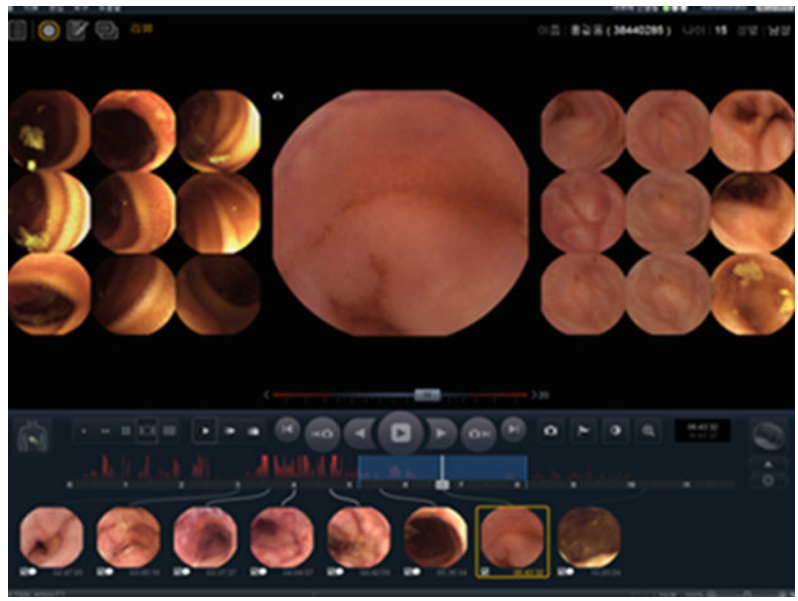


Fig. 2.25 Updated MiroView (2.5)

Fig. 2.26 MiroCam Navi (MC1000-WM)

difficult to miniaturize the proposed legged mechanisms, and thus, that was not applied to capsule locomotion. In 2004, Menciassi proposed a legged locomotion in gastrointestinal tract [95], and with this 8-legged capsule, a full colonic passage was successfully demonstrated in the ex vivo phantom model [90]. However, the multilegged locomotion capsule needs multiple actuators and controllers, which limited miniaturization and energy conservation.

An inchworm-like microrobot comprising actuation modules and clamping modules for capsule endoscopes has been proposed in Korea in 2004 [96]. However, spring-type SMA actuators in this inchworm-like microrobot were not enough to get over resistance force of small bowel and to realize long stroke with high efficacy [97–100]. In order to solve this problem, a new paddling-based locomotive mechanism was developed in 2006 [101]. This locomotive mechanism is originated from paddling a canoe. The paddle of a canoe is embodied as the legs of our microrobot, and the canoeist is replaced by the linear actuator which is composed of a reliable commercialized micromotor and a lead screw. And the more enhanced paddling-based locomotive CE was presented in 2010 and demonstrated its efficacy in vitro and in vivo experiments [102].

1. Concept design of the microrobot

At first, the paddling-based locomotive microrobot consists of a linear actuator which comprises micromotor and lead screw, an inner cylinder, an outer cylinder, multiple legs, and robot outer body [101]. The functions of this novel microrobot are illustrated as follows [101]: (1) The linear actuator moves the inner cylinder backward and forward. (2) The inner cylinder has grooves, and there is some clearance between the grooves and the legs. Owing to the clearance, the inner cylinder makes the legs rotate and moves the legs and the outer cylinder. (3) The outer cylinder is connected with the multilegs by wire-type pin and is moved inside of the robot outer body. (4) The multilegs are protruded out of the robot body and are folded in the robot body. The microrobot has six legs which are radially positioned and are in contact with the intestinal surface. (5) Finally, in order to reduce the frictional force between the robot outer body and the intestinal surface, the head of the microrobot is designed as a semisphere and the robot outer body is coated with lubricant such as silicon oil. And for the protruding and folding the legs, the microrobot outer body has the lateral slits.

