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Capsule Endoscopy: A Comprehensive Review

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1. Introduction

Until a few years ago, the small bowel was an organ which was very difficult to explore with the available endoscopic, radiological and nuclear medicine techniques due to anatomical (i.e. distance from external orifices, length) and physiological (i.e. active peristalsis) reasons. In routine practice, only the last few centimeters of the ileum was accessible to retrograde visualization by ileo-colonoscopy. Exploration from the proximal side by push, sonde or intra-operative enteroscopy were invasive procedures that did not always allow us to visualize the lesions in the small bowel (Galmi che et al.,2008). Sonde enteroscopy had been abandoned in the 90's because it was a tedious technique (long duration of the procedure) and it had several technical limitations. Push enteroscopy is limited by the depth of insertion of the scope and is poorly tolerated. Intra-operative enteroscopy is the most effective of these techniques, but it is the most invasive with a significant percentage of adverse side effects (Rondonotti et al., 2007).
The concept for small bowel capsule was developed independently by two groups. Dr. Paul Swain, a British gastroenterologist demonstrated the first live transmissions in 1996 with the broadcast of a pig's stomach. In 1997, he collaborated with Dr. Gavriel Iddan, a mechanical engineer working with the Israel Ministry of Defense(Appleyard et al.,2001;Meron,2000;Swain et al.,1996). Successful animal trials were conducted and first published in 2000. (Swain et al.,1996) Human studies followed and the use of capsule endoscopy (CE) in clinical trials was first published in 2001. (Kornbluth et al.,2004) Since the emergence of CE, more than 1000000 capsules have been swallowed worldwide and nearly 1000 peer reviewed publications have appeared in the literature. This article reviews the fundamental of wireless capsule endoscopy. Special attention is paid to the indications, benefits and drawbacks of the technique, as well as to the strengths and limitations of clinical data available to the date.

2. Technical features of the capsule

The M2A capsule (figure-1) initially, and Pillcam SB2 (Small Bowel) later, from GIVEN (Gastro Intestinal Video Endoscopy, Given Imaging Limited, Yoqneam, Israel), and endo capsule from Olympus are the capsules that have been approved for use in the clinical setting, approved in Europe by the European Medicines Agency and in the United States by the Food and Drug Administration in 2001 (Pannazio, 2006). The capsule which measures only 11 mm × 26 mm and weighs 3.7 g, holds a metal oxide semiconductor imaging chip

video camera, 6 white light-emitting diode illumination sources, 2 silver-oxide batteries and a radio telemetry transmitter. The image filed is 140 degrees, magnification is × 8 and the depth of view is 1 to 30 mm (Iddan et al.,2000;Davis et al.,2005).

