

Issue 106 • October 2007

Summary

- ✓ **The PillCam[®] Colon capsule is an ingestible miniature camera that captures images of the colon's inner lining.**
- ✓ **There is limited evidence on the use of this technology in imaging the colon. Two small, methodologically flawed pilot studies found that for patients with positive findings (i.e., abnormalities detected), the rates of detection with the PillCam Colon capsule were similar to those obtained with conventional colonoscopy.**
- ✓ **No serious adverse events were reported in the pilot studies, although some patients had delayed excretion of the capsule.**
- ✓ **A challenge for clinicians using this technology will be the time required to read the large quantity of video images produced. Further enhancements to the software system used to view the images may address this issue.**

Background

Capsule endoscopy, also called video or wireless capsule endoscopy, has been available in Canada since about 2001 for the diagnosis of gastrointestinal disorders, such as obscure bleeding.¹ Its primary indication is the imaging of areas in the small bowel that are inaccessible through upper or lower endoscopy. Developments in the technology have resulted in products that are designed for use in imaging the small bowel, esophagus, and colon. The development of a capsule intended for imaging the colon may raise questions similar to those that arose with “virtual” colonoscopy, particularly with respect to the PillCam’s role in detecting or screening for colorectal disease.

The Technology

The PillCam[™] Colon is a disposable capsule, about the size of a large vitamin pill, with miniature

cameras at each end. The cameras capture four images per second or 144,000 images over a 10-hour period as the capsule travels through the digestive system. The physician downloads the transmitted data to a computer workstation to view the images. As with other types of virtual colonoscopy (e.g., computed tomography colonography), if abnormalities are detected, further diagnostic workup (e.g., conventional colonoscopy) is needed to allow for simultaneous removal of polyps and subsequent biopsy. As with colonoscopy, patients undergo colon preparation and bowel cleansing before the capsule examination.



Image courtesy of
Southmedic Inc.

PillCam[®] Colon

Regulatory Status

The PillCam Colon (Given Imaging Ltd., Yoqneam, Israel) received a medical device licence from Health Canada in January 2007. The Given Imaging diagnostic workstation and software used to view the images are also licensed for use in Canada.² The company expects to receive US Food and Drug Administration (FDA) regulatory approval in 2007.³

Patient Group

Colorectal cancer is the second leading cause of death due to cancer in Canada.⁴ An estimated 20,800 new cases of colorectal cancer will be diagnosed in Canada in 2007, and 8,700 Canadians will die from this disease.⁴ The Canadian National Committee on Colorectal Cancer Screening recommends that all Canadians 50 to 74 years of age (approximately 8.3 million people) have a fecal occult blood test (FOBT) to screen for colorectal cancer every one or two years.⁵ This screening test is used to check the stool for blood. Initially, the main patient group for capsule colonoscopy would likely be a small subset of

individuals who have positive or suspicious test results from routine colorectal cancer screening that cannot be adequately investigated with conventional colonoscopy, or those who cannot undergo conventional colonoscopy, such as frail elderly patients; pregnant women; and patients with suspected bowel obstruction, perforation, or inflammation of the colon.

Current Practice

Individuals with positive FOBT results are followed up with conventional colonoscopy for direct imaging of the colon. Patients with symptoms of colorectal cancer, such as rectal bleeding, weight loss, or changes in bowel movements, are also evaluated using colonoscopy. Colonoscopy involves insertion of a long, flexible, lighted tube into the patient's rectum and through the colon. Patients are usually sedated for the 20- to 30-minute procedure. A video chip in the colonoscope transmits an image of the lining of the colon to a monitor. If an abnormality is detected, the doctor can remove it or take tissue samples using instruments passed through the colonoscope. Other technologies used to obtain images of the colon's inner lining include flexible sigmoidoscopy and barium enema combined with x-rays. Flexible sigmoidoscopy is similar to colonoscopy, but a shorter device is used to examine the left colon, and sedation is often not required.