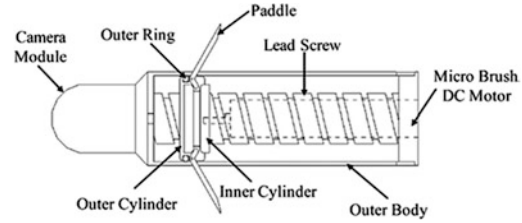


Fig. 2.27 Concept design of paddling-based locomotive capsule endoscope (Reprint with permission from Kim et al. [102])

In the modified locomotive capsule endoscope, outer ring is added to generate continuous friction between the outer body and the outer cylinder and to provide robustness in the kinematic configuration, such as the positional difference between the inner and the outer cylinders for protruding or folding paddles [102] (Fig. 2.27). As a result, the capsule endoscope can satisfactorily move inside the GI tract during repetitive movements. Moreover, this CE is teleoperated by the automatic controller, with which a reciprocating cycle for the cylinders of the capsule endoscope can be moderated by setting desired cycle time using a microprocessor on the controller [102]. This automatic control mechanism reduces power consumption and accelerates locomotion compared with the manual switching for the control used in the previous locomotive capsule endoscope [101].

2. Locomotive mechanism of the proposed microrobot

Locomotive mechanism is illustrated in Fig. 2.28. By repeating paddling motion, this capsule moves forward in the GI tract [102]. For this, the paddles linked to the outer cylinder are protruded and folded according to the direction of linearly actuating the inner and the outer cylinders along the lead screw. The clearance between inner and outer cylinders causes

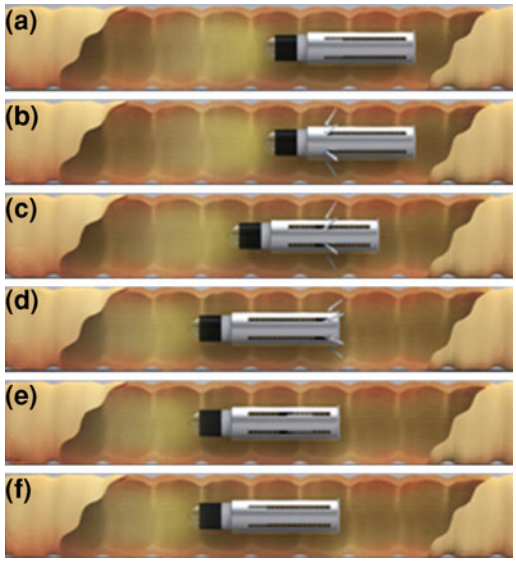


Fig. 2.28 Locomotive mechanism of the paddling-based locomotive capsule endoscope (Reprint with permission from Kim et al. [102]). **a** Initial state of the capsule-type microrobot in the intestine. **b** When the linear actuating mechanism starts to move the inner cylinder backward, the paddles linked to the outer cylinder are stretched, due to the kinematic relationship between the inner and the outer cylinders, and clamp the intestinal surfaces. **c** While the actuator moves the inner cylinder farther, the outer body of the capsule endoscope advances forward. **d** End of the stroke of the linear actuating mechanism. At this point, when the actuating mechanism is about to move the inner cylinder forward, the paddles fixed to the intestine are released and folded into the capsule body as the above kinematic relationship works inversely. **e** The cylinders and folded paddles return without the movement of the capsule body. **f** The locomotion principle returns to the same state in step A

relative position delay of the outer cylinder to the inner one during linear motion. As a result, the paddles rotate on pivotal points for protruding or folding when multiple grooves inner cylinder relatively push the end of paddles to right or left, as shown.

3. Specification of modified paddling-based locomotive capsule endoscope

The locomotive capsule endoscope is 15 × 43 mm in size and weighs 14 g. The length of the slit, meaning an actual stroke length of paddles for advancing, is 33 mm. A camera module is located in front of the locomotive capsule endoscope and had a field of view of 125 and resolution power of 320 × 320 pixels. The capsule endoscope transmits video images at 10 frames per second to outside receiver. Two cables are connected to the end of the locomotive capsule endoscope for power supply and locomotion control, and four cables transmit image data from a camera. The cables are extended to the external controller and the recorder, twisted as a bundle with a length of 2 m from the end of the capsule endoscope.