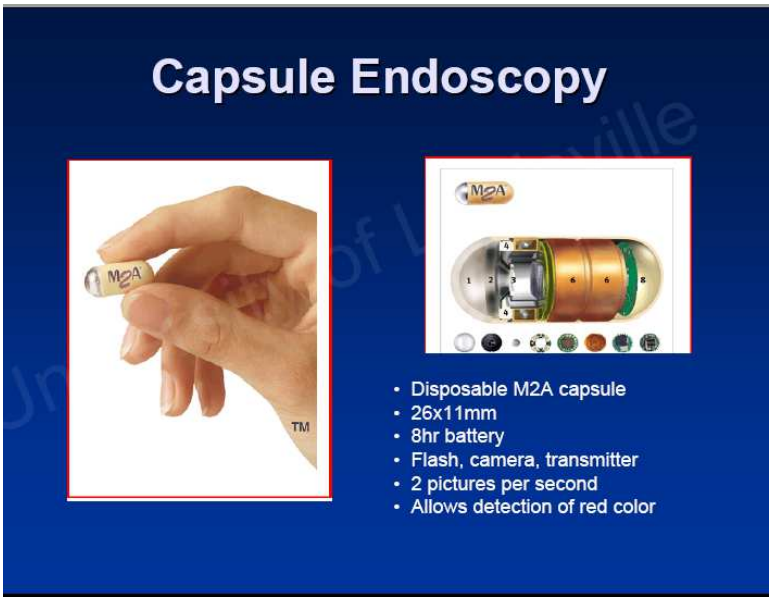

Fig. 1. M2A Capsule

Once swallowed, the capsule moves thorough the intestine via peristalsis and is excreted in the stool. The camera takes two images per second as it sweeps the intestine and transmits these to eight lead sensor arrays, arranged in a specific manner and taped to the anterior abdominal wall, connected to a recording device in the belt for the duration of the battery life, which is 6-8 h. Once the study is completed, the recording device and sensor arrays are removed and the images (50000-60000 images total) are downloaded to a computer with reporting and processing of images and data (Rapid, Given Imaging) software that displays the video images on a computer monitor. This software includes a localizing system, blood detector and some features to assist the interpreter. The suspected blood indicator is quite good at detecting active bleeding, but is not so useful at detecting other lesions and does not replace careful examination of the CE. It is recommended that patients avoid magnetic fields such as magnetic resonance imaging (MRI), and metal detectors until the capsule is excreted in the stool, which usually occurs in 24-48 h. Small bowel preparation is still a controversial issue. Some groups used fasting or clear liquids for 10 to 12 h (or even for 24 h) before the study, although some studies suggest that bowel preparation (with 2 or 4 liters of polyethylene glycol based electrolyte solution or oral sodium phosphate preparation) improves the visualization of the small intestine(Dai et al.,2005;de Franchis et al.,2005).A recent Spanish prospective multicenter trial published in abstract form, has shown that all three strategies have similar results(Pons et al.,2006). After ingestion of the capsule, patients were allowed to drink clear liquids after 2 h and eat a light meal after 4 h and were observed for 8 h at the study site.

3. Indication

Capsule endoscopy is mainly indicated (Table-1) for the evaluation of Small Bowel (SB) diseases, particularly for the diagnosis of Obscure Gastro Intestinal Bleeding (OGIB). CE can be used in a variety of conditions including Crohn's disease (CD), mal-absorption, chronic diarrhea, evaluation of refractory iron deficiency anemia, abdominal pain, polyposis syndromes, celiac disease, and detection of SB tumors.

Small Bowel
Obscure gastrointestinal bleeding
Occult (positive FOBT)
Evaluation of iron deficiency anemia
Crohn's disease
Suspected crohn's disease
Indeterminate colitis
Assessment of mucosal healing
Abdominal pain
Craft-versus-host disease
Surveillance of polyposis syndromes
Celiac disease
Suspected small bowel tumors
Follow up of small intestine Transplantation
Evaluation of abnormal SB Imaging
Evaluation of drug induced injury
Esophagus
Barrett's esophagus
Esophagitis
Variceal evaluation

Table 1. Indication

Graft versus host disease (GVHD) and follow up of small intestine transplantation are rare indications. In later years, breakthrough developments in CE technology have enabled the direct visualization of the upper (de Franchis et al.,2008;Fernandez et al.,2007)and lower segments (Deviere et al.,2008;Schoof et al.,2006)of the gut using specifically designed capsules. CE with high frame rate (PillCam Eso, Given Imaging) can be used for esophageal disorders, such as non-invasive evaluation of esophageal varices, esophagitis and Barrett's esophagus (Galmiche et al.,2008). Colon capsule endoscopy is an emerging form of colon imaging that may be useful to improve compliance with colorectal cancer screening.

3.1 Obscure GI bleeding

Obscure GI bleeding (OGIB) is the most common indication for CE examination. CE has a high diagnostic yield in OGIB, facilitates effective decision-making regarding subsequent investigations and treatments (Eliakim et al., 2008).Diagnostic yield of CE for OGIB varied between 31% and 91% (Adler et al.,2004;Costamagna et al.,2004;Ell et al.,2002;Ersoy et al.,2006;Ge et al.,2004;Golder et al.,2006;Hartmann et al 2003,2005;Lewis & Swain,2002;Mata et al.,2004;Panazio et al.,2004;Scapa et al.,2002;Saurin et al.,2003;Saperas et al.,2007;Van gossum et al.,2003;Voderholzer et al.,2003). The published studies of CE for OGIB were

reviewed and reported that sensitivity ranged from 79% to 95% and specificity from 75% to 100%(Varela Lema & Ruano-Ravina, 2008). The positive predictive value (PPV) varied from 94% to 100% and the negative predictive value (NPV) from 80% to 100%.

