Introduction

The year 2011 marked the 10th anniversary of approval of the first wireless (WCE), the M2A® (Given Imaging, Yoqneam, Israel), by the FDA. WCE technology has evolved over the past decade. The main indications for WCE were obscure gastrointestinal bleeding, Crohn’s disease, and unexplained symptoms. This review provided an update on a comprehensive evaluation of WCE and emphasizes advances in WCE in clinical practice.

Wireless capsule endoscopy systems

There are 5 WCE systems: the PillCam SB2 (Given Imaging, Yoqneam, Israel), the Endo Capsule (Olympus America, Center Valley, PA), the MiroCam (IntroMedic, Seoul, Korea), the OMOM capsule (Jinshan Science and Technology, Chongqing, China), and the CapsoCam VS1 (CapsoVision, Saratoga, CA, USA) (Table 1). However, only the PillCam SB2 and the Endo Capsule are currently approved by the US Food and Drug Administration. Preliminary studies in patients with obscure gastrointestinal bleeding (OGIB) have reported...

<table>
<thead>
<tr>
<th>Device</th>
<th>Company</th>
<th>Field of view (º)</th>
<th>Frames per second</th>
<th>Battery life (h)</th>
<th>Image sensor</th>
<th>Transmission mode</th>
<th>FDA approval status</th>
<th>Dimensions (mm)</th>
<th>Optical enhancement</th>
</tr>
</thead>
<tbody>
<tr>
<td>PillCam SB2®</td>
<td>Given Imaging, Yoqneam, Israel</td>
<td>156</td>
<td>2</td>
<td>9</td>
<td>CMOS</td>
<td>Radiofrequency</td>
<td>Yes</td>
<td>11 × 26</td>
<td>Blue-mode FICE settings</td>
</tr>
<tr>
<td>EndoCapsule®</td>
<td>Olympus, Tokyo, Japan</td>
<td>145</td>
<td>2</td>
<td>8-10</td>
<td>CCD</td>
<td>Radiofrequency</td>
<td>Yes</td>
<td>11 × 26</td>
<td>Contrast imaging</td>
</tr>
<tr>
<td>MiroCam®</td>
<td>IntroMedic, Seoul, Korea</td>
<td>150</td>
<td>3</td>
<td>&gt;11</td>
<td>CMOS</td>
<td>EFP</td>
<td>Pending</td>
<td>11 × 24</td>
<td>NA</td>
</tr>
<tr>
<td>OMOM®</td>
<td>Jinshan Science, Chongding, China</td>
<td>140 ± 10</td>
<td>2 variable</td>
<td>8</td>
<td>CCD</td>
<td>Radiofrequency</td>
<td>No</td>
<td>13 × 27.9</td>
<td>NA</td>
</tr>
<tr>
<td>CapsoCam®</td>
<td>CapsoVision, Saratoga, USA</td>
<td>360</td>
<td>16</td>
<td>15</td>
<td>Unkown</td>
<td>USB</td>
<td>No</td>
<td>11 × 31</td>
<td>NA</td>
</tr>
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CCD, charge-coupled device; CMOS, complementary metal oxide silicon imaging; EFP, electric field propagation; FICE, Fujinon Intelligent Colour Enhancement; NA, not applicable; USB, Universal Serial Bus.
Table 2. Clinical utilities and capabilities of WCE in gastrointestinal disease

<table>
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<th>Gastrointestinal bleeding</th>
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<tr>
<td>• Detection of hemorrhagic lesions: WCE diagnostic yield higher than plush enteroscopy, SBFT, angiography; WCE diagnostic yield comparable to CTE, DBE</td>
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<tr>
<td>• Selection of DBE insertion route</td>
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<tr>
<td>• Preoperative localization of bleeding site</td>
</tr>
<tr>
<td>• Real-time diagnosis in emergency room evaluation</td>
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<tr>
<td>Crohn’s disease</td>
</tr>
<tr>
<td>• Detection of lesions suggestive of small bowel Crohn’s disease</td>
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<tr>
<td>• Clarification of distribution and severity of Crohn’s disease</td>
</tr>
<tr>
<td>• Differentiation of IBD type in patients with indeterminate colitis</td>
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<td>• Complimentary use with specific inflammatory markers</td>
</tr>
<tr>
<td>• Facilitation of major scoring system for disease severity: CECDAI; Levi’s system</td>
</tr>
</tbody>
</table>

