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EDITORIAL

Capsule endoscopy and panendoscopy: A journey to the future of gastrointestinal endoscopy

Bruno Rosa, José Cotter

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Bruno Rosa, José Cotter, Department of Gastroenterology, Hospital da Senhora da Oliveira, Guimarães 4835-044, Portugal

Bruno Rosa, José Cotter, Life and Health Sciences Research Institute, School of Medicine, University of Minho, Braga 4710-057, Portugal

Bruno Rosa, José Cotter, ICVS/3B's, PT Government Associate Laboratory, Braga 4710-057, Portugal

Corresponding author: Bruno Rosa, MD, Doctor, Department of Gastroenterology, Hospital da Senhora da Oliveira, Rua dos Cutileiros, Creixomil, Guimarães 4835-044, Portugal. bruno.joel.rosa@gmail.com

Abstract

In 2000, the small bowel capsule revolutionized the management of patients with small bowel disorders. Currently, the technological development achieved by the new models of double-headed endoscopic capsules, as miniaturized devices to evaluate the small bowel and colon [pan-intestinal capsule endoscopy (PCE)], makes this non-invasive procedure a disruptive concept for the management of patients with digestive disorders. This technology is expected to identify which patients will require conventional invasive endoscopic procedures (colonoscopy or balloon-assisted enteroscopy), based on the lesions detected by the capsule, *i.e.*, those with an indication for biopsies or endoscopic treatment. The use of PCE in patients with inflammatory bowel diseases, namely Crohn's disease, as well as in patients with iron deficiency anaemia and/or overt gastrointestinal (GI) bleeding, after a non-diagnostic upper endoscopy (esophagogastroduodenoscopy), enables an effective, safe and comfortable way to identify patients with relevant lesions, who should undergo subsequent invasive endoscopic procedures. The recent development of magnetically controlled capsule endoscopy to evaluate the upper GI tract, is a further step towards the possibility of an entirely non-invasive assessment of all the segments of the digestive tract, from mouth-to-anus, meeting the expectations of the early developers of capsule endoscopy.

Key Words: Non-invasive endoscopy; Panendoscopy; Magnetically controlled capsule endoscopy; Crohn's disease; Digestive bleeding

Core Tip: Double-headed capsules are being increasingly used for pan-intestinal endoscopy, assessing the small bowel and the colon in a single non-invasive procedure, mainly to monitor Crohn's disease and to investigate cases of suspected mid to lower gastrointestinal bleeding. Recent developments on artificial intelligence and magnetically controlled capsules have further expanded the scope of non-invasive endoscopy.

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INTRODUCTION

Capsule endoscopy emerged at the start of the 21st Century as a disruptive technology, which was destined to change the world of gastrointestinal (GI) endoscopy. It consists of a swallowable pill, featuring a miniaturized imaging device inside a biocompatible resistant external casing. It is composed of an optical dome with a lens and a light source, a complementary metal oxide semiconductor image sensor, two mercury-free silver-oxide batteries and a wireless radio-frequency transmitter and antenna, which allow the transmission of endoscopic images to a receiver (data recorder). The designers of this innovative device foresaw the possibility of acquiring images of the whole digestive tract non-invasively. They named it as *M2A*, standing for the *mouth-to-anus* capsule (Given Diagnostic Imaging, Yokneam, Israel)[1]. The major achievement with these capsules at that time was the possibility to explore the small bowel, which had been until then a largely inaccessible and unexplored segment. It was known as the last frontier of digestive endoscopy. The capsule was soon rebranded as PillCam™ SB. This new endoscopic technique was eagerly accepted and rapidly incorporated in clinical practice, as a safe and effective diagnostic procedure for the investigation of small bowel diseases, mainly in cases of suspected obscure GI bleeding and suspected small bowel Crohn's disease (CD). It was also useful in suspected non-steroidal anti-inflammatory drug (NSAID) enteropathy, polyposis syndromes such as Peutz-Jeghers syndrome, some cases of refractory celiac disease and suspected small bowel neoplasia[2]. Capsules with a single optical dome remain to date the most widely used in clinical practice, with enhanced features such as a higher frame rate acquisition (up to 6 images per second), a wider angle of view, a longer battery lifespan and improved image resolution.