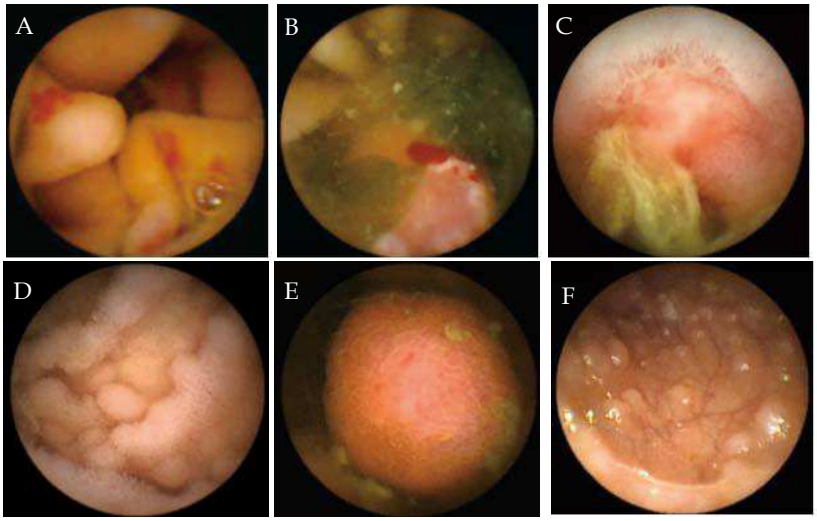

Fig. 2. VCE images of lesions found in patients with obscure-overt GI bleeding. A: Multiple angiodysplasias in the jejunum; B: A jejunal mass with active bleeding; C: An ileal ulcer in a patient with newly diagnosed Crohn's disease. D: Benign lymphoid hyperplasia located diffusely through the GI tract in a patient with CVID; E: A jejunal polyp in a patient with peutz-jeghers disease; F: Multiple small polyps in the ileum.

Capsule endoscopy led to a change in therapeutic management in 9%-77% of patients. A recent study (Albert et al., 2008) reported that CE detected the bleeding source in 76.8% of patients. The diagnostic yield of CE in OGIB depends on the type of bleeding. Highest yield of CE was 92.3% in patients with active bleeding (Pannazio et al., 2004) compared to those with obscure occult bleeding (44.2%). Researchers observed a reverse relationship between findings and time after last bleeding episode. The longer the time from last bleed, the lower the diagnostic yield. Do the lesions discovered by CE have any bleeding potential or clinical importance in terms of management change? Saurin et al., 2003 showed that CE detects more lesions, but only half of them have true bleeding potential. CE is superior to other techniques in diagnosing the source of bleeding. The yield for CE is 63% and 67% compared with 28% for push enteroscopy (PE) and 8% for barium study(Lewis,2008).

3.2 Crohn's disease

Crohn's disease (CD) is a chronic inflammatory disease that can involve any part of the Gastro-intestinal (GI) system, and disease is confined to the SB in about one-third of the patients. There is no single test to diagnose CD completely, so CD diagnosis can be established with a combination of clinical, endoscopic and histological findings. Most imaging studies lack sensitivity to identify early changes, and endoscopy does not allow total examination of the bowel. CE is able to identify mucosal changes before other technologies. It has a valuable role in the evaluation of the SB in patients with suspected or known CD. The use of CE in the

diagnosis of small bowel CD(Papadakis et al.,2005) has been examined in several studies and found to be superior to small bowel follow-through(Fireman et al .,2003;Herrerias et al., 2003;Mow et al.,2004), enteroclysis (chong et al.,2005;Liangpunsakul et al.,2003), push enteroscopy(chong et al.,2005) and CT enteroclysis (Voderholzer et al.,2005) for identifying small intestinal disease. the Diagnostic yield of CE was compared with other modalities in patients with suspected small bowel CD, yield of CE was 63% compared with 23% for barium radiography. When compared with ileo-colonoscopy, CE had a higher yield (61% vs 46%). Compared with PE, CE had a 38% higher yield, and when compared with CT enterography, the yield of CE was 69% vs 30%. Due to its high diagnostic yield, CE will have a very important place in the diagnostic workup of patients with CD, but more studies are needed to make such suggestions since there was no statistical significance in the incremental yield between CE and other diagnostic modalities in patients suspected of having CD in an meta analysis (Triester et al., 2006). However, there was a significant difference in yield of CE over alternative methods in patients with known CD, who were being evaluated for SB recurrence (Triester et al., 2006) Yield of CE is low when performed in patients with abdominal pain alone; when other criteria are added, this yield is increased (Lewis, 2008).Capsule endoscopy can be used for the assessment of mucosal healing after treatment.

The only limitation of CE is its inability to offer biopsy for histological examination. A scoring system has been proposed to evaluate CD on the basis of CE findings of villous structure, ulceration and stenosis. Each variable is assessed by size and extent of the change (Grelnek et al., 2008). However, further studies are needed to clarify the helpfulness of this system. The score provides a common language to quantify mucosal changes associated with any inflammatory process. The index does not diagnose or measure a disease, it measures mucosal change. In addition, this scoring index does not have the discriminatory ability to differentiate between illnesses. This index could be helpful in determining mucosal healing after therapy in CD (Lewis, 2008). Mucosal breaks and aphthous ulcers or erosions are also seen in asymptomatic healthy volunteers. Since non-steroidal anti-inflammatory drugs (NSAIDs) may cause ulcerations resembling those of CD, patients should be advised to stop such drugs at least one month before the CE examination (Mergener et al., 2007). It is difficult to differentiate these findings with the presence of CD.

