Gastrointestinal Imaging: The Pillcam Or Traditional Methods?

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ABSTRACT
A review of the modern imaging on the human body, by the use of a "PillCam" This is a pill that can take pictures inside the body, revolutionizing medical diagnoses.

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INTRODUCTION
Imaging the digestive tract is costly for the health service provider, traumatic for the patient and demanding in that it necessitates highly trained professionals to be present for the procedure. The process typically involves the patient having to self-administer an unpleasant bowel preparation the night before and then undergo sedation before having a flexible tube inserted into the body via either the rectum or the mouth. The doctor will observe on a nearby screen for any abnormalities. If an irregularity is found, the patient may then return to the hospital after yet another bowel preparation, undergo another sedation and have this aberration removed. This procedure can incur complications, which might include bleeding and bowel wall perforation, both of which can be costly and threatening to treat (Palimaka, Blackhouse and Goeree, 2015). Thankfully, PillCam Colon (Given Imaging Ltd, Yoqneam, Israel), has been available since 2001 (Kwack and Lim, 2016), and has transformed this entire process.

The process of capsule endoscopy is referred to by various names, including Capsule Colon Endoscopy (CCE), Video Capsule Endoscopy (VCE), and Capsule Endoscopy (CE). When used for esophageal examination, it is referred to as Esophageal Capsule Endoscopy (ECE). While patients predominantly prefer the video capsule process to the standard 'tube in the body,' it is not flawless and not always diagnostically desirable. This paper will compare PillCam to other investigations such as an endoscopy (used for the upper gastrointestinal tract) and a colonoscopy (used for the lower gastrointestinal tract), all of which are used to diagnose various gastrointestinal disorders.

MECHANISM OF ACTION
The PillCam weighs 3.7 grams and measures 11 mm by 26 mm. It contains an imaging chip video camera, six LEDs, two silver-oxide batteries, and a radio transmitter’ (Pillcamcrohns.com, 2017, How PillCam SC Capsule Works). Users, who can be aged two years or older, swallow the pill which then takes pictures of the gastrointestinal tract while in transit, typically an 8.5-hour process, and the camera is excreted naturally. Patients must fast overnight but can continue with normal activity and can eat four hours after ingesting the capsule. The images are collected at the rate of two images per second (around 50,000 images upon completion), and are all transmitted to a recorder worn by the patient and then assessed by the doctor, who does not need to be present for administration of the PillCam (Palimaka, Blackhouse and Goeree, 2015).

COMPARISON OF IMAGING CAPSULES TO ENDOSCOPY AND COLONOSCOPY
Since the inception of the PillCam, a variety of small-bowel capsules have entered the market and
include (but are not limited to) PillCam (Israel), EndoCapsule (Japan), MiroCam (Korea), OMOM (China) and CapsoCam (USA) (Kwack and Lim, 2016). It is interesting to note that in a study conducted by Höög et al., (2012) to see if any one capsule outperformed the others, 2300 capsule enteroscopy procedures, performed in four hospitals in Sweden from 2003 to 2009, were examined. Results showed that the highest rate of completed examinations occurred with the PillCam. Many studies have been conducted to compare the findings of PillCam (or other video capsule endoscopies) to traditional endoscopies. The National Institute for Health and Care Excellence (NICE) Guidelines (2004) suggest using the PillCam for investigating the small bowel, particularly in the case of obscure gastrointestinal bleeding (OGIB), which they define as ‘bleeding of unknown origin that persists or recurs after a negative initial endoscopy (colonoscopy and/or upper gastrointestinal endoscopy)’ (NICE, 2004). The PillCam is now the preferred choice for detecting small-bowel abnormalities, as neither the upper endoscopy nor the colonoscopy can reach inside to view the entire small bowel. Maeda et al. (2015), add that overt gastrointestinal bleeding (OGIB) patients may not always require intervention, therefore using the PillCam avoids costly, invasive and perhaps unnecessary procedures, as the PillCam can determine if a double-balloon enteroscopy (DBE)¹ is called for.

