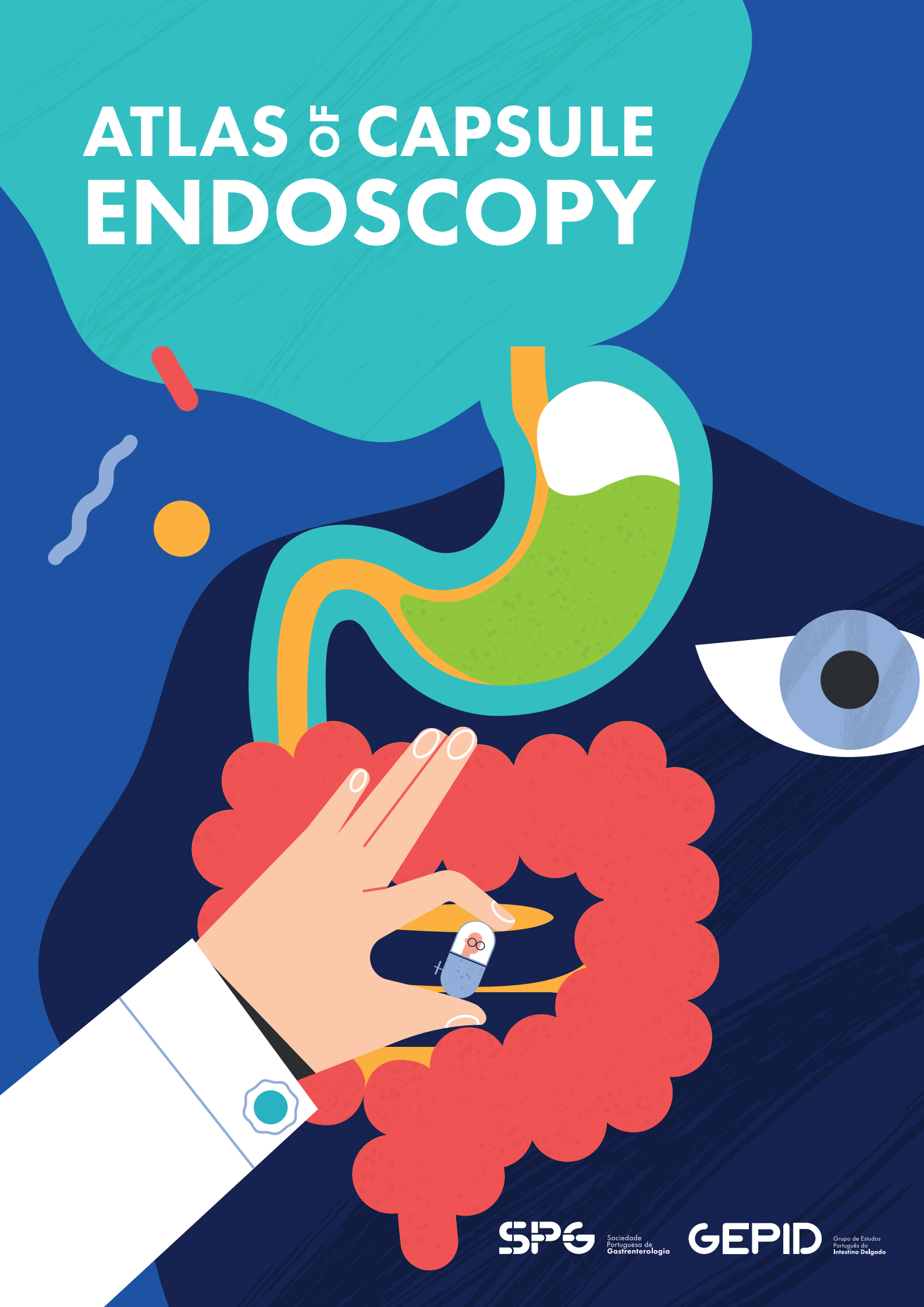
ATLAS OF CAPSULE ENDOSCOPY



SPG Sociedade Portuguesa de Gastrenterologia

GEPID Grupo de Estudos Português do Intestino Delgado

ATLAS OF CAPSULE ENDOSCOPY

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Coordenação:
Sandra Lopes
Bruno Rosa
Ana Patrícia Andrade

Organização:
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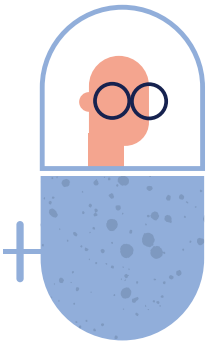

ATLAS OF CAPSULE ENDOSCOPY

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1.1. Technology

For more than 20 years, the small bowel capsule endoscopy (SBCE) has revolutionized access to and investigation of the entire mucosa of the small bowel (SB). It was independently conceptualized by Israeli engineer Gavriel Iddan and London gastroenterologist Paul Swain with clearance by the Food and Drug Administration (FDA) and obtaining CE Mark certification in 2001 (Given Imaging, Yokneam, Israel). Its technological features are packed into a single-use, swallowable and miniaturized device with a resistant and biocompatible polycarbonate coating, making it an undoubtedly non-invasive and well-tolerated diagnostic tool that can be used on an outpatient setting.

SBCE system consists of 4 industry-specific components: a computer with software, a reusable external data recorder, a reusable sensor belt and a capsule itself (Figure 1). The software program displays and analyzes the images recorded on data recorder for review by a physician at a later time. SBCE reading software tools have been developed to help physician's activity, including an advanced A-mode feature for video compilation, a localization and progress indicator of SBCE transit within the gastrointestinal (GI) tract, red pixels identification to facilitate detection of active SB bleeding, a quick-reference atlas of endoscopic images and reporting skills. During the examination, the data recorder is placed next to the patient's abdomen on a shoulder strap and connected to a simplified sensor belt that includes internal sensors. Traditional sensor arrays are no longer used, but can be considered for obese patients. The recorder can be disconnected from the patient after the lifespan of the battery has expired or after the SBCE is excreted, whichever comes first. It is then connected to the computer to download the images. Most recorders integrate an external image viewer to identify the real-time location of SBCE along the SB and determinate whether SBCE has reached the colon and consequently the study can end earlier. After activation, the capsule is swallowed by the patient and captures images as it moves passively, by peristalsis, through the patient's digestive tract. A through-the-scope capsule-loading device (AdvanCE, US Endoscopy, Mentor, Ohio, USA) is available for patients unable to swallow the SBCE, altered anatomy or motility making it difficult for the SBCE to pass into the SB or when the SBCE remains in an intragastric location for too long in real-time viewer. After ingestion, SBCE is usually excreted through patient's feces within 24-48 hours.

The typical SBCE comprises a camera, an optical dome, a light-emitting diode light source, a complementary metal-oxide-semicondutor (CMOS)

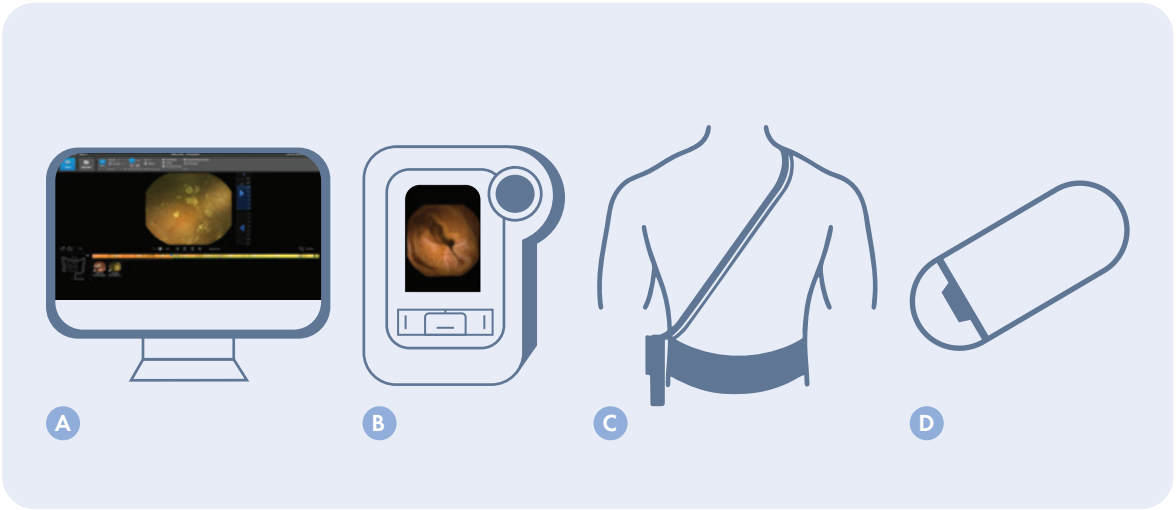

Figure 1
Components of the SBCE system. **A.** Computer with software; **B.** External data recorder; **C.** Sensor belt; **D.** Capsule.

sensor, two internal mercury-free silver-oxide batteries, a compact lens, a visible wireless radiofrequency transmitter and an antenna (Figure 2). The most common mode of transmitting data from the SBCE is via ultra-high frequency band radiofrequency telemetry or in some models via human body communications (Mirocam, Intromedic Seoul, Seoul, South Korea). The ultra-wideband technique allows the wireless transmission of images from an onbody device, transferring big data with low power consumption and features a large bandwidth that supports high-resolution images.

The first wireless SBCE, mouth-to-annus capsule (M2A), had four LEDs, 6-hour battery life, 140-degree view and image capture every 0.5 seconds (Figure 3). As research and technology into capsule endoscopy (CE) have advanced, better wireless and energy-efficient systems allowed the creation of more compact capsules and image processing systems, that improve image transmission, number of images captured per second, image resolution, field of view and battery time to boost the procedure's completion rate. Newer models of SBCE can storage images directly on the device (CapsoCam Plus, CapsoVision, Saratoga, California, USA). This reduces the medical equipment carried by the patient during the examination, but requires retrieving the capsule after it has been excreted by using a magnetic wand to extract the recorded images. The wireless SBCE with a single optical dome is the most widely used capsule for suspected SB pathology recording over

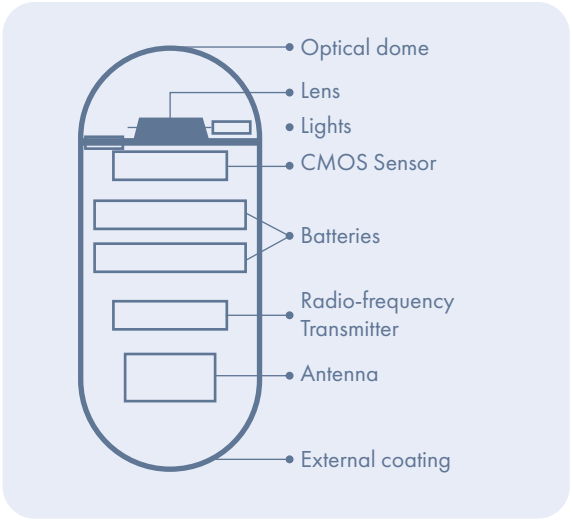

Figure 2.
Structure of the typical SBCE.

50,000 images, with an adaptative frame rate acquisition based on the movement of SBCE, a wide-angle view, an average battery life of 8-12 hours and an excellent image quality. There are currently five SBCEs on the market, which are the most widely used in clinical practice, with no superiority of one capsule over the other in terms of diagnostic yield (DY), image quality and completion rate. Technical differences between commercially available SBCEs (Figure 3) and the corresponding reading software features are listed in Table 1. Recent research has focused on incorporating artificial intelligence (AI) into existing SBCE systems in order to reduce reading

Figure 3
Commercially available SBCE (the first approved and the latest versions). **A.** M2A® (Given Imaging Limited, Yoqneam, Israel); **B.** PillCam® SB3 (Medtronic, Yoqneam, Israel). **C.** EndoCapsule® 10 (Olympus, Tokyo, Japan); **D.** MiroCam® MC1600 (Intromedic, Seoul, South Korea); **E.** OMOM® HD (Jlinshan Science and Technology Group, Chongqing, China); **F.** CapsoCam® Plus (CapsoVision, Cupertino, California, USA). Images extracted from Ciuti G, et al. (2016) and Moglia A, *et al.* (2007).

Table 1.
Differences between the latest versions of commercially available SBCE and reading software specifications.

Technical Features SBCE	PillCam® SB3	EndoCapsule® 10	MiroCam® MC1600	OMOM® HD	CapsoCam® Plus
Manufacturer	Medtronic (Yoqneam, Israel)	Olympus (Optical Co, Tokyo, Japan)	Intromedic (Seoul, South Korea)	Jlinshan Science and Technology Group (Chongqing, China)	CapsoVision (Cupertino, California, USA)
FDA approval (year)	2021	2015	2018		2020
Size (mm)	26x11	26x11	24x11	25x11	31x11
Weight (g)	3.0	3.3	3.2	3.0	4
Cameras	1	1	1	1	4
Image sensor type	CMOS	CCD	CMOS	CMOS	CMOS
Resolution (pixels)	340x340	512x512	320x320	640x480	1152x212
Lens angle (degrees)	156	160	170	172	360
Frame rate (fps)	2-6	2	6	2-10	3-5/camera (20 max)
Number of LEDs	4	4	6	4	16
Automatic light adjustment	Yes	Yes	Yes		Yes
Antennas, n	8 (or sensor belt)	8	9	4 (jacket)	
View direction	Forward	Forward	Forward	Forward	Panoramic (side view only)
Battery life (h)	12	12	11-12	12	15-20
Data transmission/ Data storage	Radiofrequency/ External	Radiofrequency/ External	Human body communication/External	Radiofrequency/ External	-/On-board storage system
Real-time viewing	RAPID real-time	Real-time viewer	MiroView express	Real-time viewer	
Reading software	RAPIDReader software - Full images with 3 reading modes, cloud reading access, server and network, quick view, image viewing (1, 2, 4, 19), semiquantitative function to inflammatory activity (Lewis score), image enhancement (FICE/Blue modes), suspected blood indicator	Endocapsule software - Image compression (software determines), image viewing (1,2,4), automatic brightness control, suspected blood indicator, contrast imaging	MiroView software - Full images with 3 reading modes, cloud reading access, rapid reader, image viewing (1, 2, 4, 19), capsule positioning, suspected bleeding, image enhancement (ALICE)	Vue Smart software - Smartscan (delete redundant images), smartfinding (select abnormalities)	CapsoView software - Image compression (software calculates, reduces images), cloud reading access, image detection of suspected bleeding and landmarks, smart motion-sense technology

SBCE. Small bowel capsule endoscopy; **FDA.** Food and Drug Administration; **CE.** "Conformité Européenne" (European Conformity); **CMOS.** Complementary Metal-Oxide-Semiconductor; **CCD.** Charge-coupled device; **LED.** Light Emitting Diode; **FICE.** Flexible spectral imaging color enhancement; **ALICE.** Augmented live-body image color spectrum enhancement.

times and the likelihood of human error, as well as improving diagnosis in the identification and characterization of lesions in the SB. Technical optimization is under development, such as image-based techniques, including the comparison of anatomical landmarks and AI-driven frame classification, as well as multimodal tracking systems integrating active locomotion and electromagnetic and vision-based data in order to improve high-precision localization, diagnostic accuracy and the ability of obtaining tissue biopsies and carrying out targeted therapy of SBCE. Wireless energy transmission is also being investigated to provide a continuous energy source for SBCE. However, current clinical translation is hindered by complexity, expense, limited availability, and standardization and regulatory challenges.

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1.2. Patient Preparation

Small-bowel capsule endoscopy (SBCE) is a noninvasive diagnostic technique for SB mucosa evaluation, indispensable for the management of multiple GI conditions. Mucosal visualization in SBCE may be compromised by the presence of debris, bubbles, bile, and enteric fluid, decreasing the small bowel visibility quality (SBVQ) and, consequently, the DY. This is especially relevant in the last SB tercile, where visibility tends to decline due to the accumulation of residues, and given that the terminal ileum is a frequent location of SB lesions. There are numerous scores used to evaluate the SBVQ, namely the Brotz score (Figure 1), which ranges from 0 to 10 and comprises five parameters (percentage of mucosa visualized, presence of bubbles, bile staining, residues, overall cleanliness). Clear visualization of the SB through adequate cleansing is essential to optimize the DY of SBCE. In that note, currently, both European and American Endoscopy Societies recommend the use of bowel purgatives before SBCE.

The European Society of Gastrointestinal Endoscopy (ESGE) recommends the ingestion of 2L of

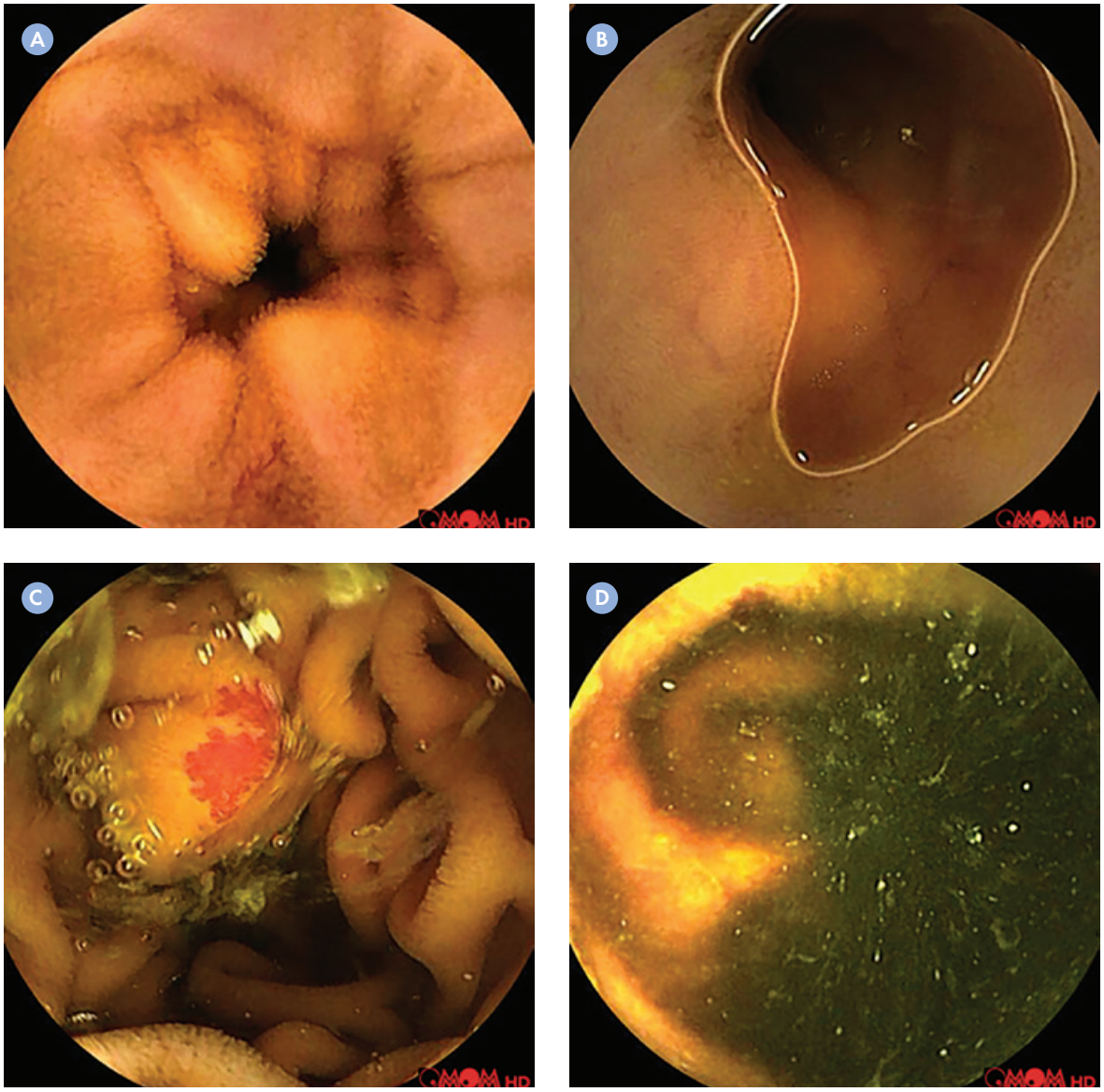

Figure 1
SBCE images showing different grades of SB preparation. In image A the SB mucosa is properly visualized. In image B there is a large bubble. In image C there is a small amount of bile staining but still allowing the identification of one angioectasia. In image D the SB mucosa is not adequately visualized due to the presence of enteric fluid.

polyethylene glycol (PEG), a purgative agent, along with antifoaming agents, since this has been associated with improved SB mucosal visualization. Moreover, split-dose regimens and lower-volume purgative protocols (1L of PEG) showed good results in SB cleansing, offering a better balance between efficacy and tolerability, thus potentially improving patient compliance. Even though booster agents have been routinely used following ingestion for colon capsule endoscopy (CCE), its application in SBCE is less clear.

Several randomized controlled trials (RCT) have investigated different modalities of purgative regimens for SBCE. Two unicentric RCT have demonstrated that taking the purgative after SBCE ingestion can enhance mucosal visibility. Among the two multicentric RCT, only one evaluated the use of intraprocedural preparation, where no differences in DY were observed. Recently, a Portuguese multicenter RCT (PrepRICE) compared four different laxative protocols using 1 L of PEG + sodium ascorbate. Two protocols involved ingestion before the procedure, and two involved ingestion after the capsule reached the duodenum: i] 0.5 L on the morning of the procedure + 0.5 L when the SB was reached, or ii] 1 L only after the SB had been reached. Patients who received intraprocedural purgatives had statistically superior SBVQ,

both globally and across individual terciles, with adequate visualization rates exceeding 90%, compared to 65%-75% in those who received only pre-procedure purgatives. These results are consistent with a recent systematic review and meta-analysis, which demonstrated that administering purgatives closer to the time of capsule ingestion improved the rate of adequate SB cleansing, with even higher rates observed when the purgative was administered after capsule ingestion.

Although most studies failed to demonstrate whether improved mucosal visualization led to an increased DY, Xavier *et al.* described a higher ability to detect angioectasia when purgatives were given after reaching the SB. Reinforcing that data, in PrepRICE, intraprocedural preparations resulted in a shorter SB transit time, higher rates of angiectasia detection and significantly higher DY in the second and third terciles.

In addition to clinical benefits, corroborating an earlier study, the PrepRICE study showed that intraprocedural purgative groups had better overall patient satisfaction, in particular the group that ingested the purgative after the capsule reached the SB, which might enhance compliance.

In summary, bowel preparation seems to be a crucial determinant of SBCE quality, and current evidence supports the use of PEG-based purgatives, possibly with a booster agent, ideally administered interprocedurally. As the field continues to evolve, future studies are expected to refine these strategies and provide tailored protocols that maximize DY while maintaining patient comfort and compliance.

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1.3. Indications

Capsule endoscopy (CE) is the forefront imaging technique to diagnose and assess SB luminal disease in most clinical instances.

While increased accessibility and technological advances may help expand indications for CE, care must be taken to avoid compromising its overall efficacy. In fact, proper indication is the first key performance measure for small-bowel capsule endoscopy (SBCE), with a minimal standard of ≥ 95%. An increase of procedures for non-recommended indication results in a decreased DY, which aggravates SBCE environmental impact and can paradoxically reduce access.

1.3.1. Common Indications

The most frequent indications for SBCE are SB bleeding, iron-deficiency anemia and suspected or diagnosed Crohn's disease (CD). The first two will be approached together for simplicity's sake as etiologies are shared, particularly in the case of occult bleeding where differentiation from iron-deficiency anemia seems many times arbitrary.

1.3.1.1. Small Bowel Bleeding and Iron-deficiency Anemia

In up to a tenth of GI bleeding cases, the culprit can be found in the SB distal to the major papilla. The presentation can be overt, with the presence of melena or hematochezia, or occult when those are absent and iron-deficiency anemia with a suspected GI source is under consideration. In either case, esophagogastroduodenoscopy and ileocolonoscopy are warranted to exclude more common sites of GI bleeding.

The potential findings are numerous and overlap with other differential diagnosis situations, such as chronic diarrhea (think Crohn's disease and celiac disease) and their frequency varies with demographics and comorbidities. Table 1 lists some of these findings which will be further discussed in various chapters of section 2 of this atlas. The most frequent causes in patients younger than 40 years are inflammatory bowel disease (IBD) and Meckel's diverticulum, whilst for older patients angioectasia are more prevalent.

Table 1.
SBCE findings in suspected small-bowel bleeding and iron-deficiency anemia.

Common causes		Rare causes
Age < 40 years	Age > 40 years	
Vascular lesions		
Dieulafoy's lesion	Angioectasia Dieulafoy's lesion	Small-bowel varices Portal hypertensive enteropathy Olser-Weber-Rendu syndrome Hematobilia Aortoenteric fistula Hemossucus pancreaticus
Neoplastic lesions		
Adenocarcinoma Polyposis syndromes Lymphoma GIST Carcinoid tumor	Adenocarcinoma Lymphoma GIST Carcinoid tumor	Kaposi's sarcoma with AIDS
Inflammatory and infectious diseases		
Inflammatory bowel disease Celiac disease	NSAID ulcers	Graft-versus-host disease Parasitic infection
Other findings		
Meckel´s diverticulum		Amyloidosis Blue rubber bleb nevus syndrome Pseudoxanthoma elasticum Malignant atrophic papulosis Ehlers-Danlos syndrome

AIDS, acquired immunodeficiency syndrome; GIST, gastrointestinal stromal tumor; NSAID, nonsteroidal anti-inflammatory drug.
Adapted from Gerson LB. Am J Gastroenterol. 2015.

Overall, when patients are carefully selected, the DY can be higher than 60%, with SBCE having the additional advantage of its established safety. Although lacking therapeutic capabilities, SBCE is very helpful in guiding device-assisted enteroscopy (DAE) need and initial route. Finally, when no significant pathology is found in a high quality SBCE examination, the risk of further bleeding is as low as 19%.

1.3.1.2. Crohn's Disease

It is well established that, albeit CD can affect any segment of the GI tract and beyond, in most instances the terminal ileum and/or the colon are affected. Therefore, SBCE can be considered as an imaging alternative to assess the SB when ileocolonoscopy is insufficient to inform the clinician.

One such scenario is when the diagnosis of CD is still being considered after a negative ileocolonoscopy, where SBCE is the recommended first-line tool to identify compatible lesions in the SB. Even when the diagnosis is established by conventional endoscopy, SBCE can be helpful in assessing disease extent at baseline.

SBCE can also be relevant in patient follow up as a mode of determining response to therapy or post-surgical recurrence, particularly when the affected bowel segment is not easily accessible by endoscopy.

Notwithstanding its excellent safety profile, especially when obstructive symptoms are absent, and favourable DY for luminal disease, other diagnostic tests such as DAE and cross-sectional imaging must be considered as an alternative or complement in each individual case.

In Table 2 we summarize the strengths and weaknesses of SBCE and its alternatives in diagnosis and follow-up.

Table 2.
Small-bowel capsule endoscopy in Crohn's disease.

Strengths	Weaknesses	Alternatives
Suspected Crohn's disease with negative ileocolonoscopy		
Identifies luminal disease out of ileocolonoscopy's reach	Can't assess extraluminal disease and complications Low risk of capsule retention	CT enterography MR enterography Ultrasonography
Minimally invasive	No tissue sampling	DAE
Crohn's disease with compatible ileocolonoscopy (initial diagnosis)		
Higher sensitivity for mucosal disease Location, extent and severity of inflammation	Can't assess extraluminal disease and complications Higher risk of capsule retention	CT enterography MR enterography Ultrasonography
Disease monitoring (post-surgical recurrence, response to therapy)		
High sensitivity form mucosal disease Can evaluate segments inaccessible to endoscopy No ionising radiation	Can't assess extraluminal disease and complications Risk of capsule retention when stenosis or obstructive symptoms are present	MR enterography Ultrasonography

CT, computed tomography. MR, magnetic resonance.

1.3.2. Less Common Indications

SBCE has proven its role in several other indications. Some examples are celiac disease and screening and surveillance of SB neoplasia. However, the total number of examinations for these causes is small given the lower frequency of these pathologies and narrower scope for SBCE use.

1.3.2.1. Celiac Disease

Evidence for celiac disease can sometimes be found in SBCE performed for iron-deficiency anemia or chronic diarrhea as these are manifestations of malabsorption syndromes where celiac disease is of chief importance in the differential diagnosis. However, suspected celiac disease is usually diagnosed

when typical histological findings are present in duodenal biopsies. The reliance in histopathologic for a definite diagnosis limits the role of SBCE to patients with a high pre-test likelihood of the disease (symptomatic patients with compatible serology markers) where conventional upper endoscopy was unable to achieve the diagnosis: either because no diseased mucosa was accessible or because endoscopy was not performed due to patient's refusal or other contraindication.
In the case of established disease, SBCE can be useful in the management in patients who remain symptomatic after sustained gluten-free diet as it can diagnose complications such as ulcerative jejunitis and malignancy and lead to a change in management in 59.3% of cases.

1.3.2.2 Screening and Surveillance of SB Neoplasia

As mentioned above, SB neoplasia can be diagnosed when SBCE is performed for suspected SB bleeding. In some instances where the incidence of these tumors is significantly high, screening and surveillance with SBCE may be warranted. That is the case of some polyposis syndromes that can affect the SB.
Peutz-Jeghers syndrome is an autosomal dominant condition where hamartomatous polyps can be found in the GI tract, namely in the SB. Even though these polyps do not have a malignant potential, their diagnosis, characterization and location are important due to the significant potential morbidity, namely the risk of bleeding, intussusception and other types of obstruction. Therefore, SBCE is recommended, even after surgery.
Familial adenomatous polyposis is another autosomal dominant polyposis syndrome where polyps can be present in the SB. As these are adenomatous, they have the potential to progress to invasive cancer. However, the clinical significance of these polyps is uncertain and it is suggested that screening and surveillance should be decided case-by-case. A possible aid is the consideration of the severity of duodenal polyposis as assessed by the Spigelman classification in duodenoscopy as it correlates with the presence of jejunal and ileal polyps, limiting SBCE to patients with Spigelman stage IV.

1.3.3. Rare and Emergent Indications

SBCE can also be indicated when abnormal SB findings are reported in imaging exams and DAE is not possible. There are several indications for SBCE that result in a low DY, such as chronic diarrhea, iron-deficiency anemia without evidence of GI bleeding and other manifestations of malabsorption. Isolated chronic abdominal pain is specifically discouraged as a justification for SBCE in some guidelines. Many other indications have been dismissed or only appear in case reports.
Notwithstanding, CE is still an evolving field and other uses are being researched, such as pan-intestinal capsule endoscopy (PCE) prior to ileocolonoscopy in suspected mid or lower GI bleeding, assessment of motility through video analysis or incorporation of novel sensors (ultrasound and chemosensors, for example) to augment diagnostic capabilities.
SBCE evaluation of SB mucosa can be helpful in many clinical instances, albeit with varying DY. Adequate knowledge is fundamental to ensure proper prescription and effectiveness of the technique.

Table 3.
Indications for SBCE.

Recommended	Low-yield	Experimental
Suspected SB bleeding	Isolated abdominal pain	Motility assessment
Iron-deficiency anemia	Iron-deficiency anemia without evidence of GI bleeding	PCE in suspected mid-lower GI bleeding
Crohn's disease (diagnosis and follow-up)	Chronic diarrhea	Ultrasound capsule endoscopy
Peutz-Jeghers syndrome and familial adenomatous polyposis	Malabsorption	
Complicated and refractory celiac disease		

GI, gastrointestinal
Adapted from Leighton JA. Gastrointest Endosc. 2022.

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1.4. Contraindications, Complications and Patency Capsule

1.4.1. Contraindications

Small bowel capsule endoscopy (SBCE) is a minimally invasive diagnostic tool for evaluating disorders of the SB and has few contraindications.

1.4.1.1. Small Bowel Obstruction

One of the principal contraindications of SBCE is SB stenosis, as the capsule may fail to pass through the GI tract. The risk of capsule retention (CR) is

greatest in patients with known or suspected strictures, fistulas, or obstructions. If the procedure is essential for a patient at risk for retention, a patency capsule (PC) should be used. This topic will be explained below.

1.4.1.2. Motility and Swallowing Disorders

Dysphagia, gastroparesis and gastric outlet obstruction are considered relative contraindications, as they can often be overcome by performing a gastroscopy (using a capsule delivery device, endoscopic net, or snare) to guide the capsule through the pylorus. The use of a real-time viewer allows detection of complications such as aspiration to the airway tract, as well as esophageal or gastric retention, enabling appropriate actions.

1.4.1.3. Implantable Devices

The presence of a cardiac pacemaker or other implanted electromedical devices is still listed by manufacturers as a contraindication for SBCE. However, technical specifications indicate that the maximum radiofrequency transmission power of most capsules is typically below the safety thresholds for such devices, making SBCE-related device malfunction unlikely.

Several studies explored the electromagnetic interference between SBCE and implantable cardiac devices like pacemakers, implantable cardioverter defibrillators (ICD), and left ventricular assist device (LVAD). Kasia *et al.* retrospectively evaluated 44 patients with pacemakers, ICD and/or LVAD. No device-related complications were reported during the procedure or within the 30-day post-procedure period. However, in a pooled analysis, image loss was noted in five cases (with LVADs) when the capsule was near the device, indicating possible interference with image transmission. Additionally, image artifacts were observed in six cases. Importantly, no adverse cardiac events were reported, and image loss did not compromise the completion rate or DY of SBCE.

In light of this data, the presence of implanted cardiac devices should no longer be seen as a contraindication for SBCE when it is clinically indicated. During the capsule recording, patients with implanted cardiac devices should avoid areas containing instruments/devices generating strong electromagnetic fields (e. g. cardiology units using telemetric monitoring, radiology units, etc.), because they may interfere with capsule data recording.

Supporting these findings, the guidelines from the American Gastroenterological Association and the European Society of Gastrointestinal Endoscopy (ESGE) state that SBCE can be safely performed in patients with pacemakers, ICDs and LVADs.

1.4.1.4. Magnetic Resonance Imaging

There are no data on magnetic resonance compatibility and SBCE so, according to that, the United States Food and Drug Administration (FDA) stated that patients should not undergo magnetic resonance imaging (MRI) until excretion of the capsule. The major concern is the migration of the capsule and potential bowel injury by heat or high forces. Only a few cases reported the use of MRI scan in patients with retained video capsules, and none reported adverse events. Manufacturers also advise against the use of SBCE in patients expected to undergo MRI within one week of capsule ingestion.

1.4.1.5. Pregnancy

During pregnancy, the GI tract is compressed by the enlarging uterus and GI transit is prolonged, factors that may complicate a SBCE procedure. Data on SBCE during pregnancy are limited, and although no adverse events have been documented, there is no information regarding potential risks for the fetus induced by the electromagnetic field generated by the capsule-recorder system.

Although SBCE is contraindicated during pregnancy, it may be considered in life-threatening situations, following thorough discussion with the patient and careful evaluation of potential risks and benefits. The lack of extensive studies on its safety during pregnancy warrants a careful approach.

1.4.1.6 Children

The use of SBCE in the pediatric population is increasing, largely due to the fact that it doesn't involve ionizing radiation, deep sedation or general anesthesia. The primary concern in children is their ability to swallow the capsule and whether it can safely pass through the GI tract. The FDA has approved CE for children aged 2 years and older, and the capsule is generally introduced into the duodenum using a gastroscope in patients under the age of 8.

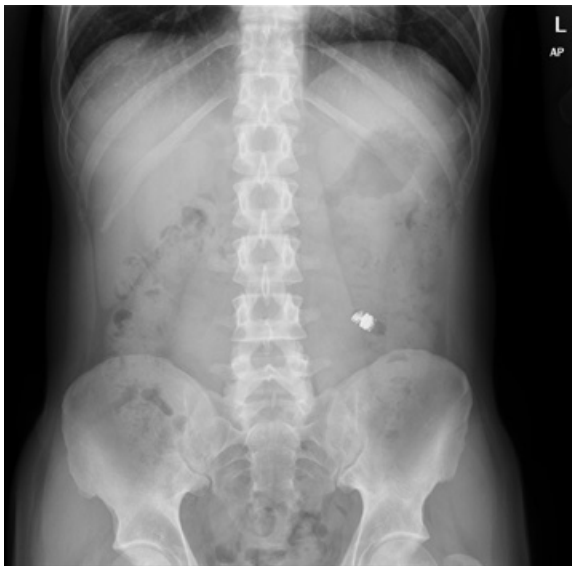

Figure 1
Endoscopic capsule retained visualized on plain X-ray.

1.4.1.7. Others

Additional concerns involve patients with **severe cognitive impairment** or those **unable to tolerate further interventions** that may be necessary (like surgery/DAE). Patients with significant cognitive limitations may struggle to follow pre-procedure instructions, potentially resulting in suboptimal outcomes or increased risk of aspiration.

1.4.2. Complications

Even though it is relatively rare, the most common complication of SBCE is **capsule retention (CR)**, a concept defined by a consensus group during the 2005 International Conference on Capsule Endoscopy. Retention is defined as a capsule remaining in the digestive tract for at least two weeks or permanently remaining in the bowel lumen unless removed surgically or endoscopically or passed following medical therapy. The overall risk of CR is low, approximately 2%, with similar rates observed in patients with suspected CD without obstructive symptoms. In contrast, patients with confirmed CD have higher retention rates, ranging from 5% to 13%. Additional risk factors include known strictures, NSAID-induced enteritis, ischemic enteritis, a history of SB surgery or abdominopelvic radiation, and suspected SB tumors. Patients undergoing SBCE should be instructed to check for excretion of the capsule and to report any symptom that may suggest CR.

In asymptomatic patients with an incomplete SBCE study and no observed capsule excretion after 15 days, the ESGE recommends a plain abdominal X-ray as the preferred method to assess CR as it is widely available, inexpensive, non-invasive and the capsule is readily identifiable (Figure 1). If the capsule recording confirms passage into the colon, additional imaging is unnecessary, as the risk of retention in such cases is negligible.

Unless malignancy is strongly suspected, conservative management is advised in most cases. Effectively, almost 50% of patients with CR will excrete the capsule naturally without any therapy. In some cases, the capsule can remain in the SB for several months without complications. Fernández-Urién *et al.*, showed in a retrospective study, that only two out of 104 CR (1.9%) reported symptomatic bowel obstruction.

ESGE recommends initial conservative or medical management in cases of CR, reserving DAE or surgery for persistent and symptomatic cases. The use of medications, including corticosteroids when appropriate, may promote capsule excretion in 20–30% of patients.

Nonetheless, a prolonged CR can be associated with complications such as bowel obstruction, perforation, or capsule fragmentation, so a shared decision-making is advised after two weeks of retention, as some case reports describe late complications. So, even in asymptomatic patients, leaving the capsule unretrieved for a long time can be harmful. Although there are no studies revealing the best timing for capsule retrieval, it is reasonable to consider retrieving the capsule after 3–6 months.

Other reported complications include **battery failure** and **aspiration** of the capsule **into the trachea** or **bronchial tree**. The latter has been addressed in a systematic literature review, which reported an overall aspiration rate of 0.1%. Although SBCE is generally considered safe in elderly patients, nearly 90% of reported aspiration cases have occurred in this population. So, in elderly patients, with swallowing disorders, a careful evaluation is required, and endoscopic placement can be performed.

1.4.3. Patency Capsule

Before performing SBCE it is crucial to identify those at risk for CR by a careful assessment of the patient's past medical history. In the presence of a high suspicion of stricture, a PC can be used before SBCE. PC has similar dimensions (11.4x 26.4mm)

and the same shape as a standard capsule, but without a camera. It consists of a biodegradable body surrounding a small radiofrequency identification tag with time released biodegradable plugs at both ends (Figure 2).

The passage of the PC within 30 hours suggests the absence of any obstruction that would preclude the use of SBCE. At 30 hours, time-controlled plugs at the ends of the capsule starts to erode, which allows intestinal fluids to dissolve the capsule body. If the PC is retained in the GI tract, it will fully dissolve in 40 to 80 hours (Figure 3). The radiofrequency identification tag is 3x13mm and can be detected by a handheld scanner or, alternatively, identified in plain abdominal radiographs or computed tomography (CT). Nondegradable parts are small enough that they can ultimately pass through tight strictures.

The PC can be swallowed without fasting, bowel cleansing or prokinetics. It is considered safe and can be administrated in adults and children older than 2 years old.

Figure 2
Intact PillCam™ Patency Capsule by Medtronic.

Figure 3
Disintegrated Patency Capsule.

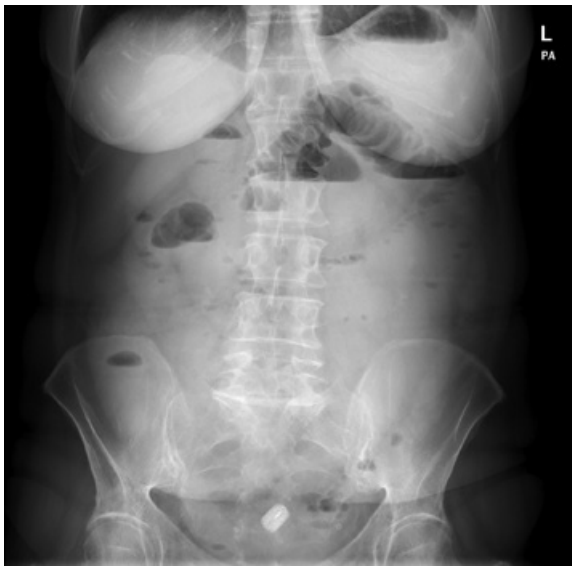

Figure 4
Patency capsule retained visualized on plain X-ray.

