Ontario Health Technology Assessment Series 2003; Vol. 3, No. 2

Wireless Capsule Endoscopy

An Evidence-Based Analysis

May 2003

Ontario

Medical Advisory Secretariat
Ministry of Health and Long-Term Care

Suggested Citation

This report should be cited as follows:
Medical Advisory Secretariat. Wireless capsule endoscopy: an evidence-based analysis. *Ontario Health Technology Assessment Series* 2003;3(2).

Permission Requests

All inquiries regarding permission to reproduce any content in the *Ontario Health Technology Assessment Series* should be directed to MASinfo.moh@ontario.ca.

How to Obtain Issues in the Ontario Health Technology Assessment Series

All reports in the *Ontario Health Technology Assessment Series* are freely available in PDF format at the following URL: www.health.gov.on.ca/ohtas.

Print copies can be obtained by contacting MASinfo.moh@ontario.ca.

Conflict of Interest Statement

All analyses in the Ontario Health Technology Assessment Series are impartial and subject to a systematic evidence-based assessment process. There are no competing interests or conflicts of interest to declare.

Peer Review

All Medical Advisory Secretariat analyses are subject to external expert peer review. Additionally, the public consultation process is also available to individuals wishing to comment on an analysis prior to finalization. For more information, please visit http://www.health.gov.on.ca/english/providers/program/ohtac/public_engage_overview.html.

Contact Information

The Medical Advisory Secretariat
Ministry of Health and Long-Term Care
20 Dundas Street West, 10th floor
Toronto, Ontario
CANADA
M5G 2N6
Email: MASinfo.moh@ontario.ca
Telephone: 416-314-1092

ISSN 1915-7398 (Online)
ISBN 978-1-4249-7285-2 (PDF)

About the Medical Advisory Secretariat

The Medical Advisory Secretariat is part of the Ontario Ministry of Health and Long-Term Care. The mandate of the Medical Advisory Secretariat is to provide evidence-based policy advice on the coordinated uptake of health services and new health technologies in Ontario to the Ministry of Health and Long-Term Care and to the healthcare system. The aim is to ensure that residents of Ontario have access to the best available new health technologies that will improve patient outcomes.

The Medical Advisory Secretariat also provides a secretariat function and evidence-based health technology policy analysis for review by the Ontario Health Technology Advisory Committee (OHTAC).

The Medical Advisory Secretariat conducts systematic reviews of scientific evidence and consultations with experts in the health care services community to produce the *Ontario Health Technology Assessment Series*.

About the Ontario Health Technology Assessment Series

To conduct its comprehensive analyses, the Medical Advisory Secretariat systematically reviews available scientific literature, collaborates with partners across relevant government branches, and consults with clinical and other external experts and manufacturers, and solicits any necessary advice to gather information. The Medical Advisory Secretariat makes every effort to ensure that all relevant research, nationally and internationally, is included in the systematic literature reviews conducted.

The information gathered is the foundation of the evidence to determine if a technology is effective and safe for use in a particular clinical population or setting. Information is collected to understand how a new technology fits within current practice and treatment alternatives. Details of the technology's diffusion into current practice and input from practicing medical experts and industry add important information to the review of the provision and delivery of the health technology in Ontario. Information concerning the health benefits; economic and human resources; and ethical, regulatory, social and legal issues relating to the technology assist policy makers to make timely and relevant decisions to optimize patient outcomes.

If you are aware of any current additional evidence to inform an existing evidence-based analysis, please contact the Medical Advisory Secretariat: MASinfo.moh@ontario.ca. The public consultation process is also available to individuals wishing to comment on an analysis prior to publication. For more information, please visit http://www.health.gov.on.ca/english/providers/program/ohtac/public_engage_overview.html.

TABLE OF CONTENT

OBJECTIVE

The objective of this health technology policy assessment was to develop a funding policy for the use of capsule endoscopy [Given® Diagnostic Imaging System] in diagnostic work up of patients with gastrointestinal [GI] disease. Capsule endoscopy is currently not an insured health benefit under the Health Insurance Act and no aspect of this service can be billed to the Ontario Health Insurance Plan.

BACKGROUND

Technological advancement in the area of diagnostic endoscopy has resulted in the development of wireless capsule endoscopy [WCE], capable of advancing beyond the reach of conventional endoscopes. The ingestible imaging capsule (known as M2A) manufactured by GIVEN® IMAGING, is a wireless miniature video camera (26 mm in length and 11 mm in diameter) which transmits digital images to an external data recorder in a belt worn by the patient. The M2A capsule is smooth and is easily swallowed by the patient. It travels through gastrointestinal tract capturing two images per second and is excreted in approximately eight hours.

CLINICAL NEED

Limitations of current diagnostic techniques in the identification of small bowel lesions has prompted a search for alternative technologies. Standard endoscopic examinations evaluate only short segments of the proximal and distal small bowel and barium follow-through [BFT] has a low sensitivity and specificity of only 10% for detecting pathologies. Hence, endoscopic examination of the entire small bowel has always been a diagnostic challenge. Limitation of the diagnostic techniques in detection of the lesions located in the small bowel are mainly due to the length of the small intestine, overlying loops and intra-peritoneal location (1). False negative examinations and radiologic misinterpretation accounted for the long delay and advanced disease at the time of diagnosis in three quarters of patients with small bowel disease (2). It would be ideal if a non-invasive diagnostic technique with high sensitivity and specificity without causing significant side effects could be used to visualize small bowel lesions.

Approximately 5% of cases of gastrointestinal bleeding remains undiagnosed with the use of conventional techniques (3). Uncontrolled trials suggest that push enteroscopy which has been used increasingly in recent years for investigation of small bowel disease can identify the bleeding source in 30-50% of cases of GI bleeding when the source cannot be identified with conventional endoscopy (4-6).

Wireless capsule endoscopy [WCE] is a new innovation that has made painless imaging of the entire small bowel possible. The technique allows visualization of entire length of the small bowel not within reach of standard upper and lower endoscopy.

INCIDENCE & PREVALENCE OF THE DISEASE

The estimated annual incidence of gasrointestinal bleeding in the United States is approximately 100 episodes per 100,000 persons result in approximately 300,00 hospitalization per year (7). Equivalent statistics in Canada are not available. Up to 5% of patients with recurrent GI bleeding remain undiagnosed following upper and lower endoscopy, the presumed source of bleeding being small bowel (8). Gastrointestinal angiodysplasia is the most common cause of iron deficiency anemia of obscure origin (9).

THE TECHNOLOGY

GIVEN DIAGNOSTIC IMAGING SYSTEM

The technology consists of three components: The wireless capsule (known as M2A®), the data recorder belt and RAPID (Reporting and Processing of Images and Data) workstation.

THE M2A CAPSULE [Also called wireless capsule] is a disposable device, measuring 11 X 26 mm (slightly larger than a large vitamin capsule) and weighting 3.7 g. The 2 dome, cylinder shaped capsule is made of a biocompatible plastic with a smooth surface that allows the peristalsis of the intestinal tract to advance the capsule through the lumen. The M2A capsule contains a complimentary metal oxide silicon chip camera, a lens, an illumination light-emitting diodes, energy source and radiotelemetry transmitter. The capsule battery life is about eight hours which is sufficient for imaging the small intestine. The M2A capsule has two operation modes; active and beacon. When the battery power is depleted, the transmitter switches the capsule to the beacon mode. In this mode, it relays the information to the recorder about the location of the capsule allowing the RAPID system to track the capsule in its pathway for 10 additional hours. The disposable capsule is constructed of specially sealed biocompatible material resistant to digestive fluids. The capsule transmits video signals and data in real time.

The M2A capsule is ingested by the patient and provides video images of the GI mucosa during its transit throughout the GI tract at a rate of two images per second. The system has the ability to acquire about 50,000 images. The capsule is naturally excreted after approximately 8 to 72 hours.

THE DATA RECORDER BELT worn by the patient around the waist, receives the signals transmitted by the capsule through an array of sensors placed on the patient's body. The sensor array [antenna] is comprised of eight identical, 4 cm diameter sensors attached to the skin by disposable adhesive pads. It receives the images from the capsule and sends signals to a data recorder. The sensors are connected to the recorder by a flexible coaxial cable.

The data recorder is a walkman-size battery-operated unit that receives the data transmitted by the capsule. It comprises a receiver, processor modules, and a hard disk drive to store the data. Eight nickel-metal 6-V rechargeable batteries are used for the operation. The data recorder is ready for operation once the sensor array and batteries and data recorder are all connected. A blue blinking light indicates that recorder is recording the data. The data recorder can download approximately 50,000 images to the RAPID workstation. The ambulatory belt permits the patient to continue normal daily activities.

A COMPUTER WORKSTATION, equipped with RAPID™ Application Software, processes the data downloaded from the data recorder. The RAPID workstation is a modified standard personal computer designed for processing of the data into a video movie and presentation. The output allows physicians to follow the path traveled by the capsule, view the lesions, and save important images and short video clips. The video movie is comprised of frames and can present from 1 to 50 frames per second. It has pausing and reversing capabilities. Usually, the movie is seen as 5 to 10 frames per second but higher or lower speeds can be selected to view the images. The physician endoscopy review time is approximately 1.5 hours.