The active movement of this novel capsule endoscope with paddling-based locomotion was demonstrated in in vivo test with an anesthetized pig [102]. The movement was fast and stable with a regular velocity (17 cm/min over 40 cm lengths) set by the automatic controller. And there were no serious complications during its active movement.

Even this paddling-based locomotive capsule endoscope has several advantages, such as long stoke, simple structure and control, and fast locomotion, the present external controller should be miniaturized and embedded in the capsule endoscope. Moreover, a wireless telemetry system should be equipped for actual operation and transmission of acquired images to recorder. A novel communication technology using human body communication [65] is a very suitable method for developing a wireless locomotive capsule endoscope due to its capability of energy conservation.

In the in vivo study, peristalsis seldom occurred in colon of the general anesthetized pigs. Actually, peristalsis might disturb the active movement of the capsule endoscope because the direction of capsule endoscope is opposite to that of peristalsis. Further study is needed to investigate the forward movement against provoked peristalsis by cholinergic drugs. Study about actual movement at anatomic obstacles, such as acute angles of recto-sigmoid junction or feces, should be evaluated. And further technologic improvement should be achieved to use in humans. A miniaturized steering module should be developed to change a direction of CE and to view at specific directions.

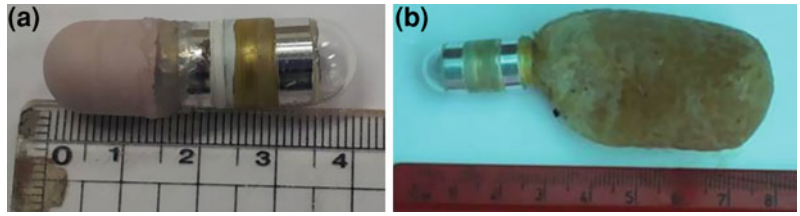


Fig. 2.29 Concept design of self-stabilizing capsule endoscope (Reprint with permission from Filip et al. [105]). **a** Modified MiroCam capsule endoscope with stabilizing component. **b** Fully expanded self-stabilizing capsule endoscope

- **Self-stabilizing colonic capsule endoscopy**

The smaller capsule is the better to swallow. However, small bowel capsule endoscope tends to tumble in larger-lumen organs such as stomach or colon [68, 103], which limits the visual field causing failure to catch significant lesions or grossly distorting the perceived dimensions of polyps [104]. Therefore, self-expanding capsule endoscope after it enters into the bowel was developed to visualize the colon without tumbling [105].

Self-stabilizing capsule endoscope is modified from MiroCam capsule endoscope coupled to stabilizing component (Fig. 2.29). This stabilizing component was a thermally treated, woven, biodegradable, liquid-permeable, flexible polyglactin 910 mesh (vicryl, Ethicon Inc., Somerville, NJ) filled with super-absorbent polymer granules (Favor PAC, Evonik Industries, Stockhausen, Germany) [106]. The expandable material was salt granules of hydrophilic, non-toxic, cross-linked polyacrylate polymer. These granules can absorb several hundred times their weight in water, but cannot dissolve because of their 3D polymeric network structure, and only the formation of a gel takes place [107]. The advantages of this super-absorbent polymer as an expandable material for the device are as follows; it is biocompatible, swells extensively, swells in a relatively short period of time, exerts a reasonable swelling pressure on the walls of the lumen, and withstands the pressure in the colon by remaining attached to the imaging component while keeping its consistency [105]. Moreover, the increased viscosity of the surrounding liquid in water allows the capsule to move smoothly in the colon, and its flexibility is enough to pass through sharp colonic turns such as the hepatic and splenic flexures [108]. This bending capability should be uniform up to the base of the expandable component that is attached to the rigid but relatively small imaging component.

