Communication from the ASGE Technology Committee

TECHNOLOGY STATUS EVALUATION REPORT

Wireless capsule endoscopy

To promote the appropriate use of new or emerging endoscopic technologies and those technologies that have an impact on endoscopic practice, the American Society for Gastrointestinal Endoscopy (ASGE)Technology Committee presents relevant information to practicing physicians in the form of technology reviews. Evidence-based methodology is used wherein a MEDLINE literature search is performed to identify pertinent clinical studies on the topic, a MAUDE (Manufacturer and User Facility Device Experience; Food and Drug Administration Center for Devices and Radiological Health) database search is performed to identify the reported adverse events of a given technology, and both are supplemented by accessing the "related articles" feature of PubMed and by scrutiny of pertinent references cited in the identified studies. Controlled clinical trials are emphasized, but in many cases data from randomized, controlled trials are lacking; in such cases, large case series, preliminary clinical studies, and expert opinion are used. Technical data are gathered from traditional and Web-based publications, proprietary publications, and informal communications with pertinent vendors. Reviews are drafted by one or two committee members, reviewed in significant detail by the committee as a whole, and approved by the Governing Board of the ASGE. When financial guidance is appropriate, the most recent coding data and list prices at the time of publication are provided. For this review, the MEDLINE database was searched through August 2012 for articles related to capsule endoscopy by using the keywords capsule endoscopy and wireless endoscopy plus esophageal disease, esophageal varices, small intestinal tumors, Barrett's esophagus, reflux, gastrointestinal bleeding, Crohn's disease, and celiac disease. Practitioners should continue to monitor the medical literature for subsequent data about the efficacy, safety, and socioeconomic aspects of these technologies.

BACKGROUND

Video capsule endoscopy provides visualization of the GI tract by transmitting images wirelessly from a disposable capsule to a data recorder worn by the patient. The first capsule model for the small intestine was approved by the Food and Drug Administration (FDA) in 2001. Over subsequent years, this technology has been refined to provide superior resolution, increased battery life, and capabilities to view different parts of the GI tract. This document will provide a review of the wireless capsule endoscopy (WCE) technology and its current role in the field of gastroenterology.

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TECHNOLOGY UNDER REVIEW

At the time of this writing, there are 3 companies that manufacture small-bowel WCE systems approved by the FDA (PillCam SB2, Given Imaging, Ltd, Yoqneam, Israel; Endocapsule, Olympus America, Inc, Center Valley, Pennsylvania; and MiroCam, IntroMedic Company Ltd, Seoul, Korea (Table 1). These are available for purchase in the United States. Capsules for esophageal imaging and colon imaging also are available from Given Imaging.

The wireless capsule system

The WCE system consists of 3 components: (1) a capsule endoscope; (2) a sensing system with sensing pads or a sensing belt to attach to the patient, a data recorder, and a battery pack; and (3) a personal computer workstation with proprietary software (RAPID v 6.5, Given Imaging; WS-1 EndoCapsule, Olympus America; MiroView, IntroMedic) for image review and interpretation. All 3 systems include handheld viewers that allow real-time review of images during WCE examinations (RAPID Real-Time, Given Imaging; Real Time Viewer, Olympus America; MiroView Express, IntroMedic).

All capsule endoscopes have similar components: a disposable plastic capsule, a complementary metal oxide semiconductor or high-resolution charge-coupled device image capture system, a compact lens, white-light emitting diode illumination sources, and an internal battery source. The mode of data transmission is either via ultra-high frequency band radio telemetry (PillCam, EndoCapsule) or human body communications (MiroCam). The latter technology uses the capsule itself to generate an electrical field that uses human tissue as the conductor for data transmission. Currently PillCam SB2 and MiroCam are available with extended battery life, which may be beneficial in patients with delayed small-bowel transit. Capsule endoscope specifications of each individual WCE system are outlined in Table 1.