Pennazio et al., (2004) studied 100 patients who underwent CCE and all of whom had negative upper and lower endoscopy findings. 26 had overt bleeding (classed as ‘Group A’), 31 had previous overt bleeding (classed as ‘Group B’) and 43 had guaiac-positive stools and anaemia (classed as ‘Group C’). In this study, CCE yielded positive findings in 92.3% of group A, 12.9% of group B, and 44.2% of group C, with Angiodysplasia² (29%) and Crohn's disease³ (6%) being the most common findings. The results of the CCE findings led to treatments that were able to resolve the bleeding in 86.9% of the patients. The authors concluded that CCE is a very effective tool for patients with OGIB, and in particular those with ongoing bleeding. Additionally, CCE ‘could shorten considerably the time to diagnosis, lead to definitive treatment in a relevant proportion of patients, and spare a number of alternative investigations with low diagnostic yield’ (Pennazio et al., 2004). It is worth mentioning that this study used the PillCam 1, which was replaced by PillCam 2 in 2011 (Pillcamcrohns.com, 2017). Given that the PillCam 2 is a more effective diagnostic tool, capsule endoscopy for OGIB is clearly here to stay.

As video capsule endoscopy (VCE) yields similar diagnostic results to the double-balloon enteroscopy (DBE) procedure, the decision of which one to use first is often controversial. Maeda et al. (2015) studied 89 patients with OGIB who had first undergone video capsule endoscopy (VCE) and then double-balloon enteroscopy (DBE). The team examined the results to see if one was superior to the other. In each of the 89 cases, VCE interpreters evaluated the necessity of performing DBE, which depended upon the results of the VCE. Thirty-seven of the patients (42%) underwent DBE, which was determined from the findings of the VCE. Of these, 29 of the patients were found to have bleeding in the small bowel. Further examination of the remaining seven patients found five to have no lesions. One patient, for whom the VCE revealed a jejunal varix ⁴, underwent a DBE from both sides but it was unable to reach the lesion site. Maeda et al. (2015) concluded that the VCE, in terms of sensitivity and negative predictive value, were 100% for both small bowel lesions and haemostasis in the small bowel. They concluded that VCE never misses relevant findings in the small bowel, and that negative VCE findings correspond to the lack of necessity for further examination’ (Maeda et al., 2015). As such, VCE is a reasonable and effective initial examination procedure for OGIB.

Busegeanu et al. (2014) studied seven patients who, after either failing a colonoscopy or refusing to have one, underwent video capsule endoscopy. All of the patients had been diagnosed with suspicious lesions, with five having colon tumours, one a gastric tumour and

¹ A technique used to visualise the small bowel that involves using a balloon at the end of an enteroscope camera and an overtube (a tube that fits over the endoscope also fitted with a balloon). Both inserted orally and pass into the small bowel.
² A small vascular malformation found in the gut.
³ A chronic inflammatory disease of the digestive tract.
⁴ A presentation of portal hypertension which is usually asymptomatic.
one a small bowel tumour. Surgery and histology later confirmed a cancer diagnosis in all of the cases. Busegeanu et al. (2014) cite the European Society of Gastrointestinal Endoscopy Colon Capsule Endoscopy Guidelines as claiming that CCE is viable, safe, cost-effective and a remarkably accurate screening tool for use in average-risk individuals. Although the colonoscopy remains preferable for high-risk patients, Busegeanu et al.’s (2014) study showed that CCE is able to detect highly suspicious lesions in high-risk, symptomatic patients who either failed or refused a colonoscopy. Carvalho et al. (2017) also showed in their 6-year study of 281 patients with bowel bleeding that CCE detected small bowel bleeding very effectively and accurately.

Health Quality Ontario (2015) undertook a study to evaluate the accuracy and safety of CCE in detecting colorectal polyps in adult patients who had either a higher risk of colorectal cancer, or signs and symptoms of such. CCE findings were compared to those of alternate procedures and a thorough literature review analyzed the data on diagnostic accuracy and safety. The findings, along with the quality of evidence, were then assessed and yielded five studies, which evaluated the PillCam COLON 2 (PCC2). From these studies, the sensitivity and specificity of colorectal polyp detection was meta-analyzed whereby a statistical view of the combined results of these studies was done to obtain a more accurate estimate.

