Chapter 5

Capsule Endoscopy: A New Era of Gastrointestinal Endoscopy

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Additional information is available at the end of the chapter

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1. Introduction

Background: Since the discovery of fiber-optic endoscopy to examine upper and lower gastrointestinal tract, diagnosis and therapy of gastrointestinal diseases were revolutionized. However, by these methods, of the small bowel, only the proximal duodenum and distal ileum could be examined. Hence, rest of the small bowel, which is more than four meters in length, remained like a black box. With the discovery of capsule endoscopy in 2000,[1] not only the small bowel became visible to the Gastroenterologist, but also it led to discovery of a new technology by which a swallowed capsule could take images of the gastrointestinal track and send these to a computer using radio-frequency transmitter. The value, safety and acceptability of this novel technology are further documented by the fact that within a year of its discovery (2001), it was approved by US Food and Drug Administration.[2] These led to an era of physiological endoscopy the scope of which is now increasing day by day to include colon and esophageal capsule endoscopy, steerable capsule and therapeutic capsule endoscopy.

Aims and Methods: The aims of this chapter are to, (a) review histotical aspects of this important development in medical science, (b) outline the principles of this technology, (c) review existing evidences on clinical impact of capsule endoscopy and its limitation, (d) project the future of capsule endoscopy. Literature was searched for studies on capsule endoscopy using various electronic search engines to review data on capsule endoscopy in relation to various gastrointestinal diseases.

2. Historical aspects of capsule endoscopy

In science, what is fiction today, may become reality tomorrow. This is amply documented once again by discovery of capsule endoscopy. Capsule endoscopy is a combination of the

device that physicist G. Iddan had developed and that devised by Paul Swain.[2], [3] This was an attempt to reproduce the movie fiction filmed by R. Fleischer in 1966, based on a story by I. Asimov.[2] The first reported use of capsule endoscopy in ten human volunteers was published in 2000 by P. Swain in Nature.[1] The first model of capsule endoscopy was made available by Israeli Company Given Imaging by the name of M2A. Within a year of first publication, the capsule endoscopy was approved by US Food and Drug Administration.[4] Subsequently, it has been widely used throughout the World for diagnosis of small bowel diseases.

3. Small bowel capsule endoscopy: The method

Indications of capsule endoscopy: Indications of capsule endoscopy are summarized in Table 1. Capsule endoscopy is indicated in various small bowel diseases such as obscure gastrointestinal bleeding, celiac disease and other types of malabsorption syndrome, polyposis, Crohn disease etc. Colon capsule and esophageal capsules are used for esophageal and colonic diseases.[5]

Organ evaluated	Diseases or conditions
Small bowel	
	Obscure gastrointestinal bleeding (overt and occult)
	Chronic small bowel diarrhea including celiac disease
	Abnormal small bowel imaging
	Chronic abdominal pain with reasonable suspicion of organic cause in the small intestine
	Evaluation of Crohn disease and its extent
	Visualization of surgical anastomosis
	Suspected small bowel tumor
	Polyposis syndrome
	Portal hypertensive enteropathy and small intestinal varices
Esophagus	
	Barrett esophagus
	Esophageal varices
Colon	
	Colon polyps and colorectal cancer

Table 1. Indications for capsule endoscopy.

The capsule: Most capsules consist of a lens, 4 light emitting diodes, a color camera, 2 batteries, a radiofrequency transmitter and an antenna (Fig. 1).[4] The camera transmits multiple (usually 2/second) images by radiofrequency through sensor to a recorder. Currently, capsule endoscopy system is marketed by different suppliers, which somewhat differ in technology and in length and weight of capsule, number of cameras and antennas, frame rate per second

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and duration of battery life. Table 2 summarizes these variables.[5] Before patient swallows the capsule, 8 skin antennas are taped to the anterior abdominal wall (Fig. 1). The capsule, while moving inside gastrointestinal tract, takes images and sends these through radio-frequency transmitters and the sensor array that are fixed at different locations on the anterior abdominal wall (Fig. 1) to the data logger, which is hang on the patient. After study completion, the images are downloaded to a computer and seen as video images with software. The use of the real time viewer may shorten procedures, as the patient can be disconnected once the cecum is visualized.[6] Recently, softwares have been upgraded with additional capabilities to assist the reader, such as ability to localize the capsule, blood indicator, a multi-viewing feature and quick view modality.