3.3 Celiac disease

Celiac disease is an immune-mediated disease characterized by chronic SB inflammation that may result in mucosal atrophy, mal-absorption and related clinical manifestations. Diagnosis is based on the combination of serologic, endoscopic and typical histological changes of the SB biopsy in clinically suspected patients. Its prevalence is around 1% in the United States. There are four endoscopic changes suggestive of villous atrophy: loss of mucosal folds, mosaic mucosal pattern, scalloping of the duodenal folds and nodularity of the mucosa (Spada et al., 2008). It is no surprise that CE provides high resolution images that contain such changes. Fourty three patients with signs or symptoms suggestive of celiac disease and positive serological markers were evaluated (Rondonotti et al., 2007). Patients underwent both CE and upper GI endoscopy. Characteristic histological changes were observed in 32 patients. Using this as a gold standard, 87.5% of patients were diagnosed by CE. Mucosal changes beyond the duodenum were detected in 18 (66.6%) patients and in 3 (11.1%) patients the whole SB was affected. Another newly published study, (Muhammad & Pitchumoni,2008) searching for celiac disease in older adults, also showed that duodenal mucosa was normal in appearance on CE in 71% of patients, but classic abnormalities of celiac disease were present distally.

Overall, CE can detect endoscopic markers of celiac disease. In addition, CE seems to be able to recognize the extent of disease and may be a tool for follow-up. CE has a high sensitivity (range, 70%-95.2%), specificity (range, 63.6%-100%) and high PPV and NPV (96.5%-100% and 71.4%-88.9%, respectively)(Biagi et al.,2006;Hopper et al., 2007; Muhammad & Pitchumoni 2008; Petroniene et al., 2005; Rondonotti et al 2007a. 2007b). When an atrophic pattern is detected by CE, the patient has a high probability of having celiac disease (Spada et al., 2008). CE has also been reported to be able to demonstrate diseases such as adeno-carcinoma, lymphoma or ulcerative jejuno-ileitis, which may complicate the course of celiac disease. A limitation is that CE is able to detect Marsh III lesions, which are associated with clear mucosal abnormalities, but may not distinguish between Marsh I and II lesions (Spada et al., 2008). At present, CE is an alternative to endoscopy with biopsy in patients with suspected celiac disease who do not consent to the conventional methods.

3.4 Small bowel tumors and polyps

Capsule endoscopy is a major advance in the diagnosis of SB tumors. Before the introduction of CE, malignant neoplasms of the SB were often diagnosed at a later stage of the disease, mostly during the work-up of obstructive symptoms. Diagnosis is delayed because conventional imaging techniques fail to detect small neoplasm's in almost half of the patients. SB tumors are a rare disease, accounting for 1%-3% of all primary GI tumors. SB mass lesions are responsible for OGIB in up to 10% of patients. (Ciresi & Scholten, 1995; DiSario et al., 1994; Lewis, 1994; Lewis et al., 2005; Kariv & Arber 2003). Early clinical studies of CE have reported a frequency of SB tumors ranging between 6% and 9% (Bailey et al.,2006; Cobrin et al.,2006; de Franchis et al.,2004; Estevez et al.,2007; Schwartz &Barkin,2007; Urbain et al.,2006). This has led to an idea that CE doubled the rate of diagnosing SB tumors. However, a recent multicenter European study showed that the frequency of SB tumors was 2.4% and the most common indication for CE was OGIB (Pennazio et al., 2008; Rondonotti et al., 2008). SB tumors appear as masses or polyps in most patients and ulcer or stenoses in a minority of patients. It is not possible to distinguish the type of tumor based only on CE pictures. Most of the tumors reside in the mid SB (Rondonotti et al., 2008).Capsule endoscopy is also useful for the surveillance of polyps in patients with inherited GI polyposis syndromes (Familial adenomatous polyposis and Peutz- Jeghers syndrome), who are at increased risk of developing polyps in the SB. Several studies comparing the yield of CE to other imaging modalities in patients with polyposis syndromes have shown that CE is accurate in the detection of polyps. The same studies also emphasized that the duodenum is a potential blind point of CE because the capsule passes quickly with tumble and results in inadequate examination. CE underestimated the total number of polyps and did not reliably detect larger polyps in that portion (Wong et al., 2006). Nevertheless, more prospective studies with longer follow-up are required, to define the role of capsule endoscopy findings in the outcome of patients with gastrointestinal polyposis syndrome.