The PC test is considered successful when there is evidence of:

1. Natural excretion of an intact PC (both plugs and body) ≤30 hours post-ingestion;
2. An egested intact PC (body and plugs) >30 hours post-ingestion (a disintegrated PC indicates inadequate intestinal patency);
3. Radiological evidence of PC projection to the colon ≤30 hours post-ingestion;
4. No abdominal pain and/or obstructive symptoms during PC passage (abdominal pain and/or obstructive symptoms during PC passage indicate inadequate intestinal patency).

Patients who undergo a PC test are usually requested to identify the excreted capsule in their feces. In cases of unsuccessful identification of physical excretion, the use of radiological confirmation is necessary to demonstrate the PC position. According to that, abdominal CT is the best method for the assessment of the exact place of impaction, with the disadvantages of radiation exposure, especially in the pediatric population. Plain abdominal X-ray can be an alternative. The risk of an adverse event is low, with PC retention being the prominent adverse event (Figure 4). No guidelines are available for the management of PC symptomatic retention, but spontaneous passage is the norm. Use of corticosteroids may reduce the inflammation of stenotic areas. Surgery is rarely required; however, in selected patients it may be the only option for prolonged symptoms or severe obstructive ileus.

According to ESGE guidelines, it is not recommended to offer a PC procedure indiscriminately to all patients undergoing SBCE and should only be offered to patients at increased risk of CR. In the particular case of CD, ESGE 2022 guidelines recommend the use of a PC prior to SBCE in patients with suspected CD and obstructive symptoms and in those with established diagnosis.

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1.5. Reading

Small bowel capsule endoscopy (SBCE) is a non-invasive and easy-to-perform method. However, this technical simplicity, does not equate to ease of image interpretation. The procedure generates an extensive video recording, within which diagnostically relevant findings may be confined to only a few isolated frames. Furthermore, as a passive endoscopic

modality, SBCE offers no real-time control over image acquisition, the operator cannot adjust the angle, focus, or distance of the camera, to optimize visualization. Additionally, it is not possible to clean the lens, aspirate intraluminal debris or perform diagnostic procedures such as biopsies. These inherent limitations may compromise image quality and, in certain cases, potentially reduce the diagnostic accuracy of the modality.

1.5.1. Before the SBCE Reading

A thorough understanding of the patient's clinical context is essential for a balanced evaluation of findings and a formulation of a meaningful conclusion in SBCE. So, before reviewing any SBCE video, clinicians should be well informed of relevant clinical details, including symptoms duration, comorbid conditions, current medications, and clinical presentation.

Given that SBCE interpretation is a time-consuming and often monotonous task requiring sustained attention and focus, it is crucial to allocate a dedicated and uninterrupted time slot for its review. According to most authors, a minimum of 45 to 50 minutes should be devoted to evaluation of each case. Ideally, the video should be reviewed in a single, continuous session, to maintain consistency and diagnostic accuracy. The reading environment should be optimized to promote concentration and minimize distractions.

1.5.2. SBCE Reading

To minimize the risk of misinterpretation, the preview–review–report method can be employed as a structured approach to SBCE analysis.

1.5.2.1. Preview Phase

The preview phase is intended to identify key anatomical landmarks – at a minimum, the first gastric, duodenal and cecal images - to confirm the completeness of SB examination.

Additionally, this phase allows for a rapid assessment of bowel cleansing quality, preliminary location of lesions, and identification of potential areas of interest for more detailed evaluation in the subsequent review phase.

In certain clinical contexts, such as suspected GI bleeding, the preview phase can also provide timely identification of critical findings.

During this stage, the entire video should be reviewed at high speed, either manually at near-maximum speed or through automated fast-reading modes that highlight potentially relevant frames or eliminate redundant sequences.

1.5.2.2. Review Phase

In this phase, the entire video is reviewed, with the primary objective of evaluating the SB in detail and capturing relevant images. These images constitute the case library allowing for efficient access and review when needed.

Although, there are no evidence-based recommendations regarding optimal frame rate for reading SBCE recordings, the most widely accepted recommendation – endorsed by the ESGE – is to review the video at a speed of 10 frames per second in a single-view mode, and up to a maximum of 20 frames per second in double- or multi-view modes. In the proximal SB - the most common site for vascular and neoplastic lesions - the risk of missed lesions is highest due to rapid transit time, angulated anatomy, and the frequent presence of bile or foam, therefore, the reading speed should be reduced to 6-8 frames per second, to optimize lesion detection. Multiframe modes have been shown to improve efficiency without compromising lesion detection accuracy, particularly in cases of diffuse SB pathology.

Automated fast-viewing modes may aid in the detection of diffuse SB pathologies, such as IBD; nevertheless, they have been associated with an unacceptably high miss rate, reported between 6.5% and 12%, predominantly involving isolated single lesions. Consequently, these software tools are not currently recommended as a substitute for conventional manual reading.

Image-enhancement tools, such as digital reprocessing software, are theoretically intended to improve the detection characterization, and definition of clinically relevant lesions. Some authors have suggested that FICE modes 1 and 2 (Fujifilm®) may enhance the visualization of angiectasias, erosions, and ulcers. However, the majority of studies indicates that these enhancements do not significantly improve DY when videos are reviewed by experienced readers. Therefore, routine use is not recommended, as it does not appear to improve lesion detection or characterization, although they may be beneficial during early training stages.

Additionally, automated systems for detecting frames with blood (or red-colored areas) have also been developed and may hold potential in patients with suspected SB bleeding; however, relevant frames can still be overlooked.

Finally, before ending video review, it is strongly recommended to reassess both the stomach and the colon, even though the SBCE is not primarily intended for their evaluation. Notably, lesions in the gastric or colonic mucosa can be detected in 7 to 15% of cases, and in some series, even up to 30%. This becomes especially relevant when no abnormalities are observed in the SB. Furthermore, in cases of negative SB examinations, is advocated, to repeat the entire review either by the same reader or, preferably, by a second, more experienced reader, to minimize the risk of missed lesions and enhance diagnostic confidence.

1.5.2.3. Report Phase (Review)

At this stage, the previously captured images — and occasionally short video clips — are individually re-evaluated. These are compared against other recordings, online databases or in-print libraries. Each selected frame should be described in detail and annotated using standardized classification or scoring methods. It's important to note that capsule movement can be bidirectional, which may result in the same finding appearing in multiple frames.

It is essential to estimate the location, size, and number of findings, as this information is crucial for planning subsequent diagnostic or therapeutic interventions, such as DAE.

The final interpretation and corresponding report are based on the comprehensive assessment of the annotated findings.

1.5.2.4. Report Phase (Post-review – Report Writing)

According to ESGE (2018), there is limited evidence to precisely define what a SBCE report must include. However, a structured format of elements is strongly recommended:

- Patient information: name, demographic details;
- Indication: clinical reason for the exam, brief summary of prior investigations, and relevant medical history;
- Procedure details: typically provided by the software, such as gastric transit time, SB transit time, and total examination duration;
- Bowel preparation protocol used and an assessment of its quality, ideally using a scoring system, even though robust scales are lacking;
- Completeness of the examination: whether the capsule reached the caecum, confirming full visualization of the SB and a complete exam;
- Findings, followed by conclusions and clinical recommendations that reflect the relevance of what was observed.

Finally, standardization is essential, ensuring that each report includes objective, quantifiable data.

1.5.3. Scoring Systems

Whenever possible, scoring and classification systems should be applied, as they offer reproducibility and help standardize terminology. Among the most commonly used are as follows:

- **Lewis Score** (Table 1): Designed to assess inflammatory enteropathy (Crohn's disease, NSAID-related injury, radiation enteritis, or vasculitis), classifying severity into three categories: severe (>790), moderate (135–790), and normal (<135).
- **CECDAI / Niv Score** (Table 2): Capsule Endoscopy Crohn's Disease Activity Index, used to quantify disease severity in Crohn's patients based on capsule findings.
- **Saurin Score** (Table 3): Classifies SB lesions by bleeding potential into P0, P1, or P2 categories.
- **SPICE Score** (Table 4): Smooth Protruding Lesion Index at Capsule Endoscopy, used to differentiate subepithelial lesions from benign bulges.
- **Brotz Scale** (Table 5): In the absence of a universally accepted cleanliness score for SB imaging — all of which remain subjective and operator-dependent — the Brotz and Park scores are the two most frequently used scores, which are also cited in ESGE documents. Given their strong correlation, one should be adopted for routine clinical use.

Table 1.
Lewis Score: parameters and descriptors

Rated for each tertile			
Parameters	**Number**	**Longitudinal extent**	**Descriptors**
Vilous appearance (worst-affected tertile)	Normal = 1	Short segment (≤10%) = 8	Single = 1
	Edematous = 1	Long segment (11-50%) = 12	Patchy = 14
		Whole tertile (>50%) = 20	Diffuse = 17
Ulcer (worst-affected tertile)	None = 0	Short segment (≤10%) = 5	< 1/4 = 9
	Single = 3	Long segment (11-50%) = 10	1/4-1/2 = 12
	Few (2-7) = 5	Whole tertile (>50%) = 15	> 1/2 = 18
	Multiple (≥8) = 10		
Stenosis-rated for whole tertile			
	None = 0	Ulcerated = 24	Traversed =7
	Single = 24	Non ulcerated = 2	Not traversed = 10
	Multiple = 20		

Lewis score: Score of the worst-affected tertile [(villous parameter x extent x descriptor) + (ulcer number x extent x size)] + stenosis score (number x ulcerated x traversed).

Table 2.
CECDAI Score: Capsule endoscopy Crohn's Disease Activity Index (CECDAI) scoring system. The SB is divided into two segments, proximal and distal, and each segment is assessed based on three parameters using a scale from 0 to 3 or 0 to 5: inflammation, disease extent, and the presence of strictures. A subscore for each segment is calculated by multiplying the inflammation score by the extent score and then adding the stricture subscore. The final score is obtained by summing the subscores of the proximal and distal segments.

Segments	A: Inflammation score (0-5)	B: Extent of disease score (0-3)	C: Narrowing (stricture) (0-3)	CECDAI
Proximal	0= none 1=mild to moderate edema/hyperemia/denudation 2=severe edema/hyperemia/denudation 3=bleeding, exudate, aphthae, small ulcer (<0,5cm) 4=moderate ulcer (0,5-2cm), pseudopolyps 5=large ulcer (>2cm)	0=none 1= focal disease (single segment) 2=patchy disease (multiple segments) 3= diffuse disease	0=none 1=single-passed 2=multiple-passed 3=obstruction	A1xB1+C1
Distal	0= none 1=mild to moderate edema/hyperemia/denudation 2=severe edema/hyperemia/denudation 3=bleeding, exudate, aphthae, small ulcer (<0,5cm) 4=moderate ulcer (0,5-2cm), pseudopolyps 5=large ulcer (>2cm)	0=none 1= focal disease (single segment) 2=patchy disease (multiple segments) 3= diffuse disease	0=none 1=single-passed 2=multiple-passed 3=obstruction	A2xB2+C2
				Total= (1)+(2)

Table 3.
Saurin Score: bleeding potential of lesions in SB.

Classification (type)	Examples	Risk of bleeding
P0	Phlebectasia, erythematous patch, diverticula without the presence of blood, nodules without mucosal break	No potential of bleeding
P1	Red spots, small or isolated erosions, possibly diminutive angiectasias	Low/uncertain
P2	Typical angiomas, large ulcerations, tumors, varices	High

Table 4.
Spice Score: Smooth Protruding Lesion Index at Capsule Endoscopy.

Criterion	No	Yes
Ill-defined boundary with the surrounding mucosa	1	0
Diameter larger than its height	1	0
Visible lumen in the frames in wich it appears	0	1
Image of the lesion lasting > 10 minutes	0	1
SPICE > 2 is predictive of subepithelial lesion.		

Table 5.
Brotz Score.

Quantitative index
Elements
Percentage of mucosa visualized (<80%=0; 80-89%=1; ≥90%=2)
Fluid and debris (severe=0; moderate=1; minimal/mild=2)
Bubble abundance (severe=0; moderate=1; minimal/mild=2)
Bile/chyme staining (severe=0; moderate=1; minimal/mild=2)
Brighteness reduction (severe=0; moderate=1; minimal/mild=2)
Total score=0-10; higher score=superior cleansing
Qualitative evaluation
Excellent: visualization of ≥ 90% of mucosa; no or minimal fluid and debris, bubbles and bile/chyme staining; no or minimal reduction of brightness.
Good: visualization of ≥ 90% of mucosa; mild fluid and debris, bubbles and bile/chyme staining; mildly reduced brightness.
Fair: visualization of < 90% of mucosa; moderate fluid and debris, bubbles, and bile/chyme staining; moderately reduced brighteness.
Poor: visualization of < 80% of mucosa; excessive fluid and debris, bubbles, and bile/chyme staining; severely reduced brighteness.
Overall adequacy assessment
Adequate
Inadequate

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1.6. Normal Anatomy

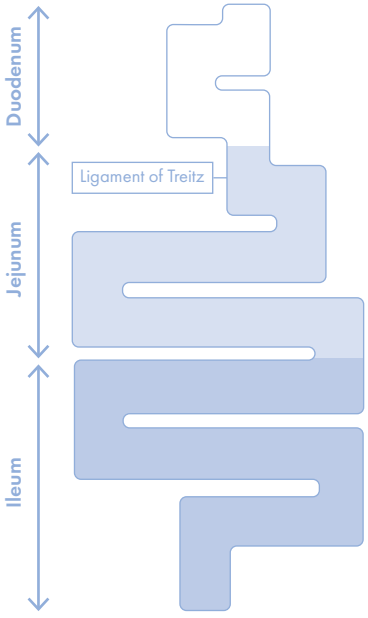
1.6.1. Anatomy of the Small Bowel

The SB is the digestive tube located between the stomach and the colon, with a total length of 6 to 7 meters, from the pylorus to the ileocecal valve. The SB is about five times longer than the large bowel but has a smaller diameter, which is why it is called 'small'. This segment of the digestive tract is divided into 3 parts: the duodenum, jejunum and ileum. The main characteristics and functions of each segment are shown in Figure 1. The predominant cell type of the epithelium is the enterocyte with absorption capability due to microvilli on the luminal surface, conferring a striated brush border appearance. The plicae circulares (or Kerckring's valves), villi and microvilli together increase the absorptive surface of the small bowel by 600-fold. The remaining epithelium cells include enteroendocrine cells, Paneth cells, goblet cells, tuft cells, cup cells, M cells, and lymphocytes and mast cells within the lamina propria, representing the largest immunoprotective tissue of the human body (gut-associated lymphoid tissue). The arterial circulation of the SB is mainly determined by the superior mesenteric artery, and the duodenum is also supplied by the gastroduodenal artery. Venous drainage is mainly via the superior mesenteric vein into the portal system. The enteric nervous system is one of the three divisions of autonomic nervous system and plays a critical role in gut motility, secretion and immune function.

The ligament of Treitz is a thin muscle that formally separates the duodenum from the jejunum, while the jejunum and ileum, although structurally different, do not have a precise division. The subdivision of the SB based on endoscopic findings in small bowel capsule endoscopy (SBCE) is quite difficult. The main endoscopic findings in SBCE to distinguish the different segments of the SB are specified in Figure 2. In clinical practice, the location estimation is based on the time elapsed between the pylorus and the first cecal image, subdivided into 3 equal parts (tertiles): the proximal third, middle third and distal third of the SB. The duodenum corresponds to the beginning of the 1st tertile and the terminal ileum to the end of the 3rd tertile.

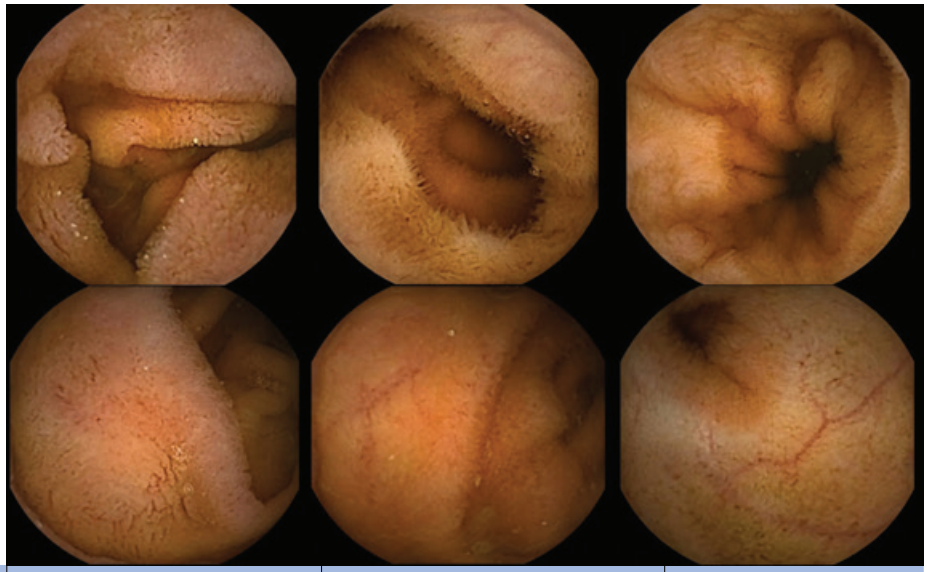
1.6.2. Normal Findings

The interpretation of SBCE images is only based on the analysis of the captured images. Unlike conventional flexible endoscopy, image optimization is not possible due to the lack of control over the



Features	Anatomic structures	Function
• 4 Sections (superior, descending, horizontal and ascending) • Retroperitoneal (except first section or duodenal bulb) • 0.25-0.30 m	First section or duodenal bulb: • Brunner's hyperplasia or foci of heterotopic gastric mucosa Second or descending section: • Major papilla (entrance for the bile and pancreatic ducts) • Minor papilla (entrance for the accessory pancreatic ducts)	Digestion of fats, proteins, and carbohydrates (Mix chyme with bile and pancreatic enzymes)
• 2.5 m		Food digestion and absorption of nutrients and water from food
• 3.5 m	• Lymphoid follicules or Peyer's patches (particularly in children and young adult)	Food digestion and vitamin B12 and water absorption

Figure 1
Main characteristics and functions of each segment of the SB (duodenum, jejunum and ileum).



Features	Duodenum	Jejunum	Ileum
Plicae circulares on the luminal surface	++ (absent of circular folds in the first section)	+++ (more prominent and closely spaced in upward direction)	+ (circular folds less developed and more widely separated, being totally absent in the terminal ileum)
Prominence of mucosal folds/ Density and length of villi	++	+++	+
Lymphoid tissue	+	++	+++ (Lymphoid follicles or Peyer's patches)
Wall thickness/Lumen diameter	++	+++	+
Visibility of mucosal and submucosal blood vessels	++	+	+++

Figure 2
Endoscopic findings of different segments of the SB in the SBCE.

movement or direction of the view, as well as the absence of tools such as aspiration or washing. Thus, the distinction between normal and abnormal is sometimes difficult, and diagnostic interpretation should take into account specific characteristics of this diagnostic modality, such as image magnification, and therefore small innocent findings should not be overestimated. The use of a standardized terminology to describe SB findings is essential to optimize the diagnosis and management of patients, such as the international Delphi consensus statement on the nomenclature and semantic description of vascular lesions in SBCE.

1.6.2.1. Normal Variants and Non-Pathological Findings

Some normal findings should not be misdiagnosed as a polyp or a mass lesion. The **retrograde view of the pylorus** appears as a circular ridge with flat pyloric mucosa surrounded by duodenal mucosa covered with villi (Figure 3A). The **major papilla** or **papilla of Vater** is not always visible in the SBCE due to the absence of luminal distension, the presence of luminal content such as bile or its rapid movement in the most proximal segment of the SB. This structure is visible in 10% of forward viewing capsules and up to 70% of panoramic

viewing capsules, appearing as a nodular lesion with a central pinpoint or slitlike opening, sometimes with bile drainage (Figure 3B). Visualization time ranges from seconds to minutes after pylorus passage, but can rarely reach hours if there is a prolonged stay of the capsule in the duodenum or retroperistalsis. The minor papilla, located immediately proximal to the papilla of Vater, is even more rarely seen. **SB nodules**, single or multiple, may represent non-pathological findings as Brunner's hyperplasia or heterotopia of the gastric mucosa (in the duodenal bulb) or lymphoid tissue forming Peyer's patches (in the terminal ileum) (Figure 3C).

1.6.2.2. Artifacts

Several artifacts should be recognized and not misdiagnosis as pathological findings, such as collapsed intestinal lumen, especially during rapid transit; observation of mucosa through an **air bubble** (Figure 3D); translucent lines at the **air/water interface** in capsules with forward light sources (Figure 3D); or the presence of **fluid or luminal debris deposited on the mucosa** (Figure 3E). Analysis of moving video images is useful to recognize these findings.

1.6.2.3. Incidental Findings

Incidental findings are common and since they do not represent abnormalities of clinical significance, they should not be misdiagnosis either. Lymphangiectasias appear as a yellowish-white speckling in the intestinal villi caused by the accumulation of chylomicrons with obstruction of the dilated lymphatic capillaries and may be single (Figure 3F) or can aggregate into a polypoid **lymphangiectasia** (Figure 3G). Diffuse lymphangiectasia can be seen in Waldmann's disease. **Xanthomas** or chylous cysts result from the accumulation of cholesterol-rich foamy macrophages within cystic dilations of large lymphatic vessels in the mucosa or submucosa of the SB, giving rise to a flat or pseudopolypoid yellowish-white appearance, with the submucosal vessels often clearly visible (Figure 3H). **Phlebectasias** or small venous ectasias are frequent findings with the appearance of flat bluish vascular dilatations of different sizes, isolated or multiple (Figure 3I). Protruding or large lesions with an irregular or eroded surface may be pathological (a potential source of bleeding) or belong to the Blue rubber bleb nevus syndrome. **Innocent mucosal bulges** can be difficult to assess in the SBCE

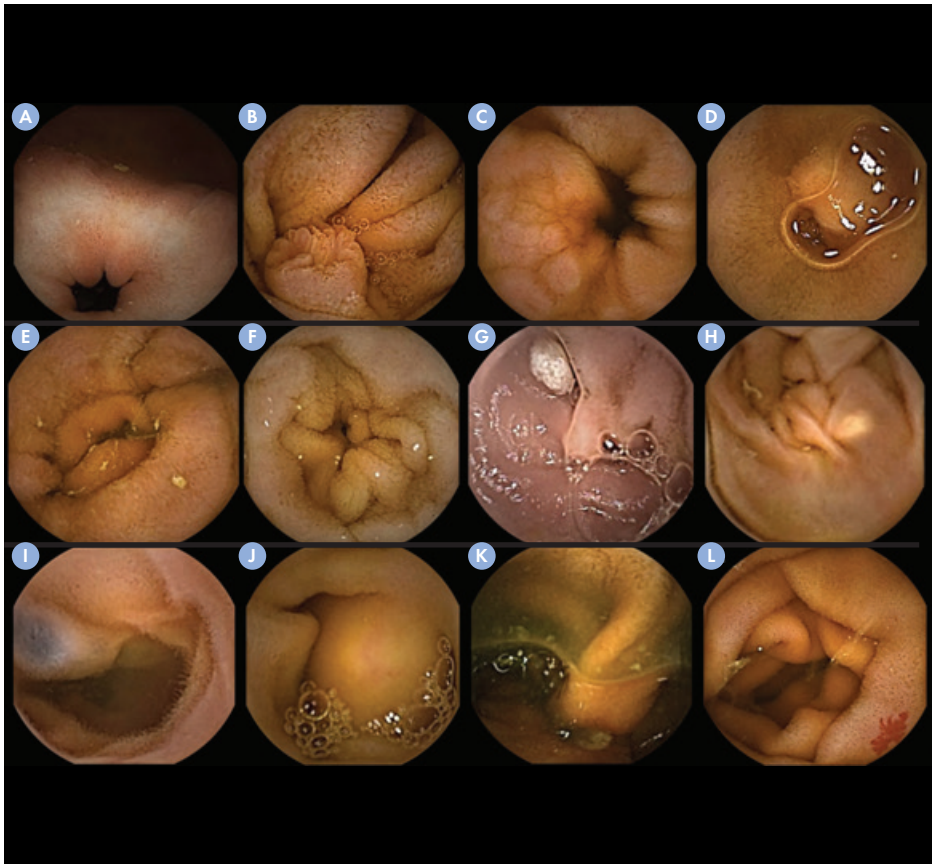


Figure 3A-L
Normal variants, artifacts and incidental findings of the SB, including retrograde view of the pylorus (**A**), papilla de Vater (**B**), Peyer's patches (**C**), air/water interface of a large air bubble (**D**), deposit of debris on the mucosa (**E**), lymphangiectasias (**F**), polypoid lymphangiectasia (**G**), xanthoma (**H**), phlebectasia (**I**), innocent mucosal bulge (**J**), ulcerated Meckel's diverticulum (**K**) and angiectasia (**L**).

(Figure 3J), especially in the absence of breaks in the overlying mucosa. Although not yet integrated into the SBCE reading software, endoscopic scores, as SPICE or Shyung scores, or three-dimensional reconstruction can help in the differentiation between pseudolesions and malignant subepithelial masses. **Acquired diverticula** of the SB are pseudodiverticula of the mesenteric surface of the intestinal wall and can occur anywhere along the SB, being most common in the second portion of the duodenum, adjacent to the major papilla. They appear as a double lumen, single or multiple, and are usually asymptomatic, although they can be complicated by bleeding, inflammation, or perforation. Acquired diverticula are rarely found in the ileum and must be differentiated from congenital Meckel's diverticulum, located on the antimesenteric side approximately 50 to 90 cm proximal to the ileocecal valve. When they contain ectopic gastric mucosa or large vessels at the edge of the opening, they can ulcerate, complicating with painless intestinal bleeding (Figure 3K). **Red spots or dots** are mucosal changes with no linear or vessel appearance, ill-defined limits and often <2 mm in size, considered to have an absent or low bleeding potential (Saurin P0/P1) and therefore with no clinical significance. These should be distinguished from angiectasias (Figure 3L), dilations of capillaries in the mucosa or submucosa of the SB and potential cause of small bowel bleeding (Saurin P2). They appear as single or multiple bright-red flat lesions, clearly demarcated, usually ≥2 mm, with well-circumscribed fernlike margins. Virtual chromoendoscopy, such as flexible spectral imaging color enhancement (FICE) setting 1 (wavelengths: red 595 nm, green 540 nm, blue 535 nm), can occasionally be useful for delineating and detecting vascular lesions, although its routine use is not indicated in European guidelines.

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2

Small Bowel Pathology

2.1. Vascular Lesions

• Miguel Mascarenhas-Saraiva, *ManopH - Laboratório de Endoscopia e Motilidade Digestiva - Porto*

• Rolando Pinho, *Serviço de Gastroenterologia, ULS de Gaia/Espinho*

2.2. Neoplastic Lesions

• Pedro Mesquita, Ana Ponte, *Serviço Gastrenterologia da ULS de Gaia/Espinho*

2.3. Inflammatory and Infectious Diseases

• Ana Isabel Ferreira, Cláudia Macedo, José Cotter, *Gastrenterologia, ULS do Alto Ave*

2.4. Malabsorption Syndromes

• Ana Teresa Ferreira, Marta Salgado, *Serviço de Gastrenterologia, ULS de Santo António*

• Catarina Araújo, Joana Frias, Hélder Cardoso, *Serviço de Gastrenterologia, ULS São João*

2.5. Other Findings

• Ana Rita Gonçalves, *Serviço de Gastrenterologia, ULS Santa Maria*

2.1. Vascular Lesions

2.1.1. Introduction

Vascular lesions of the gastrointestinal (GI) tract are a major cause of GI hemorrhage. These lesions can be solitary or multiple. They can also represent isolated abnormalities or be part of a syndrome or systemic disorder.

SB vascular lesions constitute the most frequent cause of SB bleeding in patients with negative upper and lower endoscopy.

CE has revolutionized the evaluation of these patients, offering a non-invasive, high-yield method to detect and characterize a wide spectrum of vascular abnormalities — including angioectasias, telangiectasias, varices, hemangiomas, and rare syndromic lesions. When performed early — ideally within 48 hours of overt bleeding — CE achieves higher DY, improved grading of hemorrhagic risk, and more effective therapeutic planning.

Its integration with validated scoring systems (e.g., Saurin, RHEMITT) and risk stratification tools allows for structured interpretation and consistent decision-making. The growing role of AI, particularly for vascular lesion detection and triage, further enhances reading efficiency and accuracy, supporting both experienced and less-experienced capsule readers.

Despite its limitations, CE remains central in the modern approach to suspected SB bleeding, especially in identifying clinically relevant vascular lesions that may otherwise remain undiagnosed. Optimal patient outcomes depend on a multimodal strategy that combines early diagnosis, individualized risk assessment, and — when indicated — endoscopic, medical, or surgical intervention.

2.1.2. Classification of Vascular Lesions: Congenital vs Acquired

Vascular lesions of the GI tract can be classified into congenital and acquired types, based on their pathophysiology, distribution, and clinical presentation.

Congenital lesions include telangiectasias associated with hereditary hemorrhagic telangiectasia (HHT), hemangiomas (capillary, cavernous, or mixed), and congenital arteriovenous malformations. They may also occur in the context of syndromic disorders such as blue rubber bleb nevus syndrome, Turner syndrome, or other systemic vascular malformation syndromes. These lesions tend to appear earlier in life and may be multiple or diffuse. Because they are often refractory to local endoscopic therapy, management typically requires a multidisciplinary approach involving medical, surgical, or interventional radiologic strategies.

In contrast, **acquired vascular lesions** are more frequent in older patients and are often linked to chronic comorbidities. These include angioectasias (previously termed "angiodysplasias"), phlebectasias, radiation-induced vascular injury, portal hypertensive enteropathy, hemangiomas, and iatrogenic arteriovenous malformations — such as those occurring at surgical anastomoses or as neovascular changes after mucosal injury.

2.1.3. Type of Vascular Lesions

2.1.3.1 Hereditary Hemorrhagic Telangiectasia (Osler-Weber-Rendu Disease)

Hereditary hemorrhagic telangiectasia is an autosomal dominant vascular disorder characterized by mucocutaneous telangiectasias and arteriovenous malformations (AVMs) affecting the skin, mucosa, and visceral organs.

The lesions typically present early in life, with recurrent epistaxis in childhood being the most common initial manifestation. By the age of 10, approximately 50% of patients experience GI bleeding, although severe hemorrhage is uncommon before the fourth decade. Bleeding most frequently presents as melena, while hematochezia and hematemesis are less frequent.

GI telangiectasias may affect the colon, but are more commonly found in the stomach (Figure 1) and SB, where they are also more likely to result in clinically significant bleeding.

CE has emerged as the preferred method for evaluating SB involvement in HHT. Studies have reported a prevalence of up to 56% for SB telangiectasias in HHT patients undergoing CE. These lesions may be multiple, scattered, and of variable bleeding potential. Although gastroscopy may be normal, CE provides a non-invasive means of detecting small intestinal bleeding sources and monitoring disease burden over time.

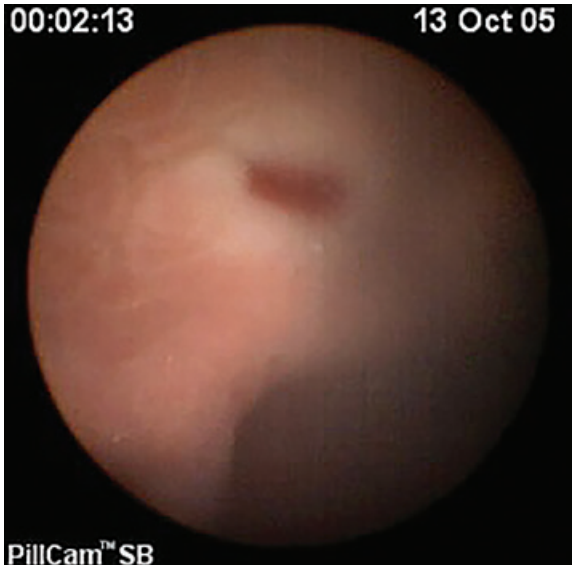

Figure 1
Gastric lesion observed on CE in a patient with hereditary hemorrhagic telangiectasia (HHT). The image reveals a flat, clearly demarcated, reddish mucosal abnormality in the gastric body, consistent with a telangiectatic lesion.

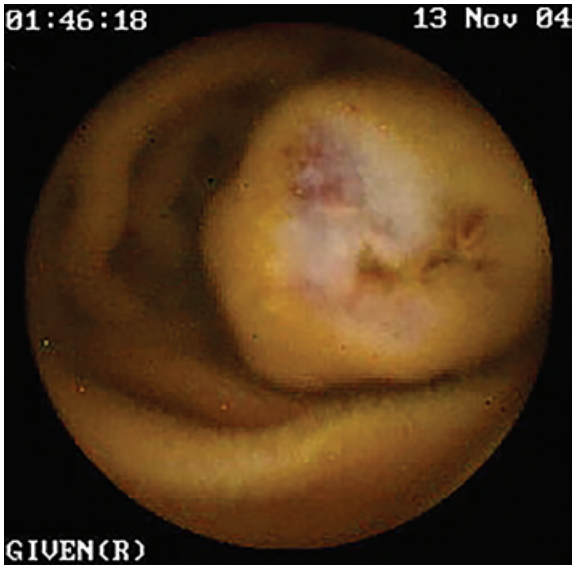

Figure 2
CE image showing a typical SB lesion in a patient with Blue Rubber Bleb Nevus Syndrome (BRBNS). The lesion appears as a bluish-red, nodular, angiomatous protrusion with a slightly lobulated surface and central ulceration, consistent with a venous malformation. Courtesy of Prof. Luís Lopes.

The role of CE in routine surveillance remains under investigation, but it is particularly useful in patients with unexplained iron-deficiency anemia or recurrent GI bleeding without identifiable source on standard endoscopy.

2.1.3.2 Blue Rubber Bleb Nevus Syndrome

Blue Rubber Bleb Nevus Syndrome (BRBNS) is a rare, sporadic vascular disorder characterized by venous malformations involving the skin and GI tract, most commonly affecting the SB. Cutaneous lesions are typically bluish, compressible nodules, while GI manifestations — particularly in the jejunum and ileum — may include occult bleeding, overt hemorrhage, or chronic iron-deficiency anemia.

The condition is associated with somatic mutations in the TEK (TIE2) gene, resulting in dilated venous channels lacking smooth muscle support, which predisposes them to bleeding. CE is the preferred modality for detecting and mapping intestinal involvement. Lesions appear as bluish-red, nodular, angiomatous protrusions (Figure 2), sometimes with a central depression or superficial ulceration. They are venous in nature and segmentally distributed, distinguishing them from the flat, clustered appearance of angioectasias.

Treatment options vary depending on severity and distribution. These include iron supplementation, endoscopic therapy (e.g., argon plasma coagulation, clipping, resection), surgical intervention for localized or refractory lesions, and medical therapy such as sirolimus or propranolol in diffuse or recurrent bleeding cases. CE remains essential for diagnosis, longitudinal assessment, and planning of therapeutic interventions.

2.1.3.3 Vascular Ectasias (Angioectasias)

Vascular ectasias — also referred to as angioectasias — are often mischaracterized as arteriovenous malformations, although they lack direct arterial-to-venous communication. Histologically, they consist of dilated, thin-walled capillaries located in the mucosa or submucosa of the GI tract and are considered the most common vascular abnormality of the GI tract, especially in elderly patients.

Their prevalence increases with age and is frequently associated with comorbidities such as aortic stenosis, chronic kidney disease requiring hemodialysis, prior abdominal radiation, and von Willebrand's disease — particularly in the context of Heyde's syndrome. While initially described in the cecum and ascending colon, CE has revealed that SB angioectasias are equally or even more prevalent in cases of obscure or recurrent GI bleeding. These lesions may be solitary or multiple, segmentally distributed, and often occur in more than one region of the GI tract.

Attributing chronic blood loss to angioectasias can be challenging, particularly when there is no active bleeding or stigmata visible during capsule examination. Typically, bleeding is low-grade and intermittent,

although massive hemorrhage may occur. In over 90% of cases, bleeding stops spontaneously, yet the recurrence rate remains high — particularly in patients with multiple lesions or significant comorbidities.

On CE, angioectasias may appear as punctate, bright-red spots (Figures 3, 4), larger ectatic lesions with central vessels and feathery extensions (Figures 5-8), or spider-like vascular formations (Figure 9). Signs of recent bleeding may include the presence of an adherent fibrin clot (Figure 10), or fresh blood (Figure 11). However, interpretation can be confused by look-alike features such as petechiae, blood droplets (Figure 12), mucosal irritation, or minor erosions. Capillary dilatations, especially in the ileum, are common and should not be misclassified as angioectasias.

Image enhancement technologies, such as FICE (Flexible Spectral Imaging Color Enhancement) - Figure 4, blue light filters (Figure 13), can improve the visualization of subtle vascular lesions and enhance diagnostic confidence, particularly in equivocal cases.

Therapeutic management depends on the number, location, and clinical impact of the lesions. Solitary or few angioectasias can be treated endoscopically using push or DAE with argon plasma coagulation (APC), bipolar coagulation, or clipping. However, in patients with multifocal or disseminated angioectasias, endoscopic treatment is often incomplete or technically unfeasible.

Pharmacologic therapy may be considered in these cases. Although hormonal therapy with estrogen and progesterone was historically used, randomized trials failed to demonstrate consistent efficacy. Somatostatin analogues such as octreotide or lanreotide have been used off-label and shown to reduce transfusion requirements in selected patients. More recently, antiangiogenic treatment with thalidomide has demonstrated promise in reducing bleeding frequency and transfusion dependence, although its adverse effect profile, particularly neurotoxicity, limits widespread use.

2.1.3.4 Phlebectasias

Venous ectasias — or phlebectasias — are relatively common findings during CE, typically presenting as bluish, flat or minimally elevated vascular dilations within the mucosa or submucosa of the SB.

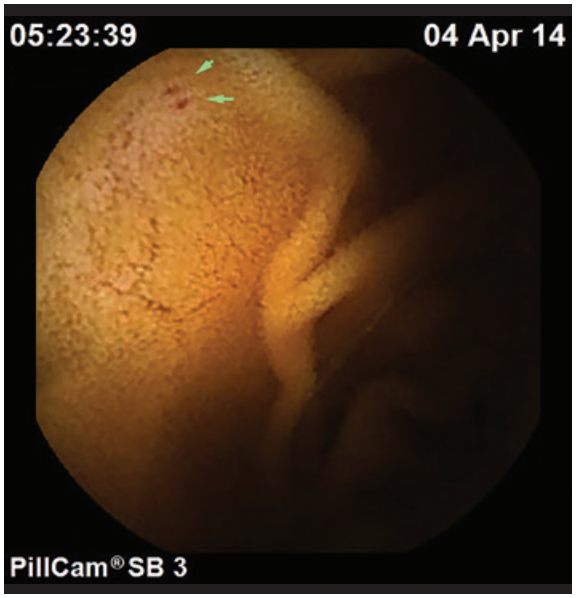

Figure 3
CE image from a PillCam® SB3 study shows a small, well-demarcated red lesion in the SB mucosa (arrows), consistent with a punctate angiectasia. The lesion appears flat and measures less than 1 mm in diameter. It is characterized by a bright red spot without central vessel prominence or surrounding vascular changes. This finding aligns with the Saurin classification P1 (uncertain hemorrhagic potential) and fits the International Delphi description of "red dot" or "diminutive angiectasia." While often incidental, such lesions may represent a source of occult bleeding, especially in the presence of multiple similar findings or anemia.

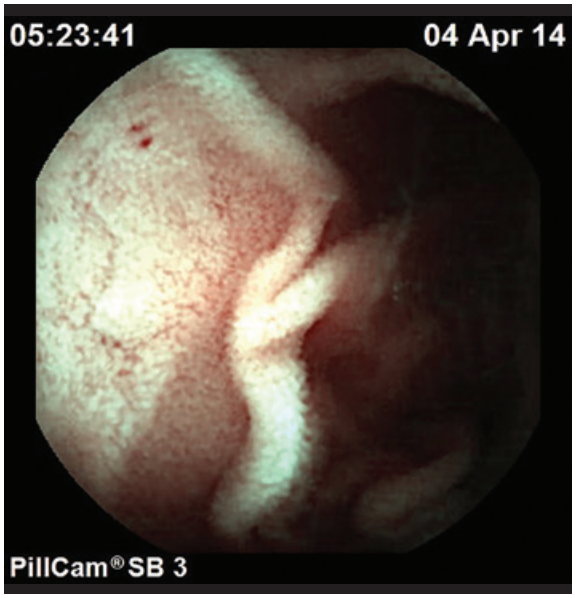

Figure 4
Same image as in figure 3, using FICE for improved delineation of the lesions.