SOFTWARE AND CAPSULE UPGRADE

M2A plus is an upgraded version of the Given Diagnostic Imaging System with additional features. Continued development and improvement of WCE has resulted in the development of a blood-sensing algorithm which uses color pattern, allowing the physician to focus more on bleeding areas. The

"Localization" feature provides an estimate of the location of the lesion inside the abdomen by showing the affected quadrant. The M2A plus has replaced the M2A sine July 2002 *[Southmedic Inc.]*.

The Rapid Viewer system is another feature added to the software and combines one image with 2 images behind, therefore, reducing the required time for reviewing the images by 30-45 min. The Rapid Viewer is available since January 2003 [Southmedic Inc.]. Additional features such as chip to carry sensors for PH, temperature and chemicals is still under investigation.

REGULATORY STATUS

FDA CLEARANCE

The M2A received clearance from the FDA as an adjunctive tool in August 2001. The clearance was based on animal and clinical studies of safety and effectiveness conducted by the manufacturer. Following the FDA approval, the distribution channel has been established in more than 40 countries.

MEDICAL LICENSE

M2A was issued a class II medical license by Health Canada in July 2001 [License number 30953]. It has been recommended that capsule endoscopy can be used as an adjunctive tool for the detection of GI diseases.

GUIDELINE

Capsule endoscopy is a new technology and no guidelines have been established for its use to date.

ALTERNATIVE TECHNOLOGIES

The sources of gastrointestinal bleeding in the majority of cases are located in regions that can be reached by standard upper and lower endoscopy. Only 2-10% of chronic bleeding sites is thought to be located in the small bowel (10). The current methods for examination of the small intestine include primarily, barium follow through (BFT) and enteroscopy. However the diagnostic yield of these tests are low. There is no *"Gold standard"* to which the diagnostic performance of the WCE can be compared.

ENDOSCOPY

Upper endoscopy generally reaches the junction of the second and the third segment of the duodenum. Colonoscopy can reach the terminal ileum for up to 30 cm (11). Enteroscopy [Endoscopy of the small bowel] is a method for identifying the lesions in the distal duodenum, jejunum and ileum. Non-surgical enteroscopy methods are push enteroscopy and Sonde enteroscopy. Intra-operative enteroscopy is the ultimate endoscopic examination of the small bowel. With the significant advances in the design of push enteroscopy, visualization of the jejunum has become possible but examination of the distal small bowel is only possible through the use of Sonde enteroscope.

PUSH ENTEROSCOPY

Push enteroscopy, which is a new generation of videoenteroscopy, has been introduced into the diagnostic work up of patients with GI disease since 1990's and currently is considered the most effective diagnostic tool to diagnose the source of bleeding in the small bowel. The push enteroscope can be advanced from the mouth up to 150 cm beyond the pylorus. During push enteroscopy, an endoscope [with the working length of up to 250 cm] is pushed deep into the jejunum. Push enteroscopy is only available at specialized endoscopic centres and the full procedure takes about 15-45 minutes (12). The actual length of the small bowel that can generally be inspected with a push enteroscope is about 50-150 cm (12). This is mainly due to anatomical barriers. The procedure requires that the patient undergoes intravenous sedation and

there is a danger of perforation. The diagnostic yield of push enteroscopy for obscure GI bleeding varies from 38% to 75% (7). However, these diagnostic yields may reflect all types of lesions that were identified including those located prior to the small bowel and not related to the source of bleeding. Thus, the true diagnostic yield of push enteroscopy for work-up of obscure GI bleeding may be more in the range of 15-35% (7). Several factors contribute to the reported differences, including dissimilar patient population and the investigators judgement. In addition, many lesions found at push enteroscopy are within the reach of standard endoscope. Hayat et al. found that the miss rate for proximal lesions at standard upper endoscopy was as high as 42% (8).

SONDE ENDOSCOPY

Sonde endoscopy allows the ileum to be reached in 77% to 84% of cases but unfortunately, it has a limited field of view and does not provide full visualization. Even in the best hands, only 50% to 70% of the small bowel may be visualized. Sonde enteroscopy relies on peristalsis to propel a long flexible endoscope to the distal small intestine. The technique is not commonly used to investigate small bowel bleeding as is a prolonged procedure (6-8 hours) with no therapeutic capability. The procedure is very uncomfortable for patients and has been abandoned.

INTRA-OPERATIVE ENTEROSCOPY

Enteroscopy with intra-operative guidance allows the entire small intestine to be explored. The proportion of patients who can really benefit from this technique is not clear. Intra-operative enteroscopy is more invasive technique and requires general anesthesia. However, it sometimes becomes necessary to establish the diagnosis. The technique is currently the most widely used diagnostic method if push enteroscopy fails to identify the source of bleeding and in this situation, the technique is successful in identifying the source of bleeding in 83% to 100% of the cases (13). Angiodysplasia is the most common cause of bleeding identified by intra-operative enteroscopy (13). The ileocecal valve or distal ileum within 2 feet of the valve can be reached on 75% of the occasions. Perforation may occur in 5% and careful observation at insertion is important. It is important that the mucosa be evaluated while advancing the instrument because iatrogenic trauma can be misinterpreted as positive finding during withdrawal (14). Long-term follow up of patients after intra-operative endoscopy shows a rate of re-bleeding between 0 and 45%.

VIRTUAL ENTEROSCOPY

Virtual endoscopy is a new method of diagnosis using 3D image datasets (such as CT or MRI) to provide simulated visualization of organs similar to those produced by standard endoscopic procedures (15-16). Virtual colonoscopy has been found to be an attractive alternative to colonoscopy but only limited research has been conducted on its use in the upper GI tract (17).

SMALL BOWEL RADIOGRAPH

BARIUM FOLLOW-THROUGH

Due to its availability, barium follow through [BFT] is still the most commonly used method of investigation in small bowel lesions. The small bowel series involves x-ray after the patient has swallowed contrast medium. BFT is not able to demonstrate flat lesions such as angiodysplasia, one of the most common causes of small bowel bleeding. It is also not very sensitive to detecting raised lesions (18). The diagnostic yield of BFT for small bowel bleeding is about 5% and has a 41.6% false negative rate (7).

ENTEROCLYSIS

Small bowel barium enema [Enteroclysis], differs from BFT in that the contrast material is administered via a small tube placed directly in the proximal intestine and allows for visualization of the entire small

bowel (19). The technique is not universally available and involves greater radiation exposure, longer procedure and patient discomfort. Enteroclysis is not very helpful in identifying vascular lesions, but can be useful in detecting small bowel tumors.

SPECIAL IMAGING TECHNIQUES

ANGIOGRAPHY

Mesentric angiography can localize the site of active bleeding (0.5-1.0 ml/min) in 50% to 72% of the patients (13). Helical computer tomographic angiography involves injection of a contrast agent and can diagnose the origin of bleeding in 72% of the patients but the technique is time consuming and not readily available in most hospitals (13).

TAGGED RED BLOOD CELL

The origin of the small bowel bleeding can be identified using the patient's ^{99m}Tc-radionuclide tagged red blood cells. The effectiveness of the radioisotope scanning has been studied mostly in colonic sites of bleeding for the detection of Meckel's diverticula [which is more common in younger patients] in the hemorrhagic phase. In a study of 103 patients, radionuclide scans failed to localize bleeding in 85% of patients and the technique has been considered not to be a useful diagnostic step in the diagnosis of small intestinal bleeding (20).

DISEASE/CONDITION

GASTROINTESTINAL BLEEDING

Gastrointestinal bleeding has substantial cost implications. Chronic GI bleeding can be challenging and requires a different strategy and management to acute GI bleeding. Chronic GI bleeding is frequently suspected on the basis of an unexplained iron deficiency anemia.

OBSCURE GI BLEEDING

Obscure GI bleeding is defined as recurrent bleeding for which no definite source has been identified by conventional endoscopic examination or barium studies (21). The most common cause of obscure GI bleeding is mucosal vascular abnormality or "angiodysplasia", which is more common in elderly patients. Obscure GI bleeding is categorized into obscure-occult [recurrent iron deficiency anemia and/or recurrent positive fecal occult blood test] and obscure-overt [recurrent passage of visible fecal blood] (7).

CAUSES OF SMALL INTESTINAL BLEEDING

Causes of small intestinal bleeding include vascular lesions, ulceration, small intestinal tumors and aortoenteric fistula.

Table 1. Causes of small intestinal bleeding

Vascular lesions	• Angiodysplasia • Telangiectasia • Hemangioma • Arteriovenous malformation • Calibre persistent artery (Dieulafoy's lesion)
Ulceration	• Crohn's disease • Non-steroidal anti-inflammatory drugs • Meckel's diverticulum • Zollinger Ellison syndrome • Vasculitis
Small intestinal tumors	• GI stromal tumors • lymphoma • Carcinoid • Small bowel carcinoma
Aortoenteric fistula	
Jejunal diverticula	

INFLAMMATORY BOWEL DISEASE

CROHN'S DISEASE

Crohn's disease [CD] is a systematic granulomatous disease that may involve any part of the GI tract but the small bowel is the affected site in 30-40% of cases. In 25-30% of the patients the symptoms start before the age of 20 years. Small bowel x-ray, colonoscopy with ileoscopy and computerised tomography (CT) are the current methodologies for identifying the disease.

LITERATURE REVIEW

OBJECTIVES

1. To perform a literature search in order to evaluate the safety, effectiveness and cost-effectiveness of the WCE technique in identifying small bowel lesions.