In living dogs, the study was conducted to evaluate the efficacy of this self-stabilizing capsule endoscopy by quantitatively comparing the detection rate of intraluminal suture marker lesions for colonoscopy [109]. Four mongrel dogs underwent laparotomy and the implantation of 5 to 8 suture markers to approximate colon lesion. Each dog consecutively administered both unmodified capsule endoscope and self-stabilizing capsule endoscopy in random order by endoscopic insertion into the proximal lumen of the colon. After capsule endoscopy, blinded standard colonoscopy was performed. The average percentage of the marker detection rates for unmodified capsule endoscope, self-stabilizing capsule endoscope, and colonoscopy, respectively, was 31.1, 86, and 100 % ($P < 0.01$). Self-stabilizing endoscope delivered a significant improvement in detection rates of colon suture marking when compared with the unmodified capsule endoscope, but there were no comparisons of small bowel transit time. Further studies are needed for the safety and efficacy of the self-stabilizing capsule endoscope in human. The worrisome problem is a premature expansion or obstruction in the small intestine or stomach. And timed launching in the cecum, detection of colon polyps, and imaging qualities should be investigated.

2.5 The Ankon Magnetic-Controlled Capsule Endoscopy Platform in the Clinical Investigation of Stomach Diseases

Abstract Gastric diseases are great burden not only in China but also worldwide. Capsule endoscopy is a noninvasive tool in the exploration of the entire gastrointestinal tract. However, conventional capsule endoscopies have shown that observation of the stomach is highly variable because of the impossibility of thorough exploration of the gastric cavity with a passive power. The steerable capsules with external magnetic field may be the most viable approaches for active control, and several explorations have showed promising benefits. We have developed a novel magnetic-controlled capsule endoscopy system (MCE) with magnetic field generated by an external industry robot (provided by Ankon Technologies Inc.), which has been demonstrated to be safe and feasible in the examination of human stomach. For the main diagnostic outcomes, MCE and gastroscopy had very similar results (the overall agreement was more than 90 %). The acceptability of MCE was much higher than gastroscopy, and most patients could tolerate ingestion of the large amount of water. This comparative study showed that MCE is a promising alternative for noninvasive screening of gastric diseases.

2.5.1 Introduction

Gastric diseases are great burden not only in China but also worldwide [110–112]. The prevalence of peptic ulcer disease confirmed endoscopically could reach to 17.2 % [113] in China, substantially higher than in Western populations. Gastric cancer remains the fourth most common malignancy and the second leading cause of cancer mortality in the world [114]. It is important to screen, diagnose, or exclude gastric diseases at an early stage. Gastroscopy is the reference method for the detection of gastric mucosal lesions. Unfortunately, it is widely regarded as uncomfortable and invasive for gastroscopy examination, thus with low patient compliance [115]. Conscious sedation in endoscopy could have potential drug-related side effects and increase medical cost, which limits its use in certain population [116]. Capsule endoscopy (CE) might offer a more patient-friendly alternative without discomfort or need for sedation. Since the first brief communication published in Nature in 2000 introducing CE, it has rapidly become the criterion standard for small intestine examination [117–119]. However, for a large organ like stomach, the random movement of passive capsule can let it observe only a small part of the whole gastric mucosa.

Since the first case report of maneuverable capsule system, published by Paul Swain et al in 2010, endoscopy companies such as Given Imaging, Olympus, Siemens, and OMOM have done some early-stage researches on this field. Capsule with propellers [120], paddles [121], and legs [122] has been studied with some success; however, a lot of work is still required for these to become clinical reality. Through recent years of efforts, the steerable capsules with external magnetic field may be the most viable approaches for active control [123, 124], and several explorations (external magnet paddle or special MRI machine) have showed promising benefits [120, 125–128]. However, these systems still have some limitations. The magnetic force generated by handheld external magnet appeared to be insufficient to prevent accidental emptying of the capsule from strong retraction of pylori [125]. The equipment derived from magnetic resonance imaging procedures provided adequate force and acceptable performance but indicated possibly fairly high cost [126].