Proprietary software is used to process and display the images in single or multiple views at rates of 5 to 40 frames per second. Representative images and video clips can be

TABLE 1. FDA-approved wireless capsule systems and specifications

WCE company	Size, mm	Weight, g	Field of view	Images/sec	Battery life	Resolution, pixels
EndoCapsule; Olympus America, Inc, Center Valley, Pennsylvania	11 × 26	3.5	145°	2	8 hours	512 × 512
PillCam SB2; Given Imaging, Ltd, Yoqneam, Israel	11 × 26	2.8	156°	2	8 hours	256 × 256
PillCam SB2EX; Given Imaging	11 × 26	2.8	156°	2	12 hours	256 × 256
MiroCam; Intromedic Co Ltd, Seoul, Korea	11 × 24	3.3	170°	3	11 hours	320 × 320
PillCam ESO2; Given Imaging	11 × 26	<4	169°	18	8 hours	256 × 256

FDA, Food and Drug Administration; *WCE*, wireless capsule endoscopy.

annotated and saved. All available software has the ability to identify red pixels to facilitate detection of bleeding lesions in the small bowel. Additional features include localization data and progress of capsule transit within the GI tract, quick reference image atlases, and report generation capabilities.

Imaging the small intestine

WCE usually is performed in an ambulatory outpatient setting. Fasting or consumption of clear liquids only for 10 to 12 hours is standard practice; some centers use a clear liquid diet for 24 hours before the study. Data are conflicting, but several studies suggest that use of a full or partial bowel preparation the night before the study yields improved visualization of the small intestine.[1-4] At the time of the procedure, the sensing system (eg, pads or a belt) is applied to the abdominal wall and connected to the data recorder that is worn by the patient.

The capsule is activated by removal from a magnetic holder. After ingestion of the capsule, patients are instructed to keep a diary of symptoms and monitor the lights on the data recorder to confirm that the signal is being received. Patients are encouraged to avoid exercise or activities that may cause the sensors to detach. A diet of clear liquids is allowed after 2 hours and a light meal after 4 hours. The reusable data-recording system can be disconnected from the patient after the lifespan of the battery has expired. The capsule is disposable and designed to be excreted.

The data recorder is subsequently connected to a workstation for transfer of the acquired images.

Imaging the esophagus

The PillCam ESO2 capsule is the only WCE system currently available for esophageal applications. Specifications on this system also can be reviewed in Table 1. The capsule dimensions, transmission wavelength, field of view, and the minimum size of the object that can be detected are similar to the PillCam SB2. However, the capsule battery life is only 20 minutes (vs 8-12 hours for small-bowel capsules), cameras are located on both ends of the capsule, and the capsule takes 18 frames per second (vs 2-3 frames per second for small-bowel capsules).

At the time of the examination, the patient should be fasting for 2 hours. The patient is fitted with 3 thoracic sensors, in a designated pattern, that are connected to the data recorder. With the traditional protocol, the patient drinks 100 mL of water while standing and then ingests the activated capsule in the supine position with a 10-mL sip of water that can be administered with the help of a syringe or straw. A 5-minute ingestion protocol is recommended, comprising a 2-minute recording with the patient supine, then 2 minutes raised to 30°, and then an additional minute at 60°, followed by an upright position for 15 minutes to maximize time for the capsule to capture images as it traverses the esophagus.[5] As with the PillCam SB2, images are transmitted to the data recorder and subsequently transmitted to the workstation for review and/or interpretation via the proprietary software.

Imaging the colon

A capsule endoscope for the colon, as well as a second-generation version, has been manufactured (PillCam Colon2, Given Imaging).The role of the colon capsule endoscope has not yet been established in the United States and it is not commercially available here, although it has been approved for use in Europe. Briefly, a meta-analysis of 8 studies (n = 837) of the first generation colon capsule (PillCam Colon, Given Imaging) found a per-patient sensitivity for polyps of any size and "significant findings" of 71% and 68%, respectively, compared with conventional colonoscopy.[6] Additionally, two randomized trials of the second-generation colon capsule have shown per-patient sensitivity for polyps ≥ 6 mm and ≥ 10 mm of 84% to 88% and 88% to 89%, respectively, compared with conventional colonoscopy.[7,8] Further details on this technology and its potential applications can be reviewed in the ASGE Report on Emerging Technology document on capsule endoscopy of the colon.[9]