2. To identify the clinical indications for the use of WCE technique and the criteria for patient selection.

3. To assess whether capsule endoscopy is superior to the conventional techniques in identifying small bowel lesions.

METHODOLOGY

INCLUSION CRITERIA

1. Studies compared the diagnostic yield of WCE to the conventional techniques in identifying the source of bleeding in small bowel.
2. Studies provided diagnostic yield for WCE in identifying the source of bleeding in small bowel.

EXCLUSION CRITERIA

1. Studies on WCE focused on the GI sites other than the small bowel.
2. Studies on WCE focused on the diseases/conditions other than the small bowel bleeding.

DATABASES AND SEARCH STRATEGY

A Medline search covering the period January 1, 2000 to April 1, 2003 was performed to identify published literature on capsule endoscopy. The key words "capsule endoscopy", "video capsule endoscopy", "Wireless capsule endoscopy" "Wireless capsule" and M2A were used as the search terms. The search was limited to the English language. Animal studies were not excluded because such studies may also provide useful information in reviewing a new technology. Cochrane database was also searched for the Health Technology Assessment on capsule endoscopy. The citation lists of all relevant articles were also examined to identify other potentially relevant publications to assure complete retrieval of studies.

OUTCOMES OF INTEREST

Selected endpoints for this assessment were: Safety, diagnostic yield, adverse events/side effects/complications, technical difficulties and the costs.

RESULTS OF LITERATURE SEARCH

All the published studies on WCE were retrieved and tabulated in Appendix F. Articles were scanned for the overall assessment of the technique and comparative studies were tabulated by the date of publication. Levels of evidence were assigned according to the scale based on the hierarchy by Goodman [1985]. An additional designation "g" was added for preliminary reports of studies that have been presented to international scientific meetings.

Table 2. Levels of Evidence: WCE studies in patients with obscure GI bleeding

Type of Study (Design)	Level of Evidence	Number of Eligible Studies Analyzed
Large randomized controlled trial, Systematic reviews of RCTs	1	
Large randomized controlled trial unpublished but reported to an international scientific meeting	1(g)	
Small randomized controlled trial	2	
Small randomized controlled trial unpublished but reported to an international scientific meeting	2(g)	
Nonrandomized trial with contemporaneous controls	3 a	3
Nonrandomized trial with historical control	3b	
Nonrandomized controlled trial unpublished but reported to an international scientific meeting	3g	10
Surveillance (database or register)	4a	
Case series, multi-site	4b	
Case series, single-site	4c	1
Case series unpublished but presented to an international scientific meeting	4g	
TOTAL		14

A review of the citation lists of the retrieved articles revealed studies on diagnostic yield of WCE presented at the international scientific meetings.

EVALUATION OF WCE TO DATE

PRELIMINARY STUDIES

The first human study was performed on ten normal volunteers (22). The study demonstrated the feasibility of the technique by showing that the capsules were easily swallowed and caused no discomfort, propelled by peristalsis and successfully transmitted video images from the stomach to the cecum. High quality images were obtained throughout the video transmission.

The first study using WCE to assess patients with obscure or uncontrolled gastrointestinal bleeding was conducted by Appleyard et al. (23). Only four patients were included in the study. The diagnostic yield of WCE was considered satisfactory and the procedure resulted in no complications.

ASSESSMENT OF COMPARATIVE STUDIES

Since the incidence of obscure GI bleeding suspected to be of small bowel origin is relatively low, the availability of subjects for the studies is limited. However, most of the studies focused on the small bowel.

To date, three published studies compared the diagnostic performance of WCE in obscure GI bleeding with an alternative diagnostic technology. Two of the studies included only patients with obscure GI bleeding (10, 24) and in one study, about two third of the patients had obscure GI bleeding (25). Comparison between WCE and PE was made in two of the studies and one study compared the diagnostic yield of WCE with small bowel barium radiograph. All the studies were conducted prospectively. The results of all the studies on WCE have been presented as "Diagnostic yield" *[Number of cases that a lesion (considered to be responsible for the bleeding) was identified divided by the number of patients]* while the optimal and reliable parameters of a diagnostic test such as sensitivity, specificity and accuracy remain unknown and the true positive rates from false positive rates cannot be differentiated.

In diagnostic testing, it is desirable to have a standard criterion as the "Gold standard". However, in comparison between capsule endoscopy and another technology, the standard criterion cannot be applied since there is none. If surgical enteroscopy, which allows histologic confirmation of a lesion is considered as the "Gold standard", not all the patients would undergo this examination. Moreover, if such an examination can be performed on a subset of patients, the results cannot be generalized to the population of patients who are eligible for capsule endoscopy.

SENSITIVITY AND SPECIFICITY OF WCE

The only study that has investigated the sensitivity and specificity of WCE is a canine study conducted by Appleyard et al (18). The investigators demonstrated that WCE is superior to the PE in detecting colored beads sutured into the small bowel (18). Nine to 13 radio-opaque, colored beads were sewn in random order inside 9 canine small bowels, half within the first meter, and confirmed with x-ray. The number of beads, their color and order were assessed. The sensitivity of WCE was 64% compared with 37% for PE [$p<0.001$]. The specificity of WCE was 92% compared to 97% for PE.

PE had a sensitivity of 94% within its range, compared with 53% for the WCE within the same range but the capsule identified significantly more beads beyond the reach of push enteroscope [median 4 per

examination versus 0, p<0.0001]. Given the greater control for manipulating the endoscope for better visualization of the lesion, the higher sensitivity of PE to identify proximal lesions is understandable. However, due to its ability to visualize the entire small bowel, the overall sensitivity of WCE is higher than PE.

STUDIES ON WCE

The studies on patients with obscure GI bleeding including three comparative studies and one study of safety and effectiveness of WCE are tabulated in table 4.

Table 4. Prospective trials on WCE in patients with obscure GI bleeding

Study	*Comparison Technique*	*Study population*	*Number (male, female)*	*Mean age*
Ell et al. 2002 (10)	WCE vs PE Complete conventional diagnostic work up was performed: Enteroclysis (32) Angiography (26) Meckel scintigraphy (21) Blood pooled scintigraphy (13) PE and WCE (32)	Patients with chronic GI bleeding and a positive guaiac test	32 (14 m, 17f)	61± 14 (23-90)
Lewis et al. 2002 (24)	WCE vs PE All the patients had to have undergone upper endoscopy, colonoscopy and BFT without discovery of a source of bleeding. PE was performed in all patients following WCE	Obscure GI bleeding	21 (9m, 12f) The data for one examination was lost and was excluded from the analysis	61 (41-78)
Costamagna et al. 2002 (25)	WCE vs BFT BFT was preceded the WCE by 4 days	Obscure GI bleeding=13 Suspected small bowel disease=7	20 (13m, 7f)	52.5 (29-78)
Scapa et al. 2002 (12)	Safety & effectiveness, Diagnostic yield	Unexplained GI bleeding/suspected small bowel disease	35 (17m, 18f)	46.5 (18-75)

WCE=Wireless capsule endoscopy; PE=Push enteroscopy; BFT=Barium follow-through

Table 5 shows the number of diagnostic procedures the study patients underwent prior to the WCE.

Table 5. Number of procedures the study patients underwent prior to the WCE examination

	Number of procedures			
Procedure	**Ell et al.**	**Lewis et al.**	**Costamagna et al.**	**Scapa et al.**
Upper gastrointestinal endoscopy	Mean = 14 ± 9 diagnostic procedures	83	87	33
Small bowel barium series		19	13	35
Enteroclysis		4		
Push enteroscopy		22 (In 9 patients)	13	8
Colonoscopy		78	82	42
Nuclear scan		12	9	1
Abdominal Angiography		3	5	
Abdominal CT				16
Intra-operative enteroscopy			1	
Total		**221**	**210**	**135**

Table 6 shows the number of blood products transfused prior to the WCE.

Table 6. History of blood transfusion prior to the WCE

Ell et al.	Lewis et al.	Costamagna et al.	Scapa et al.
Patients had been bleeding for 29 ± 24 months (range 0-120) •Mean unit of blood transfused = 17±18 (range 0-60) •Mean of hospitalization for bleeding episodes = 6 ± 7	•Patients had been bleeding for 36.5 months (range 2-144) •Average unit of transfused packed red cells = 28 units (range 0-300 units) •Average monthly transfusion = 0.8 units/month (range 0-2.8) • Mean hospitalization for bleeding episodes = 2.9 (range 0-9)	•Mean of prior bleeding episode = 8.5 (range 1-40) •Mean of units of blood transfused = 10.6 (range 0-77)	•Not mentioned in the article

The study by Ell et al. reported a significantly higher diagnostic yield for WCE compared to PE [p<0.001]. Definite sources of bleeding were identified in 21 of 32 patients (66%) including

angiodysplasia (17 patients), malignant stenosis (2 patients), inflammatory small bowel disease (2 patients). A questionable bleeding source in the small bowel was found by WCE in a further 7 patients (+22%). Definitive bleeding sources were identified by PE in 9 patients (28%) including angiodysplasia (7 patients), small bowel cancer (1 patient), and lymphoma (1 patient). A questionable bleeding source was found by PE in a further 3 patients (9%).

Conventional diagnostic procedures including enteroclysis (n=32), blood pool scintigraphy (n=13), Meckel scintigraphy (n=21) and angiography (n=26) produced positive results in only five patients (four through angiography). Similar findings have been reported in previous studies (4-6, 26).