Robotic control on magnetic capsule endoscopy based on industry robot may provide a much more cost-effective solution. An in vivo animal trial demonstrated that robotic control on magnetic steering capsule was more precise and reliable than manual operation [127]. We have developed a novel MCE system with magnetic field generated by an external industry robot,

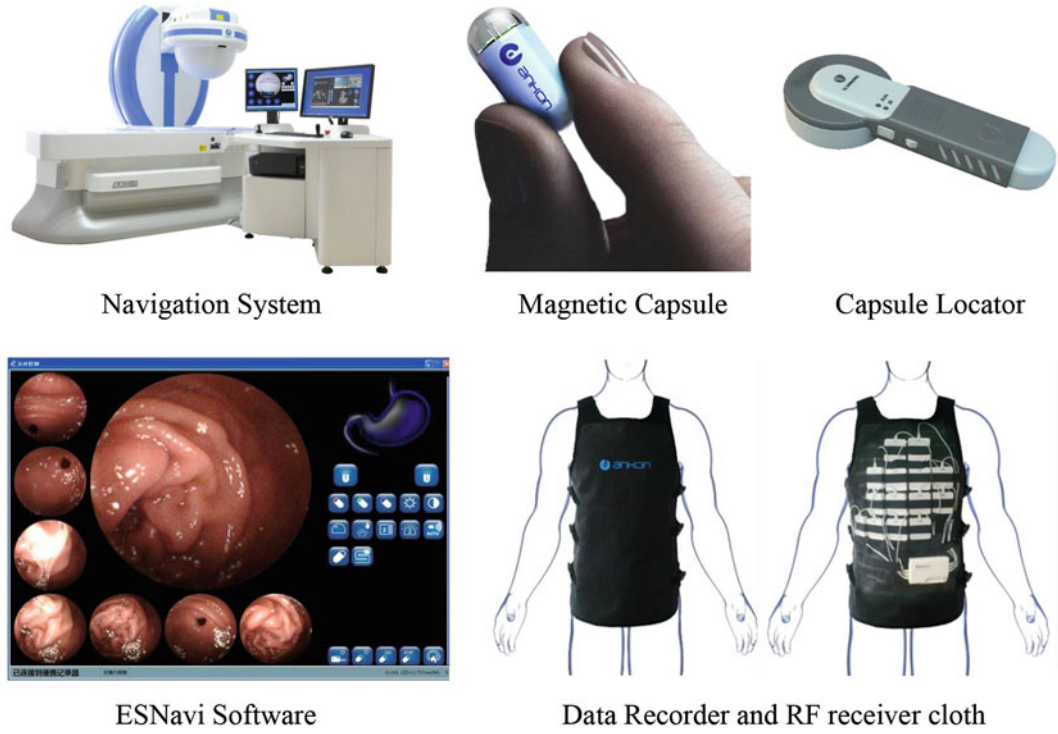


Fig. 2.30 The NaviCam MCE system

which has been demonstrated to be safe and feasible in the examination of human stomach by a pilot study of 34 healthy volunteers [129].

2.5.2 The ANKON MCE System

Ankon Technologies Inc. began its MCE research in 2009, and its NaviCam got SFDA's approval in China in 2013. The ANKON MCE system consisted of capsule endoscopy, a guidance magnet robot, a data recorder, and a computer workstation with software for real-time view and control (Fig. 2.30).

The capsule endoscopy in stomach was performed well and safe in simulator model and porcine model. The capsule has a size of 28 × 12 mm, which consisted of CMOS camera, LED, batteries, the magnet, RF transmitter, and magnetic and acceleration sensor. It has a view angle of 140° and a resolution of 480 × 480. The guidance magnet robot provides five degrees of control freedom: two rotational and three translational. The capture rate of MCE is two frames per second from a single CMOS sensor. It transmits images to the data recorder via a set of sensors placed on the patient's skin. The images are viewed in real time on monitor and stored into workstation simultaneously.

The guidance magnet robot is of C-arm type with five degrees of freedom. The complete working area on the MCE is more than $50 \times 50 \times 50\ cm^3$. The magnetic field generated by guidance robot system can be adjusted during the examination and reach 200 mT at maximum, which is much less than that from standard 1.5T MRI. Actual strength of magnetic field used to control the navigation of MCE is about 5 to 30 mT, which is 60 to 300 times greater than the Earth's magnetic field and generates magnetic force in the order of the capsule's weight. With permanent magnet, the