PCC2 showed amazing results, with a pooled sensitivity and specificity of 87% and 76% respectively for detecting colorectal polyps of minimum 6 mm in size, and 89% and 91% respectively for detecting colorectal polyps minimum 10 mm in size. Furthermore, one study, which compared PCC2 to computed tomographic colonography (CT) found it to have the same level of accuracy. Health Quality Ontario (2015) concluded that for adult patients, CCE, using the PCC2, has good sensitivity and specificity in terms of detecting colorectal polyps.

Yang et al. (2014) examined whether CCE could help 243 patients with chronic abdominal pain who had undergone a clinical evaluation which was unable to determine cause. The patients, none of whom had significant lesions, underwent CCE. In 23% of the cases the Pillcam was able to make diagnoses, which ranged from Crohn’s disease, enteritis, idiopathic intestinal lymphangiectasia, 7 uncinariasis and a small bowel tumour. The authors found that for patients with abdominal pain, CCE is an effective diagnostic tool.

The normal protocol for diagnosing coeliac disease commences with blood tests for certain auto-antibodies and is then followed with the golden standard of an esophagogastroduodenoscopy (EGD) with a duodenal biopsy (Chang et al., 2012). EGD is extremely uncomfortable, may not provide a diagnosis and may be contraindicated in certain circumstances. Furthermore, biopsies of the small bowel are not always conclusive. The authors concluded that ‘VCE can be used to diagnose coeliac disease in patients with suspected coeliac disease who have either a nondiagnostic EGD with biopsy or who are unable or unwilling to undergo EGD’ (Chang et al., 2012). The authors also note that ‘the characteristic mucosal changes of villous atrophy’ can replace biopsies as the mode of diagnosis when EGD is either declined or contraindicated, or when duodenal biopsies are negative and there remains a high index of suspicion’ (Chang et al., 2012). Urgesi et al. (2013) acknowledge that ‘the mechanisms underlying bowel disturbances in coeliac disease are still relatively unclear’ (Urgesi et al., 2013) and sought to determine if CCE could be used to measure gastric and small bowel transit times. They compared the transit times of CCE in 30 symptomatic or asymptomatic coeliac patients with a control group. The authors found ‘no statistical significant differences between gastric emptying and small bowel transit times both in coeliac and control group’ and also ‘no correlation … between transit times and age, sex and BMI’ (Urgesi et al., 2013). Surprisingly, results showed that ‘CCE reveals unrecognised gender differences and may be a novel outpatient technique for gut transit times’ assessment without

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5 Also called virtual colonoscopy, this is a special x-ray whereby a small tube is inserted a short distance into the rectum to allow for inflation with air while CT images of the colon and the rectum are taken.

6 Inflammation of the intestine and particularly the small intestine, usually causing chronic diarrhea.

7 A rare disorder whereby the lymph vessels supplying the lining of the small intestine are blocked

8 Hookworms. Also called ancylostomiasis.

9 A test for examining the lining of the esophagus, stomach, and first part of the small intestine.

10 The intestinal villi erode away.
exposure to radiation and for the evaluation of upper gut dysfunction in healthy patients suffering from constipation without evidence of intestinal malabsorption’ (Urgesi et al., 2013). These findings further support VCE as a diagnostic tool as it demonstrates promising results in respect to the small bowel.

Tomas et al. (2014), who compared many imaging techniques to disorders caused by Peutz-Jegher Syndrome\(^{11}\), added that VCE has the additional advantage of being radiation free. Urgesi et al. (2013) caution, however, that CCE, at least at the time of writing, was not the best method for studying gut transit times in untreated coeliac patients.

A software program known as 'SBI' (Suspected Blood Indicator), used in conjunction with the capsule endoscopy, has been shown to detect ‘almost all instances of small bowel active bleeding’ (Carvalho et al., 2017). The importance of this is that 'SBI was shown to swiftly detect and identify small bowel haemorrhage, assisting the reader in a fast review of the most important SBCE findings, a crucial process in the emergency setting’ (Carvalho et al., 2017).