The Evidence

A literature search from 2002 to 2007 identified two small studies, both of which were supported by Given Imaging Ltd.^{6,7} Both studies evaluated PillCam Colon capsule endoscopy using conventional colonoscopy as the gold standard for diagnosing colonic pathology. Conventional colonoscopy was performed on the same day as the capsule study, after excretion of the capsule or by the end of the day.

The first trial was a single-centre, prospective pilot study of 41 adults (including individuals with or without a personal or family history of polyps or cancer) who were scheduled for colonoscopy, for colorectal cancer screening or for unexplained abdominal pain or symptoms such as rectal bleeding.⁶ Five patients were excluded during the study (four because of technical problems and one because of an inability to swallow the capsule). The capsule endoscopy and colonoscopy procedures were conducted independently by two physicians. Both physicians were blinded regarding the other set of test results. The results from 36 patients were reported. The positive findings of capsule endoscopy were similar to those of colonoscopy (Table 1). The positive predictive values for detecting three or more polyps and polyps larger than 6 mm were 36% and 46% respectively, because of a high rate of false-positives. In six patients (16%), the capsule was not expelled after the end of recording time (10 hours) and was retrieved during colonoscopy. Complete visualization of the colon was not achieved in 16% of patients because of insufficient capsule battery life.

The second trial was a larger, multi-centre, prospective pilot study of 91 adult patients who were suspected of having colonic disease and referred for colonoscopy or referred for colonoscopy for colorectal cancer screening.⁷ Seven patients were excluded during the study. One patient was unable to swallow the PillCam; two patients did not follow the colon preparation procedures; in one patient, the capsule stayed in the stomach during the examination; and in three cases, the capsule failed to record or progress during the allotted imaging time. The results from 84 patients were reported (Table 1). Each test was read three times. After the first 44 patients were tested, a second dose of oral sodium phosphate was added to the regimen to enhance excretion of the capsule. This additional dose increased the capsule excretion rate at 10 hours post-ingestion to 78%.

Table 1: Comparison of PillCam Colon capsule endoscopy with conventional colonoscopy for any findings*

	Schoofs <i>et al.</i> ⁶ n=36 (%)	Eliakim <i>et al.</i> ⁷ n=84 [†] (%)
sensitivity [‡]	76	56
specificity ^{**}	64	69
positive predictive value ^{††}	83	57
negative predictive value ^{‡‡}	54	67

* Any findings = any size of polyp; [†] Results at principal investigator (first) reading; [‡] Proportion of individuals with disease who test positive; ^{**} Proportion of individuals without disease who test negative; ^{††} Proportion of individuals with positive test results who have the condition; ^{‡‡} Proportion of individuals with negative test results who do not have the condition

The results in Table 1 are based on the first reading (by the principal investigator) rather than the third reading (by a review panel of all three investigators). For patients with significant findings, the positive results of PillCam Colon endoscopy were similar to those of colonoscopy. Colonoscopy is an imperfect gold standard, but the low negative predictive values reported in the two studies indicate that the PillCam Colon would also miss many abnormalities. Variations in the results of the three readings may reflect the learning curve of physicians for reading capsule endoscopy images.

Adverse Effects

No capsule endoscopy-related adverse effects were reported in either of the two studies. Contraindications for capsule endoscopy include pregnancy, swallowing disorders, bowel obstruction, and implantable medical devices such as cardiac pacemakers or defibrillators. Patients who do not excrete the capsule naturally may need an additional dose of laxatives, a suppository, or colonoscopic capsule retrieval.

Administration and Cost

Patients undergo colon preparation similar to that for colonoscopy (e.g., clear liquids only and ingestion of a polyethylene glycol solution the day before the examination). On the morning of the examination, the patient drinks another litre of polyethylene glycol and then ingests the capsule orally with a glass of water. [In the second study, patients were also given a 6 mg dose of tegaserod (Zelnorm) before capsule ingestion.⁷] Osmotic cleansing agents (laxatives), such as sodium phosphate, are used to enhance capsule excretion. Sedation is not required.