Other accessories

Agile patency system. Capsule retention proximal to an intestinal stenosis is a well-recognized adverse event of WCE and may necessitate removal either endoscopically or surgically. A radiopaque non-video capsule with accompanying scanner (Agile Patency System, Given Imaging; FDA-approved 2006) has been developed to help identify individuals who are at high risk for capsule retention. The Agile patency capsule has the same dimensions as the PillCam SB2, with a dissolvable body composed of lactose and 5% barium sulfate. Within the core of the capsule is a radiofrequency identification tag that is activated and detected by a handheld, battery-operated scanner.[10] The detection of a signal by the handheld scanner means that the radiofrequency identification tag is still retained within the GI tract. At 30 hours, time-controlled plugs at the end of a retained Agile capsule erode, which allows intestinal fluids to dissolve the capsule body. The non-degraded parts are small enough that they can ultimately pass through tight strictures.[10]

Several studies, including one with pediatric participants, have evaluated the use of the Agile patency capsule. All studies included patients with risks for retention (Crohn's disease, postoperative and malignant strictures, tuberculosis infection). All patients who attempted WCE after excreting an intact patency capsule without pain had uneventful examinations.[10-15] In one study, 13 patients had radiographically observed small-bowel stenoses yet were able to undergo successful examinations after passage of the Agile capsule.[12] One patient with impaction of an intact patency capsule developed symptoms of a mechanical ileus and required surgery after 33 hours of conservative management.[12] There were no cases in which the Agile capsule passed through intact but the capsule endoscope was retained. There have been two reports on the MAUDE database that have suggested intact or incompletely degraded Agile capsules retained within the GI tract beyond 30 hours after ingestion.[16]

Delivery devices. A variety of accessories have been used to deliver the capsule to the stomach or small intestine for those patients with dysphagia, gastroparesis, or known or suspected anatomical abnormalities. Historically, overtubes have been used to deliver the capsule into the stomach,[17] and standard polypectomy snares[18] and nets[19] have been used to deliver the capsule into the duodenum.

The AdvanCE (US Endoscopy, Mentor, Ohio) allows endoscopic delivery of the video capsule. The system is a disposable catheter with a sheath diameter of 2.5 mm that is preloaded through the accessory channel of an endoscope. A specialized capsule cup is screwed onto its distal end, and the activated video capsule is loaded into the cup. The upper endoscope and the device are then advanced to the desired anatomical area, and the capsule is released via a deployment apparatus at the proximal catheter. This device has been tested and is approved for use only with the Given Imaging PillCam. EndoCapsule and MiroCam may be used with AdvanCE, but this use is currently off-label because of lack of specific testing with these models.

Additionally, a capsule paired with a magnetic wand (Navi Capsule, IntroMedic, Seoul, Korea) has been created to assist with mobilizing the device through the esophagus, stomach, and into the duodenum to facilitate delivery in patients with delayed gastric emptying. This product is available outside of the United States but is not FDA approved at the time of this writing.

INDICATIONS AND CONTRAINDICATIONS

WCE has been approved for a number of indications in patients as young as 2 years. The most common applications include evaluation for (1) obscure GI bleeding (OGIB), both overt and occult, including iron deficiency anemia[20]; (2) suspected Crohn's Disease[21-23]; (3) surveillance in patients with polyposis syndromes[21-22]; (4) suspected small-intestine tumors[24-28]; and (5) suspected or refractory malabsorptive syndromes (eg, celiac disease).[29-32]

The relative contraindications include patients (1) with known or suspected GI obstruction, strictures, or fistulas based on the clinical picture or preprocedure testing, (2) with cardiac pacemakers or other implanted electromedical devices, (3) with swallowing disorders, and (4) who are pregnant.

The PillCam ESO2 is FDA approved for visualization of the esophagus. The most common applications include evaluation for suspected Barrett's esophagus, esophagitis, or esophageal varices, but its exact role in clinical practice has yet to be established.[33,34]

EASE OF USE

Capsule endoscopy is a relatively simple test for the patient, provided the patient can swallow the capsule. Once the capsule is ingested, the patient can continue normal daily activities as the pill traverses the alimentary tract. Oral intake can occur within hours of swallowing the pill. A protocol should be in place to identify cases of capsule retention. Commonly, patients are told to watch for passage of the capsule in their bowel movements, or patients are requested to have an abdominal radiograph if entry into the colon is not observed during review of the examination. It is expected that the entire small bowel can be visualized within the lifespan of the standard 8-hour battery. However, factors such as debris seen in the distal small bowel and slow gastric emptying or small-bowel transit can preclude a full examination in 17% to 25% of cases,[35] leading to the additional need for bowel preparation or prokinetics in some patients. WCE systems with longer battery life may resolve this issue.