Hagel et al. (2014) compared the Pillcam to conventional colonoscopy in terms of feasibility, sensitivity and specificity in detecting colonic pathologies. After examining 24 patients using both methods, the results were compared. Conventional colonoscopy detected 47 polyps of any size while CCE detected 43. The authors found CCE to be both feasible and safe and an ideal method for determining patient need for double-balloon enteroscopy (Hagel et al., 2014).

In addition to its benefits in detecting colon abnormalities, the Pillcam is also very effective for use in esophageal disease detection. It can detect esophageal varices\(^{12}\), Barrett’s esophagus\(^{13}\), and esophageal cancer (Kwack and Lim, 2016). Domingos et al. (2013) compared the effectiveness of ECE to methylene blue (MB) chromoendoscopy\(^{14}\) in detecting esophageal lesions in 21 patients with Barrett’s esophagus (BE) where there was also either a suspicion of cancer, the length and pattern of BE, or the presence of a hiatal hernia. The study showed that in terms of detecting esophageal lesions suspected of cancer, ECE sensitivity was 100%, negative predictive value was 100% and accuracy was 79%. In terms of assessing BE length, ECE was accurate 89% of the time, more specifically, 74% accurate in evaluating finger-like projections, 79% for circumferential BE, and 74% for mixed BE. Hiatal Hernia detection accuracy was also 74%. Kwack and Lim (2016), as well as Domingos et al. (2013) concluded that ECE is a favourable method for lesion detection, particularly in cases where cancer is suspected. It is also moderately accurate for identifying BE length and pattern. The authors both agree that ECE is not accurate for hiatal hernia detection.

**LIMITATIONS OF PILLCAM**

Even when the Pillcam is successful and safe, there are rare cases when complications can arise. One of these is *capsule retention*. Saigusa et al. (2014) define capsule retention as the capsule remaining inside the digestive tract for a period of two weeks or longer following CCE, which reportedly happens in less than 1.5% of cases. The dangers imposed by retention can include obstruction and/or perforation of the bowel. Furthermore, ‘incomplete examination,’ defined as a ‘failure of the capsule to reach the cecum during the recording time’ (Saigusa et al., 2014) reportedly occurs in 16.5 - 20% of CCE cases, with the majority of these patients remaining asymptomatic, despite capsule retention, for many months following the procedure. The authors therefore call for all CCE procedures to be routinely followed up for patients with incomplete examination, unknown excretion of the capsule, and/or ulcerative lesions, despite the lack of abdominal symptoms’ (Saigusa et al., 2014). Any CCE retention in the small intestine, they recommend, should be retrieved in order to prevent any further ulceration and perforation.

Although the PillCam is clearly beneficial in diagnostics, there are cases where it is either

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\(^{11}\) Non-cancerous growths called hamartomatous polyps develop in the gastrointestinal tract (particularly the stomach and intestines), making the risk of developing certain types of cancer greatly increase.

\(^{12}\) An abnormal and enlarged vein formation in the tube that connects the throat and stomach (esophagus).

\(^{13}\) The tube connecting the mouth and stomach (esophagus) develops tissue similar to that of the intestinal lining and replaces the ordinary tissue with it.

\(^{14}\) Applying stains or pigments to better identify, locate or characterise tissue when undergoing endoscopy. Methylene blue is an absorptive stain which is absorbed across specific epithelial cell membranes.
ineffective or unnecessary. A study comparing endoscopy to CCE found that most patients diagnosed with lesions in the small bowel who undergo CCE would be undergoing an unnecessary procedure, as small bowel capsule endoscopy would reveal lesions already within reach of conventional endoscopes (Hoedemaker et al., 2014).

Tacheci et al. (2016) also warn of false positives from CCE. They studied 42 healthy volunteers, all of whom underwent CCE, a clinical investigation, laboratory tests, completed a health-status questionnaire and agreed to a 36-month follow-up. For 11 of the subjects (26%), the endoscopy findings were normal, and the remainders were found to have minor findings, (mostly in the small intestine) such as ‘erosions and/or multiple red spots, diminutive polyps and tiny vascular lesions’ (Tacheci et al., 2016). A 36-month clinical follow-up found all 42 subjects had remained asymptomatic, with all laboratory tests normal. The authors suggest that positive findings with the CCE should be taken with caution as such findings could easily be determined as pathological when, in fact, they may have no clinical relevance (Tacheci et al., 2016).