In 2006, the first double-headed capsule was released, called the PillCam™ COLON. In 2009, the PillCam ™ COLON 2 (Given Imaging, Medtronic) was released. At 11.6 mm × 32.3 mm, it was slightly larger than the original SB capsule (11 mm × 26mm), with an increased frame rate for image acquisition (up to 35 images per second), an extended battery time and a wider angle of view (172º in each side), to allow for the coverage of the whole colonic surface. These capsules have been mainly used in the case of a contraindication to conventional colonoscopy, cases of incomplete colonoscopy due to fixed angulation or redundant colon with persistent loop formation, or in average risk populations as an alternative for colorectal cancer screening[3,4]. Two other models of double-headed capsules were released in 2017 (PillCam™ Crohn's, Medtronic) and in 2023 (OMOM CC™, Jinshan). Compared to the PillCam™ COLON, the PillCam™ Crohn's and the OMOM CC™ do not have a sleep mode, continuously acquiring images from the start of the examination. This enables the non-invasive examination of the small bowel and colon [pan-intestinal capsule endoscopy (PCE)], in a single procedure, which is safe and well tolerated by patients[5-7]. The OMOM CC™ integrates a new feature for artificial intelligence (AI) assisted diagnosis. If this is properly validated, it might overcome a current limitation of PCE, which is its time-consuming reading, reaching on average up to 120 min[8]. This will allow a faster examination, without compromising diagnostic accuracy. Table 1 summarizes the technical details of the currently available double-headed capsules, which may be used to perform PCE.

PCE PROCEDURE - BOWEL PREPARATION

For PCE, unlike for small bowel capsule endoscopy, which can be carried out without prior intestinal preparation, a demanding preparation protocol is mandatory. Optimized bowel preparation is essential to ensure an effective colon capsule (CC) endoscopy or PCE. It is not possible to irrigate or aspirate debris, insufflate or change the patient's position to improve the quality of visualization during the examination, at the risk of rendering the procedure inconclusive. This potentially poses a significant additional burden both to the patient and the healthcare system. A recently published systematic review and meta-analysis[9] described that key quality outcomes such as adequate cleansing rate (ACR) and complete examination rate (CR) remain sub-optimal for CC or PCE, with an ACR of 72.5% (95%CI 67.8%–77.5%) and a CR of 83.0% (95%CI 78.7%–87.7%). The Leighton-Rex grading scale[10], and more recently the CC CLEansing Assessment and Report (CC-CLEAR)[11,12], were created to allow a systematic description of the quality of bowel preparation in the colon at capsule endoscopy. The CC-CLEAR basically replicates the methodology of the Boston Bowel Preparation Scale [13], with which many gastroenterologists are familiar, as it is already common practice to use it routinely in conventional colonoscopy. The CC-CLEAR scale divides the colon in 3 segments: Right-sided, transverse, and left-sided, and each segment is scored according to an estimation of the proportion of clear mucosa: 0, < 50%; 1, 50%-75%; 2, > 75%; 3, > 90%. The overall cleansing classification is the sum of each segmental score, grading between 8-9, excellent; 6-7, good; and 0-5

Table 1 Technical details of double-headed capsules currently available to perform pan-intestinal capsule endoscopy

	PillCam™ COLON2 (Medtronic, Given Imaging Inc.)	PillCam™ Crohn's (Medtronic, Given Imaging Inc.)	OMOM™ CC (Jinshan)
Dimensions (mm)	11.6 × 32.3	11.6 × 32.3	11.6 × 31.5
Optical domes	2	2	2
Resolution (pixels)	256 × 256	256 × 256	360 × 360
Lens angle (degrees per side)	172	168	172
Frame rate (frames per second)	4-35	4-35	4-35
Sleep mode	Yes	No	No
Battery life (h)	≥ 10	≥ 10	≥ 10

inadequate; with any segment scoring ≤ 1 rendering the overall classification as inadequate. Although currently available data support the use of a low-fibre diet and adjunctive sennosides prior to the purgative ingestion, split dose polyethylene glycol and routine prokinetics before capsule ingestion, with sodium phosphate as the most consistent option as a booster, there is an unmet need for improvement in order to achieve more effective bowel preparation protocols. Table 2 summarizes a proposed bowel preparation protocol for CC and PCE, based on currently available evidence in the literature.