The authors suggested that WCE can help reduce the number of diagnostic procedures and could become the initial diagnostic choice in patients with obscure GI bleeding with negative upper and lower endoscopy. WCE was carried out without complications in all cases. Delayed passage of the capsule was observed in two patients (4 and 10 weeks after the ingestion). In one case the capsule did not pass a distally located stenosis due to small bowel lymphoma and was removed 6 months later during surgical resection after the completion of radiotherapy. However, no symptoms of obstruction was observed. WCE was found to be safe and comfortable for the patients.

Lewis et al. studied 21 patients with obscure GI bleeding. The bleeding site was identified by WCE in 11 of 20 patients (55%) while PE identified the bleeding source in only 6 of 20 patients (30%). This difference did not reach statistical significance probably due to the small sample size [p=0.06]. The bleeding sites identified by WCE included angioectasia (5 patients), fresh blood (4 patients), ileal ulcer (1 patient) and tumor (1 patient). WCE also identified a tumor that was not identified by previous studies including a BFT, 2 cases of drug related inflammation causing bleeding and one case of lymphectasia. PE revealed a likely source of bleeding in 6 of 20 patients (6 angioectasia). No additional lesions were identified by PE that were not seen by the capsule. In addition, WCE found the source of bleeding in distal small bowel far from the reach of PE in 5 of 14 patients (36%).

All the images were judged to be of good to excellent quality and similar findings were found by the two investigators. A questionnaire was distributed concerning patients' impression of the procedure, capsule retrieval and push enteroscopy. The questionnaire included 16 questions about swallowing, pain, discomfort during or after the ingestion, willingness to repeat the examination and the overall impression. In all areas, patients were more satisfied with the WCE compared to the PE [Reported t test p values were 0.001 to 0.003].

Costamagna et al. compared WCE with BFT in evaluation of patients with obscure GI bleeding and suspected small bowel disease. BFT was normal in 17 of 20 patients and showed ileal nodularity in 3 patients while WCE showed positive findings in 17 patients and was normal in 3 patients. WCE was considered diagnostic in 9 patients (45%), suspicious in 8 (40%) and failed in 3 patients (15%). BFT was considered diagnostic in 4 patients (20%). For obscure GI bleeding, WCE was considered diagnostic in 31%, while BFT was considered diagnostic in only 5% [p<0.05]. There were no cases where WCE missed an abnormality identified by BFT. The endoscopists and radiologists were aware of the clinical presentations of the patients. The endoscopists were blinded to the results of BFT. The degree of agreement between the three endoscopists visualizing the images was around 90%. The required time for barium study was 30-120 minutes to perform the test and 15 minutes for the interpretation of the results. The viewing time for video images was about 2 hours.

Scapa et al. reported that abnormal findings were found in 29 of 35 patients (82.9%) from which 22 patients (75.9%) had associated significant pathological findings. Diagnostic yield was therefore 62.9% (22 of 35). In patients with iron deficiency anemia in whom the mean HB was 9.2 G.%, WCE found the source of bleeding in 15 out of 20 patients. This included three patients in whom the blood clot was found but the reason for bleeding was not known. WCE found lesions compatible with Crohn's disease [CD] in 6 of 13 patients with clinically suspected CD who had normal colonoscopy, gastroscopy, and small bowel x-ray. Authors have reported that following their WCE study, many patients received definitive treatment for the first time including six Crohn's patients. Furthermore, the information provided by WCE was helpful in directing treatment (one patient underwent upper endoscopy for cauterization of bleeding found by WCE, one patient had repeated colonoscopy and deep ileoscopy to perform a biopsy for lesions found by WCE).

Table 7 shows the diagnostic performance of WCE as compared to PE and BFT .

Table 7. Diagnostic performance of WCE in patients with obscure GI bleeding: Results of four published studies

	YIELD	RESULTS REPORTED
Ell et al.	•Significantly higher diagnostic yield compared to PE as well as to conventional techniques •Yield: WCE vs PE 66% vs 28%, p<0.001 •WCE vs conventional procedures: 66% vs 16% [Positive findings of conventional procedures: Small bowel enema: 0 Blood pool scintigraphy: 1 Meckel scintigraphy: 0 Angiography: 4 (Total 5 of 32)]	•WCE was significantly superior to PE •All clear-cut findings obtained with PE were also evident on WCE •The study confirmed the previous result showing that conventional procedures are successful in only 10-20% of suspected CGB in the small bowel (4-6, 26)
Lewis et al.	•Yield: WCE vs PE %55 vs 30%, p=0.06	•WCE found a distal source of bleeding in 5 of 14 patients (36%) who had normal PE. •WCE found small intestinal bleeding sites beyond the reach of PE, while no additional information was provided by PE following WCE. •A 2 cm ileal carcinoid tumor was identified in one patient, which had not been diagnosed by previous studies.

	YIELD	RESULTS REPORTED
Costamagna et al.	•Yield: WCE vs BFT 31% vs 5%, p< 0.05 •For all patients: [WCE vs BFT, 45% vs 27%]	•WCE was found to be superior to small bowel radiograph. •WCE was diagnostic in 9 (45%), suspicious in 5 (40%) and failed in 3 (15%). •BFT was considered diagnostic in 6 (27%) and failed in 16 (73%).
Scapa et al.	•Yield: WCE 62.9%	•WCE proved to be safe, painless, ambulatory and effective procedure

Table 8 shows the safety and complications of WCE reported in the above studies.

Table 8. Reports of safety and complications of WCE: Results of four published studies

	Ell et al.	**Lewis et al.**	**Costamagna et al.**	**Scapa et al.**
Tolerance	•Well tolerated	•Well tolerated	•Well tolerated	•Well tolerated, only two mild transient abdominal pain (one was remotely related to the capsule)
Safety	•WCE was safe and was not associate with any morbidity	•WCE was found to be safe •The capsules were found to be intact	•WCE was found to be safe	•Was found to be safe
Adverse effect	•None	•None	•None	•None
Difficulty with ingestion	•None	•None	•None	•None
Capsule passage	•Delayed passage observed in two patients (4 and 10 weeks after the ingestion) •In one patient with small bowel lymphoma, the capsule did not pass and was removed during surgical resection 6 months later.	•Mean time from ingestion to passage was 31.25 hours(8-73)	•No difficulty was reported	•All capsules were retrieved 12 hours to 5 days after ingestion

	Ell et al.	Lewis et al.	Costamagna et al.	Scapa et al.
Report of dysfunction/ Processing error	•Technical defect in one case	•3 capsules failed to reach the colon during the 8- hour acquisition time. One capsule remained in the esophagus for 3 hours and 22 minutes. •One data processing failure (was excluded from the analysis)	•One patient developed battery dysfunction after 5 hours	•None
Average time taken to visualize the video movie	•50 min (range 30-120)	•56 min (34-94)	•2 hours	•Not reported
Agreement between radiologists	•Not reported	•All images were judged to be good to excellent quality •Investigators reported similar findings	•The degree of agreement between three endoscopists was 90%	•Not reported

Although, there are a limited number of studies that compared the diagnostic yield of WCE to alternative techniques, the available data seems sufficient to permit a conclusion about the effectiveness of this technique to identify the source of bleeding in small bowel.

CANADIAN CENTRES PERFORMING WCE

To date, 12 centres in Canada have WCE systems installed including 8 centres in Ontario. Clinical trials of WCE are currently underway. According to the Southmedic, there have been over 400 WCE studies in Canada.

Investigators at the St. Paul's Hospital in British Columbia performed a feasibility study and reported the result of one hundred and ninety nine capsule ingestion by 180 patients. Table 9 shows the shortfall and complication rates for WCE reported by these investigators.

Table 9. Limitations and adverse events for WCE: Report from St. Paul's Hospital, BC

Limitations/Complications	%
Complete or near complete failure to transmit	6%
Significant transmission gap	6%
Poor visualization	5.5%
Failed spontaneous excretion	2.5%
Extended period with spontaneous passage	2.5%
Did not reach the cecum prior to the end of the battery life	11%

Canadian Association of Gastroenterologists; www.cag.acg.org/cddw2003/abs/abs160.htm

Poor visualization was reported to be due to the poor patient preparation or in patients on high-dose narcotics. Of those who failed spontaneous excretion, two capsules were removed endoscopically, one was removed surgically and one was found incidentally at surgery.

The diagnostic yield of WCE in carefully selected patients with obscure GI bleeding was reported above 50%. Sixty one patients with obscure GI bleeding (33 overt, 28 occult) ingested the capsule. The definitive source of bleeding was discovered in 33 of 61 patients (54%). This included angiodysplasia (18 cases), tumors (7 cases) and ulcers (8 cases). In addition, capsule endoscopy provided information on the probable source of bleeding in 18% of the cases. Seventeen patients with obscure GI bleeding underwent laparotomy.

BC investigators are currently investigating the inter-observer agreement between readers of capsule endoscopy images on obscure GI bleeding for a sample size that is expected to reach 100 patients. Readers with varying levels of training including summer research medical student, research assistant, capsular nurses and gastroenterologists with an interest in obscure GI bleeding review the images. The gastroenterologist's interpretation is being used as a "gold-standard".