	Pillcam SB2	Pillcam eso	Pillcam colon	Mirocam	Endocapsule	OMOM
Length in mm	26	26	26	24	26	27.9
Weight (g)	3.4	3.4	3.4	3.4	3.8	6
Number of cameras	1	2	2	1	1	1
Frame rate per second	2	18	4-35	3	2	2
Image sensor	CMOS	CMOS	CMOS	CCD	CCD	CCD
Battery life (h)	8	8	8	11	9	8
Antennas	8	3	8	9	8	14
Sleeping mode	No	No	Yes	No	No	No

Abbreviations used: CMOS: complementary metal oxide semiconductor, CCD: charge-coupled device.

Table 2. Comparison of various types of capsules used in capsule endoscopic examinations

Patient preparation: Initially, capsule endoscopy was done without any preparation. However, dark or opaque fluids, food, biliary secretions, air bubbles and mucus can cause incomplete visualization of small bowel mucosa. Slow gastric emptying and small bowel transit may also lead to incomplete examination of the small bowel in 17 to 25% of patients.[7], [8] Several subsequent studies demonstrated that various methods of bowel preparation using osmotic laxatives such as sodium phosphate, polyethylene glycol, and prokinetics such as erythromycin, metoclopramide, tegaserod, domperidone may improve image quality and completeness of examination of small bowel.[8]-[14] Sodium phosphate and polyethylene glycol, which may also shorten gastric and small intestinal transit time, were found to be superior to erythromycin for this purpose.[8], [15, 16] However, a meta-analysis demonstrated that improved visualization of small bowel mucosa during capsule endoscopy with bowel preparation is independent of any effect on transit time.[17] Oral simethicone, which may reduce intra-luminal air bubble, was associated with better mucosal visibility than placebo.[18, 19] Hence, such preparation to improve small bowel visualization and 12-h fasting before the procedure and ingestion only of clear liquids 2-h hours after capsule ingestion are recommended by most capsule endoscopists.

However, the best type of preparation, its dose and time of administration remain to be determined. Concerns have also been raised in relation to use of prokinetics that shorten small bowel transit as this may lead to shorter stay of the capsule at the site of lesions raising possibility of missing the lesions and some workers even suggested that bowel preparation may reduce patients' acceptability of the procedure.[20, 21] Some studies also suggested that keeping the patient in right lateral position may hasten passage of capsule from stomach to small intestine though there are studies to contradict this.[8], [22] It is important to note that typical gastic passage time of the capsule is one hour and small bowel passage time was four hours.[8]