PCE IN CLINICAL PRACTICE

Double-headed capsules have been used in clinical practice as a pan-enteric tool, mainly in the setting of inflammatory bowel diseases (IBDs) and digestive bleeding [suspected small bowel or colon bleeding, *i.e.* mid or lower GI bleeding (MLGIB)]. Table 3 summarizes the current indications and contraindications for PCE.

CD

The use of PCE in patients with CD has been mainly devoted to patients with an established diagnosis of CD who have already been submitted to ileocolonoscopy and cross-sectional imaging such as computed tomography enterography (CTE) or magnetic resonance enterography (MRE), to evaluate the small bowel and exclude stricturing and/or penetrating phenotypes of the disease[14,15]. In this group of patients, the use of PCE seems especially appealing for monitoring disease progression and evaluating mucosal healing in response to therapy in those cases with extensive disease, *i.e.*, those that involve both the small bowel and the colon. It is estimated that approximately 40% of patients with CD have lesions limited to the small bowel, in another 20% the disease is located only in the colon, and in near 35% it involves both the small bowel and the colon[16]. It is also known that in these patients with small bowel and colonic involvement, the burden of the disease is often driven by the type of small bowel lesions, which are usually more severe, extensive and more difficult to heal. Up to 30% of patients will present with stricturing disease at diagnosis or progress to stricturing or penetrating disease over the years[17]. The subset of patients with inflammatory-type small bowel and colonic disease corresponds to approximately one-fourth of all patients with CD. Those are the patients who are good candidates for PCE as the preferred modality for disease assessment over time. The current standard recommends invasive conventional colonoscopy in addition to cross-sectional imaging of the small bowel, such as CTE or MRE. PCE offers the possibility of a one-step examination of both the small bowel and the colon, which is safe and comfortable for the patient, without the need for sedation, radiation exposure or multiple visits to the clinic. This strategy was demonstrated to be at least as effective for assessing the small bowel and the colon, when compared with colonoscopy plus dedicated small bowel cross-sectional imaging. Preliminary data indicate that under certain circumstances PCE may represent a cost-effective approach, leading to increased quality of life and life expectancy, and making it a cost-effective option[18]. Another study evaluated the cost of PCE *vs* colonoscopy, with or without MRE, in IBD patients. Although initial costs were increased due to the use of PCE and earlier introduction of biologics, an economical benefit was observed in the longer term, due to a significant reduction in the need for surgical interventions[19].

A recent systematic review and meta-analysis by Tamilarasan *et al*[20] evaluated the performance of PCE for the detection of CD lesions in the small bowel and the colon. It found a comparable diagnostic yield of PCE compared to MRE plus colonoscopy [pooled OR 1.25 (95%CI: 0.85%-1.86%). Capsule endoscopy is the only non-invasive modality for the small bowel to adequately assess the main treatment outcome, which is mucosal healing, according to the current treat to target concept for the treatment of IBDs[21]. A meta-analysis by Dionísio *et al*[22] found that capsule endoscopy has a significantly higher diagnostic yield in patients with suspected and established small bowel CD. This new approach may have significant clinical implications, as demonstrated in the multicentric study by Tai *et al*[23], where PCE

Table 2 Standard bowel preparation for pan-intestinal capsule endoscopy

	Bowel preparation protocol
Day 2	Low-fibre diet
Day 1	Clear-liquids diet
	7:00 – 9:00 PM 2 L of PEG
Examination day	06:30 – 7:30 AM 1 L of PEG
	08:15 AM 10 mg metoclopramide p.o.
	08:30 AM 100-200 mg simethicone in water for capsule ingestion
	09:30 AM check real time viewer. Additional 10 mg metoclopramide p.o. if capsule still in stomach
	First alert (capsule detected in SB) NaP 30 mL + 1 L water
	Second alert (3h after 1st booster) NaP 15 mL + 0.5 L water
	Third alert (2h after 2nd booster) 10 mg bisacodyl rectal suppository

PEG: Polyethylene glycol; p.o.: Per os; NaP: Sodium phosphate; SB: Small bowel.