For capsule interpretation, it is recommended that the examiner have undergone formal GI training and be competent in endoscopy. Familiarity with the capsule hardware and/or software is necessary. Finally, ASGE guidelines state that readers should have either undergone formal capsule training during fellowship or have completed a formal GI or surgical society–endorsed training course with proctoring of the first 10 capsule readings.[36] The ASGE and WCE manufacturers frequently sponsor hands-on learning courses to assist with capsule training on their respective systems. The average reading time varies between 30 and 120 minutes, primarily dependant on small-bowel transit time and the experience of the reader. For capsule examinations of the esophagus, the average reading time varies between 5 and 15 minutes.

EFFICACY AND COMPARATIVE STUDIES

Obscure GI bleeding

The detection rate of WCE for potential culprit lesions in OGIB ranges from 35% to 77%, with performance dependent on various factors.[37-43] Variables that have been associated with a higher detection rate includes earlier WCE (within 1 week of bleeding),[38,44] inpatient status,[39,45] overt GI bleeding with tranfusion requirement,[37,39,44] male sex,[39,45] increasing age,[42,45] use of warfarin,[42] and liver comorbidity.[42] Three prospective, randomized studies comparing different WCE systems have shown comparable diagnostic yield and moderate interobserver agreement between PillCam SB/Endocapsule (k = 0.48) and PillCam/MiroCam (k = 0.66).[46-48]

WCE appears to impact patient management and outcomes for OGIB. In a retrospective study of 75 patients, WCE diagnosed relevant lesions in 66.7%.[49] Of these patients, 50.7% received confirmatory testing and subsequent specific therapy (surgery, medical therapy, nonsteroidal anti-inflammatory drug withdrawal). Thirty-one of these patients had follow-up to 6 months, with stabilization or resolution of bleeding in all but one of them. Another retrospective study demonstrated that WCE changes management in 36.6% and 41.8% of patients with obscure-occult and obscure-overt bleeding, respectively.[50] Findings of WCE also may predict outcomes. In a prospective study of 78 patients with OGIB with at least 6 months' follow-up, 26.1% of patients with lesions detected had rebleeding compared with 4% of patients who had negative examinations.[51]

For OGIB, WCE achieves superior results compared with radiographic barium studies.[52-55] In a meta-analysis of 3 studies (n = 88), the yield for capsule endoscopy and small-bowel barium radiography for clinically significant findings was 42% and 6%, respectively ($P <$ .00001).[55] More advanced radiographic technologies may have improved performance. In a single-blinded study, 25 patients admitted for overt and occult OGIB underwent both CT angiography and standard mesenteric angiography followed by WCE. The diagnostic yield was superior in WCE (72%) compared with CT angiography (24%; $P =$ .005) but similar to that of standard angiography (56%; $P =$ NS). As a result of WCE findings, a therapeutic intervention was undertaken in 47% of patients.[56] In a recent single-center, prospective study of 189 patients with iron deficiency anemia, WCE was superior to CT enteroclysis, with diagnosis rates of 77.8 versus 22.2% ($P <$ .001), particularly in the detection of flat lesions.[57]

Historically, intraoperative enteroscopy was used to evaluate the entire small bowel. A study of 47 consecutive patients with OGIB compared WCE to intraoperative enteroscopy. WCE identified the source of bleeding in 74.5% versus 72% for intraoperative enteroscopy ($P =$ NS). Compared with intraoperative enteroscopy, the sensitivity, specificity, and positive and negative predictive value of WCE was 95%, 75%, 95%, and 86%, respectively.[58]

Push enteroscopy has been compared with WCE for evaluating OGIB. A pooled analysis of 14 prospective studies including 396 patients showed a diagnostic yield of 56% for WCE versus 26% ($P =$ .00001) for push enteroscopy.[55] In a more recent trial of 78 consecutive patients with obscure GI bleeding, participants were randomized to undergo either WCE or push enteroscopy. WCE was superior to push enteroscopy for identification of a bleeding source (50% vs 24%; $P =$ .02). In patients who underwent both studies, WCE found previously unidentified lesions in 26% of cases, versus 8% for push enteroscopy.[59]