REPRODUCIBILITY

The reproducibility of the WCE has been investigated at St. Michael's hospital, Toronto [Published abstract] (27). In this prospective trial, two successive capsule findings in patients with obscure GI bleeding were compared with push enteroscopy. One capsule was administered on day 1, and the second on day 2, and PE was performed on day 3. Endoscopists were blinded to the WCE findings. The results showed that positive findings from the two WCE were identical in 70% of subjects. WCE identified angiodysplasia as a cause of bleeding in 50% of the patients compared to 30% with PE.

INTERNATIONAL SCIENTIFIC CONFERENCES

Clinical results of several studies on WCE were presented in the form of abstracts at international conferences including the First Given Conference on capsule endoscopy, Rome, 2002, and Digestive Disease Week 2002, San Francisco. The results of the comparative studies presented at these conferences are shown in table 10.

Table 10. Studies comparing the diagnostic yield of WCE versus PE in identifying small bowel source of bleeding

Study		WCE		PE		p-value
	N	N	%	N	%	
†‡ **Van Gossum R et al.**	Belgium	21	13/21	62%	16/21	76%	Not reported
†‡ **Demendts KU et al.**	Belgium	15	12/15	80%	4/15	27%	Not reported
† **Yousufi M et al.**	USA	12	7/12	58%	2/12	17%	Not reported
† **Selby W et al.**	Australia	20	14/20	70%	9/20	45%	Not reported
† **Pennazio M et al.**	Italy	29	17/29	59%	8/29	28%	<0.05
‡ **Remke S et al.**	Germany	32	20/32	62%	7/32	21%	<0.05
†‡ **Delvaux MM et al.**	France	57	43/57	75%	32/57	56%	0.04
‡ **Mylonaki M et al.**	UK	38	21/38	55%	12/38	30%	Not reported
ǂ **Lim RM et al.**	USA	20	14/20	70%	9/20	45%	Not reported
ǂ **Rossini FP et al.**	Italy	10	7/10	70%	2/10	20%	Not reported

References: 28-37

† *Presented at the First Given Conference on capsule endoscopy, Rome, 2002; page 17-9*

‡ *Presented at the Digestive Disease Week 2002, San Francisco [published in Gastrointestinal Endoscopy 2002;55(5)]*

ǂ *Presented at the 67th Annual Scientific Meeting of the American College of Gastroenterology, October 20-23, 2002, Seattle, Washington [Published in American Journal of Gstroenterology; Sept 2002; Vol 97(9) Suppl]*

All comparative studies presented at these conferences (a total of 254 patients with small bowel bleeding) except the one by Van Gossum et al. (n=21) confirmed that WCE is superior to PE in its ability to identify bleeding abnormalities arising from the small bowel. However, in Van Gossum's study, more than two third of the cases had a proximal source of bleeding. In this situation a higher rate of detection for PE would be expected. The lesions were esophageal varices (n=2), reflux esophagitis (n=1), upper GI ulceration (n=9), tumor like angioma in the jejunum (n=1), intestinal angiodysplasia (n=4), ileal varices (n=1) and cecal angioectasia (n=1).

Liangpunsakul et al. conducted a study to compare the diagnostic yield of WCE to enteroclysis in detecting small bowel lesions in 40 patients (36 iron deficiency anemia and 4 chronic abdominal pain) (38). WCE found the potential sites of bleeding in 16 of 36 patients with chronic anemia (44%). Eight of those 36 patients with chronic anemia underwent PE with negative results while WCE found the potential bleeding sites in 6 of those cases. In one patient with chronic anemia, the capsule stayed in the same location for 120 minutes and a diagnosis of Meckel's diverticulum was made by repeat enteroclysis. The authors concluded that WCE may be more sensitive than the entroclysis in detecting small bowel ulcers.

Leighton et al. conducted a retrospective study to compare the diagnostic yield of WCE to CT and BFT (39). The study included 48 patients (41 GI bleeding, 3 IBD, 3 iron deficiency anemia and 1 chronic abdominal pain) and the imaging tests performed within 6 months of WCE examinations were reviewed. Twenty seven of 48 patients had a BFT and 15/48 had a CT with or without reconstruction. The WCE and BFT were both negative in 10/27 patients. In 16/27 patients WCE identified lesions not detected by BFT. In 1/27 patients BFT identified antral ulcer that was missed by WCE. CT identified one jejunal mass, but missed the findings in 10/15 patients. Overall, WCE identified many significant lesions missed by BFT and CT examinations.

OTHER ASPECTS OF WCE

Lewis et al. collected data regarding patient comfort and acceptance (24). The questionnaire included 16 questions concerning swallowing the capsule, pain or discomfort during and after the ingestion and questions regarding PE. An ordinal scale between 0 and 4 (higher numbers corresponding to greater comfort and acceptance) were used for each question. The results of the questionnaire are shown in table 11.

Table 11. Results of subjective assessment: WCE versus PE

	WCE (Average)	PE (Average)	p-value
Ease of swallowing/insertion	3.81	2.38	<0.001
Pain during procedure	3.81	2.95	0.003
Discomfort during procedure	3.95	3.10	<0.001
Pain after procedure	3.81	1.81	0.002
Discomfort after procedure	3.90	2.48	0.003
Overall impression	3.90	2.95	<0.001
Willingness to repeat the procedure	3.95	1.43	<0.001

Table 12 summarizes some additional aspects of WCE as compared to PE.

Table 12. Additional aspects: WCE versus PE

WCE	PE
Requires experienced gastroenterologist/radiologist	Requires experienced endoscopist
The patient can undertake daily activities	Requires 15-45 min in endoscopy room
No patient discomfort	Patient discomfort
No sedation or analgesia	Commonly requires sedation and analgesia
No disinfection required	Requires instrumental disinfection

TIME REQUIRED FOR VIEWING AND INTERPRETATION OF IMAGES

The time required to view and interpret the recorded data depends on the following factors:

1. Experience of the physician.
2. Transit time in the small intestine.
3. Number of images per second. The capsule transmits images at a rate of two frames per second for over 7 hours. This will produce over 50,000 images. However, with the recent software improvement, which allows combining one image with two images behind, the reading time has been reduced to half and it is currently estimated as 30-45 minutes.

STUDIES ON WCE IN CROHN'S DISEASE

The results of the two recently published studies have demonstrated the usefulness of WCE in suspected Crohn's disease [CD].

Fireman et al. evaluated the effectiveness of WCE in patients with suspected Crohn's disease undetected by conventional methods and determined the diagnostic yield of the WCE (40). All patients in this study had undergone small bowel x-ray and total colonoscopy with negative results. Ileoscopy had been performed only in six patients. Each capsule study was reviewed independently by two experts with 100% agreement between the two readers. Seventeen patients with suspected CD (mean age 40 years) underwent capsule examination. Twelve were diagnosed with CD of the small bowel (Diagnostic yield: 71%). There were no side effects to the procedure. In two patients, the recording stopped before entry into the colon, possibly because of slow transit time due to the inflammation in small bowel.

Eliakim et al. reported superior results for WCE in comparison to BFT and CT in patients with suspected Crohn's disease (41). Twenty patients (mean age 31 years) underwent BFT as their initial examination, followed by WCE and CT. Only 13 patients underwent entero-CT.

WCE identified lesions as "medically significant" in 14 of the 20 patients (Diagnostic yield 70%). Capsule findings included ulcer and erosions (36%), erythema (22%), aphthae (17%), absent or blunted villi (14%), and nodular lymphoid hyperplasia (5.6%). BFT and CT found abnormalities in 50% of the cases. The abnormalities included wall thickening (23%), nodularity in terminal ileum (17%), and ulcers (5.6%). These procedures identified lesions as "medically significant" in regard to the patient's complaints in 7 patients (diagnostic yield 35%). The abnormalities found in these 7 patients included nodularity of the terminal ileum, thickening of the terminal ileum/cecum/valve (22%), enlarged mesentric nodes (11%) and terminal ileitis (33%). WCE was found to be superior to the conventional radiological methods in establishing the diagnosis in patients with suspected Crohn's disease of the small bowel [70% vs 35%, $p<0.04$].

Colonoscopy and ileoscopy with biopsies confirmed WCE findings in 8 patients in which there were conteroversial results between WCE and radiological methods. WCE found all the lesions that were found by radiology. In addition, WCE confirmed radiological findings in 6 patients, extended the region of involvement in 3 patients, and ruled out the diagnosis of suspicious CD in 3 patients (all of which were confirmed by ileoscopy and biopsy). No adverse events were reported during or after WCE. There was full agreement between the two readers in 80% of cases.

WCE examination in Crohn's disease is currently being performed in research settings. The above studies are the only available data and no conclusion can therefore be made in regard to the usefulness of WCE in diagnostic work-up of patients with suspected Crohn's disease at this time. In addition, more studies are required to compare WCE to the ileoscopy in these patients.

SUMMARY AND CONCLUSION

- © Wireless capsule endoscopy is a truly innovative technology, which provides endoscopic Images of the GI tract.
- © The design of the WCE is suited for imaging the small bowel.
- © There has been a growing interest in capsule endoscopy studies and to date several studies have been published and large number of abstracts of the completed studies have been submitted to the scientific journals or academic meetings.
- © The enthusiasm for this new technology has increased with reports of its successful application in obscure GI bleeding.