3.5 Other indications

Abdominal pain is one of the most common symptoms of patients referred to the gastroenterologist. Use of CE for the evaluation of abdominal pain is debated. Although some serious causes are identified in such patients, CE is mostly unyielding. If patients with other signs and symptoms of inflammation were selected, than the diagnostic yield was considerably higher (El-Matary, 2008). Capsule endoscopy may be helpful in the diagnosis of the following diseases: surveillance for NSAID side effects, Henoch Schönlein purpura,

indeterminate colitis, protein losing enteropathy, intestinal lymphangiectasia, Meckel's diverticulum, follow-up of SB transplantation, GVHD, and bowel changes in refractory pouchitis (El-Matary,2008).

4. Contra-indication and safety issue of capsule endoscopy

Capsule endoscopy is a safe and contraindications (Table-2) include the presence of intestinal obstruction, fistulas and strictures. Swallowing abnormalities, esophageal stricture, pseudo-obstruction, severe motility disorder are other contraindications for the procedure. Relative contraindications are pregnancy, numerous diverticuli, Zenker's diverticulum, gastroparesis, and previous pelvic/abdominal surgery.

Absolute
Bowel obstruction
Extensive and active Crohn's
Disease ± strictures
Intestinal pseudo-obstruction
Young children (<10 years)
Relative
Cardiac pacemakers
Implanted electro-medical Devices
Dysphagia
Previous abdominal surgery
Pregnancy
Diverticulosis

Table 2. Contra Indication

Other former contraindications such as implanted cardiac pacemakers or other electro-medical devices and patients with swallowing disorders have been excluded since some studies showed no interference between capsule endoscopy and pacemaker or implantable defibrillators functioning (Leighton et al.,2004,2005) and endoscopic placement of the capsule into the gut (Leung & Sung,2004). The retention of the device is the main complication of the procedure and is defined when CE remains in the digestive tract for a minimum of 2 wk (Cave et al.,2005).The frequency of this problem varies, depending mostly on the clinical indication for CE, and ranges from 0% in healthy subjects, to 1.5% in patients with obscure gastrointestinal bleeding, to 5% in patients with suspected Crohn's disease (Mata et al.,2008) and to 21% in patients with intestinal obstruction(Pennazio,2006).How to prevent capsule retention has yet to be defined since neither radiologic studies nor the "patency capsule" has shown conclusive results so far. The clinical setting of each patient, as well as some features related to intestinal strictures (previous small bowel surgery, NSAIDs, suspected small bowel Crohn's disease), have to be analyzed prior to the study. Patients should be informed about the possibility of capsule retention and further treatment.

5. Technical limitations

It cannot be used to obtain biopsy specimens or for endoscopic treatment and it cannot be controlled remotely (Pennazio,2006). CE has also some clinical limitations which are

problems in sizing and locating small bowel lesions(Rondonotti et al.,2008), a possible false-negative CE result, global miss rate is about 11%, ranging from 0.5% for ulcerative lesions to 18.9% for neoplastic disease and almost 20% of procedures the capsule does not reach the cecum while it is active (Waterman & Eliakim,2009).

6. Esophageal capsule – PillCam ESO

The esophageal capsule (PillCam™ ESO) which was approved by the FDA in November 2004, has a double head with the potential of 14 frames per second. The new-generation capsule endoscopy SB2 takes 18 frames per second. The battery life is only 20 minutes. The capsule has two cameras, each taking seven frames per second in the first 10 minutes, then four frames in the remaining 10 minutes. The patient does not need sedation, there is no recovery time, and no intubation or insufflations is used. The two FDA-approved indications for the esophageal capsule are screening and follow-up of esophageal varices and screening for Barrett's esophagus in gastro-esophageal reflux patients.

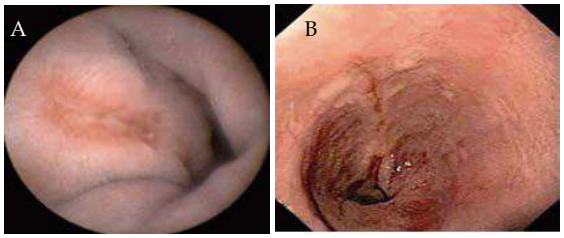

Fig. 3. **A:** PillCam™ ESO image of erosive esophagitis; **B**: endoscopy image of distal esophagus in the same patient.