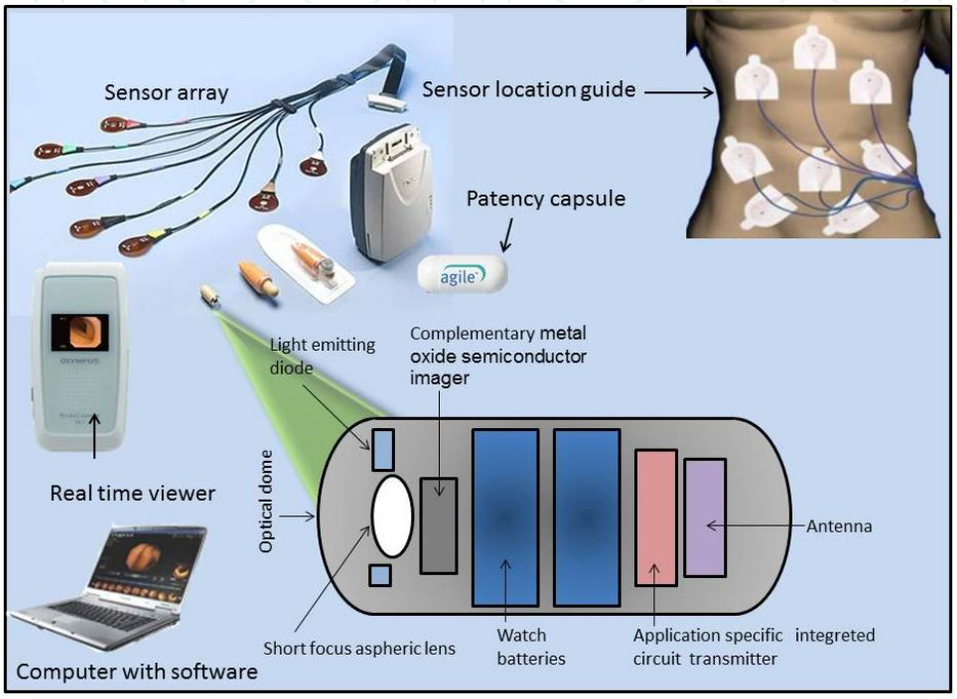

Figure 1. Components of capsule endoscopy system including schematic representation of parts of capsule and sensor location guide.

Clinical impact of capsule endoscopy: Several meta-analyses documented that small bowel capsule endoscopy is superior to other methods of small bowel evaluation such as barium small bowel series, CT enteroclysis, double balloon and single balloon endoscopy.[23], [24] Table 3 summarizes yield of capsule endoscopy in patients with obscure gastrointestinal bleeding in some series published during last decade. Capsule endoscopy detected lesions in small bowel in 45-89% patients with obscure gastrointestinal bleeding. Most series showed that lesions are detected more often in patients with obscure overt than occult gastrointestinal bleeding[25], [26] though a few series did contradict this observation.[27] It has also been shown that if capsule endoscopy is performed early after a bleeding episode, it detects lesion more frequently than if it is done late. In some studies, authors showed that second capsule endoscopy may pick-up some of the lesions missed by first study.[28], [29]

Other diseases of small bowel in which capsule endoscopy is indicated are summarized in Table 1. However, capsule endoscopy done in some of these conditions has limitations. For example,

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in celiac disease,[30] taking biopsy is very important to detect villous atrophy. However, in other conditions such as Crohn disease, small intestinal tumor, polyposis syndrome and portal hypertensive enteropathy and varices, capsule endoscopy is useful.[31]-[36] In endemic areas, hookworm infestation is not uncommonly detected in patients undergoing capsule endoscopy for obsure gastrointestinal bleeding.[27], [37], [38] Fig. 2 (A to F) and 3 (A to F) depict some of these findings on capsule endoscopy. Fig. 4 outlines a practical approach to use various small bowel endoscopic techniques in patients with obscure gastrointestinal bleeding.

Study	Location	Year	Number of patients	Indications	Overall diagnostic yield
Albert JG et. al.[55]	England	2008	285	OGIB	76.8%
Almeida N[56]	Australia	2009	15	Severe overt OGIB	73.3%
Apostolopoulos P[57]	Germany	2006	51	Occult OGIB	57%
Apostolopoulos P[58]	United States	2007	37	Acute mild-to-moderate OGIB	91.9%
Ghoshal UC[27]	India	2011	86	Occult and overt OGIB	74.4%
Ben Soussan E[59]	France	2004	35	OGIB overt (n=17) and occult (n=18)	45.7%
Bresci G[60]	Japan	2005	64	OGIB	62.5%
Calabrese C[61]	Italy	2011	346	OGIB	71%
Carey EJ[26]	Unites States	2007	260	OGIB overt (n=126) and occult (n=134)	53%
Carlo JT[62]	United States	2005	532	532 studies for OGIB	49.3%
Chao CC[63]	China	2005	35	OGIB	89%
Chong AK[64]	Australia	2003	47	OGIB	68%
De Leusse A[65]	Germany	2005	64	64 OGIB (overt 69% and occult 31%)	45%
Gupta R[25]	India	2006	154	OGIB (overt 74, occult 80)	51%
Enns R[66]	Canada	2004	167	167 studies, 88 overt, 79 occult)	50.8%
Estevez E[67]	England	2006	100	OGIB (overt 52, occult 48)	68%
Fireman Z[68]	England	2004	160	OGIB	57.7%
Fireman Z[69]	Israel	2004	293	OGIB	72%

Abbreviations used: OGIB: obscure gastrointestinal bleeding.