- © Application of WCE in Crohn's disease is still under innvestigation and the results of the first two studies have been published in 2003.
- © WCE has been used in 25,000 patients world wide *(According to the Southmedic Inc)*.
- © The diagnostic performance of WCE has been documented through clinical trials in about 8,000 patients (40).
- © The data concerning application of the technology in pediatric population is scarce.
- © As a result of lack of a "Gold standard" to compare the diagnostic efficacy of WCE to an alternative technique, all the conducted studies have reported the "Diagnostic yield".

SAFETY

- © There are sufficient data for the feasibility of WCE examination.
- © The examination is done on an outpatient basis similar to the Holter monitoring.
- © Most of the authors have reported no difficulty in swallowing the capsule.
- © Most of the authors have confirmed the safety of WCE.
- © The complication rate for WCE is low, the main complication being that the capsule may become entrapped in a stricture or an obstructed area during its passage in GI tract.
- © There are reports showing that endoscopic removal has been required to remove entrapped capsule in cricopharyngeal and appendiceal stump.
- © There are reports showing that surgical removal of the entrapped capsule in unsuspected strictures became necessary.
- © The safety of WCE has not been tested in pregnant women.
- © There is no report of accidental leakage of the battery.
- © Overall, no serious complications have been reported.

CLINICAL INDICATIONS

- © To date, obscure GI bleeding is the most widely accepted indication for WCE examination.
- © Presently, the evidence is not sufficient to evaluate the effectiveness of WCE in Crohn's disease though recently, positive results have been published.
- © Currently, push enteroscopy is the standard approach to evaluate obscure GI bleeding.
- © WCE has performed well in trials of patients with obscure GI bleeding.
- © To date, a total of 286 WCE examination *(Two published studies and 9 clinical trials published in the form of abstracts)* have shown superior results for WCE in diagnosing a source of bleeding in small intestine as compared to the PE.
- © To date, only one study (n=21) demonstrated superior results for PE in diagnosing a source of bleeding in the small intestine as compared to the WCE. In this study, over two third of the patients had proximal source of bleeding.
- © WCE has produced superior results in diagnosing the source of bleeding in small intestine as compared to BFT.
- © The sensitivity and specificity of WCE as compared to PE has been studied in dogs because conducting such study in human is impossible.
  - The study showed higher sensitivity of PE within the reach of the push enteroscope, while the overall sensitivity of WCE was significantly higher than PE.
  - The greater overall sensitivity of WCE is because it has the ability to visualize the entire small bowel.
- © WCE has rarely been performed in pediatric population, yet there are ongoing trials to investigate the feasibility and usefulness of WCE in children with chronic diarrhea and malabsorption.

CONTRAINDICATIONS FOR USE

1. Narrowing, fistula formation or blockage in the intestine.
2. Diverticuli.
3. Implanted electromagnetic devices using radio frequency signals and cardiac pacemaker.

ADVANTAGES

© The entire small intestine can be imaged.
© Ease of use and non-invasiveness.
© WCE does not create discomfort for the patients, is well tolerated and does not require analgesia or sedatives.
© WCE does not require air inflation of the bowel.
© WCE does not carry the risk of perforation.
© The patients are free to continue their daily routine during the examination.
© Images can be viewed multiple times or by multiple clinicians.

DISADVANTEGES

© No biopsy or treatment-related procedures can be performed.
© Cannot be used in the presence of the stricture or stenosis.

PRACTICAL LIMITATIONS

© The exact site of the abnormal finding has been challenging. The M2A Plus has new features that help estimate the location of the capsule within 1-2 inches.
© In some patients, the capsule may not adequately image the entire small bowel as a result of variations in patient GI motility.
© Technical defects in the capsule and failure to transmit the data may occur very occasionally.

CONCERNS ABOUT WCE

© There is a concern that the capsule may tumble in the small bowel. Since images are obtained every 0.5 second, if the capsule happen to rotate along its long axis, the probability of missing the images of the small bowel mucosa would be minimal.
© There is a concern that visualization may be hampered by coating of the capsule with residue or intestinal mucosa. The quality of the images shows that the dome of the capsule is cleaned as it passes through the intestine. WCE examination requires bowel preparation.

CONCLUSION

© WCE is a technological break through that allows the entire small bowel to be examined.
© WCE provides quality color images of the intestinal mucosa, therefore, superficial and mucosal lesions such as ulcers, erosions, and arteriovenous malformations can be seen clearly.
© The technique has the potential to be adopted for a range of digestive system diseases. To date the main focus has been gastrointestinal bleeding originating in the small bowel.
© Presently, the evidence is not sufficient to evaluate the effectiveness of WCE in Crohn's disease but quite recently, some positive results have been published.

- © Other possible indications for WCE include inflammation and suspected enteric tumors.
- © The newly added feature, a blood-sensing algorithm allows the origin of bleeding to be identified.
- © The newly added Rapid Viewer system reduces the required time for reviewing the images by half (30-45 min).
- © Based on the available data, capsule endoscopy is indicated for use in the investigation of GI bleeding where the bleeding site is located in the small intestine and cannot be reached through upper or lower endoscopy.
- © WCE is recommended to be used as an adjunctive technique to upper and lower endoscopy and should always be preceded by these techniques.
- © A small bowel radiograph is necessary prior to the WCE examination to rule out the possibility of bowel stenosis or fistula.
- © WCE can help to reduce the number of diagnostic procedures in patients with chronic gastrointestinal bleeding and negative upper and lower GI endoscopies.
- © WCE has the potential to become the initial diagnostic choice in small bowel bleeding in selected patients.
- © The cost driver for economic evaluation of WCE to a large extent is the cost of disposable Capsule ($920).

BIBLIOGRAPHY

1. Chen RY, Taylor AC, Desmond PV. Push enteroscopy: a single centre experience and review of published series. ANZ J Surg. 2002 Mar;72(3):215-8.

1. Maglinte DD, O'Connor K, Bessette J, Chernish SM, Kelvin FM. The role of physician in the late diagnosis of primary malignant tumors of the small intestine. Am J Gastroenterol 1991;86:304-8.

3. Szold A, Katz LB, Lewis BS. Surgical approach to occult gastrointestinal bleeding. Am J Surg. 1992;163:90-93.

4. Van Gossum A. Obscure digestive bleeding. Best Pract Res Clin Gastroenterol. 2001 Feb;15(1):155-74.

5. Rossini FP, Pennazio M. Small-bowel endoscopy. Endoscopy. 2000 Feb;32(2):138-45.

6. Cellier C, Tkoub M, Gaudric M, Guimbaud R, Auroux J, Chaussade S, Couturier D, Barbier JP, Landi B. Comparison of push-type endoscopy and barium transit study of the small intestine in digestive bleeding and unexplained iron-deficiency anemia. Gastroenterol Clin Biol. 1998 May;22(5):491-4.

7. Goldfarb NI, Phillips A, Conn M, Lewis BS, Nash DB. Economic and health outcomes of capsule endoscopy: Opportunities for improved management of the diagnostic process for obscure gastrointestinal bleeding. Disease management 2002. 5(3);123-35.

8. Hayat M, Axon AT, O'Mahony S. Diagnostic yield and effect on clinical outcomes of push enteroscopy in suspected small-bowel bleeding. Endoscopy. 2000 May;32(5):369-72.

9. Crichlow RW, Mosenthal WT, Spiegel PK, House RK. Arteriovenous malformations of the bowel: an obscure cause of bleeding. Am J Surg. 1975 Apr;129(4):440-8.

10. Ell C, Remke S, May A, Helou L, Henrich R, Mayer G. The first prospective controlled trial comparing wireless capsule endoscopy with push enteroscopy in chronic gastrointestinal bleeding. Endoscopy. 2002 Sep;34(9):685-9.

11. Lewis BS. Enteroscopy. Gastrointest Endosc Clinics North Am 2000. 10(1); 101-16.

12. Scapa E, Jacob H, Lewkowicz S, Migdal M, Gat D, Gluckhovski A, Gutmann N, Fireman Z. Initial experience of wireless-capsule endoscopy for evaluating occult gastrointestinal bleeding and suspected small bowel pathology. Am J Gastroenterol. 2002 Nov;97(11):2776-9.

13. Ghosh S, Watts D, Kinnear M. Management of gastrointestinal haemorrhage. Postgrad Med J. 2002 Jan;78(915):4-14.

14. Cave DR, Cooley JS. Intraoperative enteroscopy. Indications and techniques. Gastrointest Endosc Clin N Am. 1996 Oct;6(4):793-802.

15. Robb RA. Virtual endoscopy: development and evaluation using the Visible Human datasets. Comput Med Imaging Graph. 2000 May-Jun;24(3):133-51.

16. Schreyer AG, Herfarth H, Kikinis R, Seitz J, Scholmerich J, Geissler A, Feuerbach S.

3D modeling and virtual endoscopy of the small bowel based on magnetic resonance imaging in patients with inflammatory bowel disease. Invest Radiol. 2002 Sep;37(9):528-33.

17. Fockens P. Future developments in endoscopic imaging. Best Pract Res Clin Gastroenterol. 2002 Dec;16(6):999-1012.

18. Appleyard M, Fireman Z, Glukhovsky A, Jacob H, Shreiver R, Kadirkamanathan S, Lavy A, Lewkowicz S, Scapa E, Shofti R, Swain P, Zaretsky A. A randomized trial comparing wireless capsule endoscopy with push enteroscopy for the detection of small-bowel lesions. Gastroenterology. 2000 Dec;119(6):1431-8.