In the first pilot study, the mean time required for the physician to read the capsule endoscopy images was 62 minutes (range 45 to 90 minutes).⁶ In the second study, the reading times were not recorded but were estimated to be approximately 40 minutes each.⁷

The current list price for the PillCam Colon is C\$1,000 (Derek McGowan, Southmedic Incorporated, Barrie, ON: personal communication 2007 Jul 26). The procedure is estimated to cost about C\$2,000.⁸ It is unclear what is included in this estimate, though it likely includes the cost of the PillCam capsule. In comparison, a 2005 study, based on Alberta health care costs, estimated the mean

direct cost of a diagnostic colonoscopy at \$546.64. A colonoscopy including polypectomy had a mean direct cost of \$667.66. These estimates included costs of physician and nursing services, medical supplies and drugs, equipment cleaning, and overhead.⁹

Concurrent Developments

Virtual colonoscopy is another alternative to endoscopic colon imaging. This procedure can be performed using computed tomography (CT colonography) or magnetic resonance imaging (MR colonography). After bowel preparation, the colon is inflated with air or fluid, and a scan of the abdomen is performed to produce a series of two-dimensional cross-sections along the colon. A computer program can also construct three-dimensional images. The examination takes about 10 to 20 minutes (with additional time for the radiologist's review) and does not require sedation. If abnormalities are detected, the patient will need conventional colonoscopy for follow-up.

Rate of Technology Diffusion

The anticipated rate of technology diffusion in Canada is still unknown. According to the Canadian distributor, two Toronto centres are currently awaiting delivery of their systems (Derek McGowan, Southmedic Incorporated, Barrie, ON: personal communication 2007 Jul 26). The application of this technology may expand to broader use in colorectal cancer screening, depending on provincial reimbursement decisions and whether more compelling evidence emerges to support this use. The PillCam Colon will not replace colonoscopy, because any abnormal finding would require further investigation using colonoscopy.

Implementation Issues

The evidence to support the use of this technology for diagnostic purposes is limited, consisting of small, methodologically flawed studies that were funded by the manufacturer. Larger, multi-centre trials that compare capsule endoscopy with colonoscopy are needed. The evidence to support the use of capsule endoscopy in screening for colorectal cancer is also lacking. Physicians will need training to ensure an accurate interpretation of the capsule endoscopy video images. Viewing the capsule endoscopy images is time-consuming, and this has been an issue with earlier versions of the technology. Further

enhancements to the software system used to view the images produced by the capsule may reduce the time involved.¹⁰

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Cite as: Tran K. *Capsule colonoscopy: PillCam® Colon* [Issues in emerging health technologies issue 106]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2007.

Thanks to Raymond Banks, Information Specialist for this bulletin.

CADTH takes sole responsibility for the final form and content of this bulletin. The statements and conclusions in this bulletin are those of CADTH and not those of advisory committee members or its reviewers.

CADTH thanks the external reviewers who kindly provided comments on an earlier draft of this bulletin. Reviewers: **John K. Marshall, MD, MSc, FRCPC**, McMaster University, **Laura Targownik, MD, MSHS**, University of Manitoba.

Production of this report is made possible by financial contributions from Health Canada and the governments of Alberta, British Columbia, Manitoba, New Brunswick, Newfoundland and Labrador, Northwest Territories, Nova Scotia, Nunavut, Ontario, Prince Edward Island, Saskatchewan, and Yukon. The Canadian Agency for Drugs and Technologies in Health takes sole responsibility for the final form and content of this report. The views expressed herein do not necessarily represent the views of Health Canada or any provincial or territorial government.

ISSN 1488-6324 (online)
ISSN 1488-6316 (print)
PUBLICATIONS MAIL AGREEMENT NO: 40026386
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TECHNOLOGIES IN HEALTH
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