Table 3. Summary of some studies on small bowel capsule endoscopy

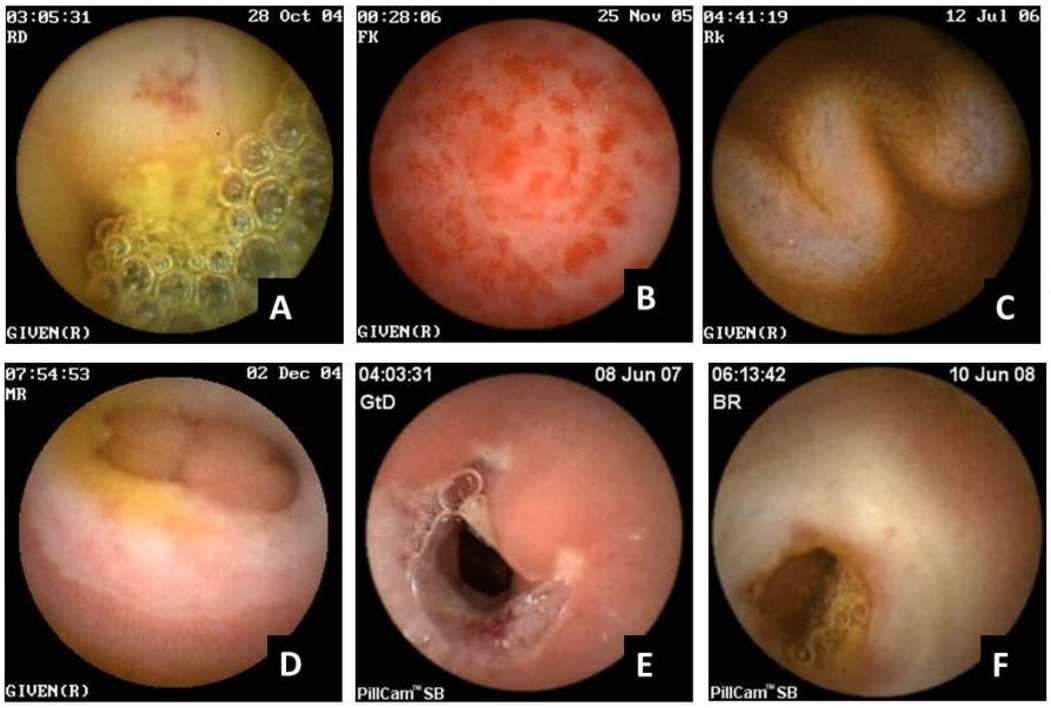

Figure 2. Representative pictures of capsule endoscopy in patients with small bowel angiodysplasia (A), portal hypertensive jejunopathy (B), varices (C), ileocecal ulceration in a patient with intestinal tuberculosis (D), small bowel stricture in a patient with intestinal tuberculosis (E) and in a patient with Crohn disease (F).