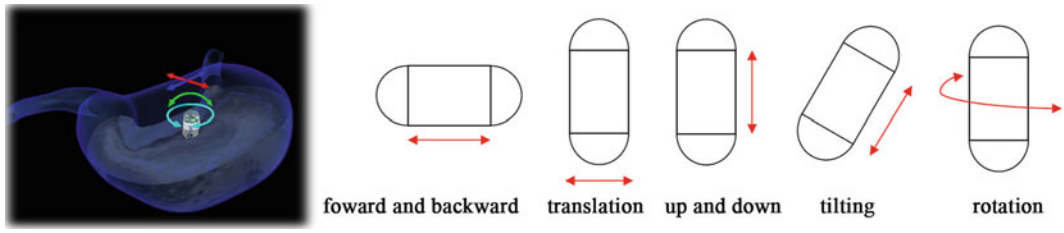


Fig. 2.31 Movements of the capsule

guidance magnet robot runs very quiet and consumes low electric power requiring no cooling system at all.

During examination, the doctor sits in front of the workstation with dual monitors. The left monitor displays the real-time view of stomach from the capsule and the view of patients from cameras. The right monitor is the operating interface collecting the information about strength of magnetic field, attitude of capsule, and so on. The ESNavi can also show the real-time location of capsule in the three-dimensional mode. The attitude information of capsule is obtained through simulation on the basis of the magnetic field generated by the guidance system. MCE can be controlled by the magnet guidance robot through a joystick or automatic mode by which the MCE can make linear movement or rotation without manual control (Fig. 2.31). The capsule could reach from the lower to the upper side of gastric wall, no matter what content the stomach is full of (water, air, or the mixture). When the stomach is partially filled with water, the capsule can float stably at the water level (Fig. 2.32).

2.5.3 Procedure

The patient arrived at the hospital between 8:00 am and 10:00 am after fasting overnight (>8 h). All subjects drank 500 ml of clear water and 5 ml simeticone about 1 h before capsule ingestion, another 500 ml of clear water 15 min before ingestion, and 6 g air-producing power (Tianzhili Biological Technology, Fuzhou, China) with 5 ml of water 5 min before ingestion. The air-producing powder served to distend the stomach through releasing about 540 ml CO_2 every 6 g. After swallowing the MCE together with 5 ml of water, the patient immediately lies down on the bed attached to the guidance robot. The position of the bed was adjustable for optimal gastric imaging and maximal magnetic force for capsule navigation.

During the examination, the patient lies down on the bed and kept minimum movement. After the MCE reached stomach, the doctor moves the joystick to control the movement of the magnetic head based on the real-time images and parameters displayed on the operating interface (Fig. 2.33). The doctor performed the following

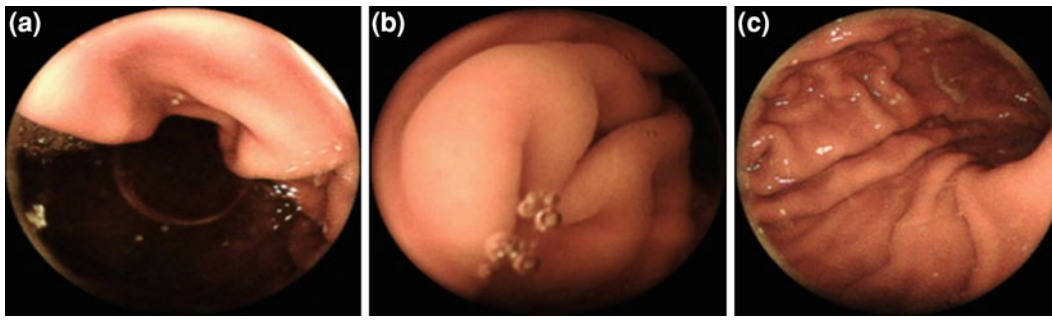


Fig. 2.32 **a** Floating view; **b** capsule under the water; and **c** capsule in the air