Table 3 Indications and contraindications for pan-intestinal capsule endoscopy

Indications	Contraindications
CD Inflammatory-type (non-stricturing, non-penetrating), extensive (affecting small bowel and colon) Scheduled monitoring to evaluate mucosal healing in response to treatment (to justify and guide treatment change) Evaluate disease distribution and severity: stratify patients to low *vs* high risk (prognosis); asymptomatic CD patients with abnormal analysis; exclude active CD or investigation of symptoms unrelated to disease activity Establish diagnosis in patients with IBD-U, suspected CD or atypical ulcerative colitis **Gastrointestinal bleeding** Suspected mid-lower intestinal bleeding (overt or occult)	(1) Known or suspected intestinal strictures and/or fistulae (if patency not proven based on cross sectional imaging and/or patency capsule assessment[14]); (2) Magnetic resonance imaging examination scheduled for same-day or following days (requires prior confirmation of capsule excretion); and (3) Special conditions and relative contraindications: pregnancy; children under 8 yr of age; swallowing disorders; gastric surgery; implanted cardiac electric devices: Pacemakers, defibrillators, ventricular assist devices, telemetry; allergy or contraindications to any of the drugs or products used in the protocol; patients unable to walk for short periods and/or with neurological and/or psychiatric condition potentially favouring protocol deviations

CD: Crohn's disease; IBD-U: Inflammatory bowel disease - type unclassified.

determined a change in disease management in 46,5% of patients with established CD. Another international multicentre prospective study recently evaluated PCE *vs* ileocolonoscopy plus MRE in 158 patients with non-stricturing CD. It found a high performance of PCE for assessing CD mucosal activity and extent as compared to MRE and/or ileocolonoscopy, without the need for multiple tests[24]. MRE, ileocolonoscopy, and PCE reading were performed by blinded central readers using validated scoring systems. The gold-standard was defined by a consensus panel composed of independent experts. Overall sensitivity for active inflammation (PCE *vs* MRE and/or ileocolonoscopy) was 94% *vs* 100% (P = 0.125), and specificity was 74% *vs* 22% (P = 0,001). PCE sensitivity was superior to MRE in the proximal small bowel (97% *vs* 71%, P = 0.021), and similar to MRE and/or ileocolonoscopy in the terminal ileum and colon (P = 0.5-0.625). A study by Yamada *et al*[25], using double balloon enteroscopy as the gold-standard, reported PCE sensitivities for scars, erosions, and ulcers of 83.3%, 93.8%, and 88.5%, respectively, the specificities being 76%, 78,3%, and 81,6%, respectively.

In up to 10%–15% of cases, IBD remains unclassified after conventional colonoscopy[26]. In such cases, PCE may also have an important role in clarifying the diagnosis, by evaluating the small bowel while simultaneously reassessing the colon. In a study which used the PillCam™ COLON or PillCam™ COLON 2 in patients with ulcerative colitis, 7.1% of patients changed the diagnosis from ulcerative colitis to CD due to inflammatory activity observed in the small bowel[27].

The use of validated scoring systems to objectively evaluate small bowel and colonic lesion, such as the Capsule Endoscopy CD Activity Index (CECDAIic) or the novel PillCam Crohn's™ capsule score (Eliakim score), allows for the standardization of reporting, increasing reproducibility and inter-observer agreement of PCE[28-32].

Regarding safety, in a recent meta-analysis the reported capsule retention rate was 2% for all indications, and it was higher in the setting of CD (relative risk = 4%)[33]. A retention rate of 4.63% (95%CI: 3.42-6.25) in patients with established CD, *vs* 2.35% (95%CI: 1.31-4.19) in patients with suspected CD[34]. The risk of capsule retention can be reduced with the use of small bowel imaging modalities such as CTE or MRE, and/or patency capsule, when indicated. When capsule endoscopy is considered in patients with history of obstructive symptoms, known stricture or surgical anastomosis[35-37], a patency capsule is advisable even in cases of unremarkable cross-sectional imaging[14,35]. PCE has been proven safe in most series, and the occurrence of capsule retention has been rarely described and usually resolved conservatively[38,39].