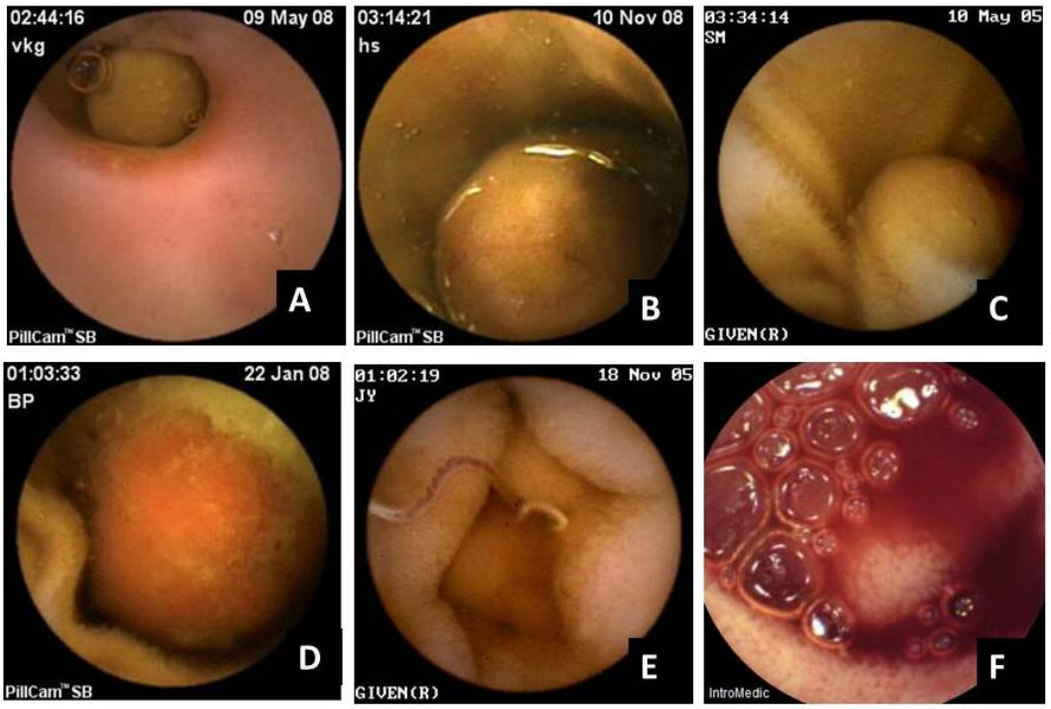

Figure 3. Representative pictures of capsule endoscopy in patients with intestinal stricture due to tuberculosis with enterolith (A), small bowel tumors (B, C, D), hookworm (E) and active bleeding without an identifiable causative lesion (F).

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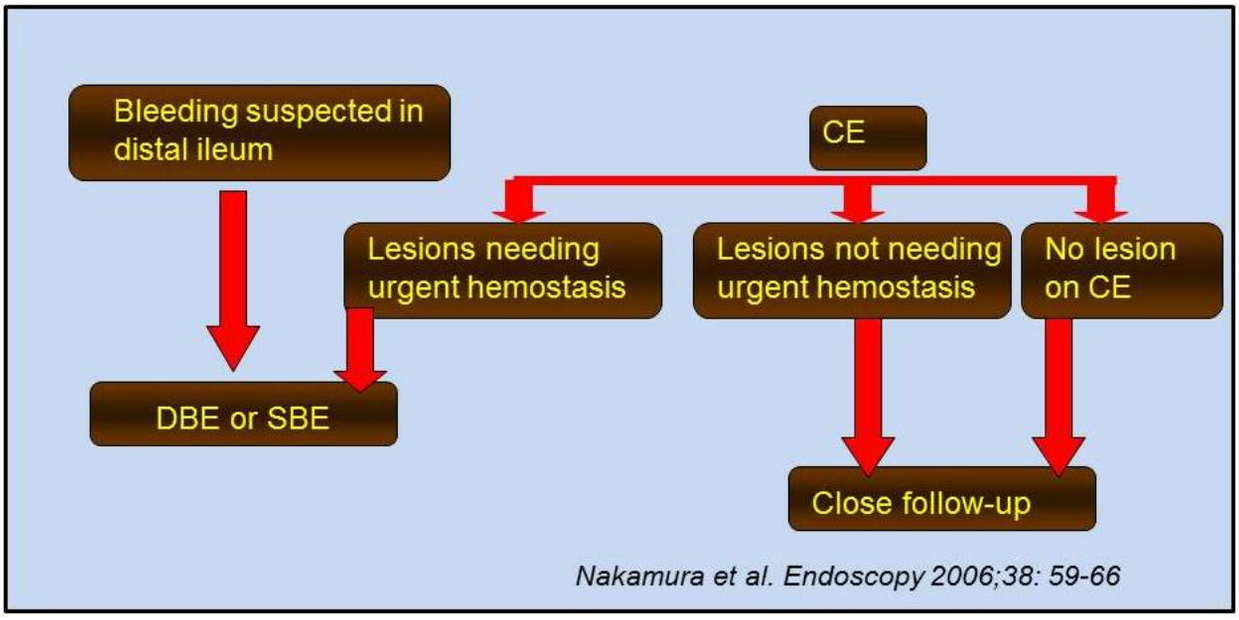

Figure 4. An outline of diagnostic algorithm of patients with obscure gastrointestinal bleeding.