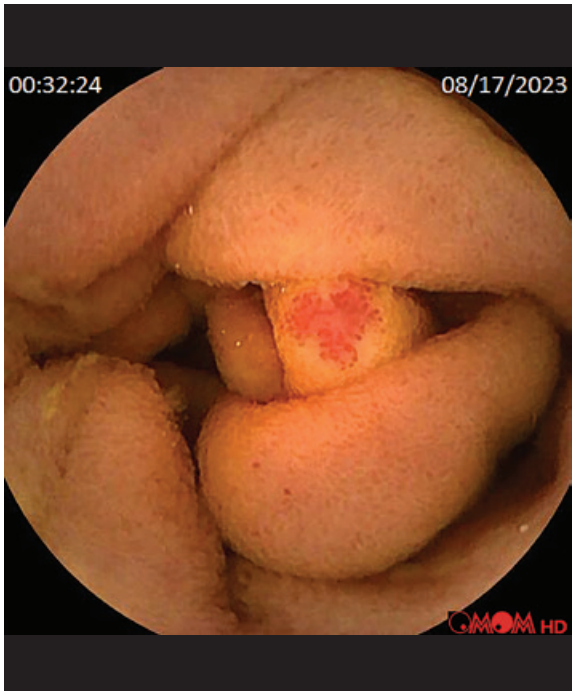

Figure 5
CE image from an OMOM HD capsule showing a flat, well-defined erythematous lesion with radiating, punctate capillaries, typical of vascular ectasia.

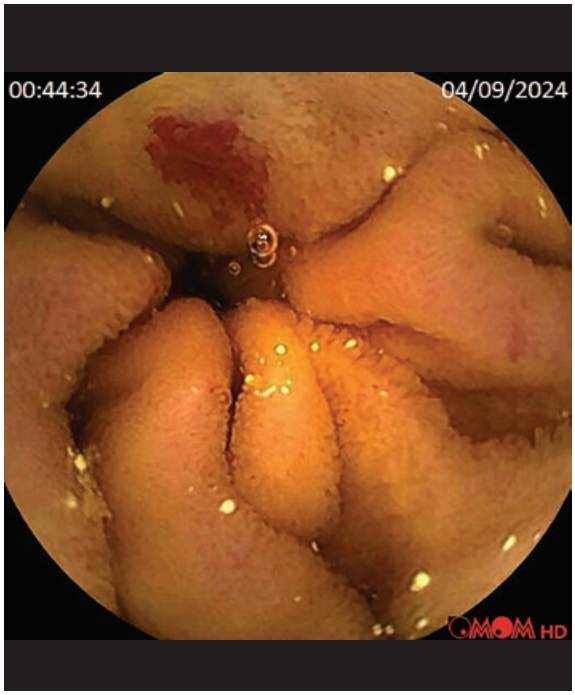

Figure 6
CE image from an OMOM HD capsule showing a well-defined, flat vascular lesion with a bright red hue and radiating, arborizing capillary pattern, consistent with angiectasia. No associated ulceration or active bleeding is observed.

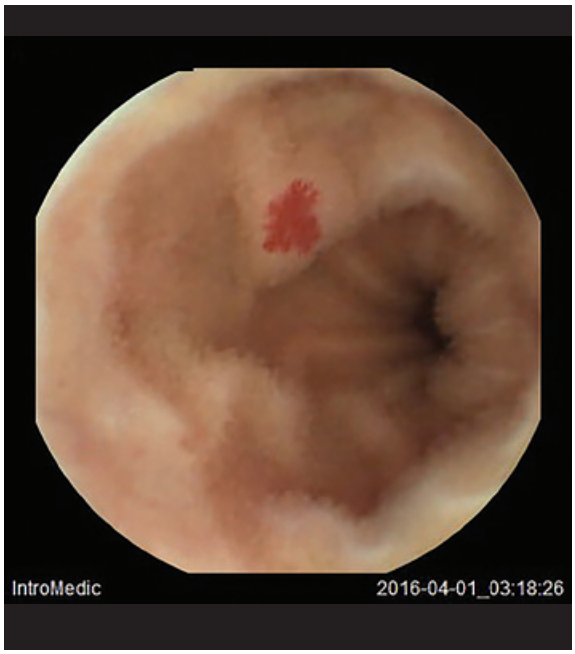

Figure 7
CE image from a Mirocam capsule platform with a solitary, well-circumscribed, flat, bright red vascular lesion with a stellate or clustered pattern of capillaries, consistent with angiectasia. No signs of bleeding or mucosal disruption are noted.

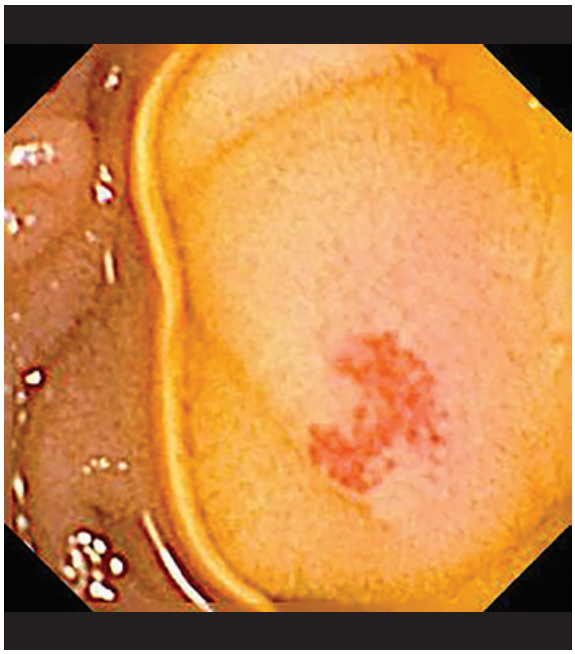

Figure 8
Flat, well-defined erythematous lesion with a cluster of punctate, dilated capillaries, forming a semicircular pattern over normal mucosa. The lesion is characteristic of SB angiectasia and is well visualized in this high-resolution Olympus CE image. No signs of active bleeding or ulceration are present.

These lesions may occur in isolation (Figure 14) or as multiple scattered findings (Figure 15).
Phlebectasias differ from other vascular entities such as SB varices or blue rubber bleb nevus lesions in that they are non-nodular, lack central pulsatility, and tend to have a smooth, compressible appearance. They are often asymptomatic and incidentally found, with unclear clinical significance.

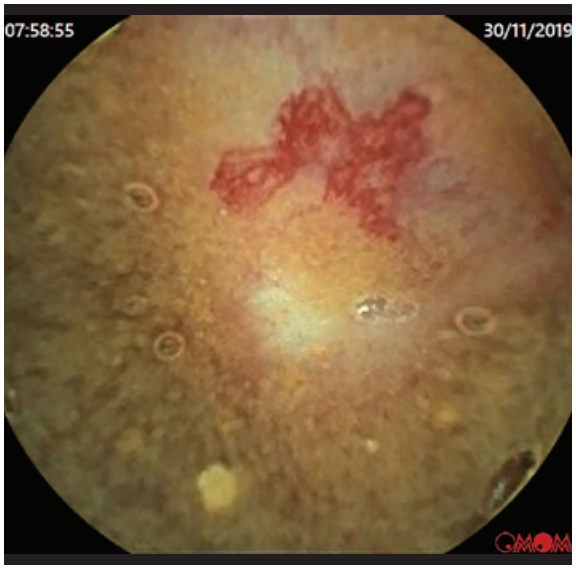

Figure 9
CE image from the OMOM platform with a flat, well-demarcated vascular lesion with a **central red nidus** and **radiating capillary branches**, forming a **spider-like configuration**. Surrounding mucosa appears normal. This morphology is typical of angiectasias found in the small intestine and is a potential source of occult or overt bleeding.

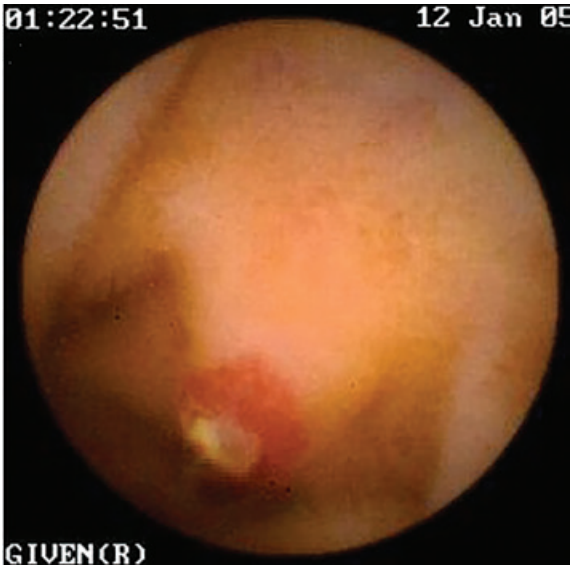

Figure 10
CE image from the GIVEN platform showcasing an irregular, erythematous vascular lesion with a central yellowish fibrin plug or adherent clot, consistent with an **angiectasia with recent or intermittent bleeding**. The surrounding mucosa appears normal, and the lesion is slightly raised, suggesting possible recent oozing.

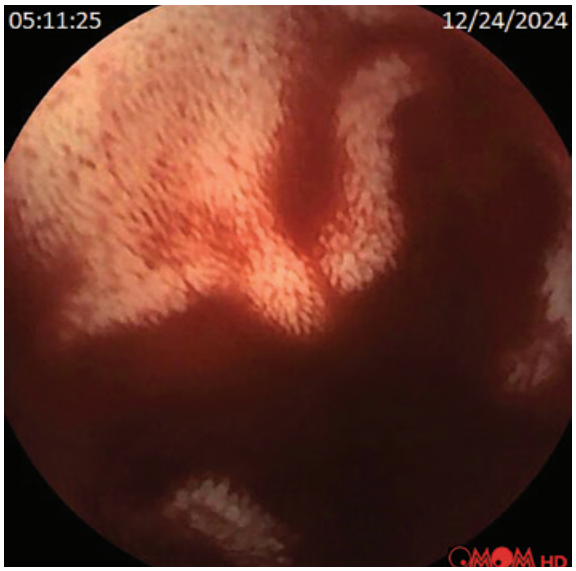

Figure 11
CE image from the OMOM HD platform revealing **active bleeding probably from a vascular lesion**, consistent with **angiectasia**, characterized by **diffuse oozing of blood** without a discrete ulcer or mass.

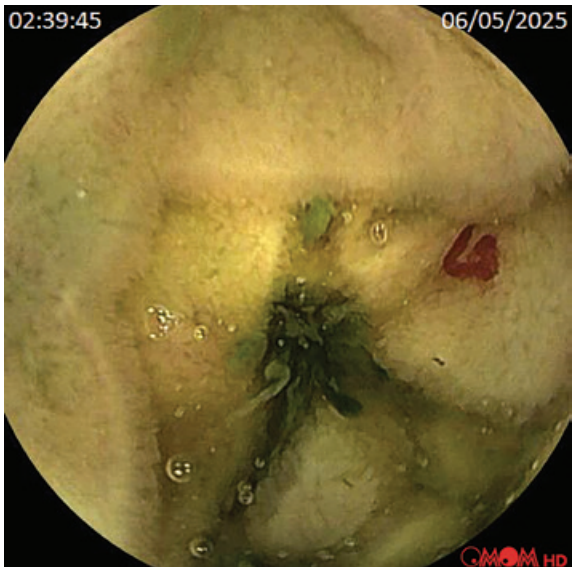

Figure 12
CE image from the OMOM HD platform showing a small, well-circumscribed red focus is observed on otherwise normal mucosa. Its morphology suggests two possibilities: 1) a **punctate angiectasia with early bleeding**, or 2) an **isolated blood droplet** from a proximal, non-visible lesion. A central vessel or vascular tufts are not clearly delineated, but the focal nature, color intensity, and location raise the suspicion of a **bleeding-prone vascular lesion**.
No surrounding inflammation, ulceration, or mucosal disruption is seen.

However, some authors propose that phlebectasias may represent early-stage or precursor lesions to angioectasias, particularly in older patients or those with vascular fragility.

While most phlebectasias are not considered a source of chronic bleeding, there are rare reports of occult or overt GI hemorrhage attributable to these lesions. Nevertheless, in the absence of ac-

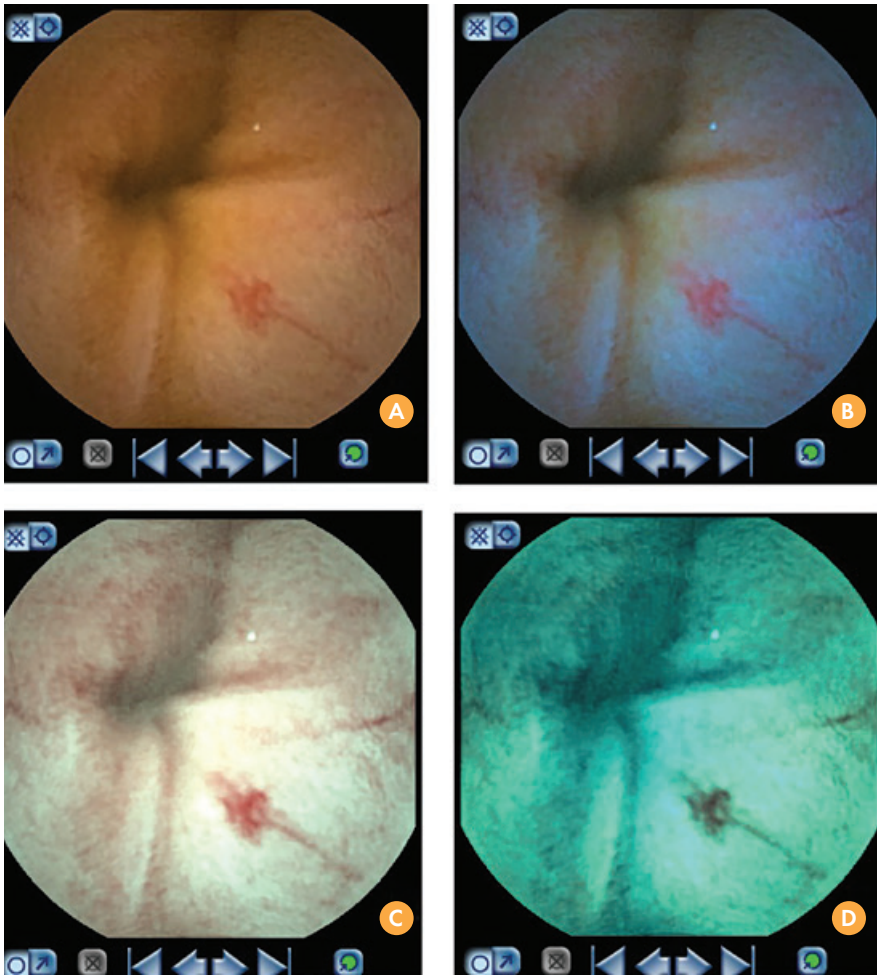

Figure 13
A vascular lesion consistent with **angiectasia** is demonstrated using multiple imaging modes in the GIVEN platform. Each mode highlights specific features of the lesion, improving its detection and characterization: **A** - Standard Image; **B**- Blue filter; **C**- FICE 1; **D**- FICE 2.

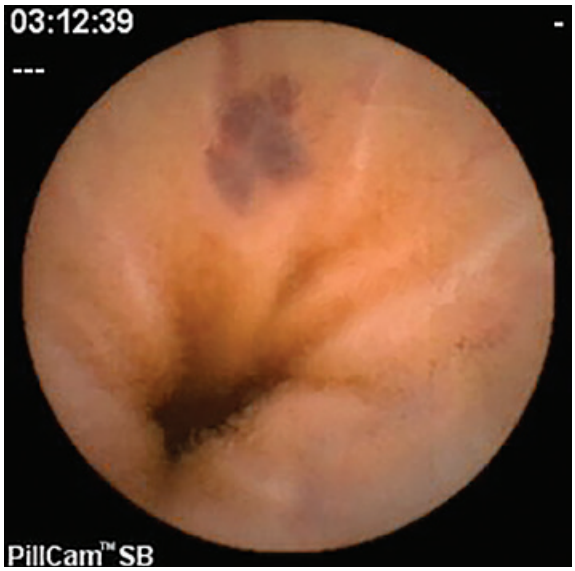

Figure 14
The image shows a CE image from the Pillcam SB platform with a **bluish, submucosal vascular lesion** with a branching or tufted appearance, consistent with **phlebectasia**. Unlike angiectasias, which are superficial and bright red, phlebectasias are **deeper, venous lesions**, often appearing **bluish to violaceous** and located beneath intact mucosa. No signs of active bleeding or mucosal disruption are seen.

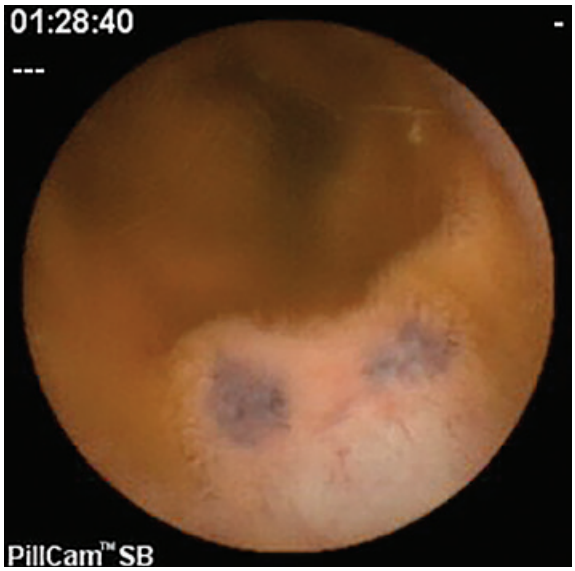

Figure 15
In this image, also from the Pillcam SB platform, two phlebectasias are seen in close proximity. These appear as rounded, violaceous foci beneath intact mucosa, without signs of ulceration or active bleeding.

tive bleeding or stigmata, therapeutic intervention is not usually indicated — even when multiple lesions are present.

2.1.3.5 Hemangiomas

Hemangiomas of the GI tract are benign vascular malformations generally regarded as hamartomatous in origin and are typically present from birth. They may occur as solitary or multiple lesions and, in some cases, as part of diffuse or syndromic angiomatoses. Histologically, they are classified into **capillary** (Figure 16), **cavernous** (Figures 17, 18), or **mixed types**, depending on the vessel architecture and caliber.

Although more commonly observed in the colon, hemangiomas may also affect the small intestine, where they account for approximately 5–10% of benign SB tumors. Most are less than 2 cm in size, though larger lesions have been reported.

CE enables noninvasive visualization of SB hemangiomas. The lack of luminal insufflation during capsule progression helps preserve the native morphology of these lesions, facilitating detection. They typically appear as bluish, nodular, angiomatous protrusions, often with a smooth or lobulated surface.

Several case series have documented the ability of CE to identify SB hemangiomas — including capillary subtypes — with histologic confirmation following surgical or endoscopic resection. This highlights its value in the investigation of obscure or overt GI bleeding when conventional endoscopic techniques are inconclusive.

Although many hemangiomas are asymptomatic, some may cause iron-deficiency anemia or overt hemorrhage, especially if ulcerated. Management options include endoscopic therapy or surgical excision for symptomatic lesions, while observation may be appropriate in stable, asymptomatic cases.

2.1.3.6 Dieulafoy's Lesion

Dieulafoy's lesion is a rare but potentially life-threatening cause of GI hemorrhage. It most commonly occurs in the proximal stomach, particularly along the lesser curvature, but it can also be found in the duodenum, jejunum, colon, or even the esophagus. The lesion consists of a persistently large-caliber submucosal artery that maintains its diameter as it approaches the mucosa, usually with a minimal or absent mucosal defect.

Diagnosis is often difficult, especially in the absence of active bleeding. Intermittent hemorrhage, mucosal retraction, and inconspicuous overlying mucosal changes may all contribute to diagnostic challenges. When bleeding is not active, the only visible sign may be an adherent clot

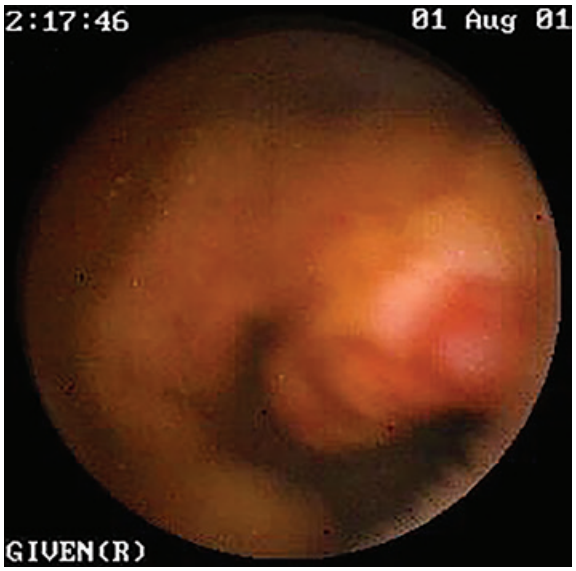

Figure 16
CE image from the GIVEN platform showing a capillary hemangioma. This image demonstrates a **raised, reddish, lobulated lesion** consistent with a **capillary hemangioma**. The lesion appears subepithelial but with a vascular surface, possibly compressible and prone to intermittent bleeding. The lesion contrasts with flat angiectasias or phlebectasias by its **protruding, nodular morphology**.

Figure 17
CE image of a cavernous hemangioma identified with the GIVEN capsule endoscopy platform. A pale, dome-shaped subepithelial lesion with a **reticulated, bluish surface pattern** typical of a **cavernous hemangioma**. No active bleeding is seen, but the lesion has a characteristic clustered appearance of dilated venous channels beneath intact mucosa.

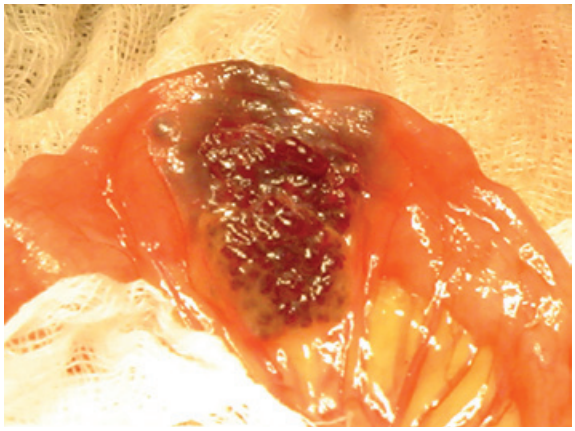

Figure 18
Surgical specimen from the same patient from figure 17 showing a well-defined, dark red to bluish submucosal mass with a lobulated surface. The lesion appears spongy and compressible, consistent with a **cavernous hemangioma**, composed of large, dilated vascular spaces.

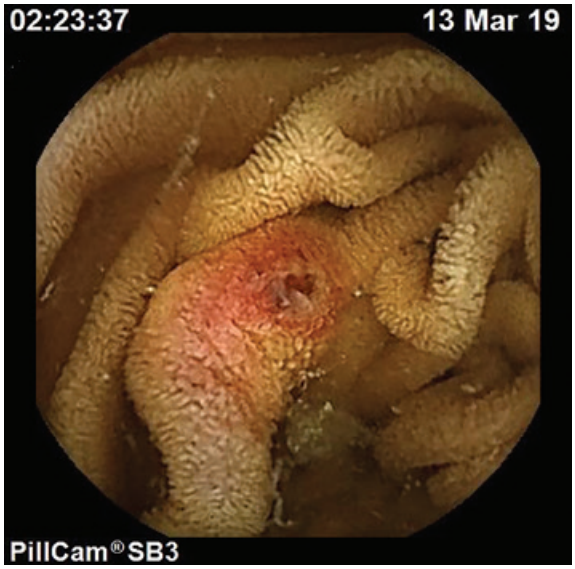

Figure 19
CE image from the Pillcam SB3 system with a Dieulafoy lesion - a **solitary, pinpoint mucosal defect** with surrounding erythema and an exposed central vessel, without a visible ulcer crater or mass. These features are consistent with a **Dieulafoy's lesion**, a rare but significant cause of **acute or recurrent GI bleeding** (Courtesy of Dr. Bruno Rosa, ULS Alto Ave - Guimarães).

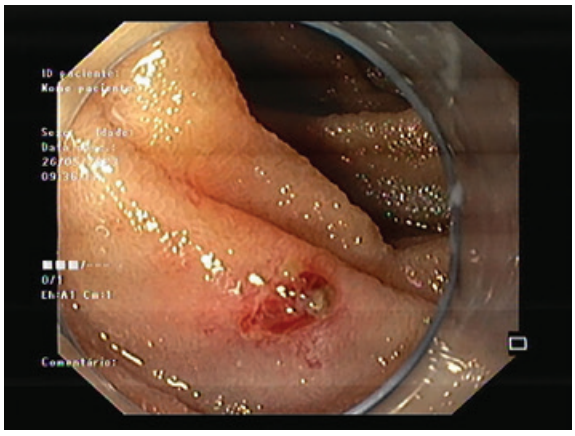

Figure 20
Enteroscopy image of the same Dieulafoy from image 19, with a pinpoint mucosal erosion with a **visible vessel and adherent clot**, surrounded by normal-appearing mucosa. This lesion fits the classic criteria: Protruding arterial vessel through a small mucosal defect; Absence of surrounding ulcer base or mass; High-risk for **massive or recurrent bleeding**. (Courtesy of Dr. Bruno Rosa, ULS Alto Ave - Guimarães).

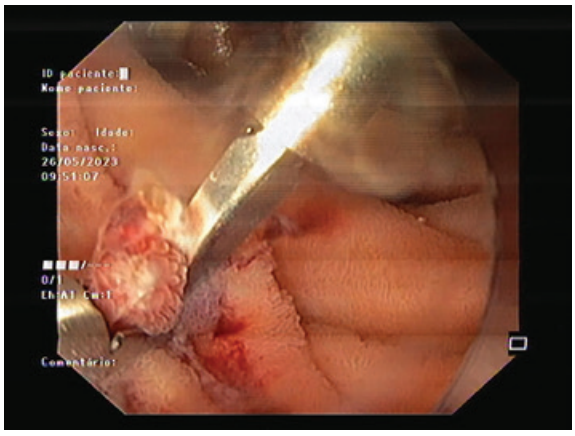

Figure 21
Same lesion from image 20 showing **successful endoscopic treatment** of the SB **Dieulafoy's lesion**. The lesion appears as a pinpoint mucosal defect with recent bleeding stigmata. Two **hemoclips were applied** across the lesion to fully encompass and compress the bleeding submucosal artery. (Courtesy of Dr. Bruno Rosa, ULS Alto Ave - Guimarães).

or a shallow erosion on otherwise normal mucosa (Figures 19-21).

During active bleeding, CE or conventional endoscopy may reveal arterial spurting from an apparently normal mucosal surface. In the SB, CE has proven effective in localizing obscure bleeding, allowing subsequent confirmation and treatment by DAE. Cases involving jejunal lesions have been successfully managed with endoscopic therapy following localization by CE, demonstrating the importance of early evaluation and integration of diagnostic modalities.

Treatment typically involves endoscopic clipping, thermal coagulation, or band ligation. In refractory or recurrent cases, angiographic embolization or surgical resection may be necessary.

2.1.3.7 Small Bowel Varices

Small bowel varices (SBVs) are rare but clinically significant vascular anomalies, typically resulting from el-

evated mesenteric venous pressure. They are most commonly associated with advanced liver cirrhosis and portal hypertension, but may also arise from mesenteric venous obstruction secondary to infiltrative neoplasms (such as pancreatic adenocarcinoma) or postsurgical changes involving venous ligation, thrombosis, or fibrosis following pancreaticobiliary procedures.

Although uncommon, SBVs are an important and potentially under-recognized cause of SB bleeding, particularly in patients with a history of chronic liver disease or abdominal surgery. Because they are not accessible by conventional upper or lower endoscopy, diagnosis is often delayed or missed.

CE enables direct visualization of SBVs, which typically appear as bluish, nodular, or serpiginous mucosal elevations, often located in the jejunum or ileum. These lesions may present as solitary (Figure 22, 23) or clustered (Figures 24-27) and can be surrounded by erythema, edema, or signs of recent bleeding. Morphologically, they may resemble hemangiomas or phlebectasias; however, SBVs are usually larger, tortuous, and more irregular in contour.

Differentiating SBVs from other vascular lesions is crucial, as their management differs significantly. While angioectasias may be treated with endoscopic ablation or pharmacotherapy, SBVs often require a multidisciplinary approach involving interventional radiology or surgical management, especially in the context of portal hypertension.

When identified by CE, careful documentation of the number, location, and associated findings is essential. Confirmation and potential treatment may be achieved with balloon-assisted enteroscopy, although intervention can be technically challenging due to the fragility and submucosal nature of these varices.

2.1.3.8 Portal Hypertensive Enteropathy

Portal hypertensive enteropathy (PHE) refers to a spectrum of mucosal and submucosal abnormalities in the SB caused by portal hypertension, most often due to cirrhosis, but also occurring with non-cirrhotic portal vein obstruction or extrahepatic thrombosis. These changes are significantly more frequent in cirrhotic patients and may lead to chronic iron-deficiency anemia, occult bleeding, or recurrent melena.

CE frequently reveals angioectasia-like lesions (Figure 28), edematous folds with punctate erythema (Figure 29), dilated submucosal venous lakes—especially in the jejunum—scattered petechiae, and a characteristic reticulated (mosaic/honeycomb) pattern representing subepithelial venous congestion. This mosaic pattern is more readily appreciated using high-definition capsule systems (Figure 30).

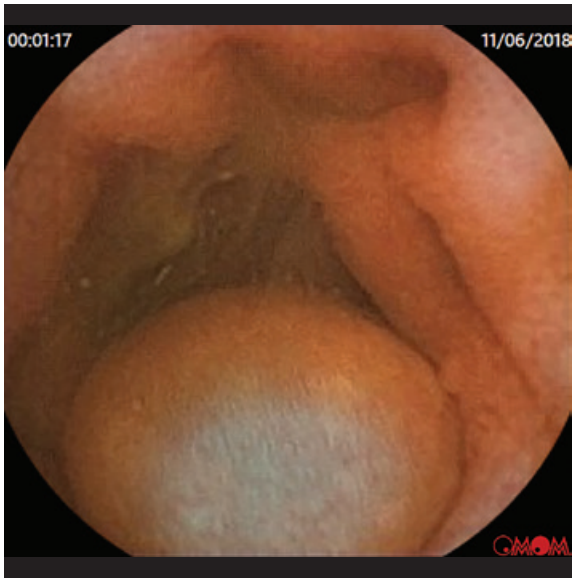

Figure 22
An image from the OMOM HD platform that reveals a **prominent, rounded, bluish submucosal bulge** consistent with a **dilated vein** (varix) protruding into the SB lumen. The lesion is covered by intact mucosa and located within otherwise normal-appearing folds. The appearance is typical of SB varices — serpiginous, compressible, and subepithelial.

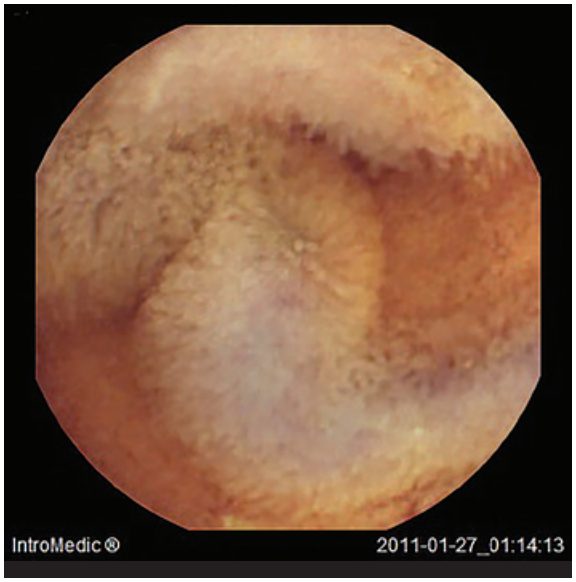

Figure 23
A CE image from the Mirocam platform with a **bluish to violaceous submucosal area**, with smooth overlying mucosa and no visible erosion or active bleeding. The discoloration is focal and rounded, suggestive of a **SBV**.

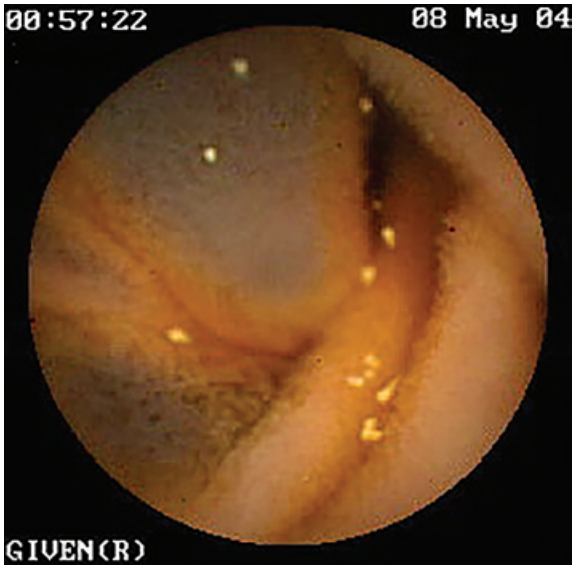

Figure 24
CE image from the GIVEN system with **rounded, bluish submucosal protrusions** with smooth contours, clearly demarcated from the surrounding mucosa — classic for a **SBVs**. The lesions appear as a **dilated venous channel**, consistent with **portosystemic collateral circulation** secondary to **portal hypertension**.

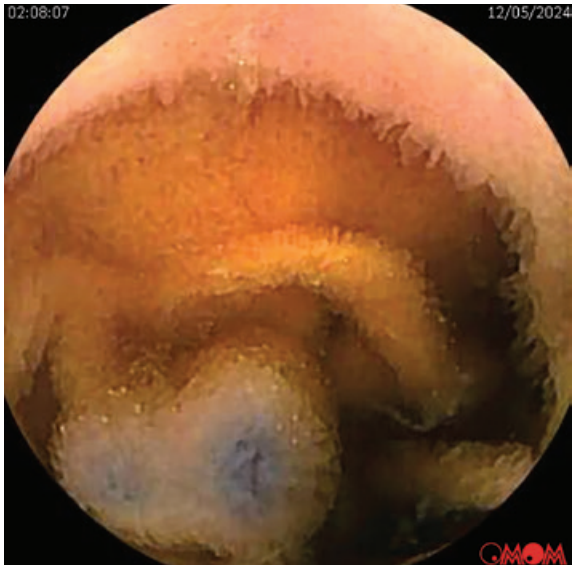

Figure 25
CE image from the OMOM platform with prominent **bluish submucosal lesions** protruding into the SB lumen. The lesion are well-defined, rounded, and covered by intact mucosa, typical of **SBVs**. The bluish hue and slightly lobulated architecture are consistent with a **dilated venous structure**, often found in the context of **portal hypertension or mesenteric venous collaterals**.

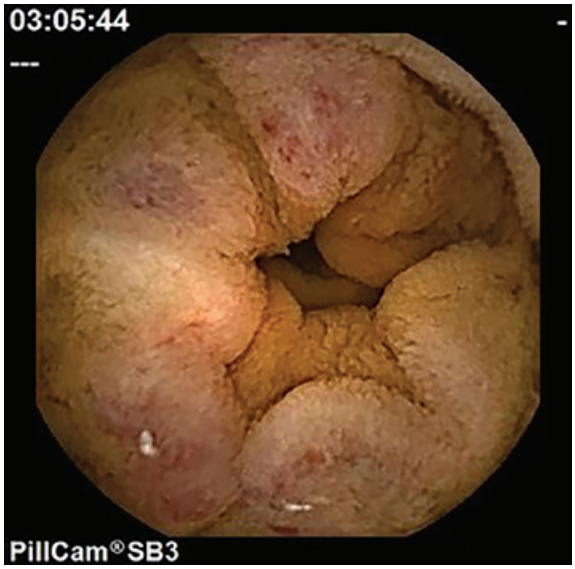

Figure 26
Pillcam SB3 image showing **multiple erythematous, edematous, nodular or granular mucosal folds**, with patchy vascular congestion. In the lower corner varices are evident. These findings are typical of **PHE with SBVs**, a condition affecting the SB in patients with **portal hypertension**, analogous to portal hypertensive gastropathy and colopathy.

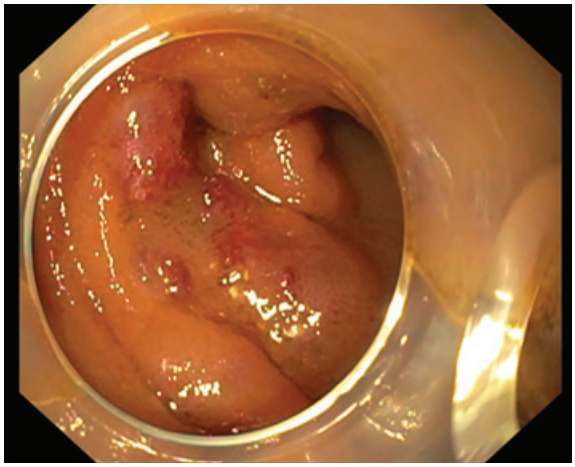

Figure 27
DAE image from the same patient in figure 26 confirming **jejunal varices**. Multiple **submucosal, bluish to violaceous, serpiginous structures** are visible beneath intact mucosa. These are characteristic of **SBVs**, typically seen in the setting of **portal hypertension**, most commonly due to cirrhosis or portal vein thrombosis. The overlying mucosa has multiple **raised, erythematous, nodular folds**, prominent **red spots and petechial lesions and** congested and edematous mucosa, consisting with simultaneous PHE.

Although often asymptomatic, PHE can manifest clinically as occult bleeding or intermittent overt hemorrhage and can exacerbate anemia in cirrhotic patients. The severity of SB mucosal changes often correlates with portal hypertension markers, such as splenomegaly, esophageal varices (Figure 31), and transient elastography scores.

Management focuses on supportive care, including iron supplementation, and avoidance of NSAIDs or anticoagulants when possible. In severe or refractory cases, decompression of the portal system (for example, via TIPS) may result in improvement of SB mucosal lesions.

2.1.4. Scoring Systems and Practical Reading Tips in Vascular Lesion Assessment

CE frequently detects multiple vascular lesions throughout the SB. Not all have clinical significance, and therefore, standardized scoring systems and structured reporting strategies are essential for prioritization and therapeutic planning.

2.1.4.1 Saurin Classification

Widely adopted in CE and recommended by ESGE:

- **P0** – No bleeding potential - e.g., phlebectasias (Figure 14, 15), red patches (Figure 32)
- **P1** – Uncertain or low bleeding potential - e.g., small red spots - (Figure 3, 4, 33)
- **P2** – High bleeding potential - e.g., typical angioectasias (Figure 5-9,35), tumors, varices (Figure 22-27)
- **P3** – Actively bleeding lesions (Figure 11, 34) - proposed in recent updates.

This score assists in determining urgency of treatment and follow-up.

2.1.4.2 Yano–Yamamoto Classification

Initially designed for DAE, applicable in CE:

- **Type 1a/1b** – Angioectasias (Figures 5-9, 35)
- **Type 2a/2b** – Dieulafoy lesions (Figures 19-21)
- **Type 3** – AVMs with venous components
- **Type 4** – Atypical/unclassified vascular lesions

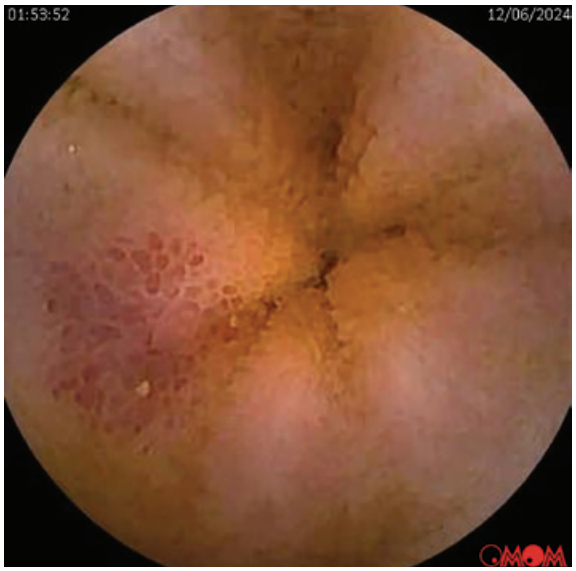

Figure 28
CE image showing a segment of SB mucosa with **congestion** and a patch with ectatic blood capilaries. The lesion appears as a flat, reddish area with a **patchwork of dilated capillary loops**, typical of **mucosal vascular changes in PHE**.

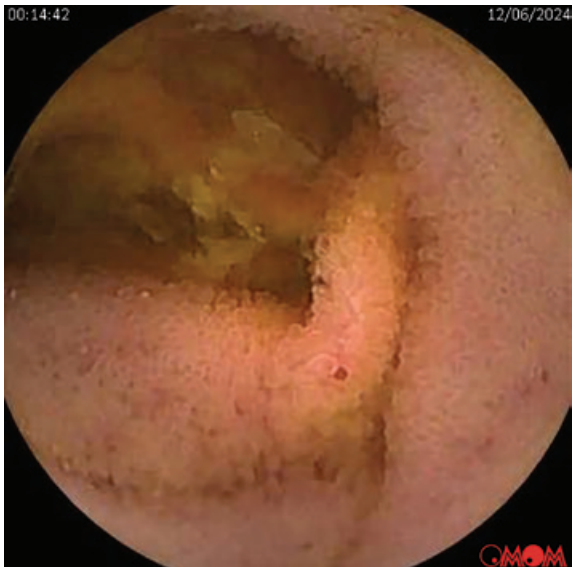

Figure 29
This CE image demonstrates **mild mucosal changes** suggestive of **PHE**. The intestinal folds appear **thickened and edematous**, with scattered **punctate erythematous spots** and mild vascular congestion.