CECDAI, capsule endoscopy Crohn’s disease activity index; CTE, CT enterography; DBE, double balloon enteroscopy; SBFT, small bowel follow through; WCE, wireless capsule endoscopy.

established indications

1. Obscure gastrointestinal bleeding

WCE is indicated for initial testing for overt or occult OGIB of presumed small intestinal origin (Table 2). OGIB has been defined as bleeding from the gastrointestinal tract persists or recurs after a negative initial evaluation using bidirectional endoscopy and radiologic imaging with barium contrast medium such as with SB follow through (SBFT) or enteroclysis. With the technological advances inherent to WCE and balloon-assisted enteroscopy (BAE), most limitations of older diagnostic test have been overcome, leading to a major paradigm shift in evaluation and management.

A meta-analysis of studies that compared WCE and push enteroscopy (PE) for OGIB showed that WCE had an incremental yield of 30% (56% vs 26%) for clinically significant findings. Similarly, WCE had an incremental yield of 36% over SBFT (yield, 42% vs 6%). On the basis of these results, WCE is currently recommended as the third test of choice for OGIB after a negative upper endoscopy and a negative colonoscopy.

A meta-analysis of 11 studies comparing WCE to DBE for SB disease showed a comparable diagnostic yield (60% vs 57%) for all findings. The yields were also similar to those for vascular, inflammatory, and neoplastic lesions. Another meta-analysis of 8 studies also found no difference in diagnostic yield (odds ratio, 1.21; 95% confidence interval, 0.64-2.29). However, in patients with OGIB, WCE had a higher yield than DBE using a
single approach (odds ratio, 1.61; 95% confidence interval, 1.07-2.43) but a significantly lower yield than DBE using a combined antegrade-retrograde approach (odds ratio, 0.12; 95% confidence interval, 0.03-0.52; \( P<0.05 \)).

The main utility of WCE for evaluation of OGIB lies in its high positive predictive value (94-97%) and its high negative predictive value (83-100%). Specifically, it can be used to identify the bleeding lesion and help direct further therapeutic intervention or surgery. WCE findings that lead to endoscopic or surgical intervention or a change in medical management have been reported in 37-87% of patients. In addition, 50-66% of patients have been reported as remaining transfusion free without recurrent bleeding at follow-up. Moreover, the rebleeding rate is quite low (33%) after a negative WCE.

WCE also guides further diagnostic testing and therapeutic planning. WCE can help select DBE insertion routes with excellent accuracy and is useful for localizing bleeding sites prior to intraoperative endoscopy or surgical resection. Whether VCE improves outcome is less certain. In a study in which patients with gastrointestinal bleeding were randomly allocated to initial VCE or small bowel barium radiography, no differences were observed in subsequent diagnostic interventions, therapies or hospitalizations over a period of 12 months.

2. Crohn’s disease

WCE is useful for diagnosing Crohn’s enteritis and defining anatomical distribution and severity in those with established disease (Table 2). In a meta-analysis of individuals with suspected CD, WCE showed superior diagnostic yields compared with barium radiography (52% vs 16%), CT enterography (CTE) (68% vs 21%) and ileocolonoscopy (47% vs 25%). In the same analysis, WCE yields in those with established Crohn’s disease were higher than for contrast radiography (71% vs 36%) and push enteroscopy (66% vs 9%). More importantly, the capsule was negative in 48% of symptomatic patients, potentially helping avoid unnecessary therapy. Ultimately, larger prospective studies are needed to determine the role of WCE in evaluating suspected and established CD and influencing clinical outcomes.

The high negative predictive value of WCE is an important advantage when evaluating patients with suspected CD. A pooled analysis of the results of 24 WCE trials comprising 530 patients found that WCE had a low miss rate of 0.5% for SB ulcerations, compared with 78.7% for other modalities (SBFT, PE, or ileocolonoscopy). Thus, the diagnosis of WCE can possibly be excluded in most patients with a negative capsule study. Other potential uses include noninvasive assessment of mucosal healing and endoscopic response to therapy, diagnosis of postoperative recurrence, and evaluation of indeterminate colitis.

The potential for capsule retention because of structuring CD mandates caution when performing WCE in patients with this condition. Retention rates vary from 5-13% in patients with established CD to 1-2% in those with suspected disease. Use of the patency capsule in patients with suspected obstruction has led to a clinically significant reduction in the incidence of capsule retention.