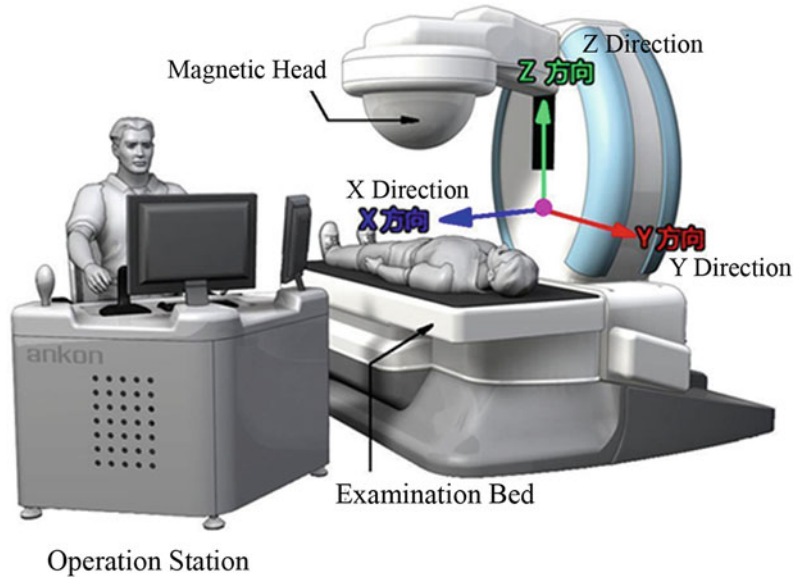


Fig. 2.33 Capsule navigation system operation

steps: lifting the capsule away from the posterior wall, rotating and advancing the capsule to the fundus and cardiac region, then rotating capsule to observe stomach body, and finally observing the angulus, antrum, and pylorus. If the distension was insufficient, ingestion of additional air-producing powder or water was repeated. The whole examination duration lasted for about 30 min.

2.5.4 Indications

1. Patients with upper gastrointestinal symptoms, including abdominal discomfort, pain, acid reflux, dysphagia, belching, and hiccups.
2. Screening for gastric cancer.
3. Follow-up examination for gastric ulcer, atrophic gastritis, and precancerous lesions.

2.5.5 Contraindications

1. Patients with impaired bowel movement from ileus or organic digestive diseases
2. Patients with known large and obstructing tumors of the upper GI tract
3. Patients after upper GI surgery or abdominal surgery altering GI anatomy
4. Patients under full anticoagulation
5. Patients in poor general condition
6. Patients using equipment that may be affected by magnetic field, such as pacemakers and defibrillators
7. Pregnancy or suspected pregnancy
8. Patients allergic to materials or drugs involved
9. Patients mentally ill or unable to cooperate.

In our pilot study of 34 healthy volunteers, the cleanliness was evaluated as good in 88 % subjects [129]. The distention of gastric cavity was evaluated as good in the 85 % subjects. Maneuverability of the MCE to movements of the guidance magnet robot was graded as good in 85 % subjects. More than 75 % gastric mucosa was visualized in 79 % subjects and 50 % to 75 % in 20 % subjects. Visualization of the gastric cardia, fundus, body, angulus, antrum, and pylorus was subjectively assessed as complete in 82, 85, 100, 100, 100, and 100 %, respectively. No entire gastric mucosa was observed in all subjects for three reasons: (1) small amounts of fluid blocked the view of the most apical parts of the fundus; (2) insufficiency

of gastric distention; and (3) difficult for guidance MCE in the cardiac region. The removal of mucus by drugs will need further researches because it is a critical issue with regard to capsule navigation and visibility.

In another double-center comparative trial of MCE and standard gastroscopy, both of them had very similar results of the main diagnostic outcomes (the overall agreement was more than 90 %). The acceptability of MCE was much higher than gastroscopy, and most patients could tolerate ingestion of the large amount of water. This study also showed that MCE is a promising alternative for noninvasive screening of gastric diseases.

In spite of initial and encouraging advancement in different kinds of MCE, there were many concerns in its practical value at present [130]. The drawbacks of current MCE comparing with the standard gastroscopy are clear: (1) complicated gastric preparation; (2) lack of biopsy capacity; and (3) long examination time. However, in our view, all these drawbacks may be solved in the future with the advancement of technology. As pointed by Rey, after balancing the pros and cons of standard gastroscopy and MCE, the latter might be a more cost-effective use of medical and social resources [126]. In the future, MCE may be adopted as the screening examination tool for gastric disease, especially for the elderly with sedation contraindications.