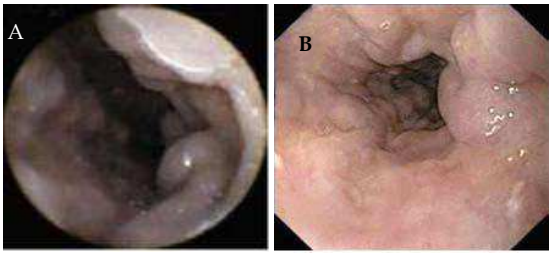

Fig. 4. **A:** PillCam ESO™ image showing esophageal varices; **B:** Upper endoscopy image of distal esophagus in the same patient.

According to the guidelines of the American Society of Gastrointestinal Endoscopy, established cirrhosis and cholestatic liver disease with a low platelets count are clear indications for esophago-gastro-duodenoscopy(EGD)(Qureshi et al.,2005).Large varices dictate treatment with propranolol or ligation. Capsule endoscopy may replace EGD for diagnosis of varices. Grading of varices according to the capsule endoscopy study is simpler than that of EGD. Three grades were evaluated: C0 = no varices, C1 =small and non-tortuous varices<25% of the circumference of the frame, and C2 =large varices>25% of the frame circumference. A recent multicenter international study with PillCam ESO prior to EGD was performed in 97 cirrhotic patients (Eisen,2006).EGD was performed within 48

hours by endoscopists blinded to the results of capsule endoscopy, while the PillCam ESO study was read by a blinded second investigator.Complete agreement was demonstrated in 84 of the 97 patients. The sensitivity and specificity of the capsule endoscopy for esophageal varices were 86.6% and 86.7%, respectively. A recent study (Galmiche et al.,2008) demonstrated 79% sensitivity and 94% specificity of capsule endoscopy for Barrett's esophagus in 77 patients. However, these results could not be demonstrated in another recent paper and there was a significant variation between observers.

7. Colonic capsule – PillCam colon

The colonic capsule was ready for research in 2006 and had been studied by Israeli, American and European groups of investigators (Eliakim et al.,2006; Fireman & Kopelman, 2007). The capsule had great potential for colorectal cancer screening since the procedure is not invasive. The first generation of the colonic capsule had two cameras on both heads, taking four frames per second. It is 5 mm longer than the small bowel capsule. The main limitation of this examination is the colonic preparation before the procedure as the colon must be perfectly clean without any remnants of stool. Sedation is not needed, and radiation, intubation and insufflation are not involved. The capsule procedure may become the first-line examination of the colon. It can be performed instead of colonoscopy when there is a contraindication to colonoscopy, is suitable for people unwilling to undergo colonoscopy or complete failed colonoscopy, and it can be used for screening colitis patients. It is believed that compliance for capsule endoscopy as a screening tool will be higher than for colonoscopy.

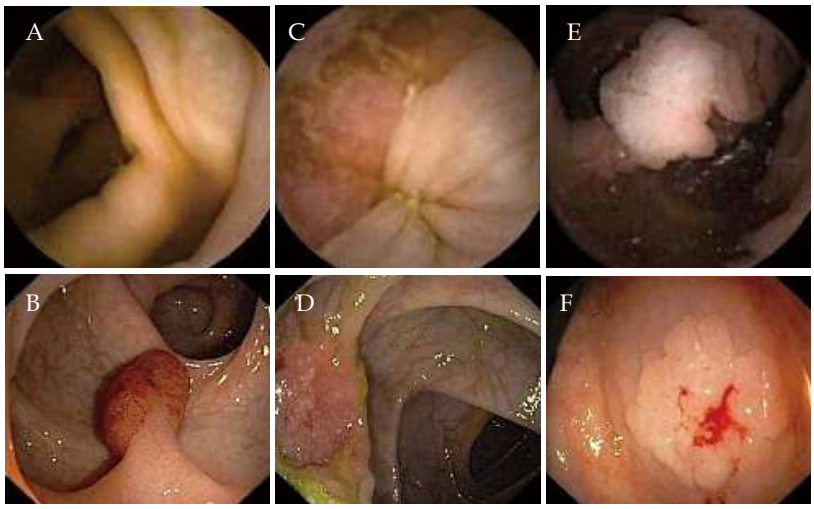

Fig. 5. Images captured by the Pillcam™ Colon and conventional colonoscopy. **A** and **B**: Pedunculated polyp in the sigmoid colon; **C** and **D**: Ulcerated tumor in the transverse colon; **E** and **F**: Flat adenoma in the ascending colon.