3. Small bowel tumors and polyps

WCE has been compared with other diagnostic modalities for diagnosis of SB tumors, specifically SBFT and PE, and was found to be superior to SBFT. WCE proved particularly helpful in identifying lesions beyond the
reach of PE; thus, the two procedures are complementary. A meta-analysis also found WCE to be superior to both SBFT and PE. With this growing body of literature supporting the increased yield of WCE in identifying SB tumors, it will become the diagnostic procedure of choice in these patients.

Several series have also examined the use of WCE in evaluating patients with polyposis syndromes. Compared with other tests, WCE identifies more polyps, but these are usually small and difficult to evaluate quantitatively. Thus, the role of WCE in the management of polyposis syndromes is not clear at this time. Patients with Peutz-Jeghers syndrome may benefit from WCE vs SBFT, particularly for surveillance and when there is OGIB.

New techniques and innovations

The advent of WCE for gastrointestinal imaging has created a major paradigm shift in gastrointestinal endoscopy. Areas of innovation include new type of capsule, improved optics, better propulsion, the ability to perform biopsies and therapeutics, targeted drug delivery, and the evaluation of SB motility.

The Sayaka device (RF Systems, Nagano, Japan)—not available in any country at this time—includes an inner capsule that spins and a lens on its lateral surface that obtains high-resolution sidewall images at 30fps to provide 360° inspection of the luminal wall. Furthermore, a dual camera capsule was developed to test if two cameras are complementary in assessing small bowel lesions. In 41 patients, 42% of 68 findings were not detected by one camera, whereas 44% were not detected by the other. Overall, more lesions were detected by dual rather than by single camera, but diagnostic yield was not clearly affected by the number of the cameras.

For the enhanced mucosal imaging, computed virtual chromoendoscopy (FICE) simulated NBI in three different wavelengths without optical filters and might be able to discriminate and demarcate lesions found on white light such as tumors, polyps, and angioectasias. In addition, other imaging techniques using fluorescence and computer assisted texture recognition with 3D imaging may further improve disease recognition.

The potential benefits are enhanced detection of pathologic images and better tissue characterization. Image analysis methods have been proposed to facilitate the identification of normal, healthy gut anatomical structures (automated capsule localization). One technique used color image analysis to discriminate between the esophagus, stomach, small intestine and colon.

For enhanced maneuvering, magnetic forces are being studied that will control the movement and location of the capsule within the gastrointestinal tract. This might improve procedure time, real-time image viewing, and back-and-forth navigation. The feasibility of an 8-legged locomotion capsule has also been discussed. It uses a novel propelling mechanism featuring electromechanical legs.

One attribute lacking in even the latest CE technology is the ability to perform biopsies. However, research is being conducted on a spring-loaded device similar to the Crosby capsule that is guided by real-time imaging capability and remote manipulation to obtain mucosal biopsies. Other biopsy devices include a capsule with single-crystal silicon planar microspikes and protruding barbs for microscale biopsy that uses micro-electro-mechanical systems technology.

Targeted drug delivery is also on the horizon. The iPill (Intelligent Pill; Philips Research, Royal Philips Electronics, Eindhoven, the Netherlands) is a plastic capsule with a medication reservoir that has a tiny pump to deposit medicine all at once or in bursts at a specific location. The capsule, which has been tested in animals,
has sensors that detect acidity and temperature and can react to pH changes. Finally, capsule technology may allow for endoluminal analysis to evaluate patients with motility disorders. This would permit detection of contractile events, noncontractile patterns, types of contents, and detection and movement of parietal and endoluminal structures. SB motor function can be evaluated quantitatively, with computer algorithms providing analysis of various endoluminal features.

Conclusions

WCE has become an essential component in the management of several conditions. Established indications for WCE include unexplained gastrointestinal bleeding, small bowel Crohn’s disease, localization of small bowel tumors and a broad range of miscellaneous abnormalities. New investigations have focused on optical improvements, advances in intestinal cleansing and risk reduction strategies to optimize WCE methodologies in clinical practice and to expand the potential utility of WCE, novel devices that can manoeuvre within or insufflate the gut lumen, tag or biopsy suspect lesions, or target drug delivery to specific sites are in development.

References