Double-balloon enteroscopy (DBE) is a newer alternative technology for evaluation of the small intestine, with the added benefit of therapeutic capabilities. An Italian multicenter study of 193 patients showed that WCE and DBE had a moderate overall agreement of k = 0.46 (95% confidence interval [CI], 0.38-0.54) but excellent agreement specifically for vascular (k = 0.72) and inflammatory findings (k = 0.78). DBE was superior to WCE in cases where capsule findings showed only blood in the lumen (10 vascular lesions, 6 neoplasia, 1 ulcer, and 5 diverticula).[60] A single-blinded study of 32 patients undergoing both WCE followed by DBE showed no difference in diagnostic yields but demonstrated the ability to perform additional treatment or biopsy the DBE in 13 of these patients.[61] Three meta-analyses of DBE versus WCE showed similar diagnostic yields in patients with OGIB.[62-64] A retrospective study of 162 patients demonstrated an advantage of WCE in areas inaccessible to DBE and superiority of DBE in patients with Roux-en-Y loop anatomy and diverticula.[65] Overall, the diagnostic yield for DBE versus WCE appears to be similar. WCE has the advantage of being noninvasive and is more likely to achieve total small-bowel enteroscopy. However, no therapy can be applied.[65]

Crohn's disease

Capsule endoscopy is useful in the evaluation of the small intestine in patients in whom the diagnosis of Crohn's disease has been elusive.[66,67] Many studies have shown that this is a valuable adjunctive diagnostic test after conventional endoscopy and colonoscopy with ileoscopy.

In a cohort study of 27 consecutive patients with suspected Crohn's disease with median follow-up of 21 months, WCE had sensitivity of 93% and specificity of 84%.[68] A study in 39 patients, the majority of whom had known Crohn's disease, estimated the sensitivity and specificity of WCE to be 89.6% and 100%, respectively.[69] A retrospective study of 86 symptomatic patients with known Crohn's disease demonstrated findings of active disease in 78% of patients, leading to a change in medical or surgical management in 74% of patients.[70]

WCE has been compared with other radiologic studies for the diagnosis of Crohn's disease with somewhat disparate results. One prospective, blinded trial of 41 patients with known or suspected Crohn's disease demonstrated no significant difference between WCE and CT enterography or small-bowel follow-through in detecting active disease (83% vs 82% vs 65%, respectively). Furthermore, WCE had a significantly lower specificity compared with these tests (53% vs 89% vs 94%; $P < .05$).[71] However, other studies have shown superiority of WCE over various radiographic modalities. In a blinded study of 35 patients with suspected Crohn's disease, a diagnosis was made in 77% by using a capsule study versus 23% by small-bowel follow-through and 20% by CT scan.[72] WCE also has been shown superior to CT enteroclysis.[73,74] In a prospective, blinded study of 31 patients with known Crohn's disease, the diagnostic yield of WCE was superior to CT enteroclysis in terminal ileal disease (71% vs 25.8%; $P < .001$) and in proximal small-bowel disease (46% vs 13%; $P < .001$).[74] A large, prospective, blinded study of 93 patients with newly diagnosed Crohn's disease examined the performance of ileocolonoscopy, magnetic resonance enterography, CT enterography, and WCE. WCE was superior over magnetic resonance enterography and CT enterography for both sensitivity (100% vs 81% vs 75%, respectively) and specificity (91% vs 86% vs 85%, respectively) ($P < .05$).[75] Overall, most studies suggest that WCE has a superior sensitivity for the detection of small bowel Crohn's disease compared with other radiologic studies, with variable specificity.