GI BLEEDING

Recently, the use of PCE has been evaluated for suspected small bowel or colon bleeding[6,40], in patients with iron deficiency anaemia, with or without overt bleeding, and with a non-diagnostic esophagogastroduodenoscopy (EGD). Following current standards of practice, patients are initially submitted to conventional colonoscopy, and then proceed to small bowel capsule endoscopy, when the colonoscopy is also non-diagnostic. However, the diagnostic and therapeutic yields of colonoscopy in this setting are quite low[41]. PCE appears as a possible game changer in the clinical management of these patients, giving the opportunity for a non-invasive and adequately timed pan-intestinal evaluation. This may guide subsequent management, depending on the type and location of the potentially haemorrhagic lesions (PHLs) when present, which may contribute to avoiding further unnecessary examinations[40]. The earlier evaluation of the small bowel which is achieved with this PCE-first approach is expected to increase the diagnostic yield in patients with suspected small bowel bleeding, particularly for patients presenting with overt bleeding[42]. Capsule endoscopy has been shown to be able to detect proximal lesions missed by EGD in a non-negligible proportion of patients[43,44].

A fundamental premise in Medicine is to be able to offer all patients, when clinically indicated, the access to diagnostic and therapeutic procedures that are effective, safe and proportionate, with as minimum degree of invasiveness and discomfort possible. This supported by the Hippocratic principle of "*primum non nocere*". Capsule endoscopy falls perfectly within these principles, as a promising and valuable diagnostic tool that is expected to play an increasingly central role in the upcoming paradigm shift in the field of digestive endoscopy. Indeed, clinicians are expected to make rational use of all the diagnostic modalities available to make a correct diagnosis, which is an essential element before planning an adequate therapeutic and follow-up strategy. There is also a principle of minimum invasiveness, *i.e.*, patients should receive the safer and less invasive diagnostic or therapeutic approach, among the available equally effective alternatives. Invasive interventions should be restricted to those cases where they are required, based on the results of preliminary non-invasive studies, with better safety and tolerability profile, as is the case of imaging tests or endoscopic capsules. Such strategies should also be cost-effective before being adopted in clinical practice.

Timely access to capsule endoscopy in patients with iron deficiency anaemia or melena, no suspected lower intestinal bleeding and negative EGD, results in shortened hospital stays, increased diagnostic yield, and a significant two-third reduction of the number of colonoscopies, when compared to those patients who receive the small bowel capsule endoscopy only after negative upper and lower GI endoscopy have been performed[45]. Mussetto *et al*[46] also assessed the use of PCE in patients presenting with melena and non-diagnostic EGD. PCE was safe and allowed for the identification of the bleeding site in 83% of 128 patients included, leading to small bowel therapeutic interventions in 50% of the cases, therefore avoiding unnecessary invasive colonoscopy. In another retrospective investigation which analyzed 100 consecutive patients[6], PHL were observed in 61% of the cases. The capsule was able to detect small bowel lesions in 68% and colonic lesions in 81% of patients, no further invasive procedures being required in approximately 65% of the patients with negative gastroscopy.

A recent prospective study[47] included 100 consecutive patients with suspected small bowel or colonic bleeding also presenting with iron-deficiency anaemia and/or overt bleeding after non-diagnostic EGD. Colonoscopy detected PHL in 23% of the cohort, which means 50% (23/46) of all patients with PHL, while for PCE the overall diagnostic yield was 44%, meaning 95.7% (44/46) of all patients with PHL, $P < 0.001$. Colonoscopy had a sensitivity of 23/46 = 50%, a specificity of 54/54 = 100%, positive predictive value (PPV) 23/23 = 100% and negative predictive value (NPV) 54/77 = 70.1%, while for PCE the sensitivity was 44/46 = 95.7%, specificity 54/54=100%, PPV 44/44 = 100% and NPV 54/56 = 96.4% for PHL. The authors concluded that PCE was safe and more effective than colonoscopy in identifying PHL, both in the small-bowel and colon. Moreover, PCE was negative in more than half of patients with suspected MLGIB, avoiding further invasive endoscopic investigations. These results support the potential use of PCE as a first-line examination in patients with suspected small bowel and/or colonic bleeding.