In a recently published European multicenter study of 328 patients (Von Gossum et al.,2009), the sensitivity and specificity of capsule endoscopy for detecting polyps ≤ 6 mm in size were 64% (95% confidence interval 59–72) and 84% (95% CI 81–87), respectively, and for detecting advanced adenoma sensitivity and specificity were 73% (95% CI 61–83) and 79%

(95% CI 77–81) respectively of 19 cancers detected by colonoscopy, 14 were detected by capsule endoscopy (sensitivity 74%, 95% CI 52–88). For all lesions, the sensitivity of capsule endoscopy was higher in patients with good or excellent colon cleanliness compared to those with fair or poor colon cleanliness.

8. Next generation capsule endoscopy

What, would be the ideal capsule of the gastroenterologist's Wildest imagination? Would we prefer a single capsule that, in one ''shot'', can give us the entire view from the oral cavity to the anal canal, or are we hoping that someday there will be an "intelligent" capsule that specializes in each section of the GI tract? Unfortunately, the anatomical and physiological differences in the GI tract make it impossible to use the same capsule for both purposes. Small bowel, esophageal and colonoscopy capsules are now commercially available. The latter two are equipped with miniature cameras on both ends of two video cameras. How we would love to be able to pinpoint drug deliveries in specific diseases such as Crohn's disease! The problem is that it would have to be done daily over a long period and this would be time consuming and costly. A pre-programmed non-viewing (i.e. no camera) capsule for drug delivery would be much cheaper and one can imagine a combination of viewing and non-viewing capsules that can be used to make this treatment efficient and cost effective. For clinicians, the capsule's motility feature in the small bowel would open a window to study the patho-physiology of relatively elusive medical entities such as irritable bowel syndrome. Malagelada et al., 2008 were the first to publish their findings on CE motility in the clinical setting and they found that CE was useful in diagnosing patients with irritable bowel syndrome. Next in our dream of CE are zooming or magnification capabilities. Why not? Think of chromo-endoscopy, narrow band imaging, ultrasound imaging and the delivering of therapy including tissue coagulation and immunologically or chemically targeted optical recognition of malignancy as it exists in endoscopy, capable of spraying fluid (methylene blue, Lugol solution, etc.) in specific areas of the small bowel. At present, the capsule cannot obtain biopsies, aspirate fluid or brush lesions for cytology. These techniques require real-time viewing as well as radio-controlled triggering and remote controlled capsule manipulation if they are to be used with precision. However, optical biopsy seems feasible (DaCosta et al.,2005).We can easily visualize our capsule eventually becoming a complete miniature laboratory with the functions of bio-sensing luminal contents and biopsy (probably by optical technologies) as well.

The quality of current CE images is inferior to that of conventional endoscopes and the solution awaits advances in microelectronics that will lead to image sensors with a smaller pixel size that enable higher resolution. In addition, current CE systems use image data compression which causes blurring at the edges of objects and leads to lower image quality, a major limitation of CE. In particular, depletion of the two silver oxide batteries used in current devices may prevent complete imaging of the small intestine if the pill remains in the stomach for too long. The problem becomes most apparent by the inability to view the cecum (the marker of a complete examination) in 10%-15% of CE examinations of the small bowel(Neu et al.,2005;Triester et al.,2006).This will eventually be overcome by using power transfer methods from outside the body. In the short term, this problem can partly be solved by using more efficient power management algorithms that enable an 11 h recording time. There have been important "breakthroughs" in battery design with the advent of carbon nanotubes (Buckytubes) which have the intrinsic characteristics desired in the material used as electrodes

in batteries and capacitors. Other methods that are under consideration for development for solving imaging issues include control units that vary the frame rate. One example is the OMOM capsule, developed at Chongqing Jinshan Science and Technology Group (Chongqing, China), which can switch from 0.5 frames per second (fps) inside the stomach to 2 fps after entering the pylorus (DaCosta et al.,2005).In a well-conducted randomized prospective study of 50 patients in China, the cecum was visualized in the 25 subjects who ingested the capsule in the switching frame rate mode compared with 18 of 25 in whom the pill functioned at a steady frame rate of 2 fps (Moglia et al.,2008). The benefit from size reduction and power efficiency is best exemplified by MiroCam by Intromedic (Seoul, South Korea). This is the first endoscopic capsule that uses the human body instead of radiofrequency to transmit data, reducing power consumption. In the first clinical trial on 45 patients in South Korea, MiroCam captured images from the whole small intestine as far as the cecum in all the subjects. Because the device does not use image compression, the bowel mucosa was viewed without blurring or distortion in over 90% of patients(de Franchis et al.,2005)This system also uses fewer components for remote transmission, thus saving space for the possible addition of modules for biopsy or locomotive guidance (Liao et al.,2009).