4. Contraindications of capsule endoscopy

Contraindications of capsule endoscopy include suspected intestinal stricture (in which patency capsule may be used to evaluate tightness of the stricture),[39] cardiac pacemaker (recently capsule has been found safe and Capsovision type of capsule is quite safe),[40], [41] gastroparesis and esophageal motility disorders (capsule can be endoscopically delivered in the small bowel).[27] Even if capsule gets retained in stricture, it can be retrieved by single balloon and double balloon enteroscopy. Moreover, precipitation of small bowel obstruction by retained capsule is rare.[27] Pregnancy is also a contraindication to capsule endoscopy.

5. Complications of capsule endoscopy

Capsule retention is considered as a complication of capsule endoscopy. Capsule retention is defined as having a capsule remain in the digestive tract for a minimum of two weeks. Frequency of capsule retention in various studies varies from 0-13%.[42], [43] In a large series of 900 patients undergoing capsule endoscopy for obscure gastrointestinal bleeding, seven (0.77%) had capsule retention.[43] Interestingly, six of these seven patients had retention in spite a normal barium series. Several subsequent studies showed that normal barium does not prevent possible capsule retention.[27] Hence, a barium small bowel series is not indicated before capsule endoscopy. Moreover, yield of small bowel barium series is low to pick up causes of obscure gastrointestinal bleeding.[23] In an attempt to prevent capsule retention, patency capsule has been developed. This self-dissolving capsule (Fig. 1) of size same as

endoscopy capsule, consists of a cellophane-walled cylinder filled with lactose and 10% barium for radio-opaqueness.[42] It is protected by wax plague at one end with a hole that allows influx of small bowel fluid, which dissolves lactose within 5 days. The patency capsule also has a transpoder device inside that helps in its detection using a hand-held scanner placed close to anterior abdominal wall.[42] However, the patency capsule can itself gets impacted in small bowel stricture.[44] Hence, it may not be entirely safe. Moreover, it increases the cost of capsule endoscopy. Hence, it has been suggested that obtaining a good medical history is the best method to avoid capsule retention.[44] Moreover, even if capsule gets retained, which occurs infrequently, precipitation of clinical obstruction is further uncommon. The retained capsule can be retrieved using balloon enteroscopy. Surgical removal, if needed, not only allows retrieving the capsule but also removes the pathology that led to capsule retention.

6. Esophageal and colon capsule endoscopy

Table 2 summarizes technical differences between esophageal and small bowel capsule endoscopy. Initial studies on esophageal capsule endoscopy did not find it very rewarding for detection of esophageal varices and Barrett esophagus in comparison to conventional esophagogastroduodenoscopy.[45], [46] Subsequently, string-controlled esophageal capsule endoscopy was tried to overcome some of the limitations.[47] However, it has to be noted that esophageal capsule endoscopy is expensive as compared to conventional esophagogastroduodenoscopy, will not have therapeutic potential and is not maneuverable. Hence, esophagogastroduodenoscopy remains the modality of choice for screening for Barrett's esophagus.[48]

Table 2 summarizes technical specifications of colon capsule endoscopy. Colon capsule endoscopy may score over conventional colonoscopy as it will reduce patients discomfort and need for sedation. However, its efficacy for colon cancer screening, which is likely to be its major indication,[49] remains to be proved in large studies though a few meta-analysis have been reported.[50], [51] If it is effective, it may be useful to improve compliance with colorectal cancer screening. However, this technology is currently only a diagnostic method, any positive finding requires conventional colonoscopy for tissue sampling or polypectomy. There is currently no video capsule device cleared by the US Food and Drug Administration for dedicated colon imaging. This technology requires more research before it can become clinically applicable as standard of care.

Future of capsule endoscopy: Limitations of the current system of capsule endoscopy include inability to steer the capsule, inability to biopsy lesions, and lack of therapeutic potential. Localization and estimation of size of the lesions using capsule endoscopy is often inaccurate. False negative and false positive diagnoses are other limitations. Moreover, in almost 20% of procedures the capsule does not reach the cecum while it is active. However, advances have been made to overcome these limitations. For example, now some of the capsules can be magnetically steered to pass through gastrointestinal tract.[52] Some capsules also provide ability to real time imaging so that the operator can see while the capsule is passing down the

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GI tract.[6] Works are also ongoing to provide therapeutic potential to the imaging capsules.[53] Several methods are being developed to improve image quality by improvement in the software or by chromoendoscopy (FICE).[54]

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