19. Zuckerman GR, Prakash C, Askin MP, Lewis BS. AGA technical review on the evaluation and management of occult and obscure gastrointestinal bleeding. Gastroenterology. 2000 Jan;118(1):201-21.

20. Voeller GR, Bunch G, Britt LG. Use of technetium-labeled red blood cell scintigraphy in the detection and management of gastrointestinal hemorrhage. Surgery. 1991 Oct;110(4):799-804.

21. [No authors listed]. American Gastroenterological Association medical position statement: evaluation and management of occult and obscure gastrointestinal bleeding. Gastroenterology. 2000 Jan;118(1):197-201.

22. Iddan G, Meron G, Glukhovsky A, Swain P. Wireless capsule endoscopy. Nature. 2000 May 25;405(6785):417.

23. Applyard m, Glukhovsky A, Swain P. Wireless capsule diagnostic endoscopy for recurrent small bowel bleeding. N Engl J Med 2002. 344(3);232-33.

24. Lewis BS, Swain P. Capsule endoscopy in the evaluation of patients with suspected small intestinal bleeding: Results of a pilot study. Gastrointest Endosc. 2002 Sep;56(3):349-53.

25. Costamagna G, Shah SK, Riccioni ME, Foschia F, Mutignani M, Perri V, Vecchioli A, Brizi MG, Picciocchi A, Marano P. A prospective trial comparing small bowel radiographs and video capsule endoscopy for suspected small bowel disease. Gastroenterology. 2002 Oct;123(4):999-1005.

26. Lingenfelser T, Ell C. Lower intestinal bleeding. Best Pract Res Clin Gastroenterol. 2001 Feb;15(1):135-53.

27. Beejay UA, Haber GB, Rasul I, et al. A pilot trial comparing the diagnostic utility and reproduceability of Given Diagnostic Imaging System to conventional enteroscopy in the evaluation of chronic obscure gastrointestinal bleeding. AJG September Suppl 2002;S299.

28. Van Gossum A, Francois E, Schmit A, Deviere J. A prospective comparative study between push enteroscopy and wireless video capsule in patients with obscure digestive bleeding. Gastrointest Endosc 2002; 55(5): AB88.

29. Demedts I, Gevers AM, Hiele M, et al. Wireless capsule enteroscopy is superior to push enteroscopy for identification of small intestinal source of obscure gastrointestinal bleeding. Gastrointest Endosc 2002; 55(5): AB146.

30. Yousufi M, Sharma V, Leighton J, et al. Video capsule endoscopy (VCE) for obscure gastrointestinal bleeding (OGIB) and iron deficiency anemia (IDA). First Given conference on capsule endoscopy, Rome, 2002. P 17-9.

31. Selby W, Shackel N. A comparison between the M2A capsule and push enteroscopy for the investigation of obscure gastrointestinal bleeding. J Gastroenterol Hepatol September 2001;16 (Suppl 11) - [First Given conference on capsule endoscopy, Rome, 2002. P 17-9].

32. Pennazio M, Santucci R, Rondonotti E, et al. Wireless capsule endoscopy in patients with obscure gastrointestinal bleeding: results of the Italian multicentre experience. First Given conference on capsule endoscopy, Rome, 2002. P 17-9.

33. Remke S, Helou L, Mayer G, Ell C. Wireless capsule endoscopy and push enteroscopy in chronic gasrointestinal bleeding: A prospective controlled trial. Gastrointest Endosc 2002; 55(5): AB125.

34. Delvaux MM, Saurine JC, Gaudin J et al. Comparison of wireless endoscopic capsule and push enteroscopy in patients with obscure occult/overt digestive bleeding: results of a prospective, blinded, multicentre trial. Gastrointest Endosc 2002; 55(5): AB88.

35. Mylonaki M, Fritscher-Ravens A, Swain PC. Clinical results of wireless capsule endoscopy. Gastrointest Endosc 2002; 55(5): AB146.

36. Lim RM, O'Loughlin CJ, Barkin JS. Comparison of wireless capsule endoscopy (M2A) with push enteroscopy in the evaluation of obscure gastrointestinal bleeding. AJG September Suppl 2002;S83.

37. Rossini FP, Pennazio M, Santucci R, et al. Early experience with wireless capsule diagnostic endoscopy patients with small bowel bleeding. AJG September Suppl 2002;S111.

38. Liangpunsakul S, Chadalawada V, Maglint D, et al. Wireless capsule endoscopy detects small bowel ulcers in patients with state of the art normal enteroclysis. AJG September Suppl 2002;S80.

39. Leighton JA, Sharma VK, Hara AK. Video capsule endoscopy (CE) compared to small bowel follow through (SBFT) and abdominopelvic CT scan (CT) for detecting lesions in the small intestine (SI). AJG September Suppl 2002;S80.

40. Fireman Z, Mahajna E, Broide E, Shapiro M, Fich L, Sternberg A, Kopelman Y, Scapa E. Diagnosing small bowel Crohn's disease with wireless capsule endoscopy. Gut 2003. Mar;52(3):390-2.

41. Eliakim R, Fischer D, Suissa A, Yassin K, Katz D, Guttman N, Migdal M. Wireless capsule video endoscopy is a superior diagnostic tool in comparison to barium follow-through and computerized tomography in patients with suspected Crohn's disease. Eur J Gastroenterol Hepatol. 2003 Apr;15(4):363-7.

APPENDICES

LIST OF ABBREVIATIONS

BFT	Barium follow-through
CD	Crohn's disease
CGB	Chronic gastrointestinal bleeding
CT	Computerized tomography
FDA	Food and Drug Administration
FOB	Fecal occult blood
GI	Gastrointestinal
IDA	Iron deficiency anemia
PE	Push enteroscopy
RAPID	Reporting and Processing of Images and Data

CAPSULE ENDOSCOPY PUBLICATION REFERENCE LIST
UPDATED 4/1/2003

Year	Author	Title	Journal
2003	Hartmann D, Schilling D, Rebel M, Zender F, Hahne M, Adamek HE, Riemann JF.	Diagnosis of a high-grade B-cell lymphoma of the small bowel by means of wireless capsule endoscopy	Z Gastroenterol 2003 Feb;41(2):171-4
2003	Becker C.	And now, live from your lower intestine...capsule endoscope proves to be a breakthrough tool for gastrointestinal diagnoses, with the pill often removing the need for some painful procedures.	Mod Health 2003 Feb 10;33(6):50-2, 54
2003	Soares J, Lopes L, Villas-Boas G, Pinho C	Ascariasis observed by wireless-capsule endoscopy.	Endoscopy 2003 Feb;35(2):194
2003	Nageshwar Reddy D, Sriram PV, Rao GV, Bhaskar Reddy D.	Capsule endoscopy appearances of small-bowel tuberculosis.	Endoscopy 2003 Jan;35(1):99
2003	Van Gossum	Capsule endoscopy in patients with obscure GI bleeding.	Gastrointest Endosc. 2003 Apr;57(4):629
2003	Stiffler HL.	Capsule endoscopy: a case study of an 11-year-old girl.	Gastroenterol Nurs 2003 Jan-Feb;26(1):38-40
2003	Fireman Z, Mahajna E, Broide E, Shapiro M, Fich L, Sternberg A, Kopelman Y, Scapa E.	Diagnosing small bowel Crohn's disease with wireless capsule endoscopy.	Gut 2003 Mar;52(3):390-2
2003	Levin B, Brooks D, Smith RA, Stone A.	Emerging technologies in screening for colorectal cancer: CT colonography, immunochemical fecal occult blood tests, and stool screening using molecular markers.	CA Cancer J Clin 2003 Jan-Feb;53(1):44-55
2003	Hollerbach S, Kraus K, Willert J, Schulmann K, Schmiegel W.	Endoscopically assisted video capsule endoscopy of the small bowel in patients with functional gastric outlet obstruction.	Endoscopy 2003 Mar;35(3):226-9
2003	Jonnalagadda S, Prakash C.	Intestinal strictures can impede wireless capsule enteroscopy	Gastrointest Endosc 2003 Mar;57(3):418-20
2003	Waye JD.	Small-bowel endoscopy.	Endoscopy 2003 Jan;35(1):15-21
2003	Fleischer DE, Heigh RI, Nguyen CC, Leighton JA, Sharma VK, Musil D.	Videocapsule impaction at the cricopharyngeus: A first report of this complication and its successful resolution.	Gastrointest Endosc 2003 Mar;57(3):427-8
2003	Mascarenhas-Saraiva M, Lopes L, Mascarenhas-Saraiva A.	Watermelon stomach seen by wireless-capsule endoscopy.	Endoscopy 2003 Jan;35(1):100