We eagerly look forward to the day that we will be able to ''control and steer'' the CE as endoscopists are able to do in standard endoscopy. Two research projects supported by the European Union are currently pursuing this goal. One is VECTOR (Versatile Endoscopic Capsule for gastrointestinal Tumor Recognition and therapy) and the other is NEMO (Nano-based capsule-Endoscopy with Molecular Imaging and Optical biopsy). The former aims to develop a self-propelled miniaturized robotic pill for advanced diagnostics and treatment in the digestive tract. Over the last few months, the topic of the feasibility and effectiveness of the combined use of external static magnetic fields to achieve wirelessly controllable and precise camera steering has been published(Gao et al.,2010;Swain et al.,2010;Valdastri et al.,2010)The second study is looking into the detection of surface and deep seated pathology by photonic technologies that enable optical biopsies. This would eliminate the need to take biopsy specimens and perform histological examination (Swain, 2008).

9. Conclusion

Capsule endoscopy is the latest evolution in gastrointestinal endoscopy and the first to enable complete investigation of the small bowel. It is a simple and well-tolerated procedure. Capsule retention is the major complication. Care must be taken in patients with symptoms suggesting partial obstruction and CD. SB series and computerized tomography enteroclysis before CE may reveal stenosis. The newly developed patency capsule may be an alternative for detection of stenoses. The value of CE in patients with OGIB appears to be high and is supported by high yields in the literature. CD and celiac disease appear to be areas where use of CE would be helpful. There may also be an indication for CE in CD surveillance and follow-up. The diagnostic role of CE extends beyond the SB. Recent new developments in the field of capsule endoscopy include the esophageal capsule (PillCam ESO™) and the colonic capsule (PillCam Colon™). More research is needed to explore the feasibility of CE in these contexts. Blind spots of CE such as the duodenum should be examined by a second look endoscopy before the CE procedure, especially in patients with OGIB. After negative endoscopic examinations, CE should be recommended as a first-line investigation over balloon assisted enteroscopies in view of its noninvasiveness, higher probability of visualizing the entire small intestine and the similar diagnostic yield of both

investigations. Such an approach may decrease the time between diagnosis and intervention. A second look CE may reveal more findings in up to 35% of patients who had prior non diagnostic CE.

The ideal next generation CE of the gastroenterologist's imagination should be capable of performing an ordinary biopsy as well as carry out an online analysis (an "optical" biopsy) and ''stop'' bleeding by an adrenaline injection, a heat probe, argon plasma coagulation, etc. The ultimate capsule would include special detectors for white blood cells and be capable of checking oncological markers (e.g. CEA, CA 19-9), perform serology tests (e.g. anti-endomysial, IgE) and measure various cytokines, pH, temperature and pressure, in addition to delivering drugs. The capsule's motility feature in the small bowel may open a window to study the patho-physiology of relatively elusive medical entities such as irritable bowel syndrome (Fireman & Kopelman, 2007; Fireman et al, 2004; Nakamura & Terano, 2008; Kochman & Swain, 2007; Swain, 2008). Finally, the optimal capsule needs to contain a computerized system for automatic detection of pathologies such as the design of a holter electrocardiographic recording in order to overcome the drawback of time-consuming viewing the video. Future gastroenterologists will have a number of types of capsules from which to choose according to whether the purpose of the evaluation is diagnostic and/or therapeutic.

10. References

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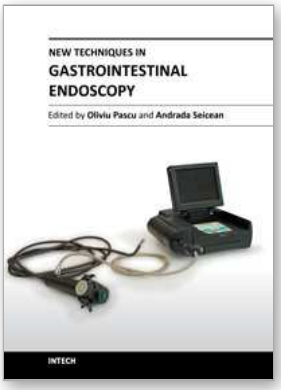

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As result of progress, endoscopy has became more complex, using more sophisticated devices and has claimed a special form. In this moment, the gastroenterologist performing endoscopy has to be an expert in macroscopic view of the lesions in the gut, with good skills for using standard endoscopes, with good experience in ultrasound (for performing endoscopic ultrasound), with pathology experience for confocal examination. It is compulsory to get experience and to have patience and attention for the follow-up of thousands of images transmitted during capsule endoscopy or to have knowledge in physics necessary for autofluorescence imaging endoscopy. Therefore, the idea of an endoscopist has changed. Examinations mentioned need a special formation, a superior level of instruction, accessible to those who have already gained enough experience in basic diagnostic endoscopy. This is the reason for what these new issues of endoscopy are presented in this book of New techniques in Gastrointestinal Endoscopy.

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