Significant limitations of WCE in the diagnosis of Crohn's disease are the lack of validated capsule criteria and the inability to obtain biopsy specimens for confirmation of the diagnosis.[21] This is particularly relevant with concurrent use of NSAIDs, which is also associated with small-intestine ulcers and strictures.[53] Furthermore, up to 13.8% of asymptomatic healthy volunteers not taking NSAIDs can have mucosal breaks and other lesions seen on WCE which are not related to Crohn's disease.[76] The ability to take biopsy specimens is an advantage of enteroscopy over WCE, but capsule endoscopy is a less-invasive examination of the small bowel and is favored over balloon enteroscopy by patients.[77] Only one recent analysis of a single-center experience has compared diagnostic yields between DBE and WCE. The report demonstrated superior results with DBE (52% vs 29%). However, these yields were not measured within the same cohorts.[78]

Severity scales have been developed for Crohn's disease: the Lewis score and the Capsule Endoscopy Crohn's Disease Activity Index. These scales are based on parameters measured by the WCE, and a calculator for the Lewis score is actually included on the Given Rapid v 6.5. These may be useful tools for diagnosing Crohn's disease of the small bowel, and validation studies are ongoing.[79,80]

Small-intestine polyps and tumors

WCE can be feasible and safe in patients with known or suspected polyposis syndromes such as familial adenomatous polyposis or Peutz-Jeghers syndrome, even after prior intestinal surgery.[24,26,28,81,82] In familial adenomatous polyposis patients with duodenal polyps, WCE was effective in detecting additional polyps in the jejunum and ileum in 24% to 57% of patients in 2 prospective studies totaling 54 patients.[26,82] However, WCE may not be able to adequately visualize the ampulla of Vater,[81,82] suggesting a limitation of this test as a solitary screening examination.

WCE offers an alternative to radiologic tests for screening of patients with polyposis syndromes, particularly in Peutz-Jeghers syndrome patients who may require screening starting at a young age. In a prospective, blinded study of 24 patients with GI polyposis syndromes, WCE was able to detect polypoid lesions in more patients than small-bowel follow-through (27% vs 12.5%) and more polyps overall (44 vs 12 polyps; $P < .02$).[25] A small study of 11 patients with Peutz-Jeghers syndrome demonstrated that WCE was as sensitive as barium enterography as well as being the more comfortable and preferred test.[83]

WCE has been compared with magnetic resonance enterography as a screening test for small-intestine tumors. A study of 20 patients with either familial adenomatous polyposis or Peutz-Jeghers syndrome demonstrated that there was no difference in identifying polyps that were larger than 15 mm (11 vs 8 polyps), but a significant advantage was measured in the ability of WCE to detect polyps <5 mm in diameter (386 vs 0 polyps).[27] Magnetic resonance enterography and WCE had similar detection rates of polyps >15 mm in a prospective series of 19 Peutz-Jeghers syndrome patients.[84] However, magnetic resonance enterography also provides extraintestinal information as well as more accurate data on size and location of polyps.[84,85]

Finally, WCE has been compared with DBE in the evaluation of patients with polyposis syndromes. In a small study of 9 patients who had both examinations, DBE was superior to WCE for identification of small-bowel polyps.[86]

Small-bowel tumor detection rates have been reported in WCE examinations performed for other indications. A pooled analysis of 24 prospective WCE trials for bleeding and nonbleeding indications showed that although WCE was superior to small-bowel follow-through and CT for the detection of small-bowel tumors, this modality still had a miss rate of 19%.[87] Two retrospective studies case series described 7 patients referred for WCE who had negative examinations but later were found to have small bowel masses by other diagnostic modalities (2 adenocarcinomas, 2 stromal tumors, malignant melanoma, Peutz-Jeghers syndrome polyp, inflammatory fibroid polyp).[88,89] In a retrospective, single-center study, WCE performance was compared with CT enterography for detection of small-bowel tumors. In 17 patients, CT enterography had superior sensitivity (94.1% vs 35.3%; $P = .004$).[90] Finally, in a retrospective review of 183 patients undergoing investigation for GI bleeding, 18 were found to have a small-bowel mass by DBE. Fifteen of these patients underwent WCE as well, which identified only 5 of the mass lesions.[91] Taken together, these studies suggest that WCE may have a role in the evaluation of small-bowel tumors, but a negative examinations should not preclude further work-up if a lesion is highly suspected.