2003	Eliakim, Rami	Wireless Capsule video endoscopy is a superior diagnostic tool compared to barium follow through and computerized tomography in patients with suspected crohn's disease	Eur J Gastroenterol Hepatol. 2003 Apr;15(4):363-7
2002	Hahne M, Riemann JF.	Inflammatory bowel diseases: diagnosis (including new procedures for small intestine examination)	Schweiz Rundsch Med Prax 2002 Nov 20;91(47):2023-8
2002	Yamaki G, Higashi K.	Mass screening of gastric cancer--limits and prospects	Gan To Kagaku Ryoho 2002 Nov;29(11):1883-7
2002	Caunedo Alvarez A, Rodriguez-Tellez M, Barroso Relinque N, Garcia Montes JM, Pellicer Bautista FJ, Herrerias Gutierrez JM.	Role of capsule endoscopy in the management of patients with obscure gastrointestinal bleeding	Rev Esp Enferm Dig 2002 Aug;94(8):482-92
2002	Fork FT, Toth E, Benoni C.	The enteroscopy capsule--a swallowable instrument for video examination of the small bowel	Lakartidningen 2002 Nov 28;99(48):4842-6
2002	Rosch T, Ell C.	Topical clinical indications for capsule endoscopy -- a paper by the Endoscopy Section of DGVS as of 1.11.2002	Z Gastroenterol 2002 Dec;40(12):971-8
2002	Danielsson A, Suhr O.	Video capsule--a promising "bean"	Lakartidningen 2002 Nov 28;99(48):4830-2
2002	Barouk J, Sacher-Huvelin S, Le Rhun M, Galmiche JP.	Wireless capsule endoscopy: a promising technology?	Gastroenterol Clin Biol 2002 Oct;26(10):879-82
2002	Costamagna G.	A Prospective Trial Comparing Small Bowel Radiographs and Video Capsule Endoscopy for Suspected Small Bowel Disease	Gastroenterology October 2002
2002	Seitz U, Bohnacker S, Soehendra N.	A simple method to determine the location of the capsule and thus whether prokinetic drugs are needed during video capsule endoscopy.	Endoscopy 2002 Dec;34(12):1027
2002		Capsule endoscopy	Clin Privil White Pap 2002 Jul;(203):1-12
2002	LewisB., Swain P.	Capsule Endoscopy in the evaluation of Patients with suspected Small Intestine Bleeding: The Results of a Pilot Study	Gastrointestinal Endoscopy Sept 2002
2002	Fleischer	Capsule Endoscopy: The Voyage is Fantastic- Will it change what we do?	Gastrointestinal Endoscopy Sept 2002 Vol 56 No 3
2002	Sung JJ.	Changing role of endoscopy in the new millennium. Bushell Lecture, Asia-Pacific Digestive Week 2001	J Gastroenterol Hepatol 2002 Apr;17(4):369-73

2002	Faigel D., Fennerty	Cutting the Cord for Capsule Endoscopy	Gastroenterology Oct 2002 Vol 123 No 4
2002	Goldfarb N, Phillips A., et al	Economic and Health Outcomes of Capsule Endoscopy: Opportunities for Improved Management of the Diagnostic Process for Obscure Bleeding	Disease Management Sept 2002
2002	Lee SD, Cohen RD.	Endoscopy of the small bowel in inflammatory bowel disease.	Gastrointest Endosc Clin N Am 2002 Jul;12(3):485-93
2002	Lewis BS.	Enteroscopy: endangered by the capsule?	Endoscopy 2002 May;34(5):416-7
2002	Scapa E, Herbert M, Fireman Z.	First histologic confirmation of the diagnosis made by the new wireless-capsule endoscopy	Surg Laparosc Endosc Percutan Tech 2002 Oct;12(5):364-6
2002	Adamek HE, Hartmann D, Hahne M, Schilling D, Riemann JF	In Process	MMW Fortschr Med 2002 Dec 17;144(51-52):34-5
2002	Scapa E, Jacob H, Lewkowicz S, Migdal M, Gat D, Gluckhovski A, Gutmann N, Fireman Z.	Initial experience of wireless-capsule endoscopy for evaluating occult gastrointestinal bleeding and suspected small bowel pathology.	Am J Gastroenterol 2002 Nov;97(11):2776-9
2002	Gay G., Delvaus M	Localization of colonic origin of obscure bleeding with capsule endoscope; a case report	Gastrointestinal Endoscopy Nov 2002 vol 56, No 5
2002	Yu, Marcia	M2A Capsule Endoscopy, A Breakthrough Diagnostic tool for Small Intestine Imaging	Gastroenterology Nursing 2002 Vol 25, No1
2002	Nelson DB.	New technology in the endoscopy center	Gastrointest Endosc Clin N Am 2002 Apr;12(2):325-34
2002	Tang SJ, Jutabha R, Jensen DM.	Push enteroscopy for recurrent gastrointestinal hemorrhage due to jejunal anastomotic varices: a case report and review of the literature	Endoscopy 2002 Sep;34(9):735-7
2002	Rossini FP	Quo vadis capsule endoscopy?	Dig Liver Dis 2002 Aug;34(8):537-9
2002	Kovacs TO, Jensen DM.	Recent advances in the endoscopic diagnosis and therapy of upper gastrointestinal, small intestinal, and colonic bleeding.	Med Clin North Am 2002 Nov;86(6):1319-56
2002	Rossini FP, Pennazio M.	Small-bowel endoscopy.	Endoscopy 2002 Jan;34(1):13-20
2002	Ell C., Remke S., et al	The First Prospective Controlled Trial Comparing Wireless Capsule Endoscopy with Push Enteroscopy in Chronic Gastrointestinal Bleeding.	Endoscopy 2003 34(9): 685-689
2002	Cappell MS, Friedel D.	The role of esophagogastroduodenoscopy in the diagnosis and management of upper gastrointestinal disorders.	Med Clin North Am 2002 Nov;86(6):1165-216

2002	Fritscher-Ravens A, Swain CP.	The wireless capsule: new light in the darkness.	Dig Dis 2002;20(2):127-33
2002	Mylonaki M, MacLean D, Fritscher-Ravens A, Swain P.	Wireless Capsule Endoscopic Detection of Meckel's Diverticulum after Nondiagnostic Surgery.	Endoscopy 2002 Dec;34(12):1018-20
2002	Hahne M, Adamek HE, Schilling D, Riemann JF.	Wireless capsule endoscopy in a patient with obscure occult bleeding.	Endoscopy 2002 Jul;34(7):588-90
2002	Fireman Z, Glukhovsky A, Jacob H, Lavy A, Lewkowicz S, Scapa E.	Wireless capsule endoscopy.	Isr Med Assoc J 2002 Sep;4(9):717-9
2002	Ginsberg GG, Barkun AN, Bosco JJ, Isenberg GA, Nguyen CC, Petersen BT, Silverman WB, Slivka A, Taitelbaum G.	Wireless capsule endoscopy: August 2002	Gastrointest Endosc 2002 Nov;56(5):621-4
2002	Rabenstein T, Krauss T, et al	Wireless Capsule Endoscopy-Beyond the Frontiers of Flexible Gastrointestinal Endoscopy	Med. Sci. Monitor 2002, 8(6): RA 128-132
2002	Bar-Meir S, Bardan E.	Wireless capsule endoscopy--pros and cons.	Isr Med Assoc J 2002 Sep;4(9):726
2002	Gonzalez-Suarez B, Guarner C, Escudero JR, Viver E, Palmer J, Balanzo J.	Wireless capsule video endoscopy: a new diagnostic method for aortoduodenal fissure.	Endoscopy 2002 Nov;34(11):938
2002	Seidman EG	Wireless capsule video-endoscopy: an odyssey beyond the end of the scope	J Pediatr Gastroenterol Nutr 2002 Apr;34(4):333-4
2002	Cave D	Wireless Video Capsule Endoscopy	Clinical Perspectives in Gastroenterology July/Aug 2002
2001	Mosse CA, Mills TN, Appleyard MN, Kadirkamanathan SS, Swain CP.	Electrical stimulation for propelling endoscopes	Gastrointest Endosc 2001 Jul;54(1):79-83
2001	Gilger MA.	Gastroenterologic endoscopy in children: past, present, and future	Curr Opin Pediatr 2001 Oct;13(5):429-34
2001	Waye JD.	Small-intestinal endoscopy	Endoscopy 2001 Jan;33(1):24-30
2001	Stiefelhagen P.	Video images from the small intestine. A capsule delivers better results than currend endoscopy	MMW Fortschr Med 2001 May 17;143(20):20
2001		Wireless capsule endoscopy in obscure digestive tract bleeding	Tecnologica MAP Suppl 2001 Dec 6;:42-3

2001	Barroso Relinque N, Caunedo Alvarez A, Rodriguez Tellez M, Herrerias Esteban JM, Pellicer Bautista F, Herrerias Gutierrez JM.	Wireless endoscopy	Rev Esp Enferm Dig 2001 Sep;93(9):598-605
2001	Appleyard M, Glukhovsky A, Swain P.	Wireless-capsule diagnostic endoscopy for recurrent small-bowel bleeding	N Engl J Med 2001 Jan 18;344(3):232-3
2000	Appleyard M, Fireman Z, Glukhovsky A, Jacob H, Shreiver R, Kadirkamanathan S, Lavy A, Lewkowicz S, Scapa E, Shofti R, Swain P, Zaretsky A.	A randomized trial comparing wireless capsule endoscopy with push enteroscopy for the detection of small-bowel lesions	Gastroenterology 2000 Dec;119(6):1431-8
2000	Bradbury J.	Journey to the centre of the body	Lancet 2000 Dec 16;356(9247):2074
2000	Meron GD.	The development of the swallowable video capsule (M2A	Gastrointest Endosc 2000 Dec;52(6):817-9
2000	Iddan G, Meron G, Glukhovsky A, Swain P.	Wireless capsule endoscopy	Nature 2000 May 25;405(6785):417
2000	Gong F, Swain P, Mills T.	Wireless endoscopy	Gastrointest Endosc 2000 Jun;51(6):725-9