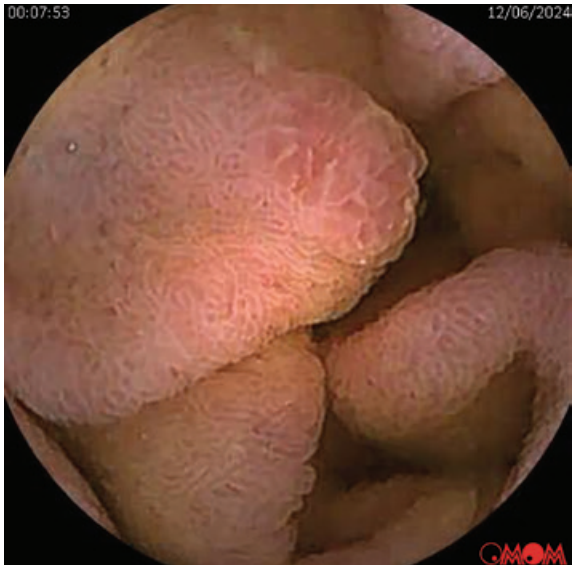

Figure 30
This high-definition CE image shows **dilated villi with a prominent reticulated (mosaic/honeycomb) pattern**, representing **subepithelial venous congestion**. The villous architecture appears swollen, with **visible submucosal venous lakes**, giving a cobblestone or honeycomb-like appearance. This vascular congestion pattern is highly specific and should raise suspicion for clinically significant portal hypertension.

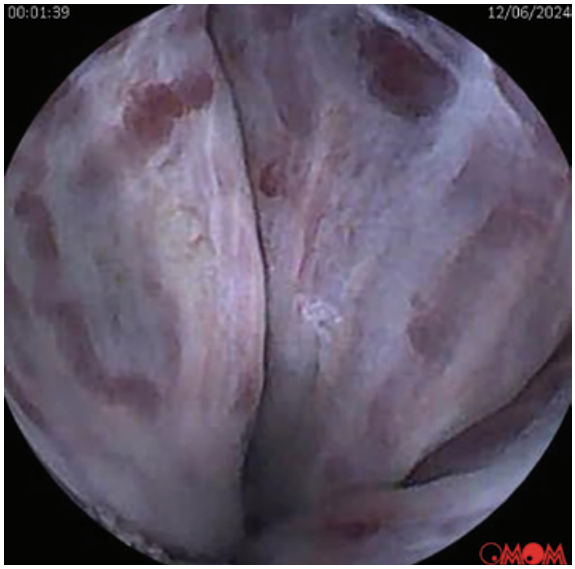

Figure 31
This CE frame, obtained in the **esophagus**, shows multiple **longitudinal, bluish submucosal protrusions** with smooth surfaces and segmental distribution — findings consistent with **esophageal varices**. The varices are serpiginous and run parallel to the esophageal folds, some with red markings suggesting recent or impending bleeding risk. These varices confirm the presence of **clinically significant portal hypertension**, in line with the extensive findings of **PHE** observed throughout the SB in the same patient.

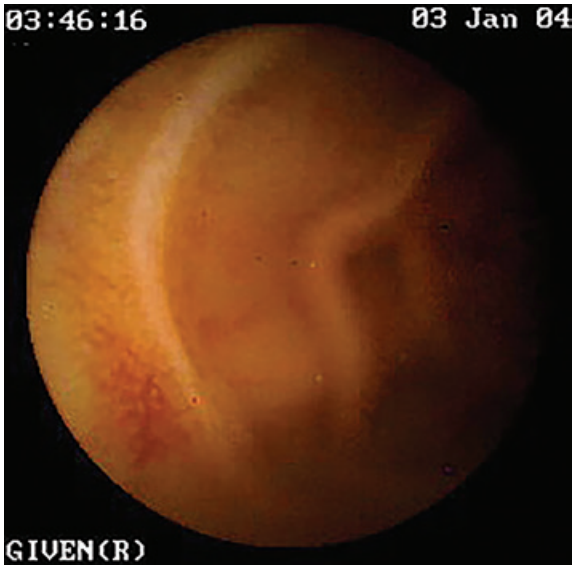

Figure 32
CE image from the GIVEN platform depicting a **flat red patch** seen on the mucosal surface, composed of **ill-defined erythema** without active bleeding or ulceration. The lesion is non-elevated and lacks visible vascular structures, consistent with a **P1 lesion** (Saurin classification) of **uncertain bleeding potential**.

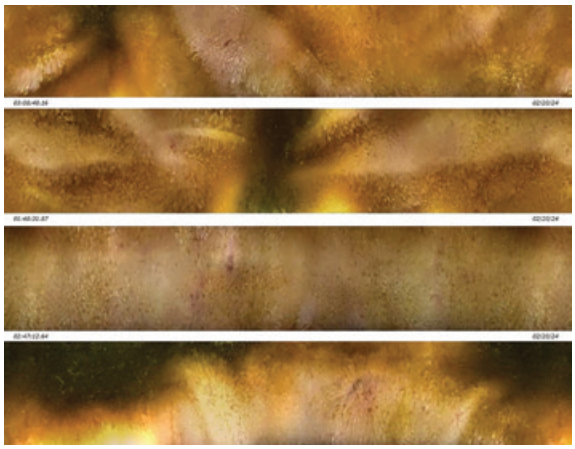

Figure 33
Series of four CE images from the Capsocam platform illustrating multiple **punctate red spots** scattered over the SB mucosa. The lesions are flat, non-pulsatile, without signs of active bleeding, and are not associated with ulceration or surrounding inflammation. These lesions fall under the **P1 category of the Saurin classification**, indicating **uncertain hemorrhagic potential**.

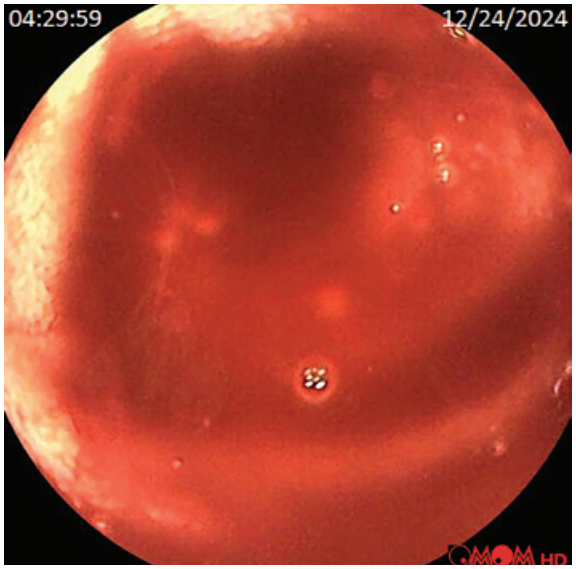

Figure 34
Image from OMOM HD showing **dense intraluminal blood** occupying the visual field, with a **bright red appearance** suggestive of **fresh, ongoing hemorrhage**. Although no specific lesion is visible in this frame, the pattern and volume of blood indicate **active bleeding** from a proximal vascular source. This finding corresponds to a **P3 lesion** under the **modified Saurin classification**, denoting **definite bleeding** with high clinical relevance and urgency for further investigation or intervention.

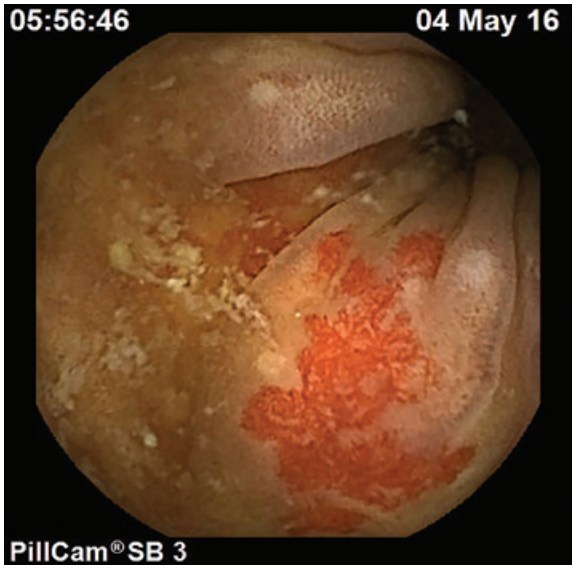

Figure 35
CE image from the PillCam SB3 platform showing an image of the colon. This image captures a **flat, well-demarcated vascular lesion** consistent with a **colonic angioectasia**, located over colonic folds (corresponding to a **P2 lesion,** Saurin classification). The lesion exhibits a **tufted, fern-like pattern of dilated capillaries**, without signs of active bleeding, and is situated within mucosa displaying patchy dark pigmentation — typical of **melanosis coli**. Importantly, this lesion was **not identified in a prior conventional colonoscopy**, highlighting a key diagnostic value of capsule endoscopy — particularly in the **right colon**, where flat vascular lesions are often missed due to preparation limitations, transient collapse, or subtle morphology. It also reinforces the need to always review extra-small bowel images.

Tips for Capsule Endoscopy Readers: Structured Interpretation of Vascular Lesions

- Always document lesion size, morphology, number, and location. Use anatomical terms (e.g., proximal jejunum, distal ileum, and extra small bowel locations, as stomach or colon - figure 35).
- Use **standardized classifications** (Saurin, Yano) in all reports.
- **Do not suspend anticoagulants or antiplatelets** before CE: evidence supports continued therapy to improve DY.
- In overt bleeding, aim to perform CE **within 48 hours**.
- Be cautious not to **overinterpret isolated flat red spots**, especially in the ileum.
- **Use image enhancement filters** (e.g., FICE) for better delineation
- When multiple lesions are found, or when anemia is severe or recurrent, consider a **therapeutic strategy** involving medical treatment or DAE.

2.1.5. Conclusion

CE has markedly enhanced our ability to detect and characterize vascular abnormalities of the SB, which are now recognized as the leading cause of mid-gastrointestinal bleeding, particularly in patients with normal upper and lower endoscopy. Its DY is significantly higher than with conventional imaging techniques.

Once identified, most vascular lesions are amenable to treatment, whether endoscopic, medical, or surgical, depending on lesion type, number, location, and bleeding risk. The introduction of structured classification systems and AI-supported reading tools has improved lesion recognition, risk stratification, and therapeutic planning.

CE has not only improved clinical outcomes but also contributed to cost savings by reducing unnecessary procedures and hospital stays. Its role is particularly relevant in patients with syndromic vascular conditions, such as HHT or BRBNS, where multiple SB lesions may otherwise go undetected.

In summary, CE is an indispensable, first-line tool in the evaluation of suspected SB bleeding, particularly of vascular origin, enabling timely diagnosis, personalized treatment, and improved long-term management.

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2.2. Neoplastic Lesions

Malignant small bowel tumors (MSBT) are relatively rare, accounting for only 3-5% of all gastrointestinal (GI) cancers. The incidence of primary MSBT is increasing, mainly due to the rise of neuroendocrine tumors (NETs). Other common MSBT include adenocarcinoma, GI stromal tumors (GISTs), and lymphoma.

2.2.1 Adenocarcinoma most commonly occurs in the duodenum and often presents at an advanced stage, making early detection challenging (Figure 1,2). Risk factors include nonresponsive/complicated celiac disease and familial adenomatous polyposis.

2.2.2 NETs primarily arise in the ileum and are slow-growing tumors (Figure 3-6). They often present with symptoms such as flushing, diarrhea, or carcinoid syndrome, particularly when liver metastases are present.

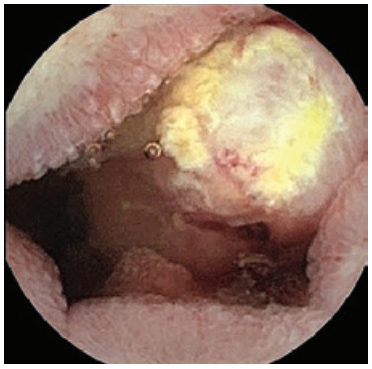

Figure 1
Ulcerated adenocarcinoma of the jejunum.

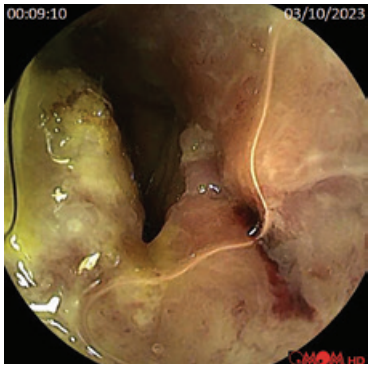

Figure 2
Duodenal ulcerated adenocarcinoma.

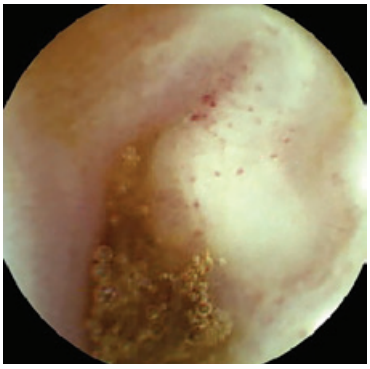

Figure 3
Ileal NET tumor.

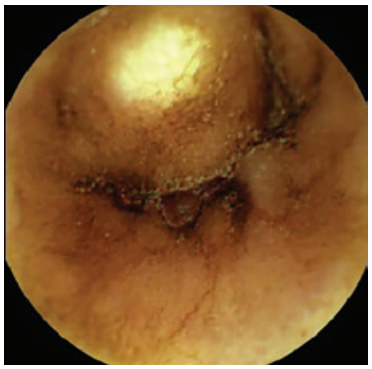

Figure 4
Ileal NET tumor presenting with a protruding lesion.

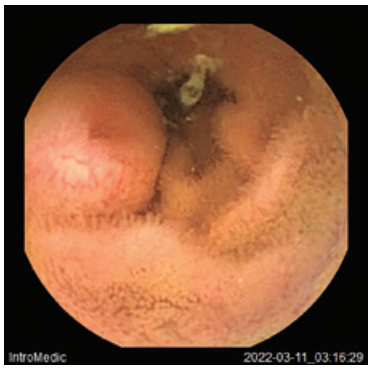

Figure 5
Ileal NET tumor presenting with a protruding lesion with a central umbilication.

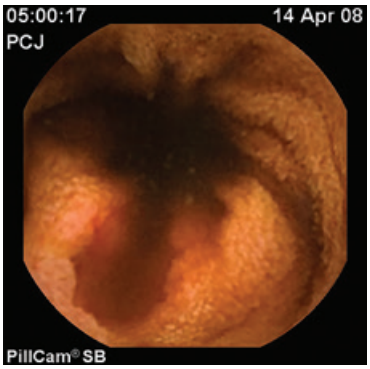

Figure 6
Ulcerated NET tumor - ileum.

2.2.3 GISTs although less common, can occur anywhere in the SB, particularly the jejunum anda ileum (Figure 7-11). GISTs tipically grow extraluminally and may not be detected until they cause GI bleeding or obstruction, making imaging modalities essential for diagnosis and staging.

2.2.4 Lymphomas (Figure 12-16) can arise anywhere in the small intestine and are most frequently non-Hodgkin types, including diffuse large B-cell lymphoma and enteropathy-associated T-cell lymphoma. They are more common in patients with nonresponsive/complicated celiac disease or immunosuppression.

2.2.5 Mast Cell Tumors in the small intestine are rare (Figures 17, 18). In humans, intestinal involvement by systemic mastocytosis is more common than true primary mast cell tumors.

2.2.6 Metastases to the small intestine are more common than primary tumors, and they may occur through direct invasion from adjacent organs, such as the ovary or colon, or through distant spread via the hematogenous route. Malignant melanoma and lung cancer are the tumors that most frequently metastasize to the small intestine. Malignant pheochromocytoma can also metastasize to the small intestine (Figure 19).

2.2.7 Diagnosis of MSBT often present with vague and nonspecific symptoms/signs, including GI bleeding, abdominal pain, weight loss, obstruction, anemia or jaundice in cases involving the duodenum, thus contributing to delayed diagnosis and poorer outcomes. Therefore, a high clinical suspicion and early diagnosis are crucial for effective management and improved outcomes, highlighting the importance of diagnostic modalities such as small bowel capsule endoscopy (SBCE), device-assisted enteroscopy (DAE), computed tomography (CT) enterography (CTE), and magnetic resonance enterography (MRE).

2.2.7.1 SBCE has revolutionized the diagnostic approach of SB pathologies, offering a non-invasive method to visualize the entire small intestine. It is particularly valuable in evaluating SB bleeding and iron deficiency anemia, a common pres-

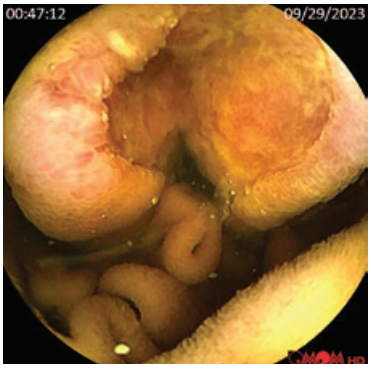

Figure 7
Ulcerated GIST stromal tumor in the jejunum.

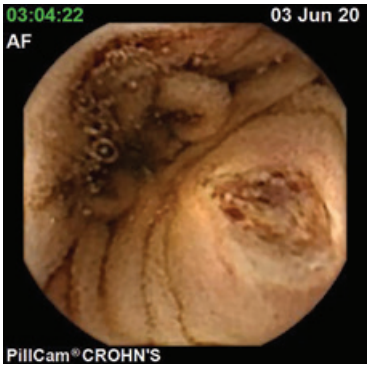

Figure 8
Jejunal ulcerated GIST stromal tumor.

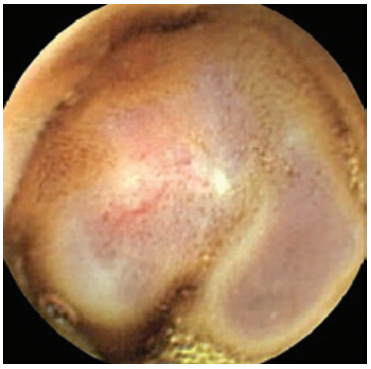

Figure 9
Jejunal non-ulcerated GIST stromal tumor.

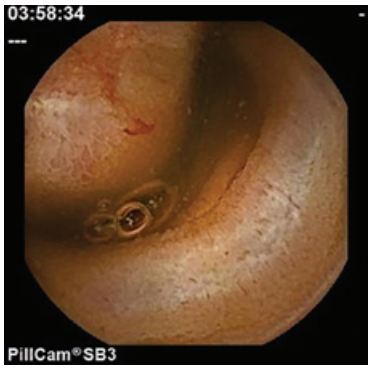

Figure 10
Jejunal ulcerated GIST stromal tumor.

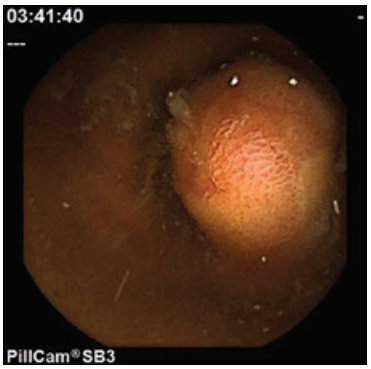

Figure 11
Ulcerated GIST stromal tumor.

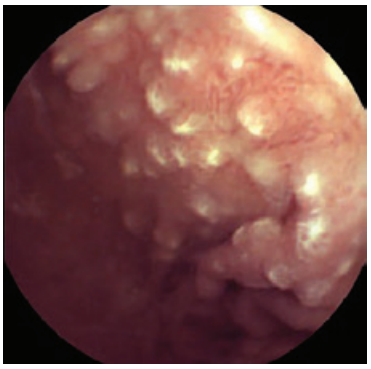

Figure 12
Marginal zone lymphoma of the duodenal bulb presenting with a nodular mucosa.

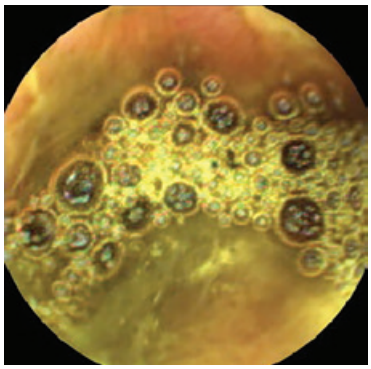

Figure 13
Diffuse large B-cell lymphoma of the ileum presenting with an ulcerated mass.

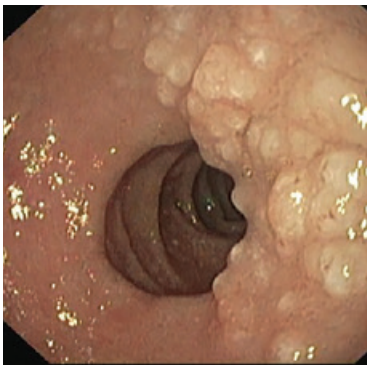

Figure 14
Small bowel follicular lymphoma - nodular pattern in jejunum.

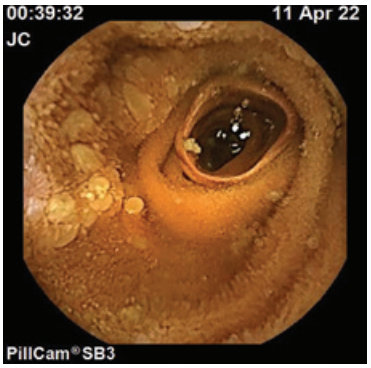

Figure 15
Small bowel follicular lymphoma - nodular pattern in ileum.

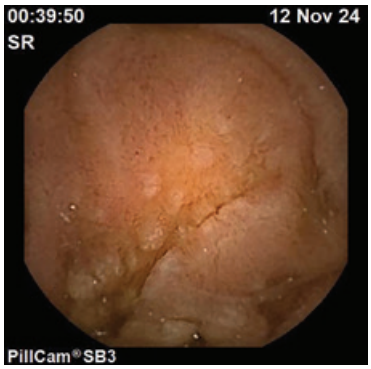

Figure 16
Duodenal follicular lymphoma.

entation of MSBT. Commonly findings suggesting MSBT include stenotic or protruding, ulcerated, bleeding lesions in SBCE. Nevertheless, SBCE has limitations as it cannot provide tissue samples for histopathological diagnosis, and its diagnostic accuracy can be compromised by fast transit times, inability to control SBCE movements, poor bowel preparation, or the presence of strictures that may lead to CR. Artificial intelligence (AI) and machine learning algorithms are being developed to improve the interpretation of SBCE and imaging studies, reducing reading times, and potentially

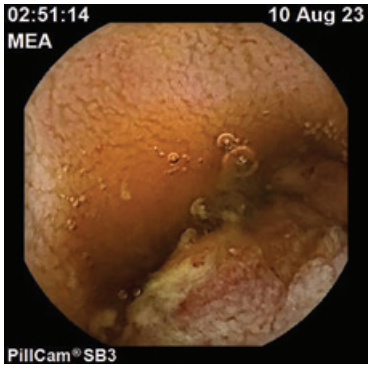

Figure 17
Mast cell tumor - Courtesy of Dr. António Curado - Centro Hospitalar do Oeste.

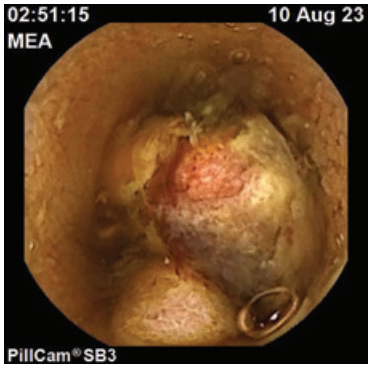

Figure 18
Mast cell tumor in ileum - Courtesy of Dr. António Curado - Centro Hospitalar do Oeste.

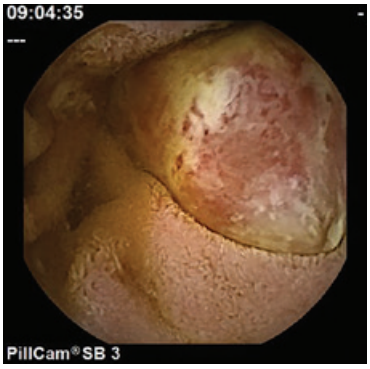

Figure 19
Metastasis of malignant pheocromocytoma.

increasing DY and reducing false positives. For acceptance of AI for automated lesion detection in SBCE, the performance of AI-assisted reading should be comparable to that of experienced endoscopists for lesion detection, without increasing and possibly reducing the reading time of the operator.

2.2.7.2 DAE, including double-balloon enteroscopy and single balloon-assisted enteroscopy, allows direct mucosal visualization, tissue sampling, tattooing of lesions for surgical planning, endoscopic resection of certain lesions and placement of self-expanding metal stents in the setting of palliative care. The DY of DAE for MSBT is similar to that of SBCE. Main limitations of DAE include its invasiveness, high rate of incomplete exams and the need for sedation.

2.2.7.3 CTE combines detailed cross-sectional imaging of CT with bowel distension techniques, allowing excellent visualization of the bowel wall, including mass lesions and wall thickening, and extraluminal disease. CTE has a high sensitivity (90%) for detecting MSBT and is particularly effective in staging MSBT as it provides valuable information on metastatic disease, particularly in the liver and mesentery. One of the main advantages of CTE is its availability and fast imaging acquisition, making it an excellent choice for initial evaluation. However, its use is limited by radiation exposure, which is a concern, especially in younger patients or those requiring multiple studies.

2.2.7.4 MRE offers excellent soft tissue contrast without radiation exposure, making it an increasingly favored modality for MSBT imaging, with sensitivity and specificity up to 91.6% and 97.6%, respectively. MRE is particularly useful in evaluating patients with contraindications to radiation or those requiring repeated imaging. MRE limitations include longer acquisition times, the need for patient cooperation, and potential contraindications in patients with certain implantable devices or severe claustrofobia.
When comparing different diagnostic modalities (SBCE, DAE, CTE and MRE), each offers unique strengths in diagnostic workup and may be complementary. SBCE and DAE have comparable DY to detect MSBT. Regarding imaging studies, MRE and CTE have comparable diagnostic accuracy in detecting MSBT. SBCE may have a lower sensitivity compared to CTE and the risk of false-negatives SBCE results has been documented in MSBT, especially for lesions located in the proximal SB or subepithelial lesions with minimal endoluminal growth, such as GISTs and NETs. Therefore, in the case of a negative SBCE, albeit with a strong suspicion of a MSBT, further CTE/MRE should be performed for confirmation. The ESGE guidelines recommend a multimodal approach in suspected MSBT, starting with SBCE, unless patient is considered to be at risk of CR. In the setting of suspected MSBT in cross-sectional imaging studies, DAE should be preferred over SBCE to avoid CR, acquire biopsies for histological diagnosis and tattoing when deemed necessary. Cross-sectional imaging is recommended for staging and planning surgery (extent and ressecability of the lesion) when there is a high diagnostic certainty in CE findings of a MSBT, obviating DAE. Conversely, when there is an uncertain diagnosis of MSBT at SBCE, DAE is indicated for biopsy sampling and tattoing. DAE provides the advantage of direct visualization and biopsy, crucial for definitive diagnosis.

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2.3. Inflammatory and Infectious Diseases

Small bowel capsule endoscopy (SBCE) is an important tool in the diagnosis and monitoring of inflammatory diseases of the SB. Inflammatory lesions of the SB may include aphthoid erosions, deep or superficial ulcerations, villous oedema, hyperemia, denudation and/or stenosis. Although these lesions are frequently typical of Crohn's disease, they are not exclusive and several differential diagnoses should be considered, including other inflammatory and infectious diseases. Villous atrophy can also occur in many of these conditions. Most infections involving the SB have a self-limited course and there is generally no need to perform endoscopic examination in these patients. However, in some cases SBCE can reveal changes in the SB mucosa. Patients with persistent diarrhea and associated symptoms such as weight loss, fever, arthralgia, neurologic deficits, or other findings such as anemia, inflammatory signs, eosinophilia or malabsorption warrant further investigation besides stool cultures.

2.3.1 Inflammatory Diseases

2.3.1.1 Crohn's Disease is an inflammatory bowel disease in which ulcerative lesions are the most typical feature, with discontinuous lesions, presence of strictures and fistulae, and perianal involvement. Clinical manifestations include chronic abdominal pain and diarrhea, associated with weight loss, fever, arthralgia, iron deficiency, elevated c-reactive protein, erythrocyte sedimentation rate and/or fecal calprotectin. There are no specific endoscopy findings, but the most common are villous edema (Figures 1-5), aphthous erosions or ulcers (Figures 6-8), large round, longitudinal or pleomorphic ulcers (Figures 9-19) cobblestone appearance, strictures (Figures 20-24), mucosal bridge, skip lesions and inflammatory polyps (Figures 25-27). The diagnosis of Crohn's disease is based on a combination of clinical, biochemical, stool, endoscopic, cross-sectional imaging and histological examinations.

2.3.1.2 Nonsteroidal Anti-Inflammatory Drug (NSAID)-Induced Enteropathy is an important differential diagnosis and an increasingly prevalent entity, mainly in older patients and those suffering from conditions that require long term NSAID use (Figures 28-32). The intestinal injury associated with these agents is thought to be multifactorial, with increased intestinal permeability due to inhibition of cyclo-oxygenase activity and suppression of prostaglandin synthesis. Symptoms are usually nonspecific, such as abdominal pain, constipation, diarrhea, iron deficiency anemia and protein loss. The characteristic features of NSAID-induced enteropathy include multiple superficial lesions with less than 1 cm, with similar distribution in the jejunum and ileum and uncommon ileocecal valve involvement. Diaphragm stenosis is a rare but pathognomonic finding. The diagnostic criteria of NSAID-induced enteropathy are a history of NSAID use; endoscopic findings, such as erosions, ulcers and diaphragm like strictures; improvement of clinical manifestations and/or endoscopic findings after stopping NSAID; exclusion of other aetiologias, such as Crohn's disease, infection and malignancy.

2.3.1.3 Behçet's Disease is a chronic, relapsing, multisystemic vasculitis that can affect any vessel type of any size. The main symptoms are recurrent oral and/or genital ulcers, uveitis and characteristic skin lesions. The causal mechanisms of the disease are not fully understood, but it has been described an association with genetic predisposition due to specific HLA genes, vascular endothelial hyper-activation and dysregulated immune response. In SB injury, neutrophilic infiltration plays an important role, leading to mucosal inflammation and medium-vessel involvement which can cause intestinal ischemia and infarction. Endoscopically, the involvement of the ileocecal area is the most common and the typical ulcerations of intestinal Behçet's disease are round and deep, the volcano-shaped ulcers, with discrete borders and in small number, generally less than 6 ulcers in total.

2.3.1.4 Other **Systemic Vasculitis** may involve the SB, with endoscopic findings similar to those of Behçet's disease including oedema, erythema, erosions and ulcers. Polyarteritis nodosa is a type of medium-vessel vasculitis in which SB involvement is relatively common and associated with a poorer prognosis. GI involvement can occasionally occur in ANCA-associated vasculitis, systemic lupus erythematosus and long-standing rheumatoid arthritis.

2.3.1.5 Graft-versus-Host-Disease (GVHD) can involve the skin, GI tract, liver and lungs, the SB being the most common intestinal location (Figures 33-36). It is frequently associated with significant morbidity after allogenic hematopoietic stem cell transplantation. SBCE has a high accuracy and DY in GVHD, identifying oedema, hyperemia, erosions and ulcers, which are due to the activation of donor T cells that recognize the host tissues as foreign.

2.3.1.6 Small Bowel Radiation Enteritis is a rare complication of abdominal and/or pelvic radiotherapy that usually affects the distal ileum. In this condition, the SB wall becomes thickened with mucosal and villous oedema and atrophy, collagenous-vascular lesions and obstruction of lymphatics. Additionally, there is also the formation of telangiectasias and ulcerations which can heal with fibrosis, leading to narrowing of the lumen.

2.3.1.7 Cryptogenic Multifocal Ulcerous Stenosing Enteritis (CMUSE) is chronic and recurrent disease characterized by idiopathic multifocal strictures and ulcerations of SB. It is a rare enteropathy with less than 100 cases reported in the lit-

erature. Characteristic symptoms include abdominal cramping, GI bleeding and anemia, with a relapsing and remitting course. The diagnosis is based on history, clinical features, CT/MR enteroclysis, SB endoscopy and histology of the SB. The SB ulcers occur predominantly in the ileum but sparing the terminal ileum. The ulcers are usually multiple and never progress to cobble-stone appearance, stricture or fistula formation, since the ulcers are restricted to the mucosa or submucosa.

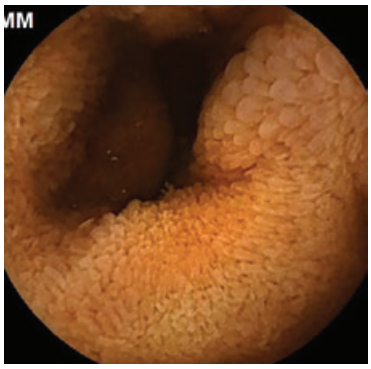
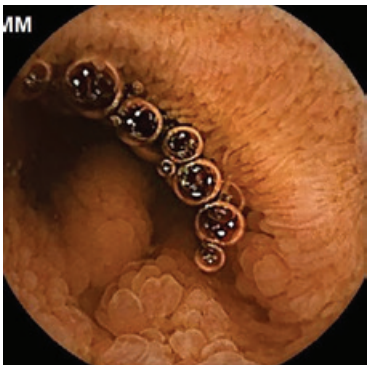



Figure 1-2
Patchy villous oedema in Crohn's disease.

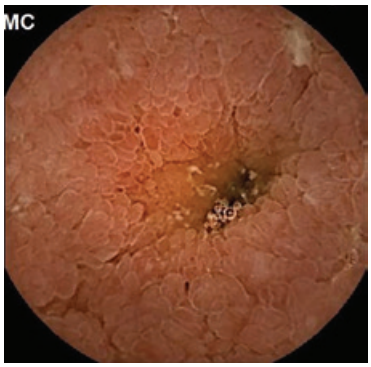
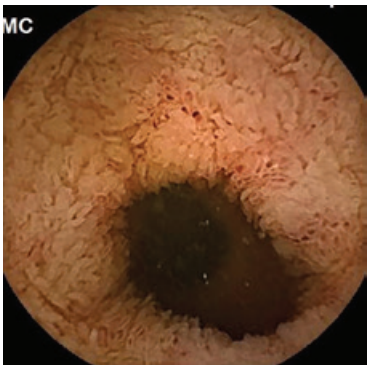
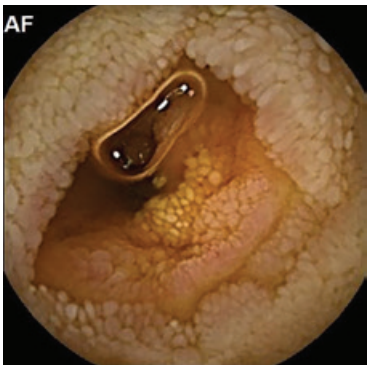




Figure 3-5
Diffuse villous oedema in Crohn's disease.

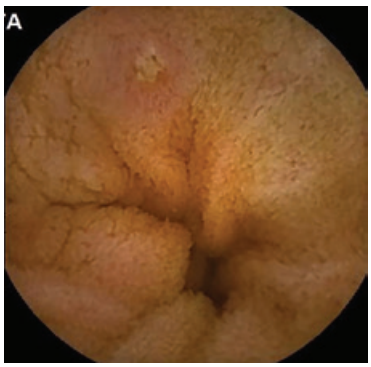
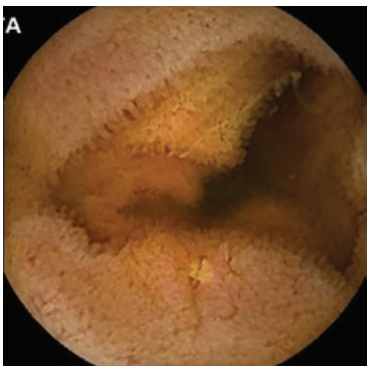
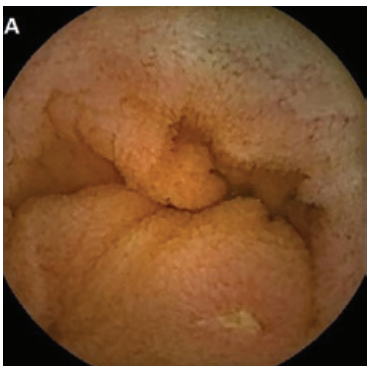




Figure 6-8
Aphthous erosions in Crohn's disease.

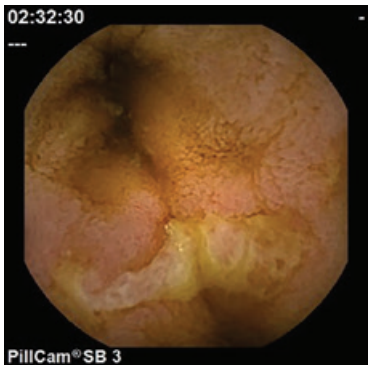


Figure 9
Ulcer with erythematous halo in Crohn's disease.

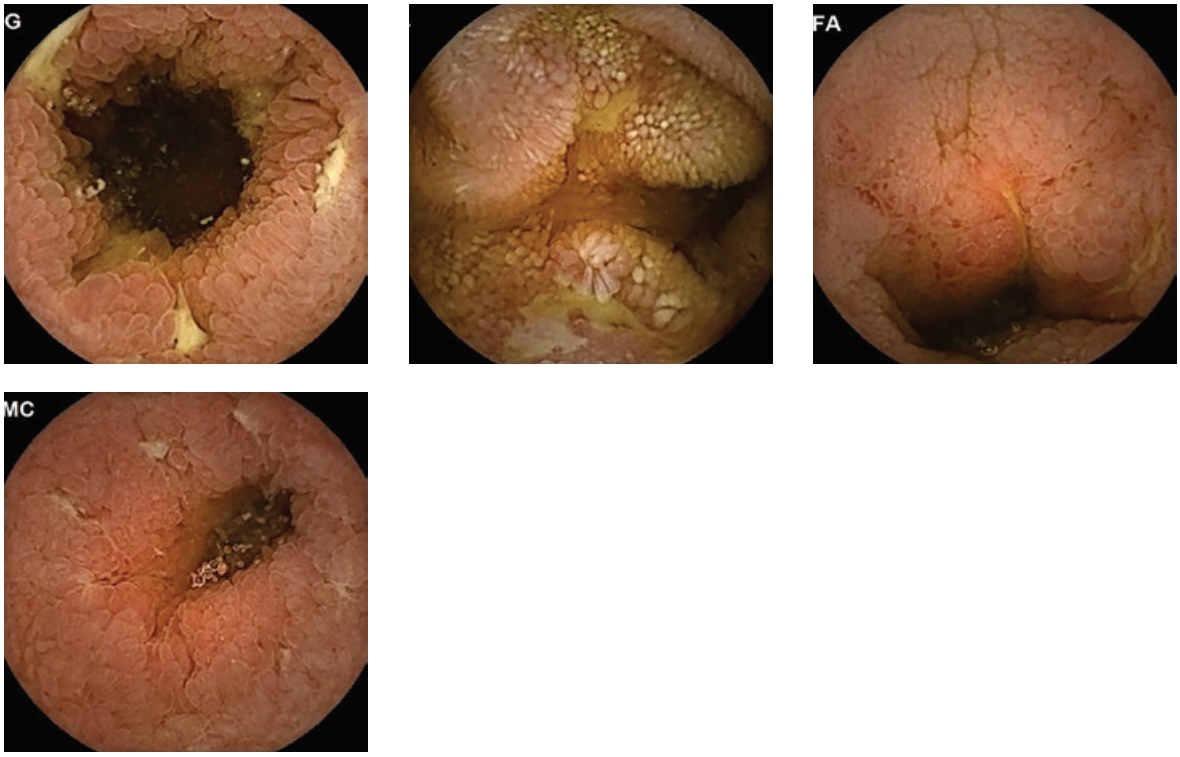


Figure 10-13
Ulcers and villous oedema in Crohn's disease.