MAGNETICALLY CONTROLLED CAPSULE ENDOSCOPY

Although conventional EGD remains the gold standard for the endoscopic evaluation of the upper GI tract, it may be limited due to poor tolerability and acceptability, or in patients at increased risk of complications[48]. Recently, the possibility of external magnetic control of the capsule [magnetically controlled capsule endoscopy (MCCE)] for non-invasive assessment of the esophagus and stomach has been available[49-54]. This novel MCCE is a comfortable, highly

acceptable alternative for patients refusing, or unfit for conventional EGD (including sedated EGD), or at a higher risk of adverse events[53]. It has the advantages of non-invasiveness, with an excellent safety profile and patient acceptance. Clinical indications for MCCE may include esophageal diseases such as esophageal varices and Barrett's esophagus[55], screening for gastric cancer[54], detection and surveillance for gastric or duodenal lesions such as ulcers, polyps, varices, erosive and atrophic gastritis, drug-related GI mucosal injury such as NSAIDs, remote gastric examination[56], stable patients with acute upper GI bleeding[57], or surveillance after partial gastrectomy or minimally invasive endoscopic treatment.

The translation of the MCCE concept and technology into a double-headed pan-intestinal capsule may soon make it possible to assess the entire mucosa of the digestive tract, meeting the expectations of the founders of capsule endoscopy, who coined and aimed for the concept of a *mouth-to-anus (M2A)* endoscopic capsule.

MCCE examination is generally safe, with a low rate of adverse events. The risks of capsule retention and aspiration should be addressed for active prevention and appropriate management[14,58]. Contraindications for MCCE include known or suspected significant GI stricture[14], pregnancy, implanted electronic devices (*e.g.*, pacemakers, cochlear device, drug infusion pumps, nerve stimulator except for MRI-compatible devices) or magnetic metal foreign bodies.

A systematic review and meta-analysis, published in 2021, compared MCCE and conventional gastroscopy in the identification of gastric lesions[59]. Seven studies were included, with a total of 916 patients and 745 gastric lesions. The mean capsule endoscopy examination time was 21.92 ± 8.87 min. The pooled overall sensitivity of MCCE was 87% (95%CI: 84%-89%). The sensitivity for identifying gastric ulcers was 82% (95%CI: 71%-89%), gastric polyps 82% (95%CI: 76%-87%), and gastric erosions 95% (95%CI: 86%-98%). MCCE was well tolerated, with minimal adverse events. The authors reported that MCCE was a relatively time-consuming process compared to conventional gastroscopy (21.92 ± 8.87 min *vs* 5.35 ± 3.01 min, respectively). However, when sedation is required during conventional gastroscopy, patients need to stay in a recovery unit after the procedure and may be incapable of following their regular activity for the rest of the day. Conversely, after MCCE they are alert and able to continue their regular activities.

MCCE still has many disadvantages that currently limit its use in clinical practice. The examination of the esophagus is an important part of routine upper GI investigation, therefore the rapid passage of the capsule through the esophagus is a limitation of MCCE. If proven effective and safe, the use of detachable strings[60] or enhanced magnetic fields to decelerate the passage through the esophagus may improve the investigation of the esophagus through MCCE. The cost of MCCE is significantly higher compared with conventional gastroscopy, and cost-effectiveness analysis in real life clinical settings is lacking[49]. The inability to perform biopsies and therapeutic procedures such as haemostasis or polypectomy, among others, may also be perceived as an important limitation for MCCE, as for any other type of capsule endoscopy. The capsule may, as in other segments of the GI tract, be regarded as a filter diagnostic examination, followed by more invasive examinations only when justified by the capsule endoscopic findings. A propensity score matching analysis[61] for large-scale screening of asymptomatic individuals reported that most patients do not require conventional gastroscopy after MCCE, while patients with GI symptoms or focal lesions detected by MCCE were more likely to require further examination with conventional gastroscopy, for biopsy or endoscopic treatment (3.8% *vs* 10%). Lai *et al*[62] reported that only 18.2% of patients needed a biopsy after MCCE. MCCE may therefore be regarded as a screening tool, allowing the identification of patients who require further evaluation with conventional gastroscopy. Regarding the role of biopsies obtained during EGD to check for *Helicobacter pylori* (*H. pylori*) status, some preliminary evidence has shown that the Kyoto classification of gastritis can be adapted to MCCE, to accurately predict *H. pylori* infection status on conventional gastroscopy[63]. In this setting, major specific findings were mucosal swelling and spotty redness for current infection, regular arrangement of collecting venules, streak redness, fundic gland polyp for non-infection, and map-like redness for past infection.