Tomas et al. (2014) citing Chong et al. (2006) point out that lesions can be missed in the small bowel (especially within the proximal portion). Tomas et al. (2014) also cite Ross et al. (2008) as reporting one study in which 10 patients who underwent VCE, which showed nothing abnormal, were found to have small bowel tumours. The authors additionally cite Soars et al. (2004) as reporting in one of their studies detecting large, small-bowel polyps, that VCE missed 20% of them. Similarly, Zagorowicz et al. (2013) found that CCE may miss neoplasms particularly when located in the proximal small bowel. Tomas et al. (2014) acknowledge that imaging the proximal jejunum and duodenum is extremely difficult with the VCE due to the rapid capsule transit and they cite and concur with Postgate et al. (2009) who believe VCE has its limitations in evaluating the size of tumours.

Some other drawbacks to the CCE, as outlined by Kwack and Lim (2016) include Air Insufflation, which they describe as the inability of the capsule endoscope, as it progresses along the GI tract, to expose the entire mucosa, due to air inflation, which could result in a failure to detect lesions. Another issue is Retention or Delayed Transition, whereby the capsule is delayed in passing through the GI tract due to longer than usual time periods for gastric emptying or transit through the small-bowel. This can result in the capsule battery dying before completing its journey to the cecum and thus result in an incomplete examination (Kwack and Lim, 2016). This outlines the fact that Low Battery Life is another limitation of the video capsule, which typically lasts for 8 to 10 hours - long enough only for a normal transit time. Lastly, once the administration is complete, the interpretation of the images it produces can often be obstructed by mucus, bile or other factors. Tomas et al. (2014) agree with Kwack and Lim (2016) and further cite Postgate et al. (2009) in lamenting that CCE cannot take biopsies nor can it offer any kind of therapy.

**CONCLUSION**

The PillCam, a tiny camera-capule, has transformed the way the upper and lower GI tract can be examined, has proved to be safe, effective and cost-saving in that it does not require the presence of trained professionals during its administration. When compared with other procedures, the PillCam is able to approximate, equal, and in some cases, outperform standard procedures. Although clearly here to stay, the PillCam must overcome several limitations before it can replace the procedures currently used. The main challenges to overcome include false positive results, missed diagnoses (especially within the proximal portion of the small bowel), evaluating the size of tumours, an inability to take biopsies, an inability to offer therapy, air insufflation, retained or delayed transition, low battery life and producing quality images.

While correcting the above imperfections may appear insurmountable, developers clearly believe in the value of CCE and are currently working on solutions to extend the battery life of the capsule while, at the same time, reducing its size, improve its diagnostic yield and perform therapeutic work (Kwack and Lim, 2016). Fortunately, many proposed solutions and improvements are already under development and/or undergoing testing, and we can soon expect ‘enhanced image modality, controlled air insufflation, decreased battery consumption, and several therapeutic and biopsy tools’ (Kwack and Lim, 2016). If, or more likely, when these improvements arrive, PillCam could well become the new golden standard for endoscopies for both the upper and lower GI tract.
REFERENCES


Parts of the product (Diagram of pillcam compartments), n.d. photograph, viewed 23 June 2017, <www.slideshare.net/shakilsid/pillcam>.


SEARCH STRATEGY

Search Strategy:
- Date of Search: June, 12th, 2017, 13:00
- Database: PubMed

Search Terms:
- ((gastrointestinal Disorder* OR Disorder* near/3 gastrointestinal) OR functional gastrointestinal disorder[MeSH Terms]) AND ((upper endoscopy OR colonoscopy OR endoscopy) OR endoscopy, gastrointestinal[MeSH Terms]) AND ((pillcam OR capsule endoscopy OR capsule endoscope) OR capsule endoscope MeSH Terms)

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