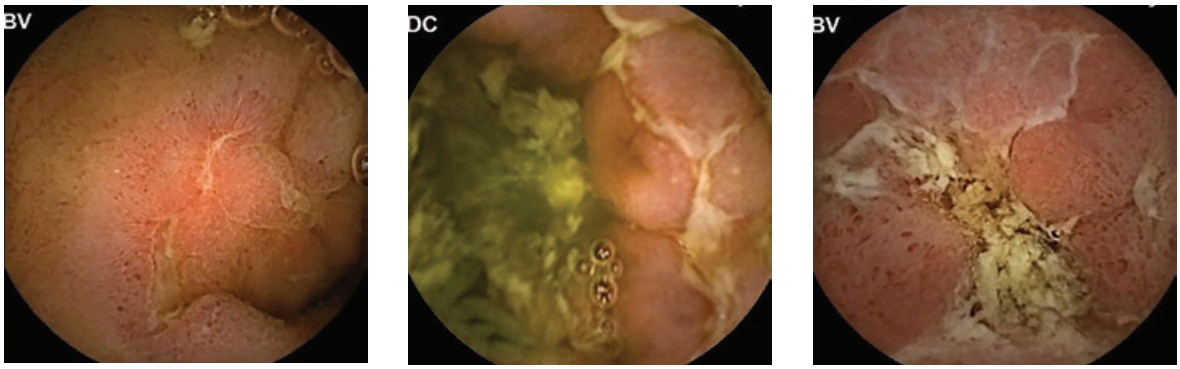


Figure 14-16
Multiple pleomorphic ulcers in Crohn's disease.

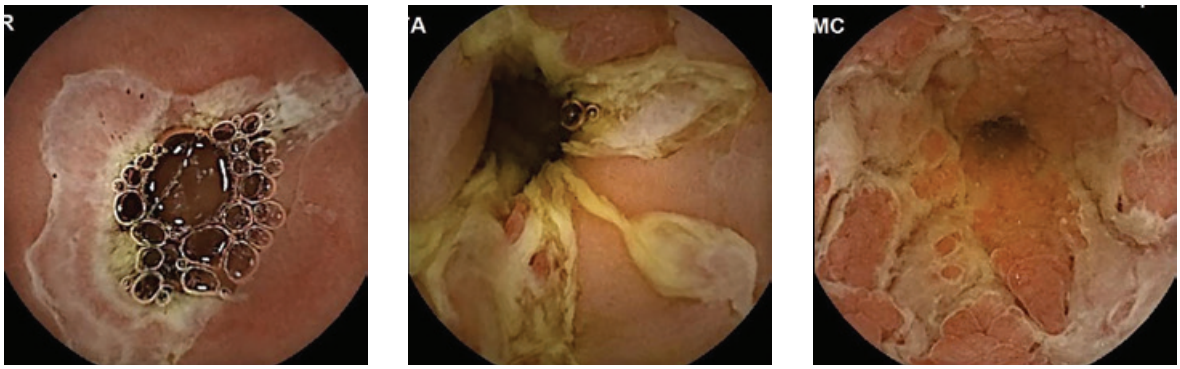


Figure 17-19
Large ulcers in Crohn's disease, occupying more than half of the lumen's circumference.

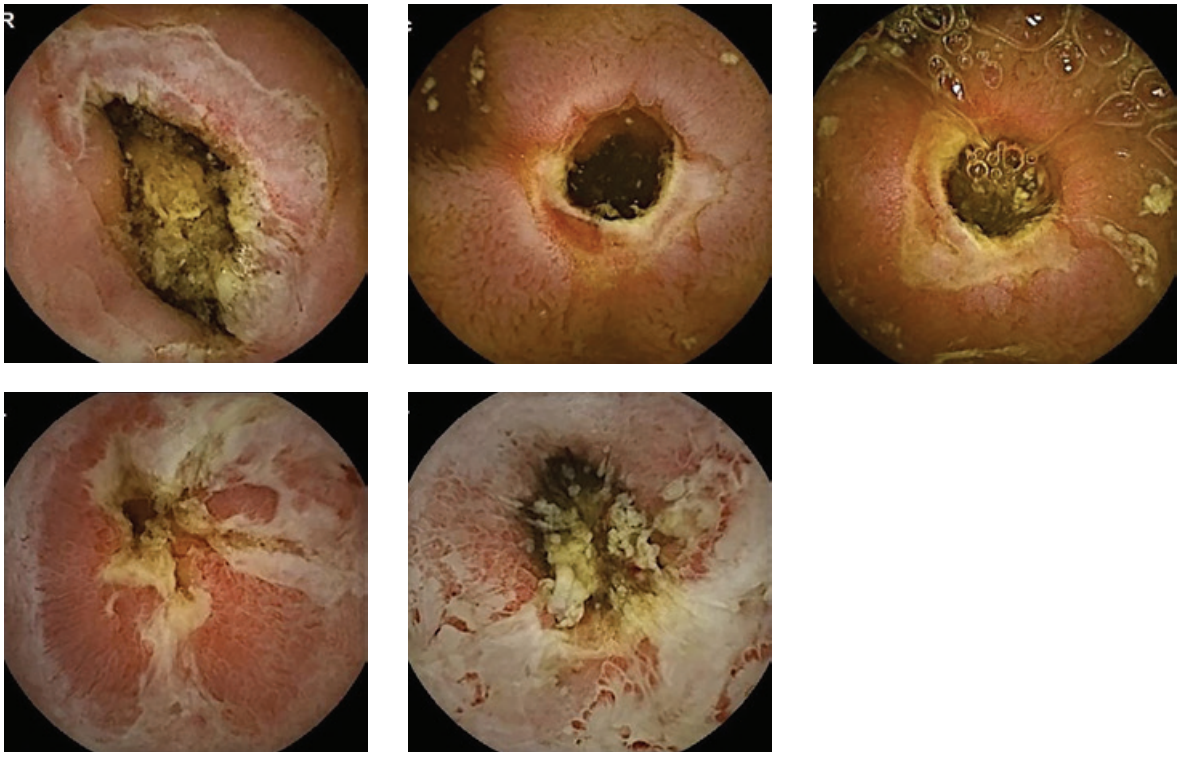


Figure 20-24
Ulcerated stenosis in Crohn's disease.

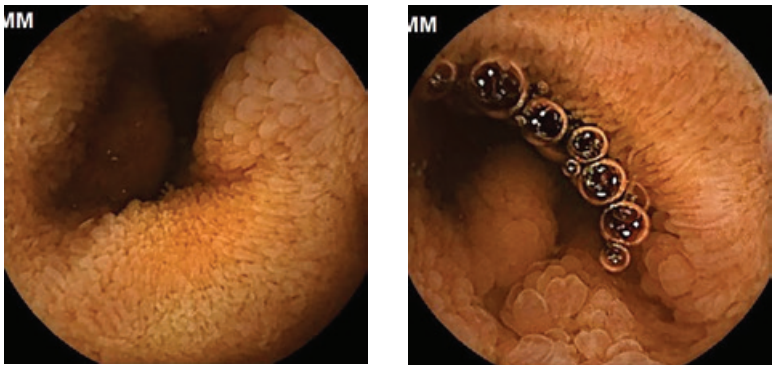


Figure 25-26
Inflammatory polyp with ulceration in Crohn's disease.

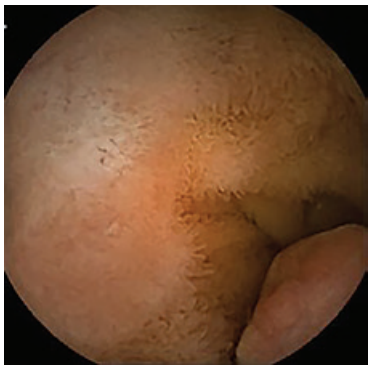


Figure 27
Inflammatory ileal polyp in Crohn's disease.

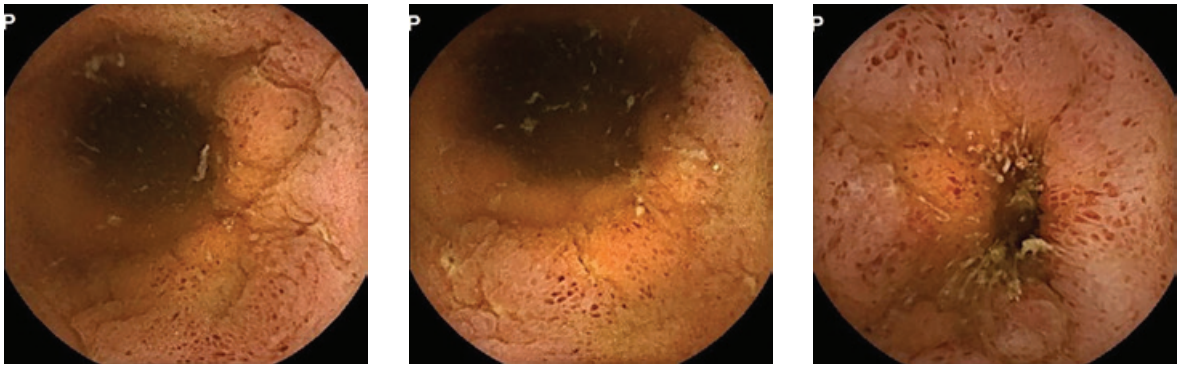


Figure 28-30
Ulcers and erosions in nonsteroidal anti-inflammatory drug (NSAID)-induced enteropathy.

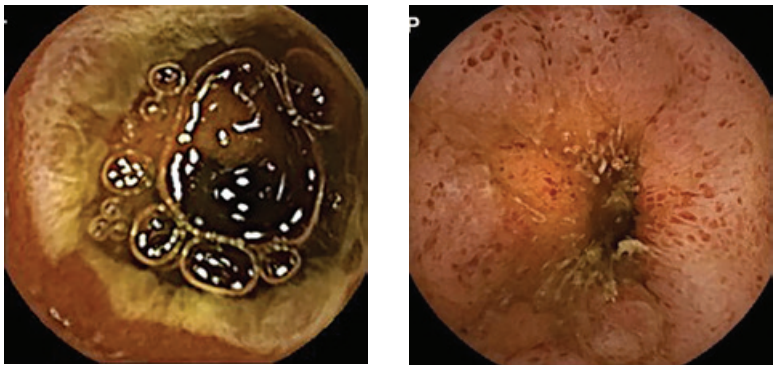


Figure 31-32
Stenosis in nonsteroidal anti-inflammatory drug (NSAID)-induced enteropathy.

2.3.2 Infectious Diseases

2.3.2.1 Intestinal Tuberculosis is caused by *Mycobacterium tuberculosis* and has a greater incidence in developing countries, although it is increasing in developed countries due to acquired immunodeficiencies. Clinical features include generalized or localized pain, weight loss, night sweats, fever and constipation or diarrhea. In endoscopy, the main findings are transverse ulcers, pseudopolyps, patulous ileocecal valve and involvement of less than 4 segments. The ileum is the most common segment involved. A definitive diagnosis of intestinal tuberculosis is performed based on positive staining for acid-fast bacilli in tissue samples, mycobacterial culture or polymerase chain reaction (PCR). The presence of necrotizing granulomas on histology or necrotic lymph nodes on imaging are very typical of intestinal tuberculosis.

2.3.2.2 Whipple's Disease is a chronic and rare multisystemic infection caused by the Gram-positive bacillus *Tropheryma whipplei,* most common in white middle-aged males. The clinical presentation generally consists of arthralgias, weight loss, abdominal pain and diarrhea. Endoscopic findings include mucosal edema with friability and bleeding, whitish-yellow plaques due to foamy lipid-laden macrophages (PAS, Periodic Acid–Schiff positive), lymphangiectasias, erosions and serpiginous ulcers (Figures 37-40). In SBCE, it has been demonstrated that this disease usually affects both the jejunum and the ileum.

2.3.2.3 Yersiniosis is an intestinal infection caused by the bacteria *Yersinia enterocolitica* and *Yersinia pseudotuberculosis,* that can cause terminal ileitis, enteritis and mesenteric lymphadenitis. Endoscopically, there are round or oval ulcers with elevated borders, and the diagnosis is performed by stool culture.

2.3.2.4 Cytomegalovirus (CMV) Infection is more common in immunocompromised patients, such as post-transplant status. Endoscopically, the typical findings may include polypoid masses and large ulcers that can cause bleeding, most often located in the jejunum.

2.3.2.5 Human Immunodeficiency Virus (HIV) Enteropathy is caused by an increased permeability of the intestinal epithelium, which occurs independently of opportunistic infections. The main clinical features are malabsorption, diarrhea and weight loss. In SBCE, it has been identified a higher

prevalence of erosions and villous atrophy with reduction or absence of Kerckring's folds, compared with controls.

HIV-positive patients can have opportunistic infections of the SB such as histoplasmosis, cryptosporidiosis and coccidioidomycosis, which are acquired immunodeficiency syndrome (AIDS)-defining diseases. Histoplasmosis can involve the terminal ileum and lead to deep central ulcers on top of pseudopolyps, hyperemia, friability and strictures. Cryptosporidiosis generally affects the duodenum and/or the terminal ileum, and endoscopy can be normal or include duodenal oedema, nodularity, loss of mucosal folds and loss of submucosal vasculature. Coccidioidomycosis can also cause multiple small ulcers in the SB.

2.3.2.6 Giardiasis is a parasitic infection by the flagellate protozoan *Giardia lamblia,* more common in children and endemic in areas of the world that have poor sanitation. Clinical features are variable, ranging from asymptomatic patients to diarrhea, weight loss and malabsorption. In SBCE, the most typical finding is villous atrophy and the diagnosis is based on a positive Giardia specific stool antigen, identification of trophozoites in duodenal specimens or aspirate, direct identification of cysts or trophozoites in fresh feces or specific Giardia PCR positive test.

2.3.2.7 Strongyloidiasis is caused by the nematode *Strongyloides stercoralis* which is endemic to tropical and subtropical countries. It should be suspected in patients with a history of travel to endemic areas and/or chronic GI and pulmonary symptoms accompanied by eosinophilia. The most common GI symptoms are nausea, vomiting, abdominal pain and diarrhea. Endoscopic findings in the duodenum include oedema, mucosal discoloration, erythema and subepithelial hemorrhages.

2.3.2.8 *Ascaris lumbricoides* Infection is the most common soil-transmitted helminthic infection, and with the increase in global migration and travel, its prevalence has increased in non-endemic regions. Most patients are asymptomatic, but symptoms and signs such as abdominal pain, bloating, intestinal obstruction, malnutrition or iron-deficiency anemia are also possible. SBCE can reveal the presence of a live helminth (Figures 41-42).

2.3.2.9 Hookworm Infection is caused by the roundworms (nematodes), more commonly in poor communities in the developing countries. This infection can cause SB bleeding or iron-deficiency anemia. SBCE usually demonstrates multiple adult hookworms in the proximal SB.

2.3.2.10 Tapeworm Infection is caused by *Taenia spp* and can cause iron-deficiency anemia. SBCE generally reveals the presence of a long, white worm, tangled in the ileum (Figures 43-44).

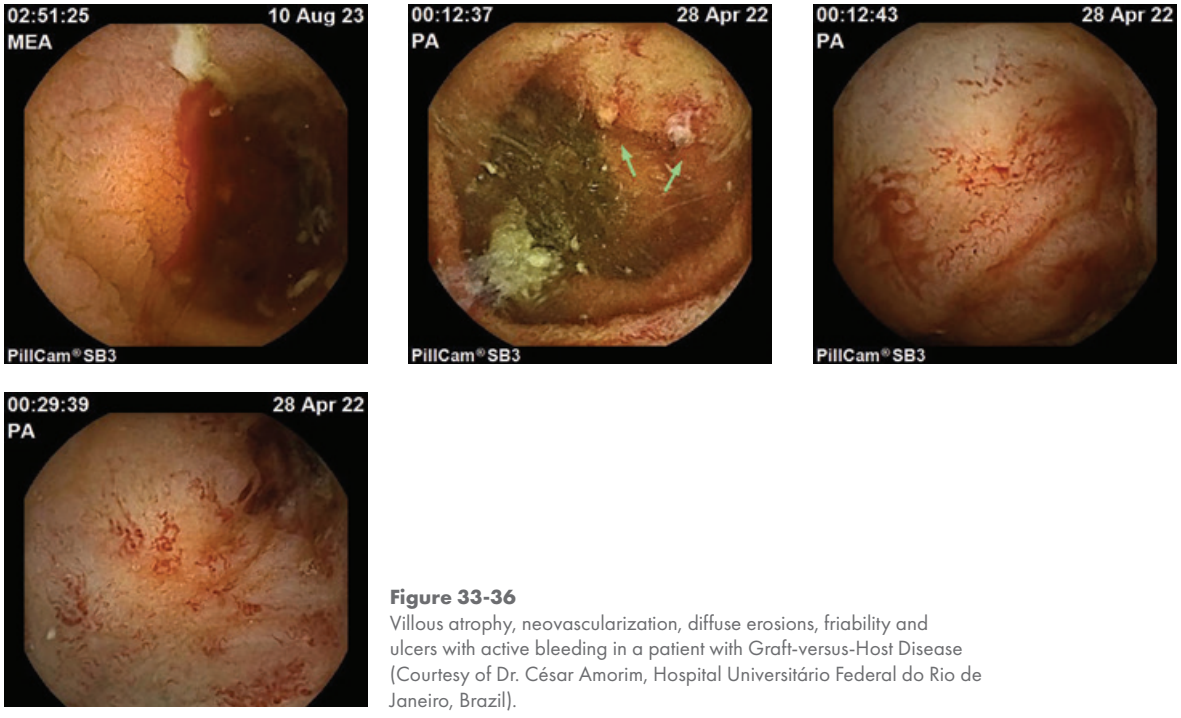
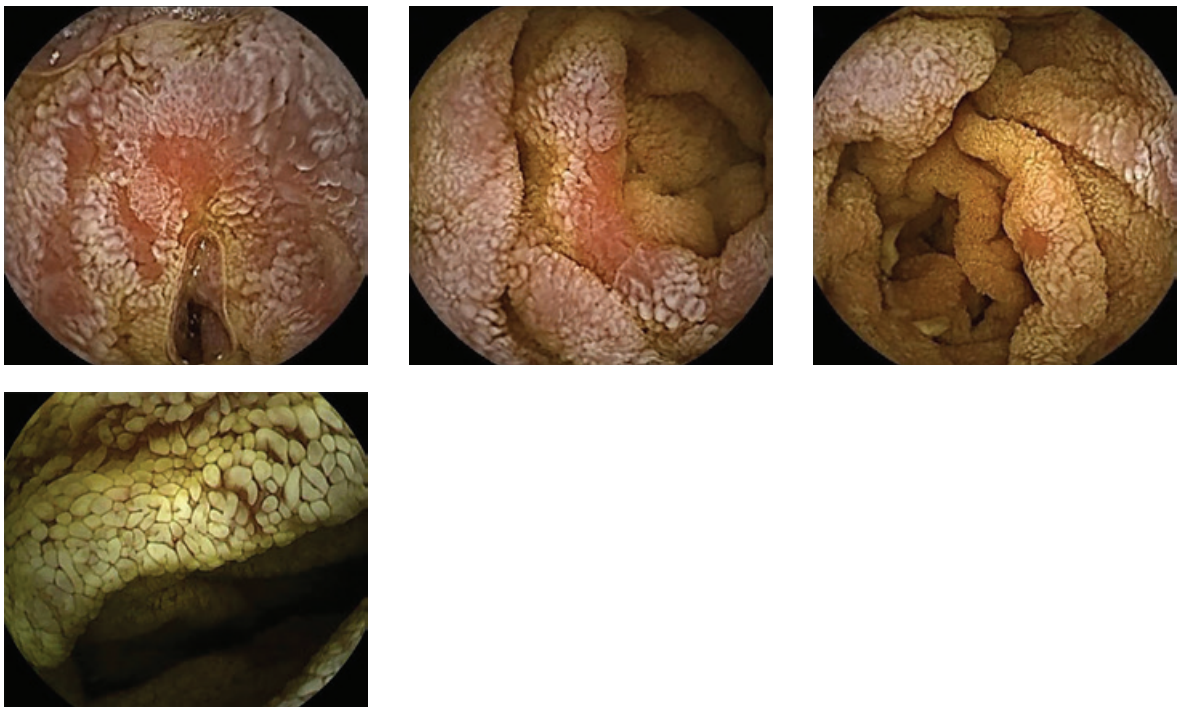
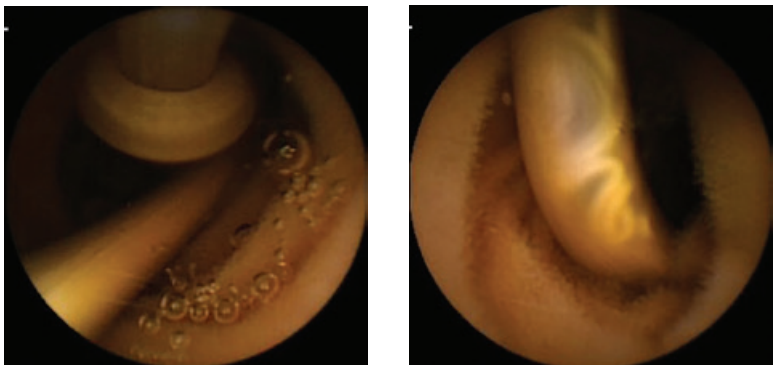


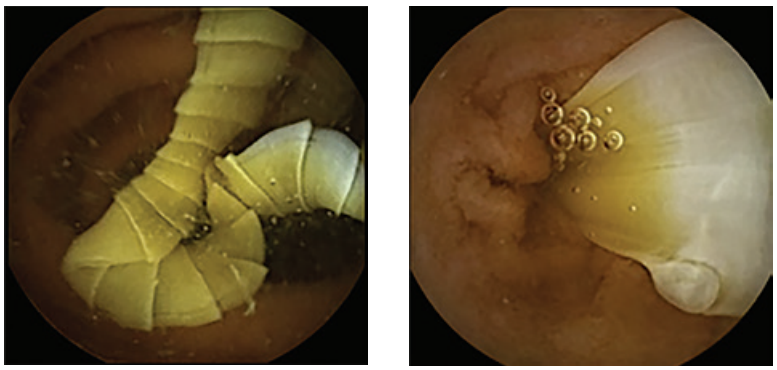
Figure 33-36
Villous atrophy, neovascularization, diffuse erosions, friability and ulcers with active bleeding in a patient with Graft-versus-Host Disease (Courtesy of Dr. César Amorim, Hospital Universitário Federal do Rio de Janeiro, Brazil).



Figures 37-40
Whipple's disease.



Figures 41-42
Ascaris lumbricoides.



Figures 43-44
Tapeworm.

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2.4. Malabsorption Syndromes

Malabsorption is a multifactorial clinical syndrome marked by impaired nutrient absorption through the intestinal mucosa into the bloodstream or lymphatics, and this process primarily involves the SB. Among those disorders that cause malabsorption, celiac disease has been pivotal in advancing understanding of SB disorders and enteropathies.

Traditionally associated with diarrhea and steatorrhea, malabsorption encompasses a wider clinical spectrum—from asymptomatic forms to severe systemic involvement.

This chapter explores malabsorption syndromes and highlights the role of CE in their diagnosis.

2.4.1 Celiac Disease

Celiac disease is a chronic, immune-mediated, multi-organ disorder triggered by the ingestion of gluten—a protein found in wheat, barley, and rye—in genetically predisposed individuals.

With a point prevalence of ~1%, celiac disease diagnoses have increased due to higher awareness and screening.

Celiac disease presents varied symptoms and malabsorption is common. While classic signs include diarrhea, steatorrhea, weight loss, and failure to thrive, many patients have manifestations like iron-deficiency anemia, neuropathy, short stature, bone disorders, elevated liver enzymes, poor pregnancy outcomes, or lymphoma.

Screening is essential in patients with malabsorption and first-degree relatives of affected individuals. Active case-finding with serological tests (while on a gluten-containing diet) is the preferred approach. IgA anti-tissue transglutaminase is the most sensitive, and total IgA should be checked to exclude IgA deficiency. IgA anti-endomysial antibody is the most specific and is useful for confirmation.

Endoscopic features include mucosal fissuring, nodular or mosaic mucosa, with a "cobblestone" appearance, duodenal atrophy with visible submucosal vessels, and scalloping or loss of intestinal folds. Although these findings are sensitive and specific, approximately one-third of newly diagnosed cases exhibit a macroscopically normal duodenum on endoscopy. Therefore, duodenal biopsies (at least two from the duodenal bulb and four from the second part of the duodenum) remain essential for confirming the diagnosis, using Marsh classification (types 1 through 3B, from the least to more aggressive disease) for histological staging.

CE has emerged as a valuable diagnostic tool for celiac disease. This modality offers the advantage of detecting characteristic mucosal abnormalities and estimating the extent of disease involvement along the entire SB.

In celiac disease diagnosis, CE is focused on detecting villous atrophy (sensitivity of 89% and specificity of 95% for diagnosis). However, its diagnostic sensitivity decreases in cases of partial villous atrophy, and early-stage lesions (Marsh types 1–2) may go undetected.

CE is also instrumental in evaluating patients with suspected complications of celiac disease, particularly those who do not respond adequately to a gluten-free diet, and guides further investigation via DAE. These complications include strictures, erosions, ulcerations, and lymphoma or adenocarcinoma.

In summary, CE serves a dual role in the context of celiac disease: it is useful both for diagnosis - when there is a clinical suspicion and serology compatible with celiac disease, but the duodenal endoscopic and histologic aspects are normal- and for monitoring disease progression - when there is a verified failure of gluten free diet, allowing surveillance of potential complications in the SB.

Figures 1-4 demonstrate typical signs of celiac disease showed in CE.

2.4.2 Whipple's Disease

Whipple's disease is a rare systemic infection by *Tropheryma whipplei*, leading to malabsorption. Classic symptoms include abdominal pain, diarrhea, weight loss, and arthralgia. However, its presentation may be heterogeneous and nonspecific, what may result in a prolonged, undiagnosed illness.

Diagnosis is confirmed by PAS-positive macrophages in duodenum biopsies during upper endoscopy. Yet, involvement may be more distal, and these biopsies may appear normal in up to 25% of cases.

CE has previously been used to aid in the diagnosis of Whipple's disease where upper endoscopy was insufficient. Findings might include villous atrophy, lymphangiectasia, and diffused, clubbed villi with possible associated luminal narrowing and nodularity.

CE examples of Whipple's disease are shown in figures 5-7.

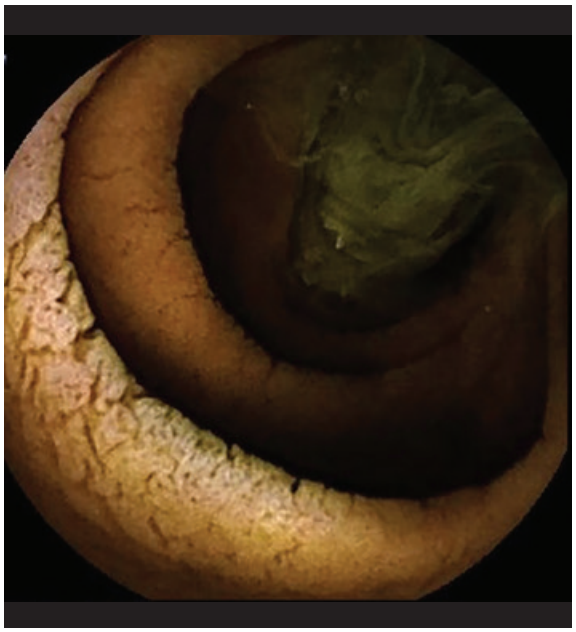

Figure 1
Scalloping of duodenal folds and villous atrophy in a patient with celiac disease.

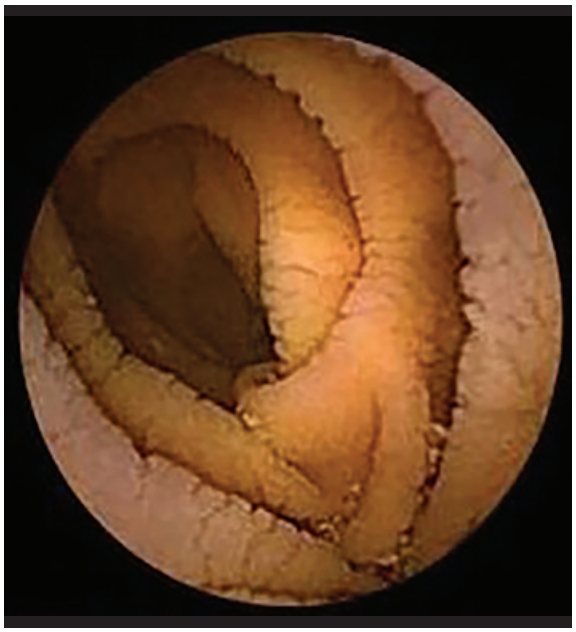

Figure 2
Scalloping of jejunal folds and villous atrophy in a patient with celiac disease.

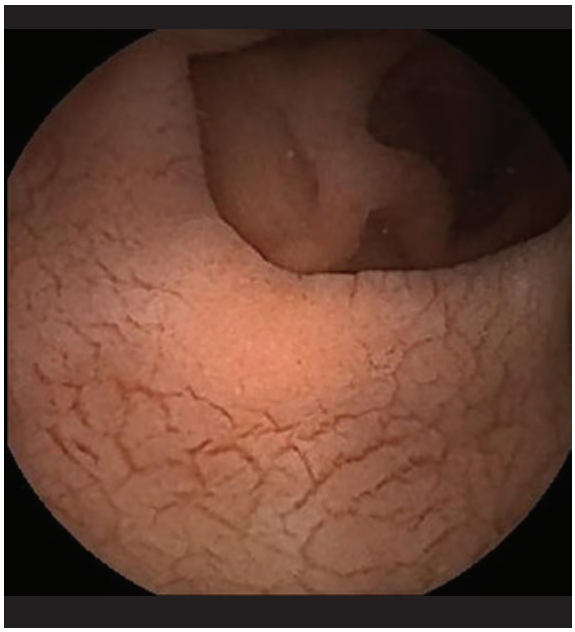

Figure 3
Jejunal mucosa with mosaic pattern ("cobblestone" appearance) in a patient with celiac disease.

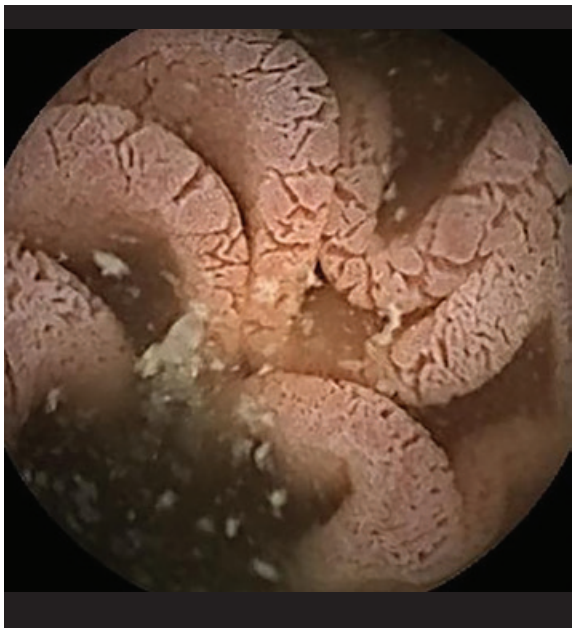

Figure 4
Ileal mucosa with scalloping of folds, edema, villous atrophy and mosaic pattern ("cobblestone" appearance) in a patient with celiac disease.

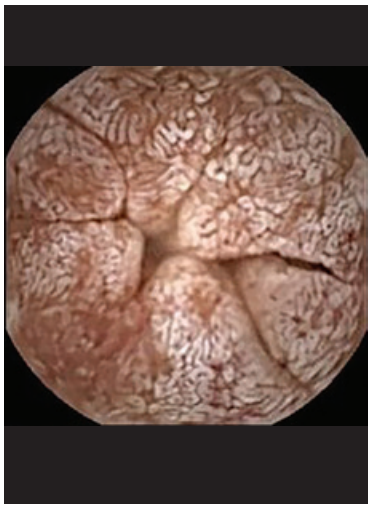

Figure 5
Duodenal mucosa with prominent lymphangiectasia in a patient with Whipple's disease.

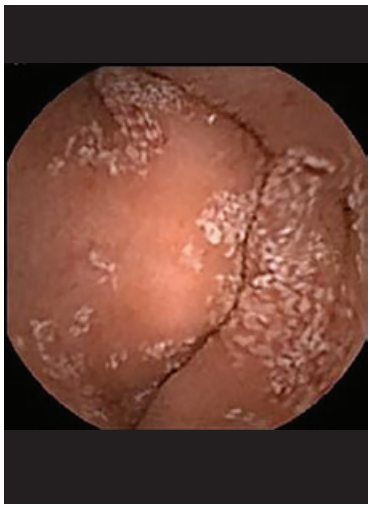

Figure 6
Jejunal mucosa with villous atrophy and clubbed villi in a "plaque" pattern in a patient with Whipple's disease.

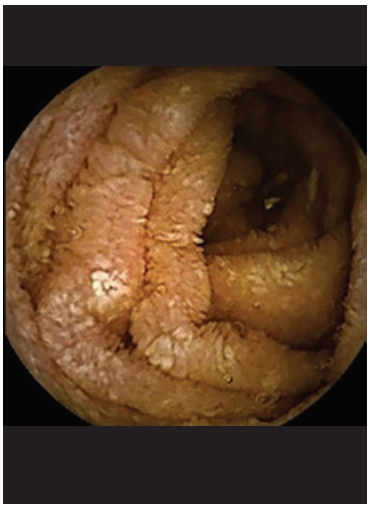

Figure 7
Jejunal mucosa with clubbed villi in a patient with Whipple's disease.

2.4.3 Intestinal Lymphangiectasia

Intestinal lymphangiectasia appears as small white spots in the SB mucosa, usually clinically insignificant. When extensive, it can cause protein-losing enteropathy due to blocked lymph drainage. This leads to hypoproteinemia, lymphocytopenia, and low serum immunoglobulins. Common manifestations are peripheral edema and ascites.

Intestinal lymphangiectasia may be primary (congenital) or secondary to conditions like abdominal or retroperitoneal carcinoma, lymphoma, chronic pancreatitis, retroperitoneal fibrosis, mesenteric tuberculosis, sarcoidosis, constrictive pericarditis, or chronic heart failure.

CE is useful for evaluating intestinal lymphangiectasia, showing diffuse dilated lymphatics as pinhead-sized white-yellow lesions. Nodular protrusions without whitish mucosa may also appear. Reported complications include bleeding, ulcers, stenosis, and lymphatic leakage.

Figures 8-9 show typical signs of intestinal lymphangiectasia that may appear in CE.

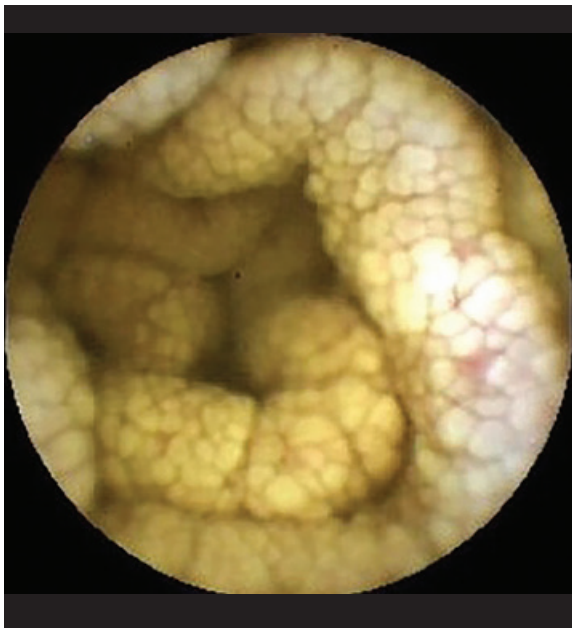

Figure 8
Enlarged white duodenal villosities in a patient with intestinal lymphangiectasia.

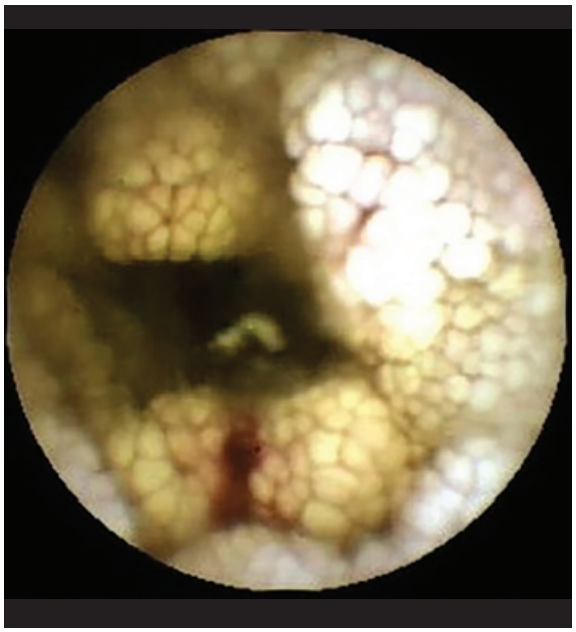

Figure 9
Enlarged white jejunal villosities and erosions in a patient with intestinal lymphangiectasia.

2.4.4 Eosinophilic Enteritis

Gastrointestinal eosinophilic disorders, including eosinophilic enteritis, are of unknown etiology and are characterized by mucosal eosinophilic infiltration and GI symptoms, after exclusion of secondary causes. Atopic comorbidities are present in about 50% of patients, with peripheral eosinophilia observed in 20–80%.

Diagnosis relies on clinical suspicion, imaging, endoscopy, and mucosal biopsies. However, histologic criteria remain controversial due to the lack of standardized thresholds.

Common manifestations include diarrhea, abdominal pain, nausea, vomiting, weight loss, bleeding, and in advanced cases, malabsorption.

Eosinophilic enteritis is difficult to diagnose due to its SB location and poor imaging sensitivity. Suggested histologic criteria for eosinophilic enteritis include 56 eosinophils per high-power field in ileal mucosal samples, presence of eosinophilic cryptitis or crypt abscesses, and abnormal distribution of eosinophils.

CE can reveal non-specific findings such as mucosal edema, erythema, salmon-colored patches, ulceration, and stenosis; while these are not pathognomonic, they can raise suspicion of this clinical entity. Diagnostic confirmation ultimately may require histological examination via DAE or, in rare cases, surgical resection.

CE plays a pivotal role in guiding diagnosis and management of eosinophilic enteritis - it helps to avoid unnecessary surgery and supports conservative treatment (typically dietary modifications and corticosteroid therapy).

CE examples of eosinophilic enteritis are shown in figures 10-11.

2.4.5 Common Variable Immunodeficiency-Associated Enteropathy

Common Variable Immunodeficiency (CVID) is the most prevalent primary immunodeficiency in adults. It is considered a rare disease (estimated prevalence from 1 in 100,000 to 1 in 10,000 individuals).

Diagnosis is based on a primary deficiency in IgG, often accompanied by reduced levels of IgA and/or IgM, and impaired/absent antibody responses to vaccination. The clinical presentation of CVID is variable, but patients typically exhibit increased susceptibility to recurrent bacterial infections—particularly of the sinopulmonary tract—as well as autoimmune conditions - such as IBD - and malignancies - especially lymphomas.

GI symptoms occur in 20–60% of patients. Around 10% experience malabsorption or weight loss; prevalence of CVID-associated inflammatory enteropathy is 2–4%.

Endoscopic findings are often non-specific and may resemble those seen in IBD, or they may

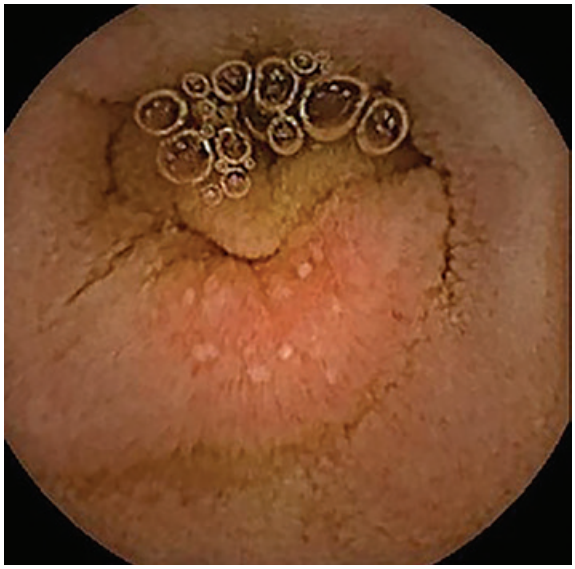

Figure 10
Patchy redness with edema in the jejunal mucosa in a patient with eosinophilic enteritis.

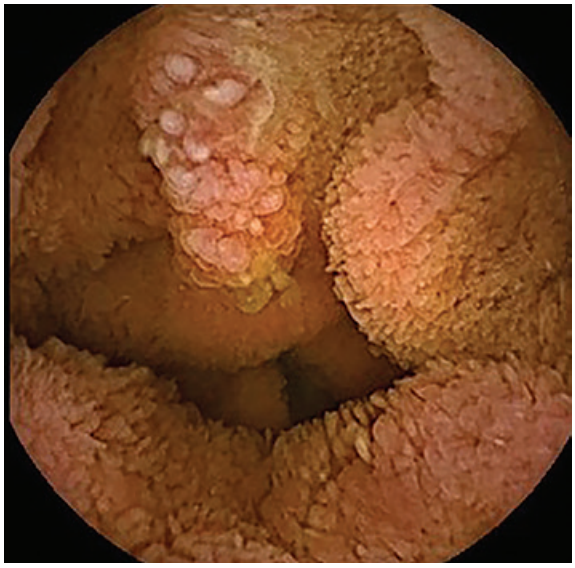

Figure 11
Erosions and edema in the jejunal mucosa in a patient with eosinophilic enteritis.

display sporadic or diffuse nodular lymphoid hyperplasia. Histologically, features include lack of plasma cells in the lamina propria, increased intraepithelial lymphocytes, crypt apoptosis, granulomas, and architectural distortion of crypts.
CE plays a critical role in evaluating GI symptoms in CVID patients with normal standard endoscopic findings. It can reveal mucosal abnormalities such as erosions, small ulcers, or extensive nodular lymphoid hyperplasia. Additionally, CE helps assessing the extent of SB involvement and can aid in detecting complications like lymphoma.
Capsule imagens of CVID are shown in Figures 12-13.