AI IN CE

There has been a huge expansion of AI models in medicine, and particularly in digestive endoscopy[64-67]. The time-consuming reading of capsule endoscopy procedures, as well as the large number of image frames which are generated, have driven the development of convolutional neural networks (CNN) for digital imaging analysis. AI is expected to tackle some of the current limitations of PCE, by reducing reading times and improving the ability to detect all the relevant lesions[68]. To date, this has been mainly tested for the small bowel[69,70], while it remains scarcely explored in the case of double-headed capsules. A few studies of CNN development for CC endoscopy revealed a very high accuracy for detection of colorectal neoplasia or protruding lesions[71-73]. Mascarenhas *et al*[74] recently developed a CNN for automatic detection of colonic blood in CC endoscopy, enabling the differentiation between normal mucosa, blood or hematic residues and pleomorphic mucosal lesions, namely ulcers and erosions, protruding lesions and vascular lesions. CNN revealed a global sensitivity of 96% and specificity of 98%. Ferreira *et al*[75] developed a CNN for automatic detection of panenteric ulcers in PillCam™ Crohn's capsule, with a sensitivity of 98%, specificity of 99% and accuracy of 99%, having a perfect discriminatory capacity for the detection of ulcers and erosions. AI implementation is expected to achieve a significant reduction in the reading times per exam. Moreover, PCE reading technique is challenging and requires specific training, and AI models are expected to contribute to assist training and shortening the learning curve for this technique. The implementation of AI-powered PCE may therefore become a disruptive change towards an effective and minimally invasive evaluation of the entire GI tract. A multicenter prospective study (n = 131)[76], described a substantial reduction in the reading time of PCE with AI in patients with suspected CD. The sensitivity and specificity for detecting CD was 97% and 90%, respectively, with a NPV of 95%, enabling a faster screening with high diagnostic accuracy in cases of suspected CD.

CONCLUSION

The horizons of capsule endoscopy are evolving. PCE is a non-invasive, effective, and safe procedure to evaluate the small bowel and the colon. Its use in CD and more recently in GI bleeding is expanding in routine clinical practice. Conventional endoscopic procedures for the esophagus, stomach and colon remain superior to PCE considering each individual segment, and have the advantage of enabling biopsy sampling and therapeutic procedures as needed. PCE, however, offers the opportunity to evaluate multiple segments of the digestive tract at the same time, in a single non-invasive procedure. Currently, clinical indications for PCE include the assessment of non-stricturing, non-penetrating and extensive CD (affecting the small bowel and colon), mainly for disease monitoring and evaluation of mucosal healing in response to medical therapy. It could also be considered to clarify the diagnosis in patients with IBD - type unclassified or in atypical cases of ulcerative colitis. PCE has been also proven valuable in patients with suspected overt or occult MLGIB, driving subsequent clinical decisions and avoiding the need for additional invasive procedures in a significant proportion of cases. The central questions that seem to be pressing for the future are: Should capsule endoscopy technology be considered a "niche" procedure to be used only in particular patients and settings? Will it remain in the shadows of the dominant gold standard which is invasive upper digestive endoscopy and colonoscopy? Could it represent the archetype of a coming revolution? The capsule is a disruptive device which has been proven to have the potential to find its place in clinical practice, able to act as a non-invasive diagnostic "filter", offering the opportunity to change the diagnostic approach of patients with digestive tract diseases in the near future. We already have the possibility to evaluate all the small bowel and the colon, non-invasively, with a capsule, in a single procedure, which is effective, safe and well tolerated. Therefore, PCE may be the key to answer the question "Who needs an invasive endoscopic procedure?", as opposed to the current practice, where "All these patients will undergo an invasive endoscopy or colonoscopy, and then some (many) will require a small bowel capsule". PCE is a possible game changer, expanding the field for non-invasive endoscopy and limiting the need for invasive procedures such as conventional colonoscopy or device-assisted enteroscopy, which should be restricted to those cases where biopsies or therapeutic procedures are required, based on the results of the PCE.

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ORCID number: Bruno Rosa 0000-0003-2885-0720; José Cotter 0000-0002-2921-0648.

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