2.6 CapsoCam

Two of limitations of capsule endoscopy are as follows: (1) incomplete examination of the small intestine due to inadequate battery life and (2) the inability to observe some areas on the side wall because the camera is located at the end of the capsule [131]. The CapsoCam (Capsovision, Saratoga, CA, USA) was a recently developed 11 × 31 mm capsule endoscopy, which represents a new concept of detecting lesions in the small intestine: 360° panoramic lateral view with four cameras [132]. CapsoCam SV-1 capsule consisted of lens, imaging sensor, light source, power source, and flash memory (Fig. 2.34). It has a high frequency of 20 frames per second during the first 2 h and thereafter 12 frames per second, with a battery life of 15 h.

Fig. 2.34 The CapsoCam SV1. Reprint with permission from Friedrich et al. [132]

2.6.1 Special Characteristics

1. 360° Panoramic View: The CapsoCam employs four cameras facing the sides of the capsule that together image a full 360° about the capsule's circumference and capture high-resolution images of the mucosa including surfaces hidden behind folds.
2. Wire-Free Technology: There is no generation and transfer of RF signals, and all the images captured are stored on board with CapsoCam. The patient does not need any form of external devices, and the clinician is free of the receiver equipment and other accessories for data retrieval. However, because of not including the recording system, the capsule has to be retrieved by the patient after expulsion in order for the video to be downloaded.
3. Smart Motion Sense Technology: The Smart Motion Sense Technology allows the cameras to be activated to capture images only during capsule motion. When the capsule does not move and is stationary, the sensor

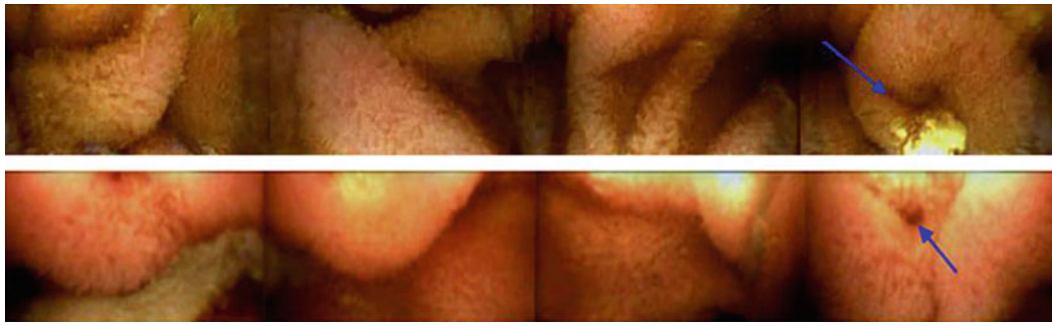


Fig. 2.35 Images of the duodenal papilla detected by CapsoCam SV1. Reprint with permission from Friedrich et al. [132]

goes into the monitoring mode before switching to active mode during motion, which also helps to conserve battery power.

2.6.2 Clinical Studies

Friedrich et al. firstly carried out a prospective dual-center study of CapsoCam in Germany [132]. The study evaluated the feasibility and completeness of small bowel examination together with secondary end points of duodenal papilla detection in 33 patients. Small bowel examination was complete in all procedures. Mean time to pass the small bowel was 258 ± 136 min. The duodenal papilla was identified in 71 % of the patients (Fig. 2.35). No adverse effect was observed. It demonstrated that CapsoCam is a safe and efficient tool in small bowel examination.

To evaluate diagnostic concordance of the PillCam SB2 and CapsoCam capsules in the same patients, a prospective comparative study was conducted in four French referral endoscopy units [133]. Seventy-three patients ingested the two capsules 1 h apart and in a randomized order. Results showed that concordant positive diagnosis was 38.3 % and a negative diagnosis 43.3 %. The kappa value is 0.63, indicating that the concordance was good. In a per lesion analysis, the CapsoCam capsule detected significantly more lesions (108 vs. 85 lesions, $P = 0.001$). Reading time was longer for CapsoCam procedures (32.0 vs. 26.2 min, $P = 0.002$). This study shows comparable efficiency of the CapsoCam and PillCam SB2 capsule systems in terms of diagnostic yield and image.

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