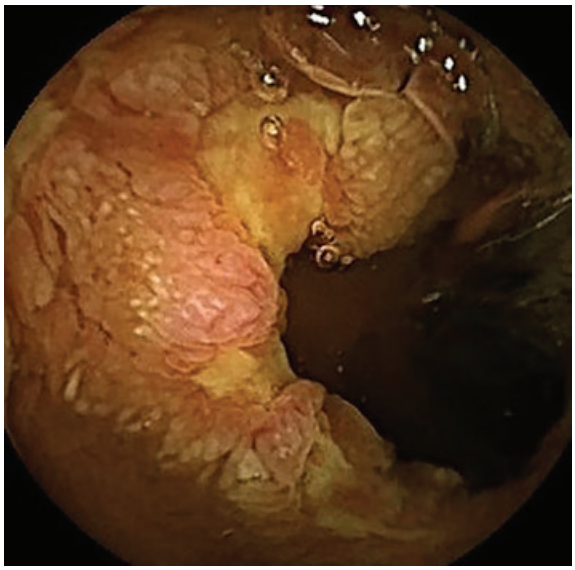

Figure 12
Jejunal mucosa with edema and ulceration in a patient with CVID.

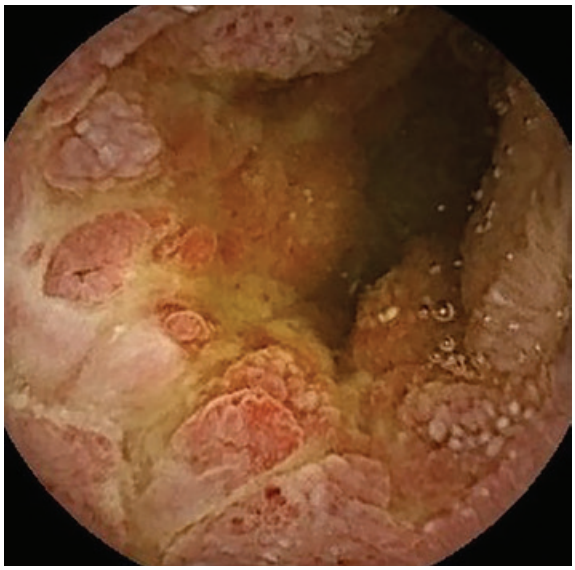

Figure 13
Jejunal mucosa with edema and ulceration in a patient with CVID.

2.4.6 Olmesartan-associated Sprue-like Enteropathy

Olmesartan-associated sprue-like enteropathy is a rare malabsorption syndrome characterized by chronic diarrhea and weight loss, developing after the use of olmesartan; symptoms typically appear months to years after initiating therapy.
Diagnosis relies on duodenal histology showing

villous atrophy, after excluding other causes. When duodenal findings are normal, CE may reveal villous atrophy in more distal regions of the SB.
Definitive diagnosis and treatment involve discontinuation of olmesartan, which usually results in rapid resolution of diarrhea. However, recovery from malabsorption—such as hypoalbuminemia—may take longer, likely reflecting the time required for mucosal regeneration and restoration of normal villous architecture.
CE examples of this entity are shown in figures 14-15.

2.4.7 Other Entities

Additional conditions that cause malabsorption include Crohn's disease, lymphoma, immunodeficiency syndromes, and reduced bowel length post-surgery.

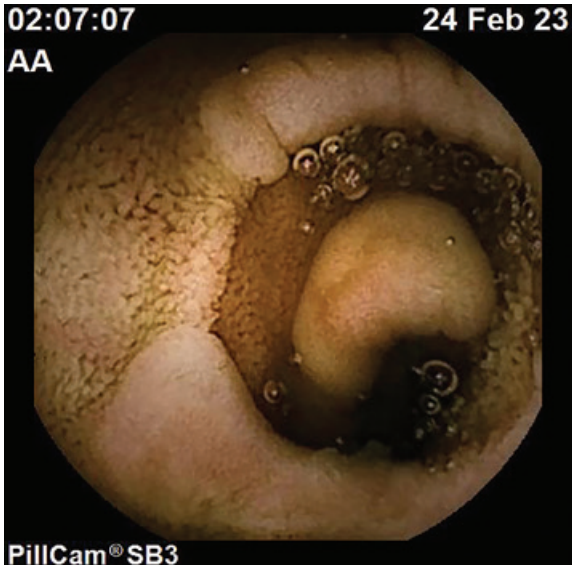

Figure 14
Villous atrophy in the jejunal mucosa of a patient with olmesartan-associated sprue-like enteropathy.

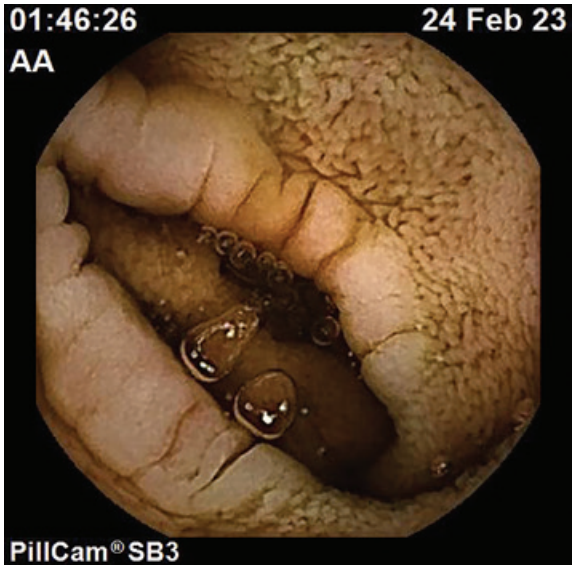

Figure 15
Fold atenuation in the ileal mucosa of a patient with olmesartan-associated sprue-like enteropathy.

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2.5. Other Findings

Pathological lesions are less common in the SB compared to other parts of the digestive system. Besides the common findings covered earlier, SBCE may also reveal various other SB abnormalities.

2.5.1. Small Bowel Mucosal Lesions

2.5.1.1. Actinic/Radiation Enteritis refers to lesions caused by SB exposure to radiation (generally after radiotherapy). Radiation leads to a progressive ischemia condition and endarteritis, which may cause early SB lesions after treatment or even some years after conclusion of treatment. It can appear in various ways such as villous denudation, diffuse lymphangiectasias, neovascularization, haemorrhagic suffusions or stenosis (Figure 1).

2.5.1.2. Polyps of the SB may occur as manifestation of familial polyposis syndromes (Familial Adenomatous Polyposis, Peutz Jeghers Syndrome (PJS)), non-familial syndromes (Cronkhite-Canada syndrome), other familial syndromes (Muir-Torre, Lynch) or may occur as sporadic polyps (Figure 2-7). Polyps of the SB can be of various types such as adenomas, inflammatory or hamartomatous. Some vascular lesions such as hemangiomas may also have a polypoid appearance.

2.5.1.2.1 Small Bowel Polyposis Syndromes have a low prevalence but are clinically relevant because of its high morbidity and mortality. In familial adenomatous polyposis and MYH – associated polyposis, adenomas are found mainly in the duodenum although the presence of extensive duodenal adenomas (Spigelman degree III and IV) are a risk factor for jejunal-ileal adenomas.

2.5.1.2.2 Sporadic Adenomatous Polyps of the SB are mainly located in the proximal jejunum; they are usually asymptomatic until they are over 2 or 3 cm. At this point, they can cause invagination episodes, intestinal obstruction or mid-gastrointestinal bleeding (Figure 2-4). Carcinogenesis in SB seems to occur in a similar way to the adenoma-carcinoma sequence occurring in colorectal cancer.

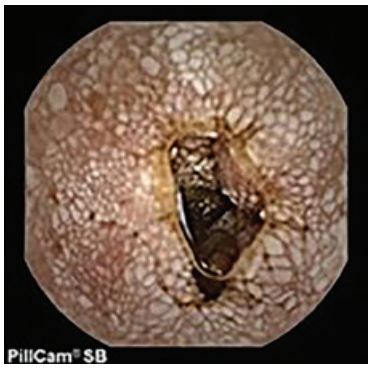
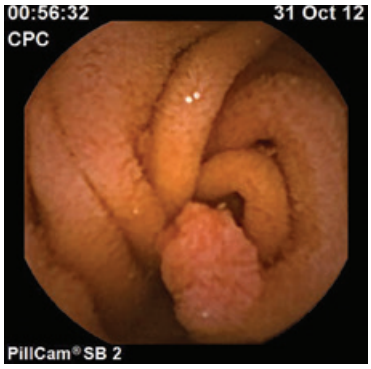
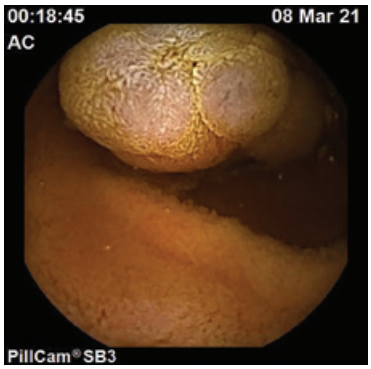
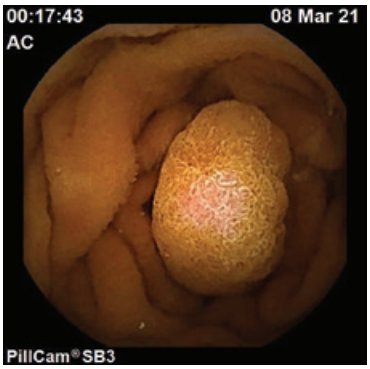


Figure 1
Actinic/Radiation Enteritis.





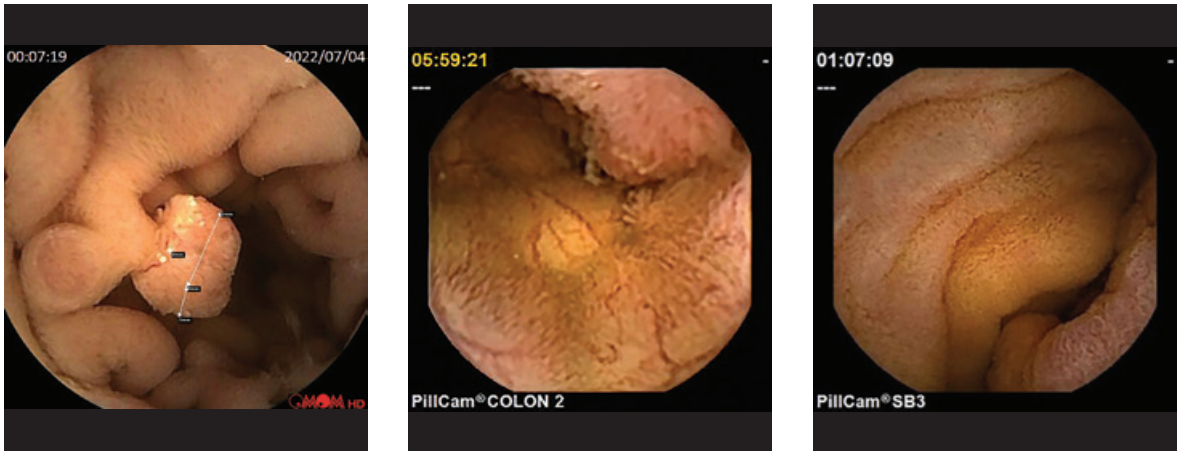


Figures 2-4
Sporadic adenomatous polyps.

However, the incidence of carcinoma is lower for sporadic polyps than for polyposis-associated forms, and it is also lower than for colonic polyps.

2.5.1.2.3 Hamartomatous Polyps generally appear in a polyposis syndrome context such as Peutz-Jeghers syndrome (PJS), Cronkhite-Canada syndrome or juvenile polyposis. They may have an irregular surface with nodular appearance or be lobulated and larger (Figure 5-7). Although the risk of malignant transformation is low, foci of adenocarcinoma have been reported. In PJS, they are present in 65% of patients; clinical symptoms due to intestinal obstruction, intussusception or bleeding appear early. SBCE should be performed at 2-3 year intervals, beginning at 8 to 10 years of age. DAE should be indicated if lesions larger than 1 cm are found in SBCE. This strategy has been shown to reduce the need for surgical intervention in these patients.

Inflammatory polyps of the SB can appear in IBD patients as a result of the healing-regeneration cycle. They are usually small although giant symptomatic pseudo-polyps have been described.



Figures 5-7
Hamartomatous polyps.

2.5.1.3. Small Bowel Lymphangiomas are exceedingly rare tumors (Figure 8 A,B). Although benign, they can become symptomatic, causing GI bleeding, intussusception or protein-losing enteropathy. Endoscopically, they present as polypoid lesions with a white-yellow surface and "strawberry-like" mucosa, reflecting the edematous mucosa along with multiple hemorrhagic red spots.

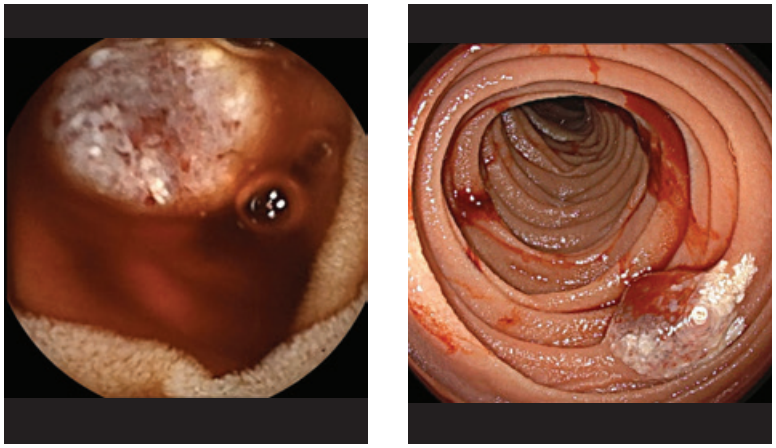


Figure 8 (A, B)
SB Lymphangioma. **A**. CE revealing a lesion with whitish surface and "strawberry-like" mucosa, and fresh blood at the proximal jejunum. **B**. Push enteroscopy showing an actively oozing 12 mm soft sessile lesion.

2.5.1.4. Small Bowel Pseudomelanosis is rarely reported (Figure 9 A,B,C). In SB pseudomelanosis, the pigments deposited within macrophages in the lamina propria are essentially iron sulfide and/or hemosiderin but deposition of lipofuscin, silicates, titanium and other minerals is also possible. It seems that there is a strong correlation between SB pseudomelanosis and oral iron therapy, although some authors defend that oral iron intake is not the sole condition associated with pseudomelanosis. In fact, association with hypertension/antihypertensive medications, end-stage renal disease and diabetes mellitus has also been described.

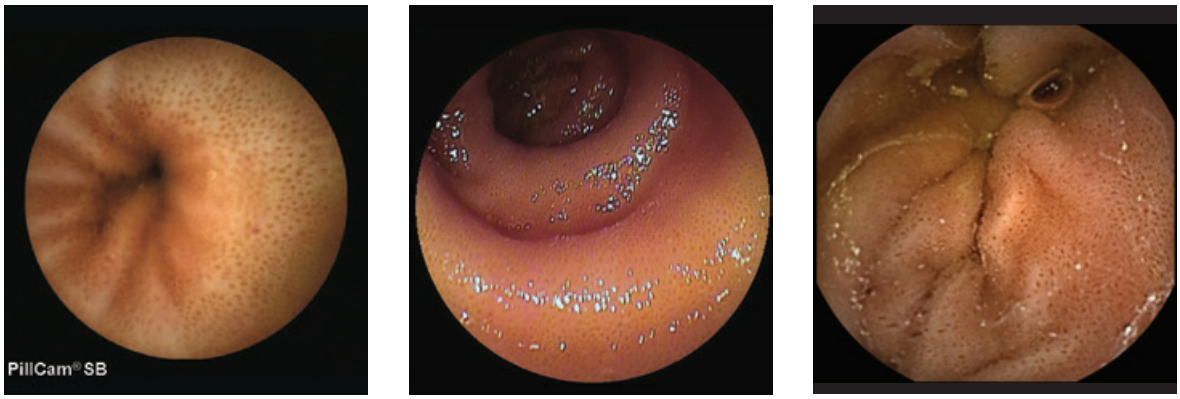


Figure 9 (A, B, C)
SB Pseudomelanosis. **A,C**. Capsule endoscopic image shows a brown pigmentation with a speckled, continuous patterns in the proximal jejunum. **B**. DAE revealed the same brown pigmentation with a speckled pattern in the proximal jejunum.

2.5.2. Small Bowel Submucosal Lesions

These comprise a group of lesions that protrude under the mucosa into the GI lumen, originating from the deeper layers. They are essentially benign (e.g., leiomyomas, lipomas) or, less frequently, may correspond to malignant tumours (see Chapter 2.4). The frequency of benign SB submucosal lesions increases from the duodenum to the ileum. The most frequent are leiomyomas and lipomas (Figure 10), followed by Brunner's gland adenomas (Brunneromas), neurofibromas, and desmoid tumors.

2.5.2.1. Lymphoid Nodular Hyperplasia a common incidental submucosal finding in SBCE, is caused by infiltration of submucosal lymphocytes through active germinal centers (Figure 11). It is a physiological process occurring in the ileum at young ages. Its presence in more proximal segments may be associated with immunodeficiencies, parasitic infections (e.g., giardiasis), or celiac disease.

2.5.2.2. Small Bowel Heterotopic Pancreas lacks both anatomical and vascular continuity with the main pancreas (Figure 12 A,B). The most common location is the duodenum, particularly the first and second portions, and it is rare in the jejunum (0.5–16.3%). It is usually detected incidentally. Symptoms and complications are related to the lesion's size (>15 mm) and its relation to the mucosal surface. A definitive preoperative diagnosis is difficult. SB endoscopy is crucial for identifying the lesion (often showing a suggestive caterpillar-like appearance) and marking it for surgical referral if it is large and symptomatic.

2.5.3. Other Findings of the Bowel Wall and Lumen

These include luminal dilatation due to distal SB obstruction, postoperative changes such as anastomoses, suture lines, and other materials like staples (Figure 13).

2.5.3.1. Diverticula appear as outpouching sacs, which may be congenital or acquired (Figure 14–15). They are most frequently found in the duodenum (79%) but may also occur in the jejunum and ileum (18%). In a series of 208 patients, those with diverticula in the jejunum and ileum had a complication rate of 46%, compared to 13% for those in the duodenum. Jejunoileal diverticula were more prone to diverticulitis, perforation and abscesses, while bleeding was more frequent with duodenal diverticula.

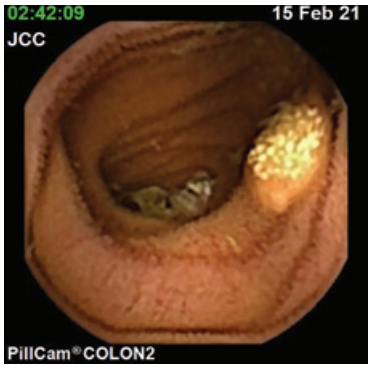


Figure 10
Lipoma with overlying lymphangiectasia.

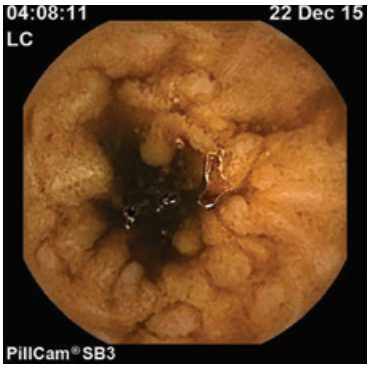
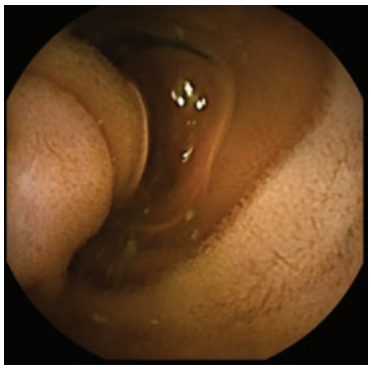


Figure 11
Lymphoid Nodular Hyperplasia.



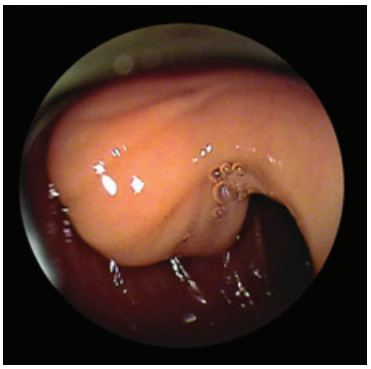


Figure 12 (A, B)
SB Heterotopic Pancreas. **A**. CE shows a subepithelial lesion at the proximal jejunum. **B**. DAE revealed a caterpillar shape subepithelial lesion with a 20 mm in diameter at the proximal jejunum.

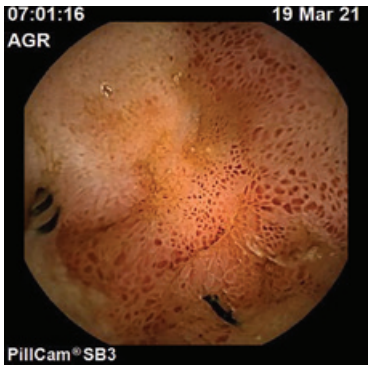


Figure 13
Surgical staples after diverticulotomy.

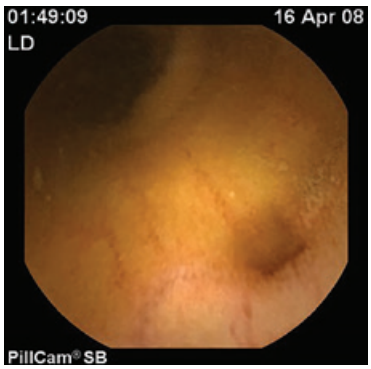


Figure 14
Small jejunal diverticulum.

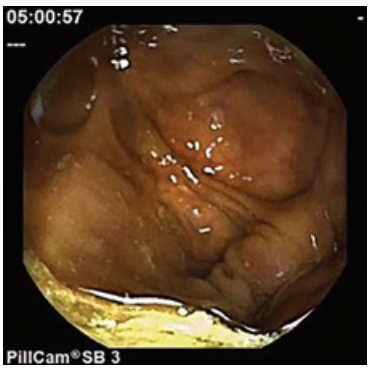


Figure 15
Large duodenal diverticulum.

2.5.3.2. Meckel's Diverticulum deserves special attention. It results from incomplete obliteration of the omphalomesenteric (vitelline) duct and contains all the normal layers of the small intestinal wall (Figure 16). It arises from the antimesenteric border of the ileum, 30–80 cm from the ileocecal valve, and has an average length of 5 to 6 cm. In approximately half of all cases, it contains ectopic tissue - most commonly gastric mucosa (60%), and it is the most frequent congenital abnormality of the GI tract, affecting about 2% of the population. Between 25–50% of symptomatic patients are under 10 years old. Complications include bleeding, intestinal obstruction, diverticular inflammation, and perforation.

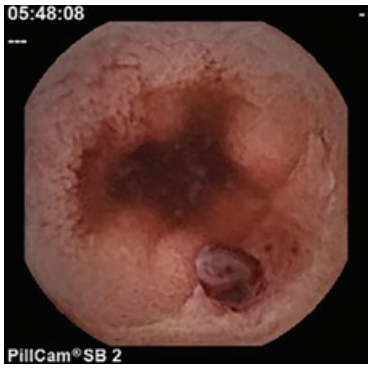


Figure 16
Meckel's diverticulum with ulceration and visible vessel.

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3

Colon Capsule Endoscopy

3.1. Technology

Colon capsule endoscopy (CCE) is a non-invasive diagnostic procedure used to visualize the colon as an alternative to colonoscopy. It involves swallowing a capsule equipped with miniature cameras, light sources and wireless transmitters. As the capsule travels through the GI tract, it captures high-resolution images that are transmitted to an external data recorder, with a real-time viewer worn around the patient's waist. Once the study is complete, data from the recorder is uploaded to a computer with specialized software that compiles the images into a continuous video.

The first generation of CCE, the PillCam™ COLON 1, was released in 2006. Since then, technological advancements have been made, and the PillCam™ COLON 2 has become the most widely used system (Figure 1). It measures 11.6x31.5 mm and is equipped with two cameras, one at each end, with 172° field of view. This capsule has an internal battery designed to last at least 10 hours and includes a sleep mode to economize energy. It captures 4 to 35 images per second, adjusting dynamically based on movement and light conditions.

Figure 1
PillCam™ COLON 2.

3.2. Patient Preparation

The rate of adequate cleansing is a quality indicator in capsule endoscopy. The cleansing protocol aims to ensure clear visualization of the colonic mucosa, reduce air bubbles and promote capsule progression before battery depletion.

Preparation typically involves a clear liquid diet the day before the procedure, followed by ingestion of bowel-cleansing agents such as polyethylene glycol (PEG), ideally in split doses, for better effectiveness and tolerability. Booster doses, commonly sodium phosphate (NaP), at low doses (45 to 55 mL), may be added to enhance cleanliness and propulsion but should be avoided in patients with electrolyte imbalance, hypovolemia, kidney disease, medications that affect renal perfusion, bowel obstruction, active colitis, and in elderly patients. Prokinetics are used if the capsule remains in the stomach for over an hour and simethicone helps reduce bubbles. Iron supplements should be stopped seven days prior to the procedure and nonsteroidal anti-inflammatory drugs (NSAIDs) for at least four weeks before CE.

A preparation protocol example is explained in Table 1.

Table 1.
CCE Preparation Protocol.

Time	Step
Day before exam	Clear liquid diet and 2L PEG (7 pm – 9pm)
Morning exam (2h before exam)	2L PEG
At the same time as swallowing capsule	Simethicone 105mg/mL (2 mL)
If 1h later the capsule stays in stomach	Prokinetic (Domperidone 10 mg)
After passing into small bowel	First booster (30 mL NaP diluted in 1L water)
3 hours after first booster	Second booster (15 mL NaP diluted in 1L water)
2 hours after second booster	Bisacodyl 10mg suppository

NaP, sodium phosphate; **PEG**, polyethylene glycol.

For a better assessment of bowel cleanliness, a qualitative grading scale was proposed (Table 2).

Table 2.
Cleasing Scale

	Rating	Description
Cleansing level scale	Poor	Inadequate Large amount of fecal residue precludes a complete examination
	Fair	Inadequate but examination completed Enough feces or turbid fluid to prevent a reliable examination
	Good	Adequate Small amount of feces or turbid fluid not interfering with examination
	Excellent	Adequate No more than small bits of adherent feces
Bubbles effect scale	Significant	Bubbles that interfere with the examination More than 10% of surface area obscured by bubbles
	Insignificant	No bubbles or bubbles that do not interfere with the examination Less than 10% of surface area obscured by bubbles

More recently, other CCE cleansing grading scales have been described and validated, such as Colon Capsule CLEansing Assessment and Report (CC-CLEAR). This score divided colon into three segments (right-sided, transverse and left-sided colon) and scored each segment according to an estimation of the percentage of visualized mucosa (0, <50%; 1, 50%-75%; 2, >75%; 3, >90%). The overall cleansing classification was a sum of each segment score, grading between excellent (8-9), good (6-7), and inadequate (0-5). Any segment scoring ≤1 resulted in inadequate overall classification.

3.3. Indications

Clinical indications for CCE remain an issue of continuous clinical research.
The 2020 update of the guidelines from the European Society of Gastrointestinal Endoscopy (ESGE) and the European Society of Abdominal Radiology (ESGAR) suggests CCE as an alternative to colonoscopy in the following cases:

- **Incomplete colonoscopy due to non-neoplastic obstruction**, preferably the same or the next day
- **Patients with non-alarm symptoms**
- **Positive fecal occult blood test (FOBT) or fecal immunochemical test (FIT) with incomplete or unfeasible colonoscopy**, within organized population screening programs.

Despite these limited formal indications, CCE is an attractive option for patients undergoing **colon cancer screening** due to its minimally invasive nature. Based on current evidence, this procedure could be an acceptable colorectal cancer screening method for selected patients.
In IBD, CCE is not recommended. While studies have demonstrated a strong correlation in endoscopic scores between CCE and colonoscopy, the inability to obtain biopsies, particularly in patients with ulcerative colitis, and the increasing use of PCE in Crohn's disease have limited its use in these disorders.

3.4. Reading

Before reading CCE it is imprescindible to know the indication for the exam and patient clinical history.

3.4.1 Software

Software allows single view, one of the two cameras per time, and double view with both cameras simultaneously (Figure 2).

It also has some special modes like Flexible Spectral Imaging Color Enhancement (FICE), that is a virtual chromoendoscopy, blue mode, suspected blood indicator, quick view, collage mode and top 100 mode (Figure 3).

Tools like polyp size estimation (Figure 4), atlas consultation (Figure 5) and capsule localization are available.

3.4.2 Environment for Reading

Reading should be performed in a quiet, well-lit environment to minimize distractions and fatigue. We should allocate dedicated time to reading CCE videos to maintain high standards and thoroughness. The official time for view should be at least 45–65 min for the first readers and at least 25–35 min for the validators.

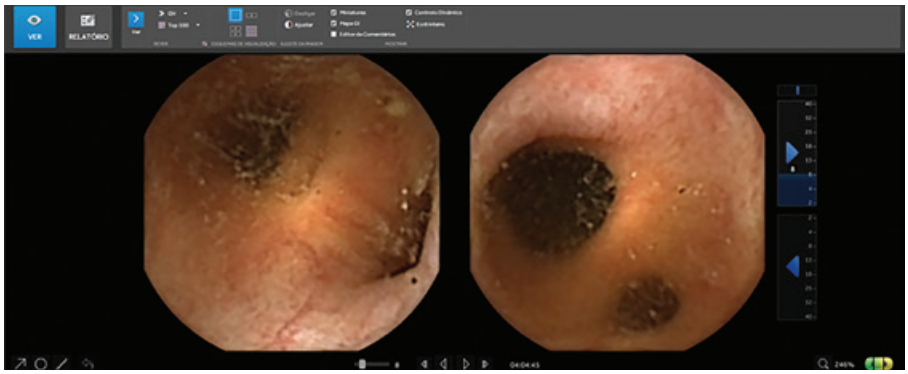

Figure 2
Double view.

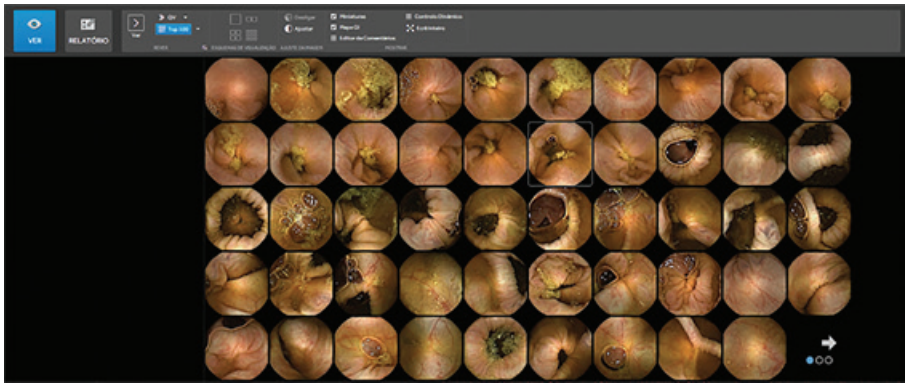

Figure 3
Top 100 mode.

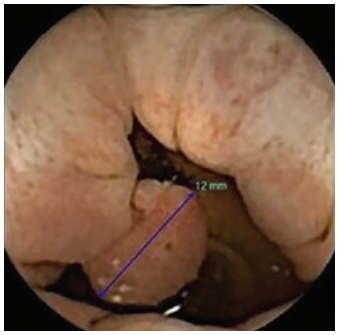

Figure 4
Polyp size estimation tool.

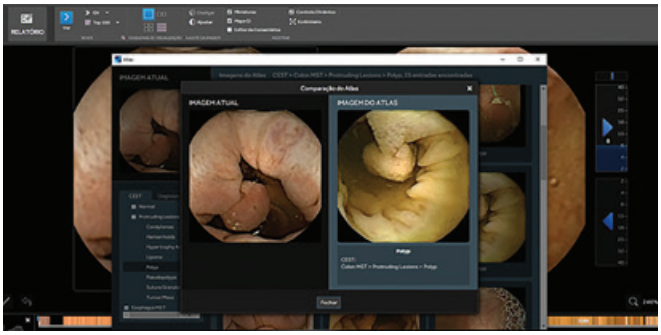

Figure 5
Atlas consultation.

3.4.3 Practical Process of Reading

There is no scientific proof supporting the optimal way to read a CCE video, but there is a strong need for a structured reading process. The following steps are suggested:

1. Quick preview of the entire video, with both cameras simultaneously
2. Look at the total length of time that the capsule needed to go through the colon
3. Identify the landmarks (caecum, hepatic and splenic flexures and rectum/anus excretion of capsule)
4. View the images from each camera alone at a frame rate max 8–15 frames per second and slow down if the capsule moving fast
5. Capture any suspected lesions and some normal images for photo documentation. Check the marked suspected lesions using white light and sometimes virtual chromoendoscopy for characterization, measure polyp using size estimation tool and count them
6. Check Top 100 and collage mode images for missed findings
7. Prepare the report

3.4.4 Report

Report should include:

1. Reason for CCE
2. Relevant clinical data (i.e. previous surgery)
3. Characteristics of study (equipment, time procedure)
4. Completeness
5. Colon transit time
6. Preparation
7. Colon and extra-colon findings
8. Significance of findings
9. Photo-documentation
10. Recommendations and follow-up

It should be noted that AI has gained importance and demonstrated its potential in the field of CCE. Several studies show its benefits in reducing reading time and improving accuracy in the detection of relevant lesions, such as polyps.

3.5. Normal Anatomy

Colon measures approximately 150–180 cm in length and is divided into five segments: cecum, ascending colon, transverse colon, descending colon and sigmoid colon.

3.5.1 Cecum: Appears as a large cul-de-sac and contains the orifice of appendix (Figure 6).

3.5.2 Ileo-cecal Valve: It is situated on the wall of the ascending colon, has a circular, bilabial or oval shape measuring from 1.5 to 3 cm in diameter (Figure 7).

3.5.3 Ascending Colon: It is larger than the left colon and is lined with a mucosa forming semicircular folds (Figure 8).

3.5.4 Hepatic Flexure: Flexure between the ascending and transverse colon and can be recognized by gray–blue colored impression of the liver (Figure 9).

3.5.5 Transverse colon: It is distinguishable by its characteristic triangular haustrations. Mucosa is greyish-pink, smooth and shiny through which the underlying fine vascular network shows up (Figure 10).

3.5.6 Splenic Flexure: At the proximal extremity of the descending colon the splenic flexure can be recognized by its dome-like appearance (Figure 11).

3.5.7 Descending Colon: Appearance of a long, straight tube marked by circular haustrations which are lower but more regular in shape and placed at more regular intervals than those of the sigmoid colon. The mucosa is smooth, shiny, thin and greyish pink in color (Figure 12).

3.5.8 Sigmoid Colon: It forms wide convolutions and is distinguished endoscopically by the presence of rather well-marked semilunar folds and by the velvety appearance of its mucosa (Figure 13).

3.5.9 Rectum: Approximately 15 cm long. The upper third is covered by peritoneum and about 10 cm of the rectum lies below the lower edge of the peritoneum (below the peritoneal reflection). It has several prominent folds, called valves of Houston (Figure 14).

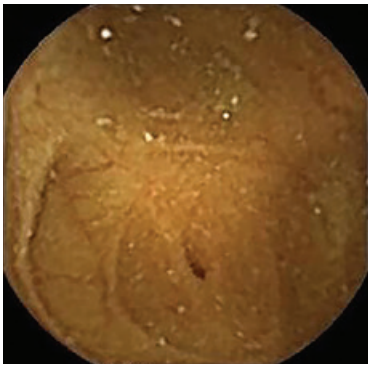

Figure 6
Appendix.

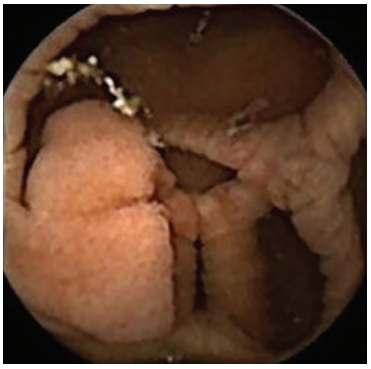

Figure 7
Ileo-cecal valve.

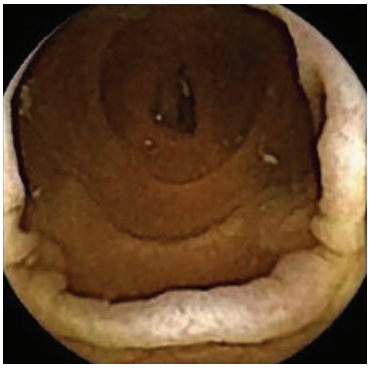

Figure 8
Ascending colon.

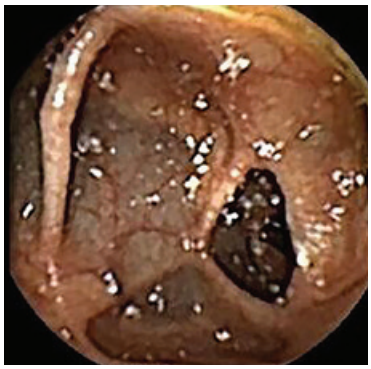

Figure 9
Hepatic flexure.

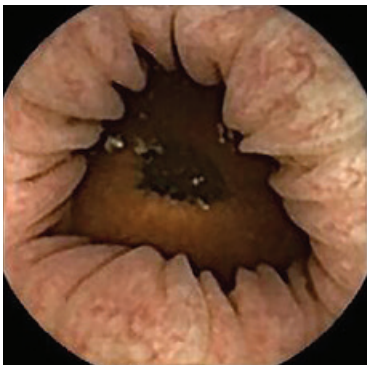

Figure 10
Transverse colon.

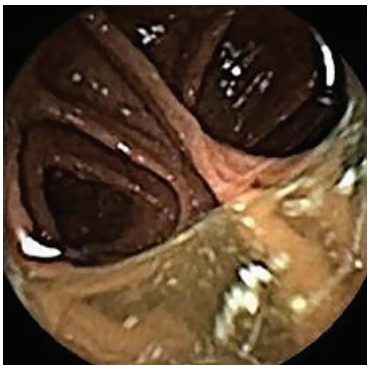

Figure 11
Splenic flexure.

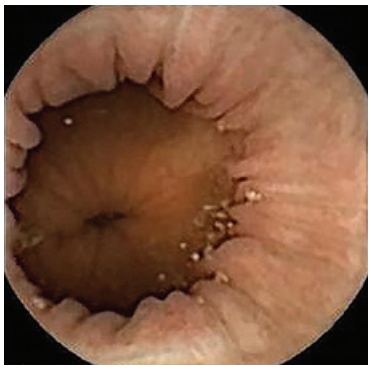

Figure 12
Descending colon.

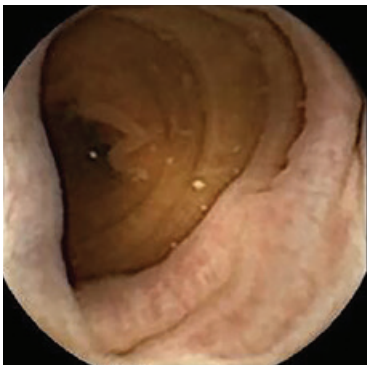

Figure 13
Sigmoid colon.

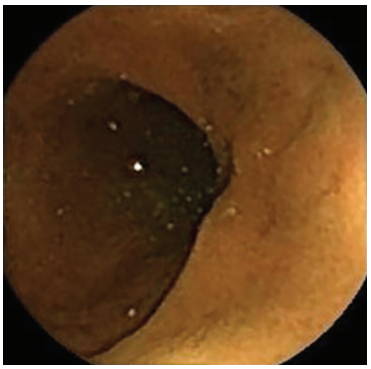

Figure 14
Rectum.

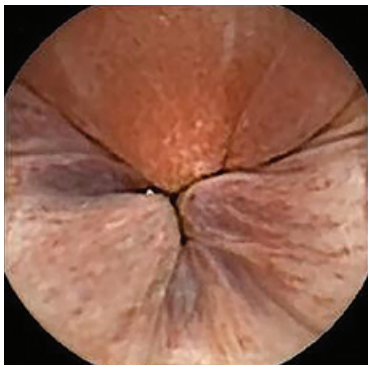

Figure 15
Canal anal.