Celiac disease

In a recently published meta-analysis of 6 studies and 166 patients with biopsy-confirmed celiac disease, WCE had a pooled sensitivity and specificity of 89% (95% CI, 82%-94%) and 95% (95% CI, 89%-98%), respectively.[92] Interobserver variability is good-to-excellent among experienced readers (k = 0.56-1.0).[25,87,88] One study also demonstrated mucosal changes beyond the proximal small bowel in 66.6% of patients, suggesting a possible advantage of WCE over endoscopy in celiac disease with "patchy" distribution.[92,93] In a prospective study of 47 patients with known celiac disease and extensive previous radiographic and/or endoscopic examinations for refractory symptoms, WCE was able to detect findings of celiac disease in 87% of cases, with unexpected findings in up to 45% of cases (neoplasms, ulcerations, and strictures). These data suggest an additional role of WCE specifically in complicated celiac disease.[29,94]

Esophageal disease

Many studies have evaluated WCE in the esophagus for the noninvasive diagnosis of complicated GERD, Barrett's esophagus, and esophageal varices.

A multicenter trial of 106 GERD patients who underwent both a PillCam ESO study and standard endoscopy showed that WCE had a sensitivity and specificity of 92% and 95% for esophageal abnormalities (eg, esophagitis, Barrett's esophagus).[33,95,96] However, a recent meta-analysis of 9 studies (618 patients) showed a pooled sensitivity and specificity for the diagnosis of Barrett's esophagus of only 77% and 86%, respectively. WCE was found to be safe and had a high rate of patient preference.[97] For detection of esophagitis, 2 studies demonstrated sensitivity ranging from 50% to 79% and high specificity.[95,96] These data indicate that WCE is currently inferior to upper endoscopy for the diagnosis of esophagitis and Barrett's esophagus.

WCE has been evaluated in the detection of esophageal varices. A meta-analysis by Lu et al,[98] comprised of 7 studies and 446 patients, calculated a pooled sensitivity and specificity for detecting esophageal varices of 82.7% and 80.5%, compared with upper endoscopy. In a recent single-blinded study of 65 cirrhotic patients, WCE had an accuracy for diagnosing esophageal varices of 63.2%, with poor accuracy in grading portal hypertensive gastropathy and detecting ulcers, gastric varices, and other significant upper GI lesions.[99] Agreement between upper endoscopy and WCE was substantial on the presence of varices (k = 0.73)[100] and was moderate on the grading of varices (k = 0.53).[101] Overall, the data suggest that WCE is inferior to endoscopy for the diagnosis and grading of esophageal varices for screening.

WCE examinations of the esophagus may be suboptimal because of rapid transit and lack of insufflation. A magnetic maneuverable capsule (MMC; Given Imaging), which attempts to counteract the forces of gravity and esophageal motility, has been developed. There are limited data on its use, and it is not commercially available.[14]

TABLE 2. List prices for available wireless capsule systems

Manufacturer	List price for workstation, data recorder, patient equipment	List price for capsule endoscope
Given Imaging	$26,940	$500
Olympus America	$12,150	$500

SAFETY

In general, WCE is a safe procedure. The main potential adverse event of WCE is capsule retention, defined as a capsule endoscope remaining in the digestive tract for a minimum of 2 weeks or one that has required directed therapy to aid its passage. Retention can occur in the setting of NSAID strictures, Crohn's disease, small-bowel tumors, radiation enteritis, and surgical anastomotic strictures. Occasional cases of retention within other sites (eg, Zenker's diverticulum, duodenal diverticulum, umbilical hernia, Meckel's diverticulum) have been reported.[97,102-113] An abdominal radiograph is recommended after 2 weeks if retention is suspected[114] and if confirmed, may require surgery or endoscopic intervention.[102,103]

TABLE 3. Current procedural terminology codes for wireless capsule endoscopy

CPT code*	Description
91110	Gastrointestinal tract imaging, intraluminal (eg, capsule endoscopy) esophagus through ileum, with physician interpretation and report. Append modifier 52 if ileum is not visualized.
91111	Gastrointestinal tract imaging, intraluminal (eg, capsule endoscopy) esophagus with physician interpretation and report.
91110-TC modifier	Gastrointestinal tract imaging, intraluminal (eg, capsule endoscopy) esophagus through ileum, with physician interpretation and report—Technical Component (The Technical Component charges are institutional charges—facility to bill TC component if billing separately from physician).
91110-26 modifier	Gastrointestinal tract imaging, intraluminal (eg, capsule endoscopy) esophagus through ileum, with physician interpretation and report—Professional Component (The Professional Component is the physician's portion of the procedure; 26 component billed by physician if billing separately from facility).
91299	For patency capsule (ie, unlisted diagnostic gastroenterology procedure).