3.5.10 Anal canal: It is the terminal portion of the digestive tract, connecting the rectum to the anus and measures about 3 cm long, extending to the dentate line, which represents the transition point between the columnar epithelium of the upper anal canal and the stratified squamous epithelium of the lower anal canal and perianal skin (Figure 15).

Some findings from CCE are shown in the following images.

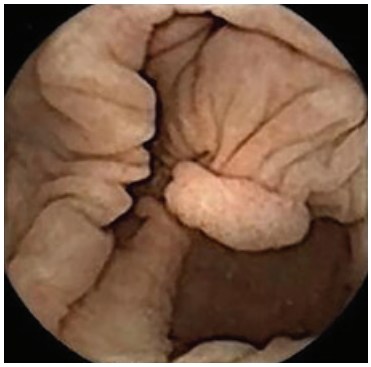

Figure 16
Sessile polyp.

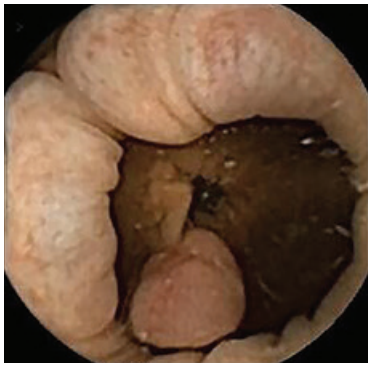

Figure 17
Pedunculated polyp.

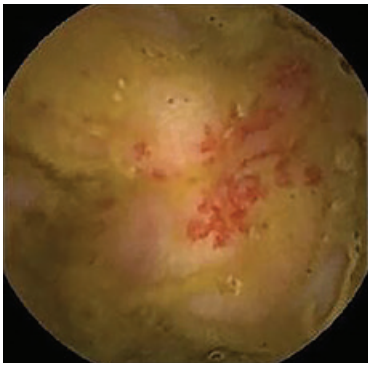

Figure 18
Colonic angioectasia.

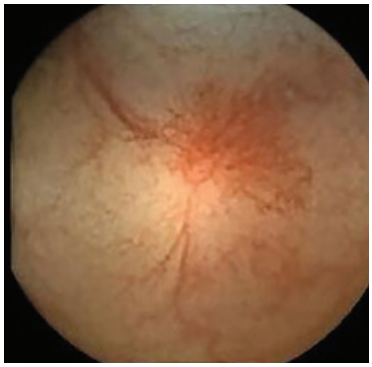

Figure 19
Colonic angioectasia.

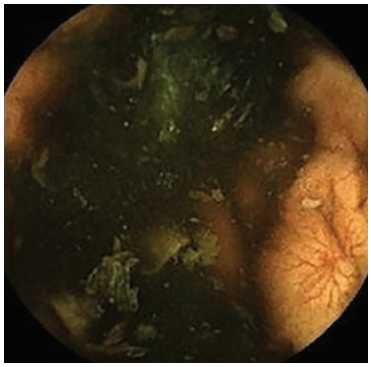

Figure 20
Colonic angioectasia.

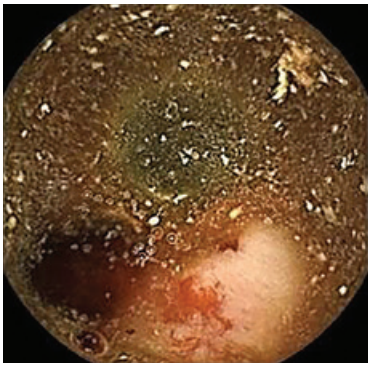

Figure 21
Bleeding colonic angioectasia.

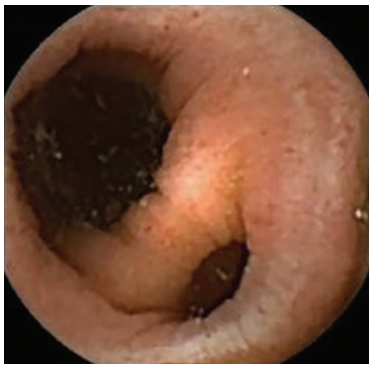

Figure 22
Diverticulum.

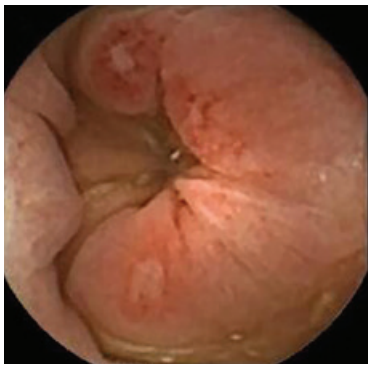

Figure 23
Colonic erosions - NSAIDs.

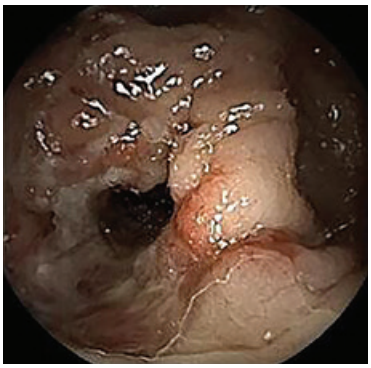

Figure 24
Colonic ulcer with exudate – Crohn's disease.

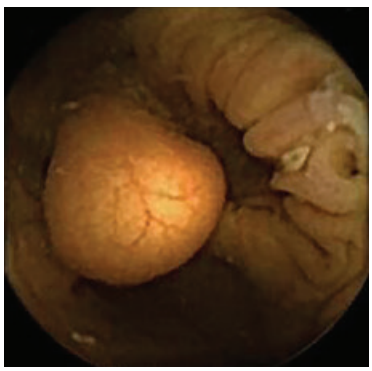

Figure 25
Lipoma.

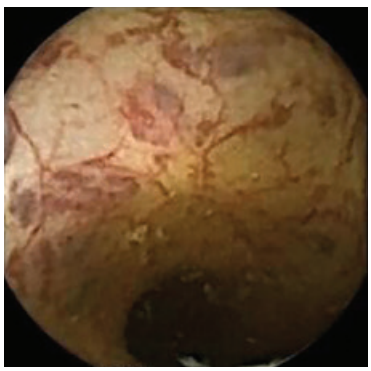

Figure 26
Radiation colitis.

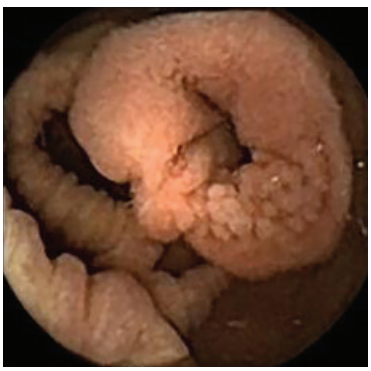

Figure 27
Protruding ileo-cecal valve with lymphoid hyperplasia.

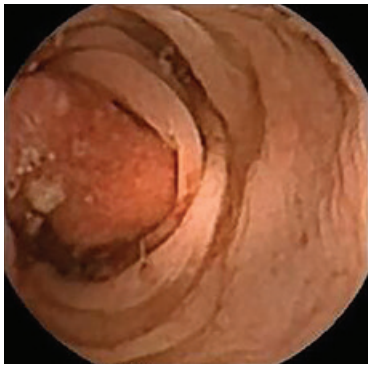

Figure 28
Sigmoid neoplasia.

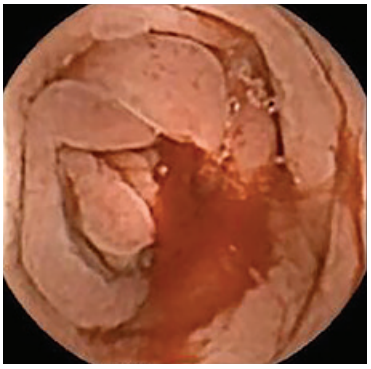

Figure 29
Active bleeding from neoplasia.

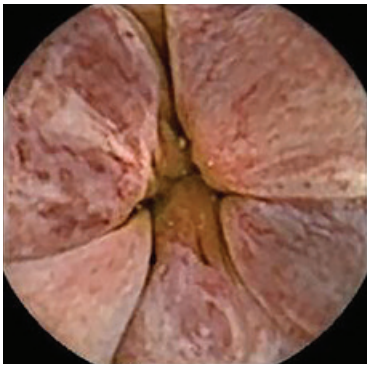

Figure 30
Congestive hemorrhoids.

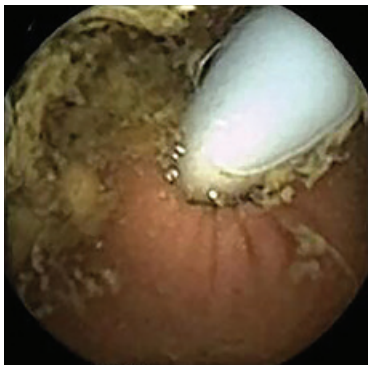

Figure 31
Rectum foreign body.

3.6. Colorectal Cancer Screening

3.6.1. Introduction

Colorectal cancer is the third most diagnosed cancer globally and the second leading cause of cancer deaths, with around 1.9 million new cases and 900,000 deaths in 2020. Early detection through screening, such as fecal occult blood tests and colonoscopy, significantly reduces colorectal cancer mortality. Colonoscopy is especially effective, as it can detect and remove pre-cancerous lesions in the same procedure. However, despite strong evidence supporting its effectiveness, its invasiveness, need for sedation, and associated discomfort result in low participation rates. As a less invasive alternative, CCE offers a promising option.

3.6.2. Preparation

Historically, high-volume polyethylene glycol (PEG) regimens—typically involving 4 liters—were used for bowel preparation. However, current evidence indicates that low-volume regimens (2 liters) are equally effective in achieving adequate bowel cleansing.

Accordingly, the ESGE now recommends a clear liquid diet on the day before the procedure, along with a split-dose regimen of PEG—administered partly the day before and partly on the day of the colonoscopy. Both 2-liter and 4-liter PEG preparations are considered effective. ESGE also recommends the use of sulfate-based solutions as adjuncts. Due to the risk of adverse effects such as acute phosphate nephropathy or kidney damage, sodium phosphate is generally not recommended.

Despite these guidelines, a recent meta-analysis suggests that split-dose regimens using less than 4 liters of PEG—particularly 3-liter volumes—may be more effective in achieving complete and adequate bowel cleansing. The study also supports the use of a low-fiber diet and the administration of prokinetic agents (e.g., 10 mg metoclopramide or 20 mg domperidone) before capsule intake. Interestingly, while sodium phosphate is typically discouraged in most guidelines, no adverse effects were reported in the study referenced.

Although guidelines exist, a universally standardized preparation protocol is lacking, and individual centers typically implement their own adapted regimens. The complexity and time-consuming bowel preparation required for CCE represents a significant limitation of the technique, contributing to suboptimal completion rates when compared with CT colonography.

3.6.3. Colorectal Cancer Screening

3.6.3.1 Indications

Alternative screening methods to traditional colonoscopy include CT colonography and CCE. According to the 2020 guidelines from the ESGE, CCE may be considered a viable alternative for colorectal cancer screening in the following situations:

- Incomplete colonoscopy;
- Patients undergoing screening who do not present with alarm symptoms;
- Incomplete or contraindicated colonoscopy combined with a positive fecal occult blood test (FOBT);
- Patient refusal to undergo colonoscopy.

3.6.3.1.1 Incomplete Colonoscopy

According to the most recent international guidelines, CCE is considered an effective method for colorectal cancer screening in patients without alarm signs following an incomplete colonoscopy. Ideally, the capsule should be administered on the same day or the following day, with bowel preparation completed using 1 liter of solution (such as PEG), supplemented by sodium phosphate as a booster.

A recent meta-analysis compared CCE and CT colonography (CTC) in this context. It found that CTC had a higher completion rate, with a pooled estimate of 98% (95% CI: 96–100%), compared to 76% for CCE (95% CI: 68–84%). However, the rate of complete colonic visualization with CCE was still relatively high at 90% (95% CI: 83–95%) and the rate of appropriate colon progression ranged from 75% to 98% across studies.

Importantly, while CTC outperforms CCE in terms of completion rate, CCE is superior in detecting colonic lesions, particularly small polyps less than 5 mm in size.

3.6.3.1.2 Diagnostic Yield of CCE

CCE demonstrates promising diagnostic accuracy for colorectal cancer screening (Figure 1). For adenomas ≥ 6 mm, CCE has a reported sensitivity of 88% and a specificity of 82%.

A multicenter study conducted in 2019 compared the effectiveness of lesion detection between CCE and CTC in a colorectal cancer screening population. The findings indicated that CCE had a significantly higher lesion detection rate than CTC. Specifically, CCE detected polyps ≥ 6 mm in 32% of cases and polyps ≥ 10 mm in 14%, whereas CTC detected polyps ≥ 6 mm in only 9% and polyps ≥ 10 mm in 6%. Sensitivity for polyps ≥ 6 mm and ≥ 10 mm was also greater with CCE (84% for both) compared to CTC (32% and 53%, respectively). However, specificity for polyps ≥ 6 mm was higher for CTC (99%) compared to CCE (93%), while specificity for polyps ≥ 10 mm was similar between the two modalities (CTC 99% vs. CCE 97%).

In individuals with a first-degree relative diagnosed with colorectal cancer, CCE has also proven to be an effective screening tool. For polyps ≥ 6 mm, CCE demonstrated a sensitivity of 91% and specificity of 88%, with a positive predictive value (PPV) of 78% and a negative predictive value (NPV) of 95%. For larger polyps (≥ 10 mm), sensitivity and specificity were 89% and 95%, respectively.

3.6.3.1.3 Use of CCE in FIT-Positive Patients

In patients with a positive fecal immunochemical test (FIT), also referred to as FTOB -positive patients, CCE is considered an effective method for detecting colorectal polyps and cancers (Figure 2).

Evidence suggests that, in FIT-positive individuals, CCE may even outperform conventional colonoscopy in certain aspects. In a study involving 126 patients who underwent both complete CCE and colonoscopy, the per-patient sensitivity of CCE for detecting polyps larger than 9 mm was 97% (95% CI: 94–100%), compared to 89% (95% CI: 84–94%) for colonoscopy. Notably, this advantage was observed only in complete CCE examinations.

Overall, the sensitivity of CCE for detecting polyps > 9 mm in FIT-positive patients ranges from 87% to 92.8%, with a specificity of approximately 92%. These findings support the role of CCE as a via-

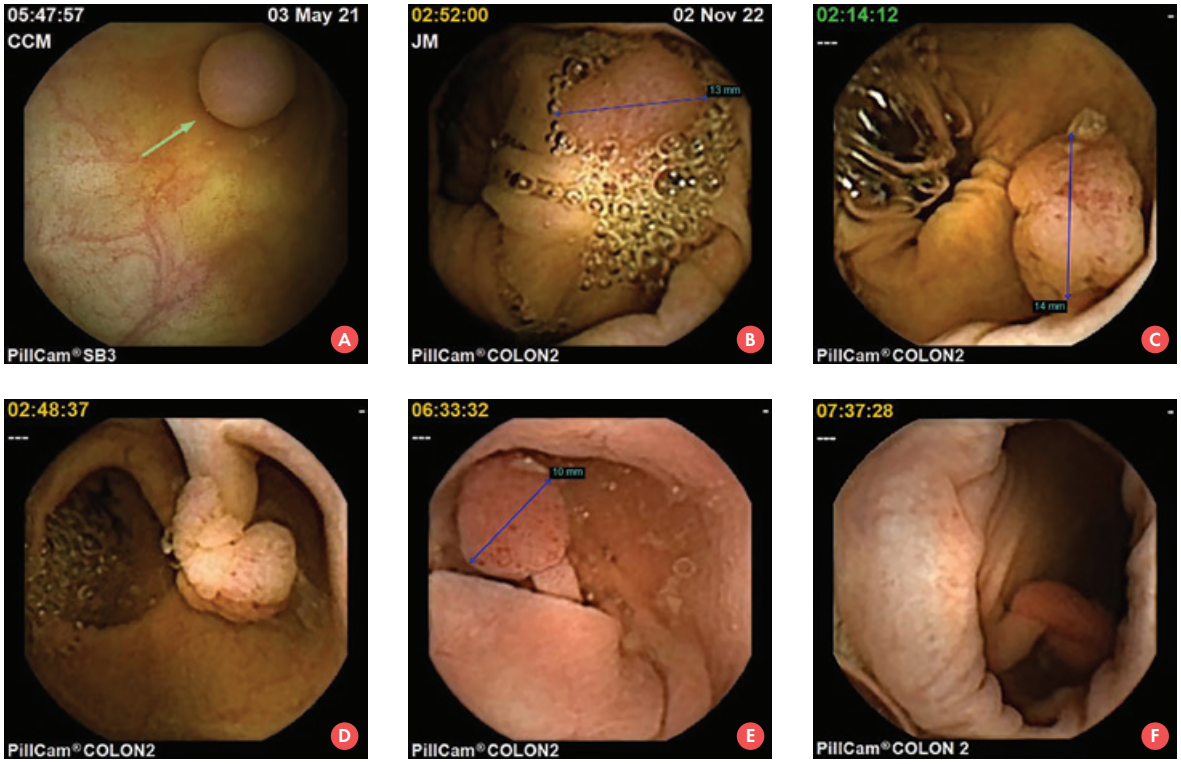

Figure 1
Multiple polyps diagnosed on CCE. (**A**) Sessile polyp (Paris 0-Is). (**B**) An 13 mm sessile polyp (Paris 0-Is). (**C**) An 14 mm semipedunculated polyp (Paris 0-Isp). (**D**) Pedunculated polyp (0-Ip). (**E**) An 10 mm pedunculated polyp (Paris 0-Ip). (**F**) Pedunculated polyp (0-Ip).

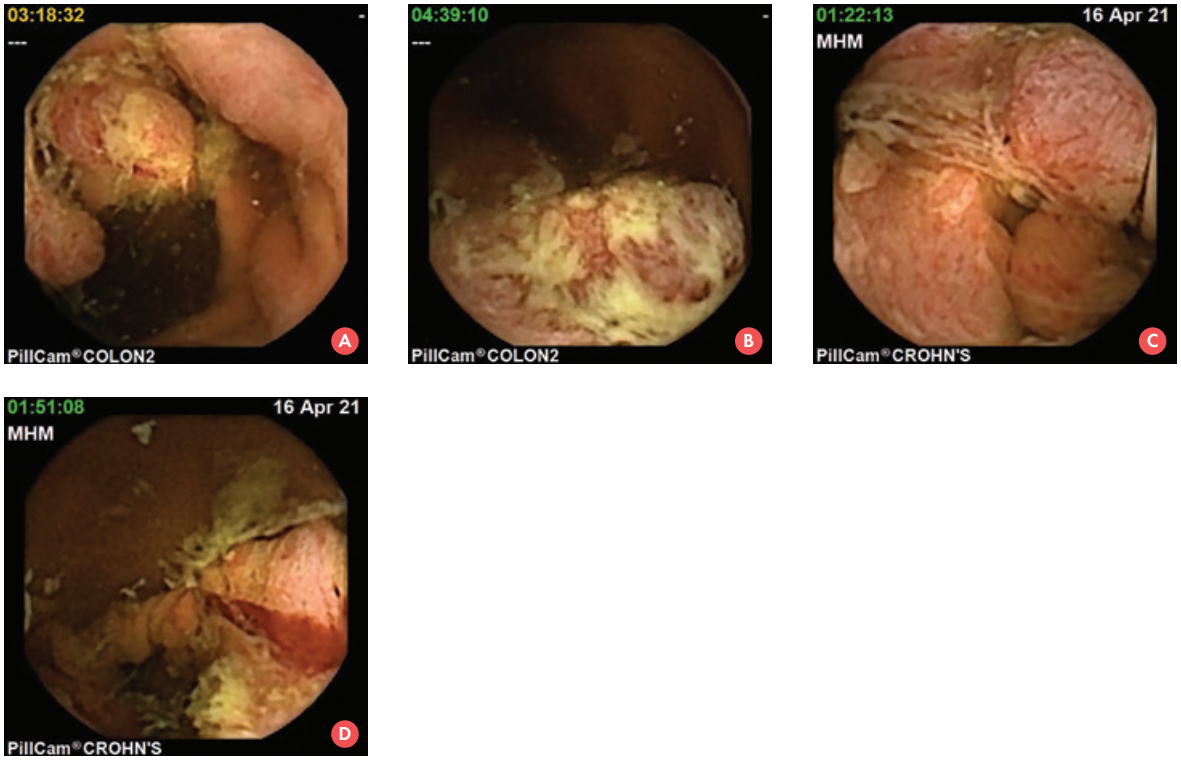

Figure 2
Colonic carcinoma. **A** and **B** shows two different lesions. **C** and **D** depict the same lesion.

ble, non-invasive alternative in colorectal cancer screening, particularly for individuals reluctant to undergo colonoscopy.

3.6.3.2 Follow-up After CCE

When polyps ≥ 6 mm are detected on CCE, patients should be referred for therapeutic colonoscopy with polypectomy. Additionally, referral is also recommended if three or more diminutive polyps (< 6 mm) are identified.

While most diminutive polyps carry a negligible risk of malignancy, the presence of multiple such lesions may warrant removal to reduce long-term risk and avoid underdiagnosis. However, in isolated cases of one or two diminutive polyps, a conservative approach may be justified, potentially avoiding the need for an additional invasive procedure.

3.6.3.3 Contraindications

According to the most recent guidelines from the ESGE, CCE should not be performed in the following situations (Figure 3):

3.6.3.3.1 High-risk Patients with Alarm Symptoms: CCE is not recommended for individuals presenting with signs suggestive of colorectal cancer, such as hematochezia, anemia, or unexplained weight loss. Although it may be considered in select cases, current evidence is insufficient to support its routine use in this context.

3.6.3.3.2 Post-polypectomy Surveillance: There is a lack of robust data supporting the use of CCE for surveillance following polypectomy.

3.6.3.3.3 First-line Screening: CCE should not be used as a primary screening tool for colorectal cancer in the general population.

3.6.3.3.4 Post-curative Surgery Follow-up: CCE is not recommended for follow-up after curative colorectal cancer surgery due to limited supporting evidence.

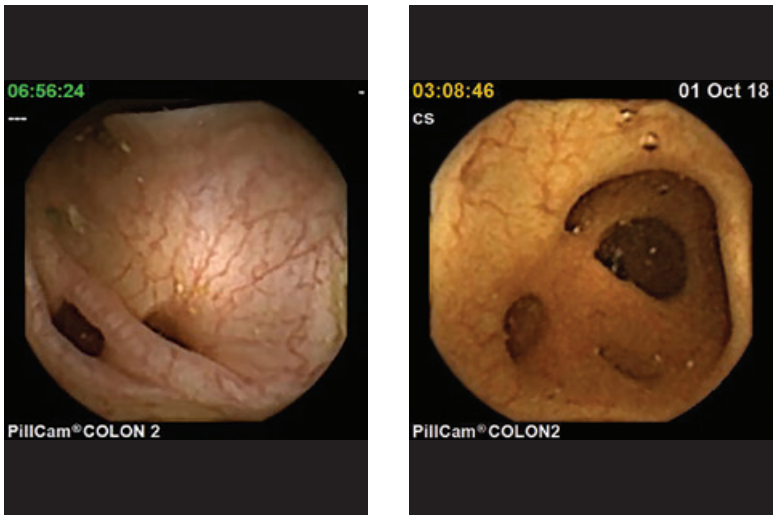

Figure 3
(**A**) and (**B**) demonstrate colonic diverticula. Colonic diverticula do not represent a contraindication for CCE.

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4

Pan-intestinal Capsule Endoscopy

• Rita Barosa • Bruno Rodrigues, *Serviço de Gastrenterologia, Hospital Egas Moniz - ULSLO*

4.1. Technology

When first emerged, CE intended to acquire images from the whole GI tract in a non invasive way. The first capsule introduced was then called the mouth-to-anus (M2A) capsule. Since then, newer capsules were designed with improvement on field of view, battery duration, frame rates and image sensor.
After the first double-headed PillCamTMCOLON (Given Imaging, Medtronic) capsule, the PillCamTMCOLON 2 was released, which was slightly larger than the PillCamTMSB capsule, had an increased frame rate for image acquisition, extended battery time and wider angle of view (Table 1). In the recent years, two new double-headed capsules were developed, the PillCamTMCROHN (Given Imaging, Medtronic) and the OMOM 2023 capsule (OMOM CCTM, Jinshan), with the particular advantage of continuously acquiring images trough the GI tract by not having a sleep mode. This enables a single procedure study of the whole SB and colon embodying the concept of pan-intestinal capsule endoscopy (PCE).

Table 1.
Comparison of Comercially Available Capsules for Pan-Intestinal Capsule Endoscopy.

Feature	PillCam™ SB3	PillCam™ COLON 2	PillCam™ Crohn's	OMOM
Manufacturer	Medtronic (Given Imaging)	Medtronic (Given Imaging)	Medtronic (Given Imaging)	Jinshan (OMOM CC™)
Dimensions (mm)	11.6 × 26.2	11.6 × 32.3	11.6 × 31.5	11.6 × 31.5
Optical domes	1	2	2	2
Field of view (°)	156	344	344	344
Image resolution	256 × 256	256 × 256	256 × 256	360 × 360
Adaptive frame rate (fps†)	2–6	4–35	4–35	4–35
Battery duration (hours)	~12	~14	~14	~10
Sleep mode	No	Yes*	No	No

Adapted from Rosa B, et. al (2024). * Can be deactivated † Frames per second.

Medtronic also developed a new software with an improved GI map providing a more immediate representation of the capsule progress through the SB and colon and of the severity of lesions found per segment in Crohn's disease (PillCam™ Crohn's). After first duodenal and first cecal images are identified, the software divides the SB into three terciles according to their length and not according to time as in previous software. There is a software-based lesion size estimation tool for PillCam™ COLON 2 and PillCam™ Crohn's capsules. For Crohn's disease PCE with PillCam™ Crohn's, the software allows to compare images, videos and treatment over time and has incorporated the Lewis and the Eliakim scores.

4.2. Patient Preparation

PCE requires a demanding bowel preparation protocol, considering that, as in other types of diagnostic endoscopy, the quality of the preparation has impact on diagnostic accuracy. Furthermore, irrigation, aspiration or patient mobilization are not possible during the procedure. Moreover, to obtain images from the whole GI tract, the capsule must be excreted prior to battery depletion,

however an excessively rapid transit may result in an increased incidence of missed lesions.
The literature supports the use of a low-fiber diet, additional laxatives, and prokinetics prior to the ingestion of bowel preparation, as well as split-dose PEG and a laxative booster during the procedure, NaP being the most extensively evaluated (Table 2).

Even though no standardized protocol is universally available, in a recent systematic review and meta-analysis the adequate cleansing rate of CCE or PCE was 72,5% (95% CI 67,8%-77,5%) and the complete examination rate was 83,0% (95% CI 78,7%-87,7%).

Table 2.
Proposed Bowel Preparation Protocol for PCE.

Day	Time	Action
2 days before	----------	Low-fibre diet
1 day before	----------	Clear liquids diet
	7:00–9:00 p.m	2 L PEG solution
Exam day	6:30–7:30 a.m	1 L PEG solution
	8:15 a.m	10 mg metoclopramide/domperidone orally
	8:30 a.m	100–200 mg simethicone in water with capsule
	9:30 a.m	Check capsule location; give another 10 mg metoclopramide if in stomach
	(Capsule detected in SB)*	30 mL NaP + 1 L water
	(3h after the 1st booster)*	15 mL NaP + 0.5 L water
	(2h after the 2nd booster)*	10 mg bisacodyl rectal suppository

Adapted from Rosa B, *et al.* (2024). * An alert is emited by the reader (PillCam®).

4.3. Indications for PCE

PCE has been used more extensively in clinical practice in IBD and in mid-lower GI bleeding (Table 3). PCE might also be an appealing option in the context of polyposis syndromes with SB and colonic involvement, namely in those where SB surveillance is well established. However, limitations related to adequate bowel preparation, incomplete examinations, and mainly the inability to provide therapeutic treatment constrain the efficacy of this option.

Table 3.
Main Clinical Indications of PCE

Indication	Clinical Utility
Inflammatory Bowel Disease (IBD)	1. Inflammatory type affecting small bowel and colon 2. Access mucosal healing (treat to target) 3. Staging: disease distribution and severity 4. Asymptomatic Crohn´s disease and abnormal lab tests: exclude active disease or concomitant diagnosis 5. Investigating IBD-unclassified: suspected Crohn´s disease or atypical ulcerative colitis
Gastrointestinal Bleeding	Investigating mid-lower gastrointestinal bleeding

Adapted from Rosa B, *et al.* (2024).

4.3.1. Inflammatory Bowel Disease (IBD)

4.3.1.1. Crohn's Disease

Crohn's disease (CD) is a pan-enteric disease of discontinuous nature where PCE can be a particularly relevant procedure to evaluate disease severity and extent. In a multicentre prospective study, PCE demonstrated at least equivalent performance to magnetic resonance enterography (MRE) and ileocolonoscopy in a single procedure, eliminating the risks associated with more invasive procedures and radiation exposure. The treat-to-target strategy in CD focuses on achieving mucosal healing, as persistent inflammation correlates with poorer outcomes. PCE supports this approach by enabling longitudinal mucosal monitoring and earlier detection of subtle inflammatory activity. Furthermore, in an observational study, PCE upstaged the disease and lead to treatment intensification, based on a higher accuracy to identify proximal SB disease. However, PCE can only detect mucosal changes and is not an adequate method to identify transmural and extramural disease.

4.3.1.1.1. Scoring Systems

Validated scoring systems enable to objectively assess the severity and extent of SB and colonic CD based on CE findings, allowing standardization of reporting and longitudinal monitoring.

CECDAI (Niv Score): evaluates inflammation severity, disease extent, and strictures. Its extended version, **CECDAIic**, also includes the colon, enabling a panenteric assessment.

Eliakim Score: designed for panintestinal assessment, quantifies most severe lesion, most common lesion, extent of the disease and the presence of strictures.

4.3.1.1.2. Safety Considerations

Capsule retention is a recognized risk in CD. While the overall retention rate in suspected CD is low (2,3%) and similar to that of procedures for other indications, it increases to 4,6% in confirmed CD. Thus, in patients with known CD, CTE or MRE and/or PC testing is recommended prior to CE. Nevertheless, in patients with obstructive symptoms, known strictures, or surgical anastomoses, the use of a PC should be considered, even in the absence of significant findings on cross-sectional imaging.

4.3.1.2. Ulcerative Colitis

While UC is limited to the colon, CE offers a non-invasive alternative for assessing mucosal inflammation, with good correlation to conventional colonoscopy. The Capsule Scoring of UC (CSUC) system was developed to evaluate vascular patterns, bleeding, and the presence ulcers, showing comparable performance to the UC Endoscopic Index of Severity (UCEIS). Moreover, CE can help reclassify misdiagnosed with UC as CD by identifying SB involvement. However, histology is crucial for diagnosis and assessment of deep remission and PCE is not adequate for dysplasia surveillance.

4.3.2. Gastrointestinal Bleeding

Currently, SBCE is the first-line diagnostic modality for GI bleeding of indeterminate origin in hemodynamically stable patients following a negative bidirectional endoscopy, to exclude mid-gut bleeding. However, PCE seems an adequate option in the diagnosis of both overt (melena/hematochezia) and occult (iron-deficiency anaemia) GI bleeding, after negative esophagogastroduodenoscopy, as it allows visualization of the SB and colon in the same procedure, may avoid unnecessary and non-therapeutic colonoscopies and may reduce costs and hospital stay. In a recent study, PCE performed in patients presenting with melena and negative esophagogastroduodenoscopy identified the bleeding site in 83% and led to therapeutic DAE in 50%, thus avoiding unnecessary colonoscopy. Furthermore, CE may detect proximal lesions missed by esophagogastroduodenoscopy.

4.4. Reading

There are no specific recommendations for PCE reading. When compared to SB and colon capsule reading, same systematic procedure should be used, same landmarks should be marked and same scores (i.e. for bowel preparation) should be employed. However, it is expert opinion that reading a pan-enteric study in CD setting has some differences when compared to CCE reading. While the SB reading time can be the same, colon images can be read with the two sides at

the same time and faster. In this setting a shorter total reading time can be achieved.

4.5. Pathological Findings

PCE enables the detection of a wide array of GI tract abdormalities in a single procedure, with diagnostic, therapeutic, and prognostic implications. These findings can be categorized as vascular or non-vascular, including infiltrative, ulcerative, inflammatory, or neoplastic lesions.

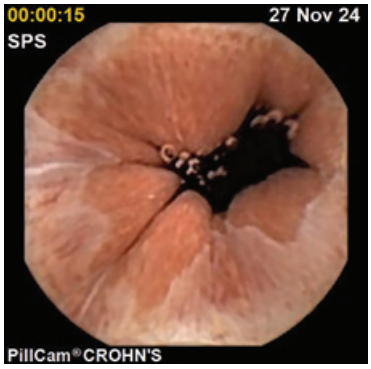

Figure 1
Normal Z-line.

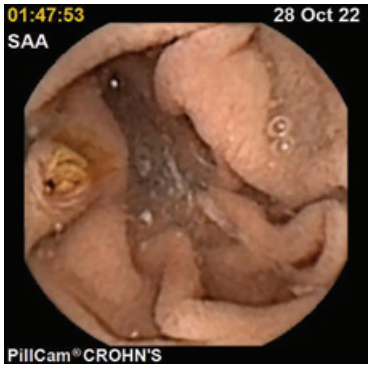

Figure 2
Normal papilla in PCE study.

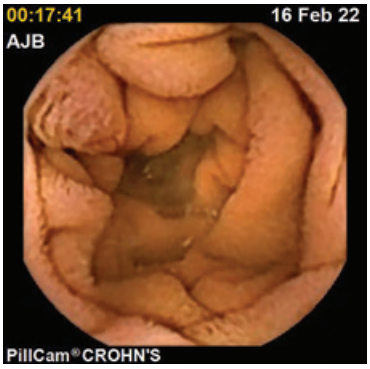

Figure 3
Normal papilla in PCE study.

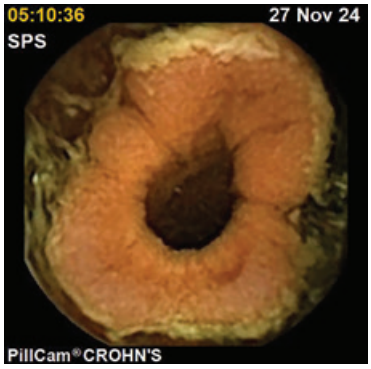

Figure 4
Normal ileocecal valve.

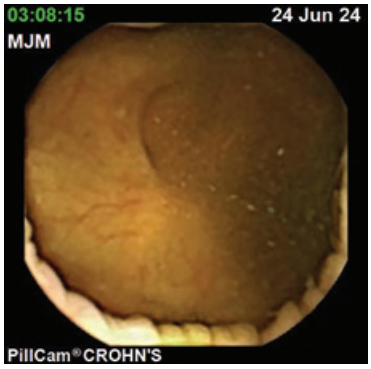

Figure 5
Appendiceal orifice in a PCE study.

Figure 6
Jejunal anastomosis.

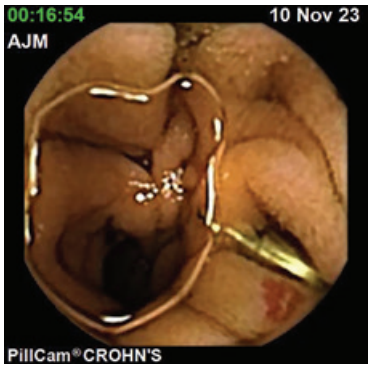

Figure 7
Patient referred with melena after esophagogastroduodenoscopy with clipping of a vascular lesion in the duodenum. PCE showing a clip in the duodenum and adjacent angiectasia.

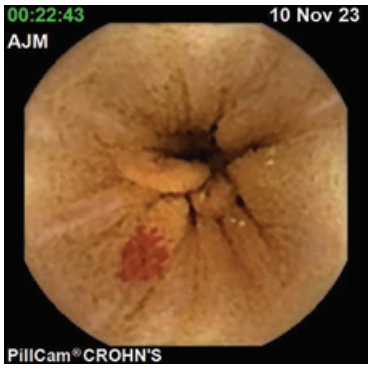

Figure 8
Small bowel angiectasia.

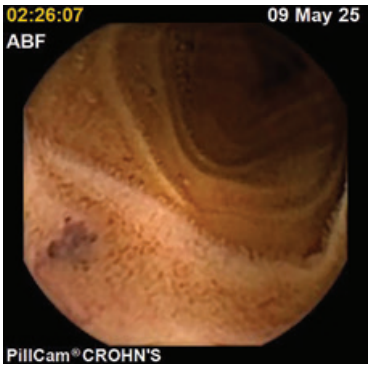

Figure 9
Small venous malformation in a Blue Rubber Bleb Syndrome patient.

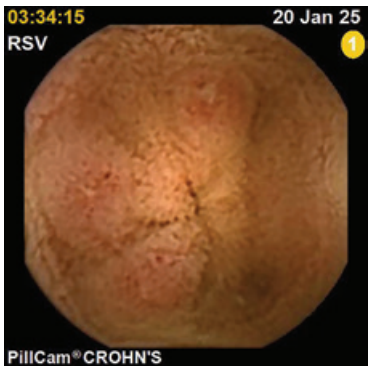

Figure 10
Ileal aftoid erosion.

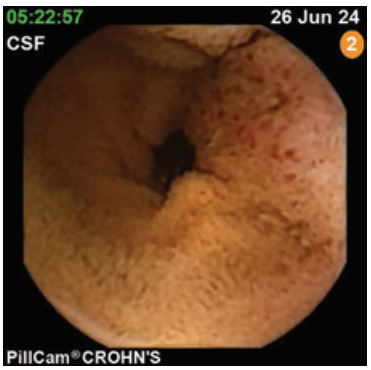

Figure 11
Ileal hyperemia and ulcer.

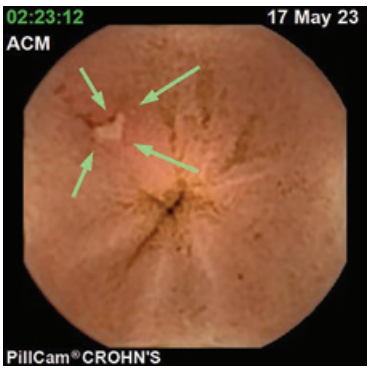

Figure 12
Small bowel superficial ulcer.

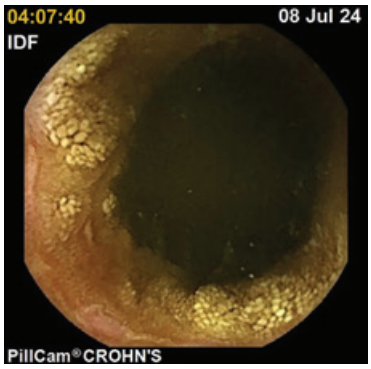

Figure 13
Proximal ileum MALT lymphoma.

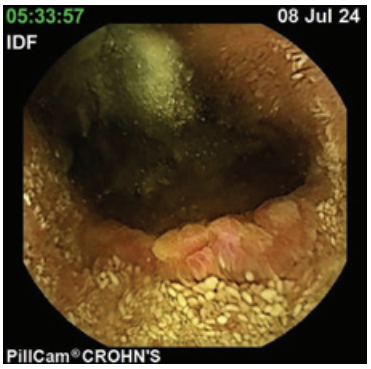

Figure 14
Proximal ileum MALT lymphoma.

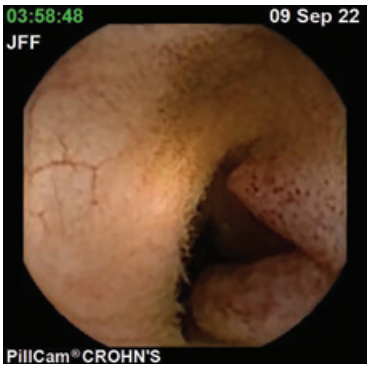

Figure 15
A patient presented with iron deficiency anemia one year after undergoing initial upper endoscopy and ileocolonoscopy. While repeat upper endoscopy was unremarkable, PCE subsequently revealed lymphoma in the terminal ileum.

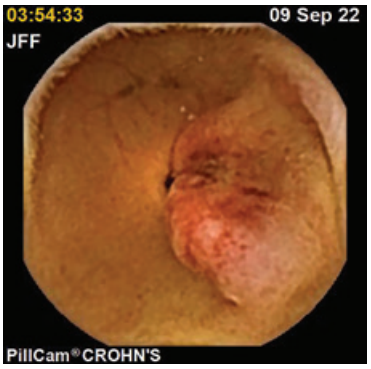

Figure 16
A patient presented with iron deficiency anemia one year after undergoing initial upper endoscopy and ileocolonoscopy. While repeat upper endoscopy was unremarkable, PCE subsequently revealed lymphoma in the terminal ileum.

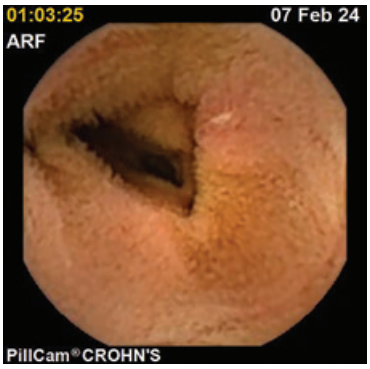

Figure 17
Proximal SB erosion in suspected Crohn's disease.

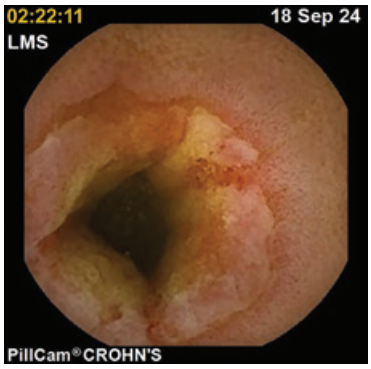

Figure 18
Crohn's disease ulcerated stenosis.

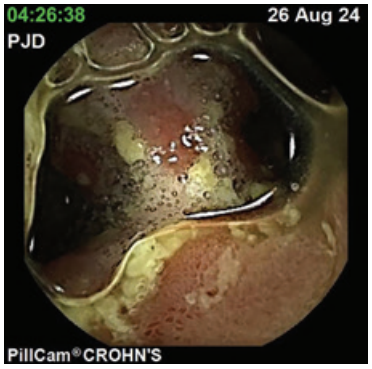

Figure 19
SB anastomosis with ulcers in Crohn's disease.

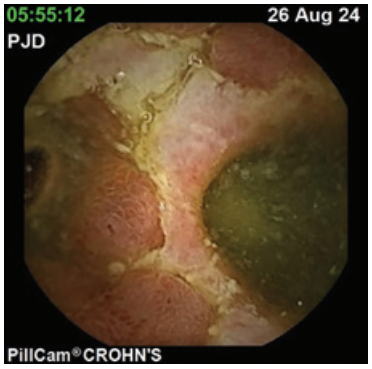

Figure 20
SB ulcerated anastomosis in Crohn's disease.

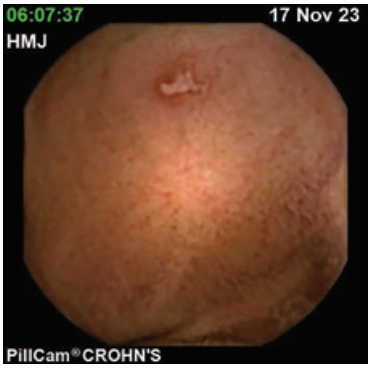

Figure 21
Proximal ileum aftoid erosion in a patient with IBD-unclassified.

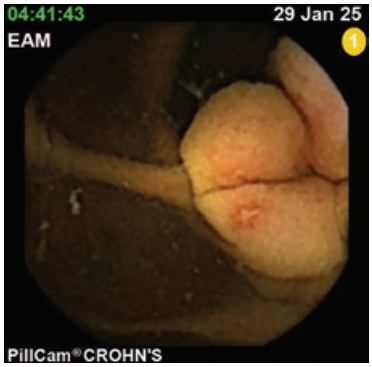

Figure 22
Ileocecal valve with erosions (colonic view).

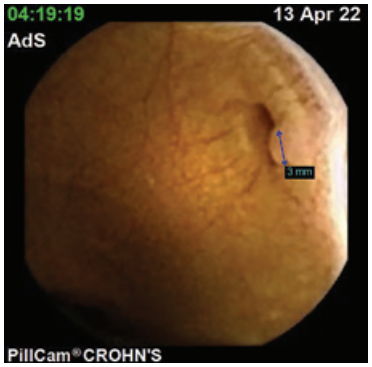

Figure 23
Small colon polyp adjacent to a colonic diverticulum.

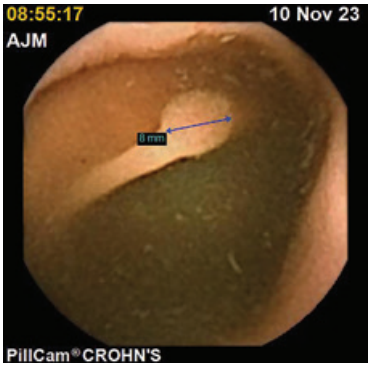

Figure 24
Colonic polyp found in PCE study for anemia.

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5

New Modalities

5.1. Magnetic-guided Capsule Endoscopy

5.1.1. Introduction

Capsule endoscopy, initially developed for the evaluation of the SB, has since been applied to other regions of the gastrointestinal (GI) tract, including the esophagus, stomach, and colon. However, the diagnostic accuracy for detecting esophagogastric lesions remains suboptimal, limiting its clinical applicability. Esophageal evaluation is limited by a short assessment time, typically lasting only a few seconds. Gastric evaluation, on the other hand, is limited by the stomach's typically collapsed architecture, which hinders luminal visualization in the absence of insufflation - particularly in the most proximal segment as the cardia and fundus. Furthermore, reliance on peristaltic movement impairs complete assessment of the gastric cavity, restricting the role of CE as a minimally invasive alternative to conventional esophagogastroduodenoscopy.

The potential for controlled navigation of capsule endoscopes has been explored over the past two decades. Initial studies employed magnetic arms or adaptations of magnetic resonance imaging (MRI) equipment to control the capsule. However, most of these devices did not progress to clinical implementation. The introduction of magnetic-guided capsule endoscopy (MGCE), first described in 2009, aimed to address this limitation. Advances in technology have since enabled fully automated control of capsule navigation, facilitating comprehensive visualization of the gastric mucosa without direct operator intervention. These developments support the potential of magnetic-guided capsules as a truly minimally invasive alternative to conventional upper GI endoscopy.

5.1.2. Technology

MGCE integrates a single-camera capsule with a fully automated robotic arm to enable controlled navigation. Two systems currently available in clinical practice are the OMOM RC® (Chongqing Jinshan Science & Technology™) and the NAVICAM® Stomach System® (AnX Robotics™). In both systems, a single-camera capsule is responsible for image acquisition, with a field of view ranging from 160° to 172°. Image capture rates vary between 0.5 and 6 frames per second for the NAVICAM® and up to 10 frames per second for the OMOM RC®. Each capsule contains a battery with an operational life of 8 to 12 hours, and image data are transmitted wirelessly to an external recorder.

Capsule navigation is achieved through a magnetic robotic arm that allows for both rotational and translational movement. In the case of the OMOM RC® system, navigation can be manually controlled by the endoscopist or conducted fully automatically based on a protocol that assesses the percentage of mucosal surface visualized. Figure 1 illustrates the key components of both magnetic-guided capsule systems.

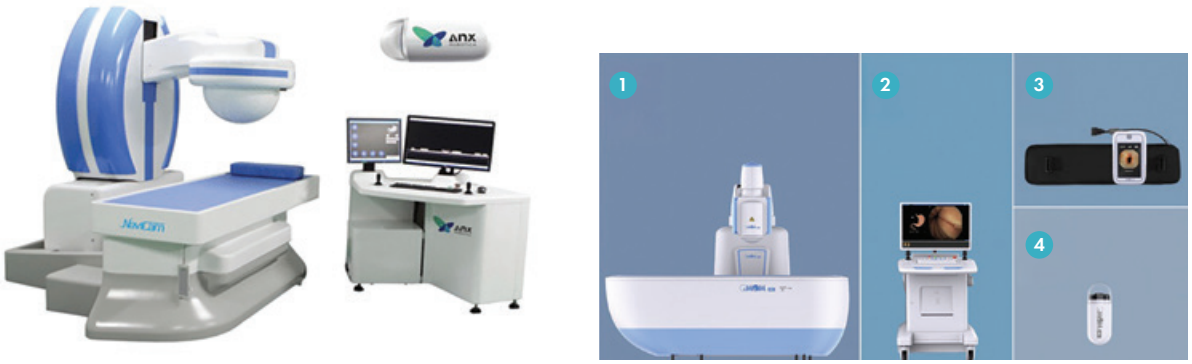


Figure 1
Main components of MGCE systems (NaviCam Stomach System® – upper scheme; OMOM RC Capsule System® – lower scheme). In both systems, the procedure requires a magnetic robotic arm (capable of rotational and translational movement), a control unit, a data recorder, and a single-camera capsule endoscope.

5.1.3. Indications

MGCE is proposed as a minimally invasive alternative to conventional upper GI endoscopy. Therefore, it should be considered in patients with contraindications to standard upper endoscopy or those in whom procedural sedation is inadvisable. In addition, it has been investigated as a tool for minimally invasive gastric cancer screening. The availability of a fully automated capsule navigation system enables minimally invasive evaluation of the gastric mucosa, as well as surveillance of esophageal, gastric, or duodenal mucosal abnormalities, and follow-up of patients previously treated for esophagogastric lesions. Moreover, because the same capsule can be used to assess the small intestine, the SB evaluation be performed immediately after the gastric evaluation protocol, allowing for extended panendoscopic assessment. This approach could be more useful in conditions potentially affecting both the stomach and SB such as Crohn's disease and polyposis syndromes.

5.1.4. Contraindications and Complications

Regarding contraindications, MGCE should be avoided in patients with contraindications to conventional CE or magnetic resonance imaging (MRI). This includes patients with implanted electronic devices (e.g., pacemakers) or metallic prostheses incompatible with MRI. Furthermore, MGCE should be avoided in patients at increased risk for CR; in such cases, a PC is recommended prior to robotic capsule deployment.

5.1.5. Patient Preparation

MGCE overcomes the limitation of peristalsis-dependent progression by enabling either manual or automated control of capsule movement. However, the typically collapsed structure of the gastric lumen necessitates a strategy to compensate for the absence of insufflation.

In this context, following a bowel preparation regimen similar to that used for SBCE, the patient is instructed to ingest 1 liter of water combined with an anti-foaming agent (e.g., simethicone) within the 10 minutes preceding the procedure. Rapid ingestion of a large volume of water improves visualization of the gastric mucosa by creating a fluid interface that facilitates capsule navigation.

After water ingestion, the patient swallows the capsule in the supine position to optimize esophageal image acquisition, followed by gastric examination, ideally performed through fully automated capsule control. Comprehensive visualization of the gastric mucosa is ensured via automatic detection of key gastric anatomical landmarks. Once the capsule progresses past the pylorus into the duodenal bulb, the pa-

Example of images

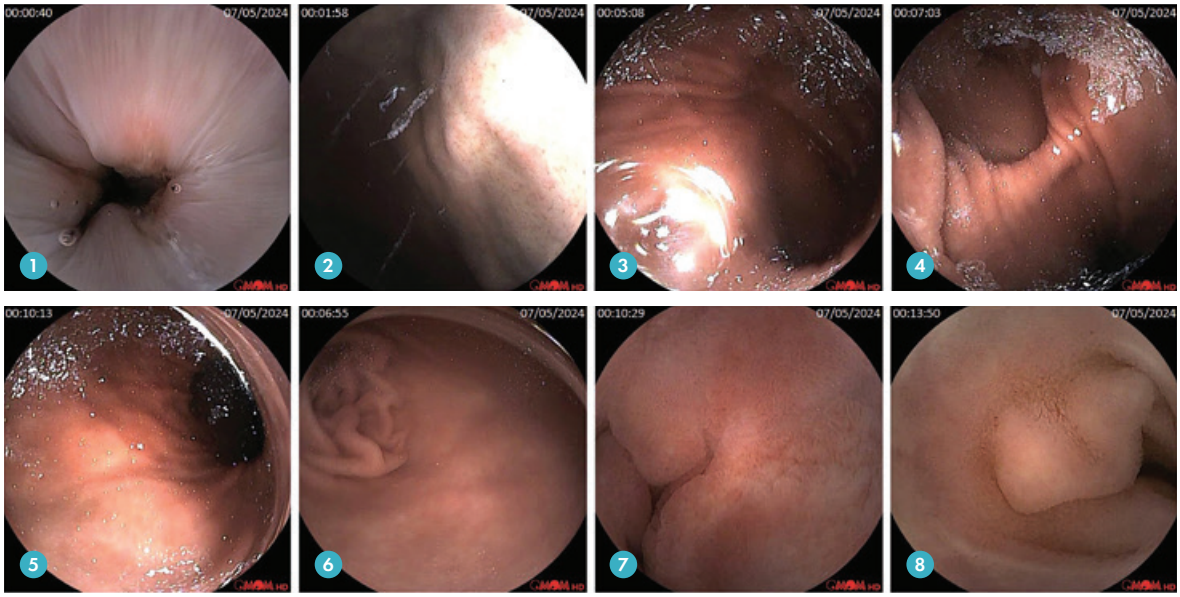


Figure 2
Gastric anatomical landmarks during MGCE: 1 – gastroesophageal transition; 2 – fundus; 3 – corpus; 4 – incisura; 5 and 6 – antrum; 7 – pylorus; 8 – duodenal bulb.

tient may proceed with SBCE, following standard protocols for this procedure.
By employing an automated protocol for gastric mucosal inspection, MGCE enables a minimally invasive evaluation of the stomach, followed by capsule enteroscopy. In this context, robotic capsule gastroscopy may serve as a valuable alternative in patients with contraindications to conventional upper endoscopy, reluctant to invasive procedures, or as a complementary procedure that enhances gastric assessment in patients undergoing capsule enteroscopy.

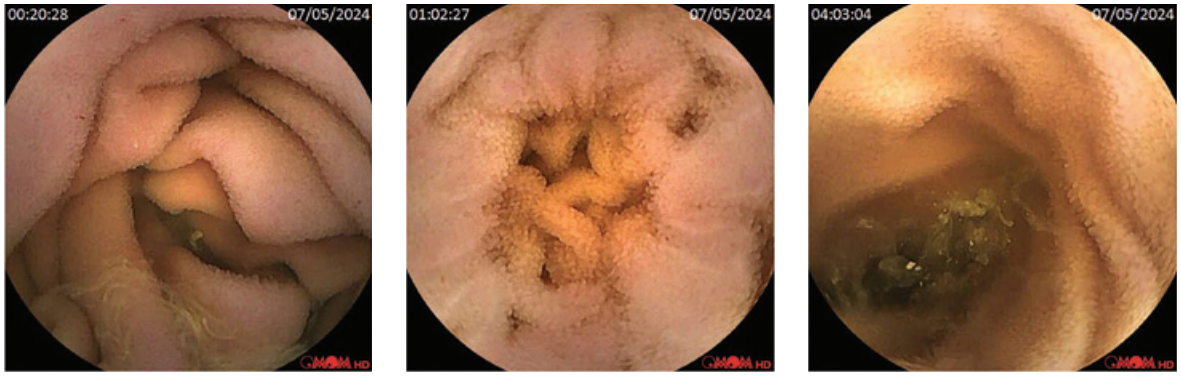


Figure 3
Normal SB (jejunum and ileum).

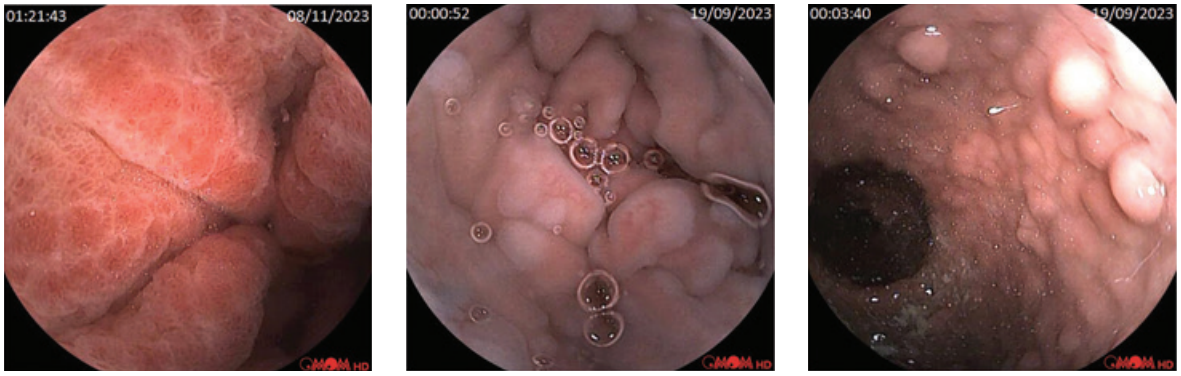


Figure 4
Gastric Antral Vascular Ectasia (GAVE) visualized by magnetic-guided capsule endoscopy.

Figure 5
MGCE frames demonstrating multiple fundic gland polyps in a patient with Cowden syndrome (PTEN mutation).

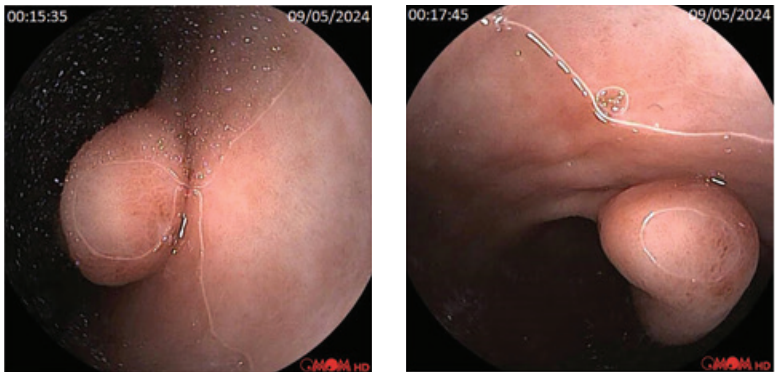
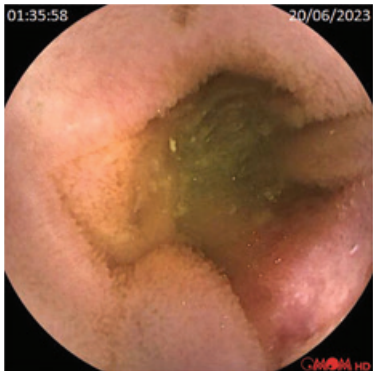


Figure 6
Gastric hyperplastic polyp.



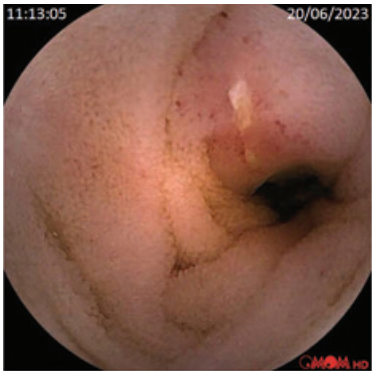


Figure 7
MGCE frames illustrating ulcerative lesions in the SB, subsequently identified as neuroendocrine tumors (NETs) through clinical correlation.

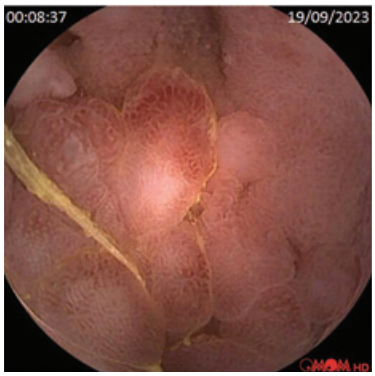
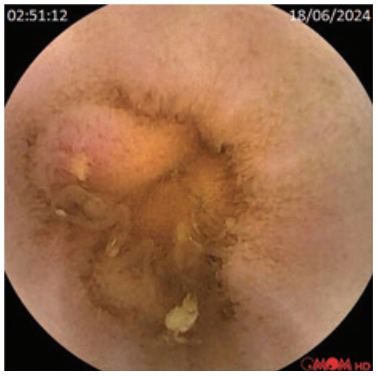


Figure 8
MGCE frames demonstrating duodenal polyps n a patient with Cowden syndrome (PTEN mutation).



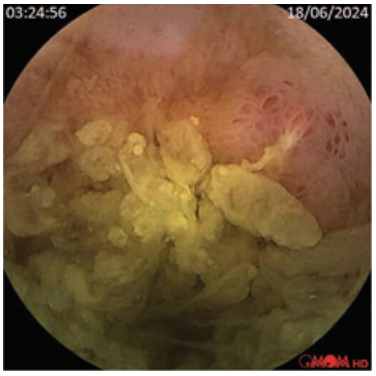


Figure 9
MGCE frames demonstrating ulcers of ileum in a patient with ileal Crohn's disease.

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5.2. Artificial Intelligence in Capsule Endoscopy

5.2.1. Introduction

Capsule endoscopy (CE) has revolutionized the endoscopic evaluation of the GI tract since its introduction in the early 2000s. This minimally invasive procedure provides a comprehensive endoscopic assessment of the GI tract, offering a minimally-invasive alternative to traditional endoscopic methods. However, the analysis of the extensive and complex video data generated by CE presents a significant challenge, which has historically limited its broader adoption.

The continuous evolution of CE technology, marked by advancements in camera resolution, image capture rates, battery life, and the development of real-time small monitors, has firmly established CE as the first-line method for SB evaluation. Subsequent development of dual-camera capsules further expanded its diagnostic capabilities, enabling pan-endoscopic assessment of the entire GI tract (from the esophagus to the colon).

Despite these advantages, manual analysis of CE videos remains time-consuming and susceptible to errors, increasing the burden for gastroenterologists and potentially leading to missed lesions. It is in this context that AI emerges as a transformative tool to optimize the CE analysis, with the potential to significantly enhance its efficiency and DY.

The exponential development of AI models in gastroenterology, propelled by recent advancements in computational power and deep learning algorithms, has demonstrated disruptive potential in CE practice. The application of this models is projected to substantially reduce the time required for CE video analysis—from the conventional 30-60 minutes to an estimated 3-10 minutes. This progress not only aims to reduce the burden on healthcare professionals but also to broaden the indications for CE utilization.

5.2.2. Application of Artificial Intelligence in Capsule Endoscopy

The integration of AI into CE presents two primary approaches for optimizing the analysis of captured video data: real-time analysis and post-hoc video pre-analysis (or summarization). Both strategies aim to enhance diagnostic efficiency through distinct methodologies (Figure 1).

In real-time analysis, AI algorithms process video frames concurrently with their display, identifying and flagging potential lesions as the video is streamed. This approach provides immediate alerts to the physician regarding areas warranting closer inspection, thereby facilitating early lesion detection. However, this method carries the inherent

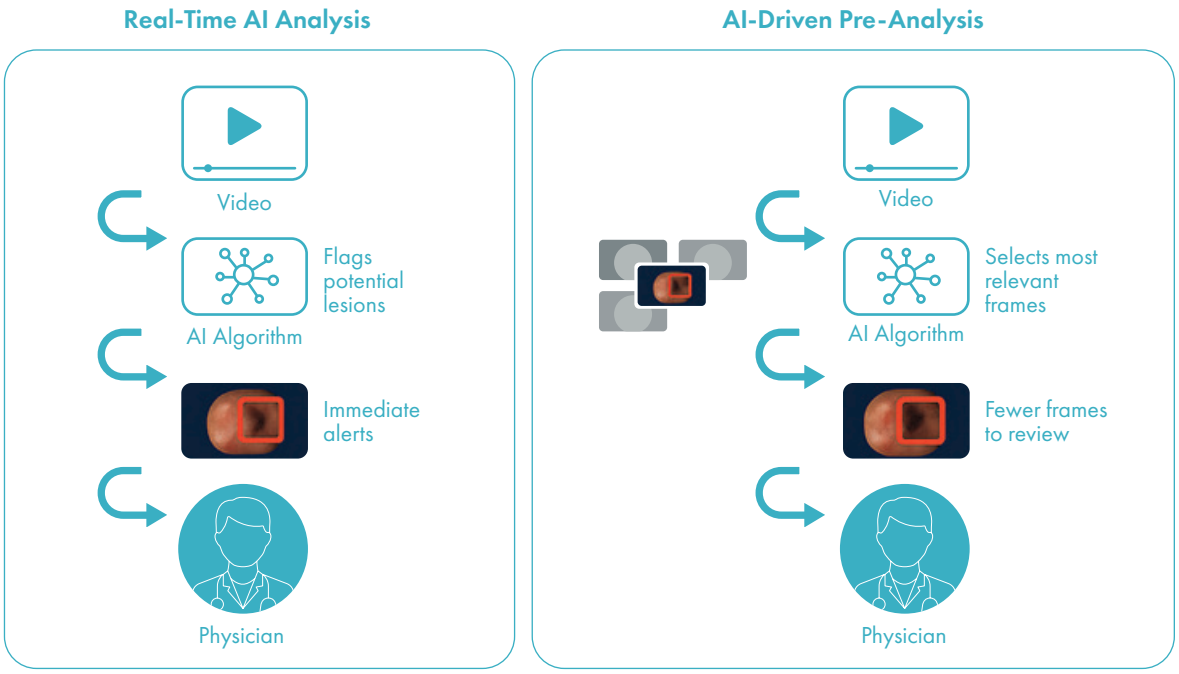

Figure 1
Proposed strategies for AI-enhanced Capsule Endoscopy.

risk of the clinician over-relying on AI-flagged regions and potentially overlooking lesions not identified by the model. Furthermore, it may not significantly reduce the overall analysis time, as the physician still reviews the entire video sequence.

Conversely, AI-driven pre-analysis involves the preliminary processing of the complete CE video. The AI software identifies and selects the most pertinent frames with the highest probability of containing lesions, effectively creating a condensed summary for physician review. This strategy offers the promise of a substantial reduction in the number of frames requiring manual assessment by filtering out normal, non-pathological images. While this approach is designed for rapid video analysis, a potential drawback is that the physician might not review the entire, unedited video, which could compromise their comprehensive understanding of the global clinical context.

5.2.3. Heatmaps and the Importance of Explainable AI

Heatmaps represent an innovative solution that bridges the gap between data science outputs and clinical interpretation in AI-assisted CE. By graphically visualizing areas within an image that exhibit a higher probability of containing lesions, heatmaps offer a more comprehensible representation of the predictions made by the AI model. These visual overlays serve as intuitive indicators, directing the clinician's attention to regions of interest with varying degrees of confidence.

The significance of heatmaps is further underscored by the observed concordance between the areas identified by the AI model and those highlighted by an experienced clinician. This alignment suggests that the AI model is identifying lesions in accordance with established clinical criteria, which consequently reinforces trust in its practical application. This principle aligns closely with the concept of Explainable AI (XAI), which is crucial for the adoption of AI in medicine.

XAI endeavors to make AI models transparent and understandable, moving beyond "black box" algorithm. Heatmaps contribute significantly to XAI by providing visual explanations for the AI's predictions, enabling clinicians to comprehend why a particular area was flagged as suspicious, thus increasing clinical trustworthiness and facilitating more informed clinical decision-making.

The following figures illustrate the practical application of AI-generated heatmaps for various lesion types commonly encountered in CE. These visual examples demonstrate how AI can pinpoint highlight areas of clinical significance, aiding efficient and accurate diagnosis.

Examples of Heatmaps for Detection and Characterization of Pleomorphic Lesion in Capsule Panendoscopy

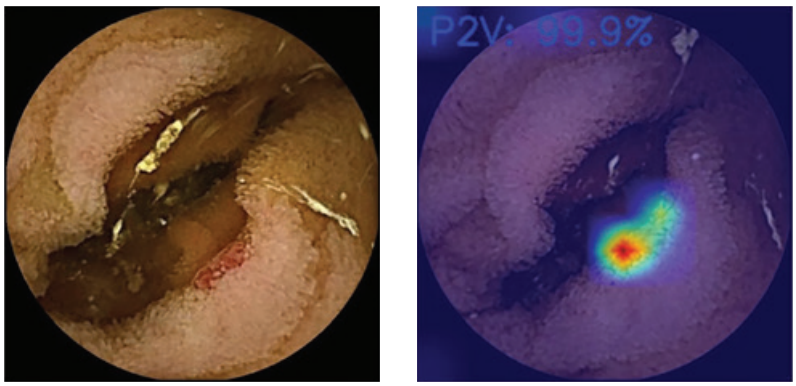

Figure 2
Vascular Lesions.

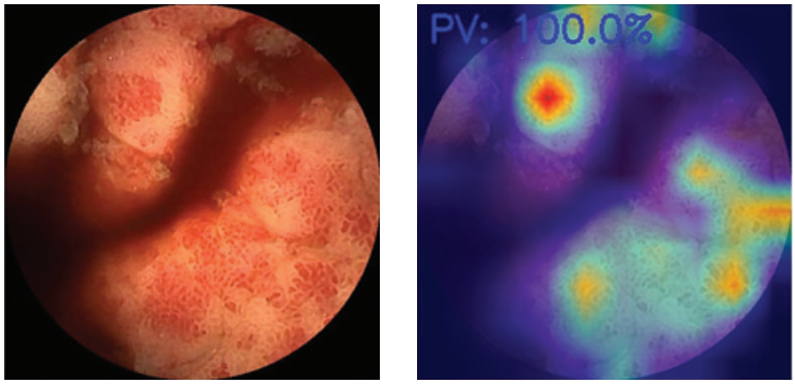

Figure 3
Vascular Lesions.

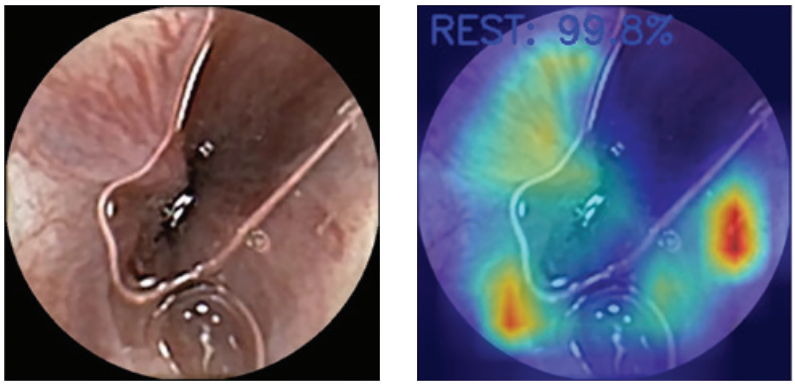

Figure 4
Vascular Lesions.

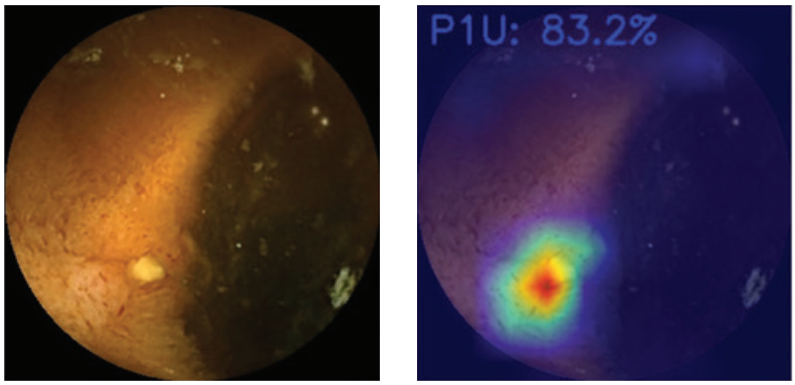

Figure 5.
Ulcers.

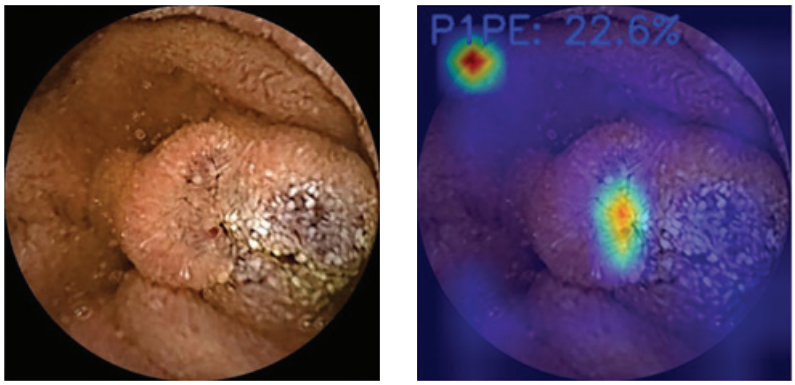

Figure 6
Erosions.

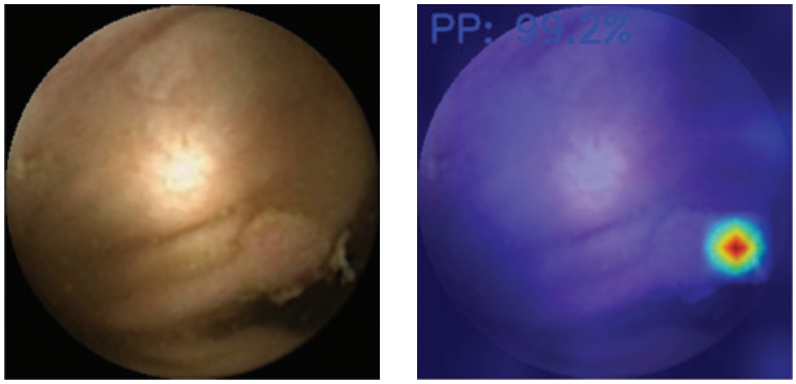

Figure 7
Protuberant Lesions.

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List of Abbreviations and Acronyms

AIDS › Acquired Immunodeficiency Syndrome

AI › Artificial Intelligence

ANCA › Anti-Neutrophil Cytoplasmic Antibodies

APC › Argon Plasma Coagulation

AVM › Arteriovenous Malformation

BRBNS › Blue Rubber Bleb Nevus Syndrome

CCE › Colon Capsule Endoscopy

CC-CLEAR › Colon Capsule CLEansing Assessment and Report

CD › Crohn's Disease

CE › Capsule Endoscopy

CI › Confidence Interval

CMUSE › Cryptogenic Multifocal Ulcerous Stenosing Enteritis

CMV › Cytomegalovirus

CR › Capsule Retention

CT › Computed Tomography

CTC › CT Colonography

CTE › Computed Tomography Enterography

CVID › Common Variable Immunodeficiency

DAE › Device-Assisted Enteroscopy

DY › Diagnostic Yield

ESGAR › European Society of Gastrointestinal and Abdominal Radiology

ESGE › European Society of Gastrointestinal Endoscopy

FDA › Food and Drug Administration

FICE › Flexible Spectral Imaging Color Enhancement

FIT › Fecal Immunochemical Test

FOBT › Fecal Occult Blood Test

GI › Gastrointestinal

GIST › Gastrointestinal Stromal Tumors

GVHD › Graft-Versus-Host Disease

HHT › Hereditary Hemorrhagic Telangiectasia

HIV › Human Immunodeficiency Virus

HLA › Human Leukocyte Antigen

IBD › Inflammatory Bowel Disease

ICD › Implantable Cardioverter Defibrillator

LVAD › Left Ventricular Assist Device

MGCE › Magnetic Guided Capsule Endoscopy

MRI › Magnetic Resonance Imaging

MRE › Magnetic Resonance Enterography

MSBT › Malignant Small Bowel Tumors

NaP › Sodium Phosphate

NET › Neuroendocrine Tumors

NPV › Negative Predictive Value

NSAID/NSAIDs › Nonsteroidal Anti-Inflammatory Drug(s)

PAS › Periodic Acid-Schiff

PCE › Pan-intestinal Capsule Endoscopy

PC › Patency Capsule

PEG › Polyethylene Glycol

PHE › Portal Hypertensive Enteropathy

PJS › Peutz-Jeghers Syndrome

PCR › Polymerase Chain Reaction

PPV › Positive Predictive Value

RCT › Randomized Controlled Trial

SBCE › Small Bowel Capsule Endoscopy

SBV › Small Bowel Varices

SBVQ › Small Bowel Visibility Quality

TIPS › Transjugular Intrahepatic Portosystemic Shunt

UC › Ulcerative Colitis

XAI › Explainable Artificial Intelligence

List of Authors

Coordenadores

Sandra Lopes
Assistente Hospitalar Graduada de Gastrenterologia da ULS de Coimbra; Coordenadora da Unidade Funcional de Doença Inflamatória Intestinal da ULS de Coimbra.

Bruno Rosa
Assistente Hospitalar Graduado de Gastrenterologia do Hospital da Senhora da Oliveira da ULS do Alto Ave; Docente da Escola de Medicina da Universidade do Minho.

Ana Patrícia Andrade
Assistente Hospitalar de Gastrenterologia na ULS de São João; Docente Convidada da Faculdade de Medicina da Universidade do Porto.

Autores

Ana Isabel Ferreira
Médica Interna de Formação Específica em Gastrenterologia do Hospital da Senhora da Oliveira da ULS do Alto Ave.

Ana Ponte
Assistente Hospitalar de Gastrenterologia da ULS de Gaia/Espinho.

Ana Rita Carreiro Silva
Médica Interna de Formação Específica em Gastrenterologia do Hospital do Divino Espírito Santo de Ponta Delgada, E.P.E.R.

Ana Rita Gonçalves
Assistente Hospitalar Graduada de Gastrenterologia do Serviço de Gastrenterologia e Hepatologia da ULS de Santa Maria.

Ana Teresa Ferreira
Médica Interna de Formação Específica em Gastrenterologia da ULS de Santo António.

Andrea Silva
Assistente Hospitalar de Gastrenterologia da ULS de Coimbra.

Antonieta Santos
Assistente Hospitalar Graduada de Gastrenterologia da ULS de Leiria.

Bruno Rodrigues
Médico Interno de Formação Específica em Gastrenterologia da ULS de Lisboa Ocidental.

Catarina Araújo
Médica Interna de Formação Específica em Gastrenterologia da ULS de São João.

Catarina Atalaia Martins
Assistente Hospitalar de Gastrenterologia da ULS de Leiria.

Catarina Costa
Médica Interna de Formação Específica em Gastrenterologia da ULS de Gaia/Espinho.

Cláudia Macedo
Assistente Hospitalar de Gastrenterologia do Hospital da Senhora da Oliveira da ULS do Alto Ave.

Elisa Gravito-Soares
Assistente Hospitalar de Gastrenterologia da ULS de Coimbra; Assistente Convidada da Faculdade de Medicina da Universidade de Coimbra.

Francisco Mendes
Médico Interno de Formação Específica em Gastrenterologia da ULS de São João.

Gonçalo Teixeira
Médico Interno de Formação Específica em Gastrenterologia da ULS de Viseu Dão-Lafões.

Guilherme Macedo
Assistente Hospitalar Graduado Sénior de Gastrenterologia; Diretor do Serviço de Gastrenterologia da ULS de São João; Professor Catedrático da Faculdade de Medicina da Universidade do Porto.

Hélder Cardoso
Assistente Hospitalar Graduado de Gastrenterologia na ULS de São João; Docente Convidado da Faculdade de Medicina da Universidade do Porto.

Joana Frias
Médica Interna de Formação Específica em Gastrenterologia da ULS de São João.

José Cotter
Assistente Hospitalar Graduado Sénior de Gastrenterologia; Diretor do Serviço de Gastrenterologia do Hospital da Senhora da Oliveira da ULS do Alto Ave; Professor da Escola de Medicina da Universidade do Minho.

José Renato Pereira
Assistente Hospitalar Graduado de Gastrenterologia do Hospital do Divino Espírito Santo de Ponta Delgada, E.P.E.R.

Maria Manuela Estevinho
Assistente Hospitalar de Gastrenterologia da ULS de Gaia/Espinho; Assistente Convidada da Faculdade de Medicina da Universidade do Porto.

Mariana Sant'Anna
Assistente Hospitalar de Gastrenterologia da ULS de Coimbra.

Marta Gravito-Soares
Assistente Hospitalar de Gastrenterologia da ULS de Coimbra; Assistente Convidada da Faculdade de Medicina da Universidade de Coimbra.

Marta Salgado
Assistente Hospitalar de Gastrenterologia da ULS de Santo António; Professora Associada Convidada do Instituto de Ciências Biomédicas Abel Salazar (ICBAS) da Universidade do Porto.

Miguel Mascarenhas
Assistente Hospitalar de Gastrenterologia na ULS de São João; Professor da Faculdade de Medicina da Universidade do Porto.

Miguel Mascarenhas Saraiva
Diretor do ManopH - Laboratório de Endoscopia e Motilidade Digestiva – Porto; Diretor do Serviço de Gastrenterologia do Instituto CUF Porto.

Miguel Martins
Médico Interno de Formação Específica em Gastrenterologia da ULS de São João.

Pedro Lima
Médico Interno de Formação Específica em Gastrenterologia da ULS de Lisboa Ocidental.

Pedro Magalhães Costa
Assistente Hospitalar Graduado de Gastrenterologia.

Pedro Mesquita
Médico Interno de Formação Específica em Gastrenterologia da ULS de Gaia/Espinho.

Pedro Narra Figueiredo
Assistente Hospitalar Graduado Sénior de Gastrenterologia; Diretor do Serviço de Gastrenterologia da ULS de Coimbra; Professor de Gastrenterologia da Faculdade de Medicina da Universidade de Coimbra.

Ricardo Cardoso
Assistente Hospitalar Graduado de Gastrenterologia da ULS de Viseu Dão-Lafões.

Rita Barosa
Assistente Hospitalar de Gastrenterologia na ULS de Lisboa Ocidental.

Rolando Pinho
Assistente Hospitalar Graduado de Gastroenterologia da ULS de Gaia/Espinho; Department of Medical Sciences, University of Aveiro.

SPG Sociedade Portuguesa de Gastrenterologia

GEPID Grupo de Estudos Português do Intestino Delgado

APOIO

NORGINE

Medtronic Engineering the extraordinary