CPT, Current Procedural Terminology.

The overall reported incidence of capsule retention has ranged widely in the literature (0%-13%) and also varies with indication for examination. Initial capsule retention rates were reported as 1.5% in the setting of OGIB and up to 5% in patients with known Crohn's disease.[114] However, recent large studies have indicated an overall retention rate between 1.3% and 1.4%.[104,105] A systematic review of 227 English-language articles including 22,840 procedures calculated pooled retention rates of 1.2%, 2.6%, and 2.1% for indications of OGIB, Crohn's disease, and neoplastic lesions, respectively.[105]

There have been two reports of intestinal perforation after capsule endoscopy, both in patients with Crohn's disease.[106,107]

Tracheal aspiration of the capsule has been reported.[108] Patients with swallowing disorders should have endoscopic placement of the capsule.

There are concerns of potential interference between transmitted capsule wavelengths and other implanted electronic devices, most notably cardiac pacemakers, defibrillators, and left ventricular assist devices. Thus far, in vivo and in vitro studies have mainly demonstrated no interference between capsule endoscopy and cardiac devices.[109] A review of available in vivo studies with cardiac pacemakers and defibrillators have shown no interference with WCE except for one study of 100 patients.[109-113,115-118] This study demonstrated interference of WCE with cardiac pacemakers of 4 patients when a test capsule was placed within 10 cm of the skin surface close to the generator and electrodes. However, the test scenario under which this interference occurred was thought to be clinically irrelevant by the authors.[111] One study showed no interference, but there was a loss of acquired images, whereas the capsule was in close proximity to a patient's abdominal pacemaker pulse generator.[113] Little data exist on the use of WCE in patients with left ventricular assist devices, but 2 case reports have shown no interference.[119-121] Product labeling states that implantable cardiac devices are a contraindication to WCE, although it has been performed off-label without adverse events in these patients.

Patients should not undergo magnetic resonance imaging after having completed a WCE until they have passed the capsule. The capsule can be easily identified on plain radiographs, and this should be performed if there is any question of capsule retention.

FINANCIAL CONSIDERATIONS

The list prices for the WCE systems are shown in Table 2. The cost for the AdvanCE capsule delivery system is $495 per box (3 devices). The cost for the Given Agile Patency technology is $500 per 10 capsules.

The approved Current Procedural Terminology (CPT) codes for WCE are listed in Table 3. Because approved indications may vary among payers, providers should check with their individual Medicare or private carriers for details on coverage.

AREAS FOR FUTURE RESEARCH

Future studies may focus on refining the diagnostic value of capsule endoscopy and determining its impact on management of patients with suspected small-bowel disease.

Additional studies are required on the use of WCE in patients with cardiac devices. Data thus far suggest no clinical interference of WCE and defibrillators, cardiac pacemakers, or left ventricular assist devices. However, given the implications of cardiac device malfunction in such patients, use of WCE will be contraindicated by manufacturers until large-scale studies are performed. Future research also

may include a comparison of the different transmission image systems (radiofrequency vs human body communications) and whether there is different potential of interference with cardiac devices.

Improvement in technology and techniques are needed to optimize WCE performance in the esophagus. These could include modified swallowing protocols to slow propulsion of capsules across the esophagus, development of a capsule capable of being controlled and/or maneuvered at the level of the gastroesophageal junction as well as a capsule that has biopsy capabilities. Some of these technologies are already in the process of being developed.

As noted earlier, new technology is also being developed to aid with capsule endoscopy delivery. Future developments may include more delivery system options such as specialized devices or capsule endoscopes that can be guided into the duodenum.

SUMMARY

Over the last decade, WCE has established itself as a valuable test for imaging the small intestine. It is a safe and relatively easy procedure to perform that can provide valuable information in the diagnosis of small-bowel conditions. Its applications still remain limited within the esophagus and colon. Future developments may include improving visualization within the esophagus and developing technologies that may allow manipulation of the capsule within the GI tract and biopsy capabilities.

Abbreviations: DBE, double-balloon endoscopy; FDA, Food and Drug Administration; NSAID, nonsteroidal anti-inflammatory drug; OGIB, obscure GI bleeding; WCE, wireless capsule endoscopy.

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