



Australian Government
Department of Health and Ageing



Horizon Scanning Technology
Prioritising Summary
PillCam ESO
February 2007



**Australian
Safety
and Efficacy
Register
of New
Interventional
Procedures -
Surgical**



**Royal Australasian
College of Surgeons**

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The production of this Horizon scanning prioritising summary was overseen by the Health Policy Advisory Committee on Technology (HealthPACT), a sub-committee of the Medical Services Advisory Committee (MSAC). HealthPACT comprises representatives from health departments in all states and territories, the Australia and New Zealand governments; MSAC and ASERNIP-S. The Australian Health Ministers' Advisory Council (AHMAC) supports HealthPACT through funding.

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PRIORITISING SUMMARY

REGISTER ID: S000019 REFERRAL FROM HEALTHPACT

NAME OF TECHNOLOGY: PILLCAM ESO

PURPOSE AND TARGET GROUP: ALTERNATIVE DIAGNOSTIC TECHNIQUE FOR PATIENTS WITH OESOPHAGEAL DISEASE

STAGE OF DEVELOPMENT (IN AUSTRALIA):

- | | |
|---|---|
| <input checked="" type="checkbox"/> Yet to emerge | <input type="checkbox"/> Established |
| <input type="checkbox"/> Experimental | <input type="checkbox"/> Established <i>but</i> changed indication or modification of technique |
| <input type="checkbox"/> Investigational | <input type="checkbox"/> Should be taken out of use |
| <input type="checkbox"/> Nearly established | |

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- | | | |
|---|-------------|-----|
| <input type="checkbox"/> Yes | ARTG number | N/A |
| <input checked="" type="checkbox"/> No | | |
| <input type="checkbox"/> Not applicable | | |

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Europe		✓	
Israel		✓	
United States		✓	

IMPACT SUMMARY:

Given Imaging (Israel) provides the PillCam ESO with the aim of diagnosing oesophageal diseases (Gastro-oesophageal reflux disease, oesophageal varices etc.). The technology is available to gastroenterologists or endoscopists as an alternative to conventional endoscopy for patients requiring diagnosis/evaluation of oesophageal diseases.

BACKGROUND

Oesophageal diseases, especially gastro-oesophageal reflux disease (GORD) and its complications (oesophagitis, stricture, Barrett's oesophagus) often require upper oesophageal endoscopy to evaluate symptoms or to screen for complications, especially in chronic cases. Despite being the preferred technique to evaluate the oesophageal mucosa, conventional upper endoscopy is often hindered by its invasiveness, which therefore limits its utilisation in many patients with suspected or established oesophageal disease (Sánchez-Yagüe et al. 2006). Tolerance to upper oesophageal endoscopy has improved with the use of conscious and deep sedation, however these steps lead to longer procedure times, higher costs and increased risk of complications (Lapalus et al. 2006).

A potential alternative method of examining the oesophagus is capsule endoscopy. Previously, capsule endoscopy has been utilised as a method of examining the small bowel, the specific capsule utilised for this purpose was the PillCam SB. Recently, a new capsule, known as the PillCam ESO, has been developed by the same company (Given Imaging Inc., Israel) that produced the PillCam SB. The PillCam ESO video capsule is a wireless, disposable capsule (11 x 26 mm) that was designed to glide smoothly through the oesophagus. It was developed specifically to view the inner lining of the oesophagus and is equipped with miniature cameras on both ends that are capable of capturing 14 frames per second. The potential advantage of the PillCam ESO is the possibility of higher compliance rates as it is a less invasive procedure compared to conventional upper endoscopy which does not require sedation. The PillCam ESO is one component of the Given® Diagnostic System, the system's two other essential parts: the Data recorder set and the RAPID® workstation. As the capsule travels down the oesophagus, it transmits the acquired images via digital radiofrequency communication to the data recorder unit located outside the body. Upon completion of the examination, the physician transfers the accumulated data in the data recorder to the RAPID workstation for processing and interpretation (Given Imaging 2006, Eliakim et al. 2005). To date, the PillCam ESO has been utilised in the examination of patients with GORD and oesophageal varices, both of which will be discussed in this summary.

CLINICAL NEED AND BURDEN OF DISEASE

The clinical need and burden of disease will be limited to GORD and oesophageal varices as these are the two indications where the PillCam ESO has been utilised. Previous studies have estimated that symptomatic GORD affects at least 5-7% of the global population, while up to 30% of the population in western countries are affected by this disorder (Eliakim et al. 2004). In Australia, the prevalence of GORD is not known, however based on conservative global prevalence rates (~5%), approximately 1 million Australians may be affected by this disorder (based on population of 20,718,000). The national separation due to GORD in 2004 to 2005 is 57,923 (AIHW 2000).

Oesophageal varices are responsible for approximately 5 to 11% of upper GI bleeding. In Western countries, alcoholic and viral cirrhosis are the leading causes of portal hypertension and oesophageal varices (Azer 2006). There is no Australian data on the prevalence of oesophageal varices, however cirrhosis is estimated to occur in 70 per 100,000 males and 50 per 100,000 females and is responsible for 9836 hospitalisations from 1997 to 1998 (AIHW 2000), thus providing a conservative estimate of the potential prevalence of oesophageal varices.

DIFFUSION

At the time of writing, the PillCam ESO has been granted FDA approval for marketing purposes in the United State in October 2004. In addition to this, the PillCam ESO recently received the CE mark of approval in October 2006.

COMPARATORS

The current gold-standard diagnostic procedure for oesophageal diseases is conventional endoscopy. At the time of writing, there are no alternative oesophageal pill cameras available; other than the predecessor of the PillCam ESO, the PillCam SB (small bowel). One study (Eliakim et al. 2005) inferred that future generations of oesophageal capsules with higher frame rate speeds are currently in trials.

SAFETY AND EFFECTIVENESS ISSUES

A total of six studies have been included in this summary. Four studies utilised the PillCam ESO to visualise GORD while the remaining 2 studies utilised the PillCam to examine the oesophagus for varices.

Safety/Technical Performance

The multicentre trial by Eliakim et al. (2005) (n = 109) compared the accuracy of *oesophageal capsule endoscopy* (OCE) utilising the PillCam ESO compared with conventional upper endoscopy in patients with chronic gastroesophageal reflux diseases. No oesophageal related adverse events were noted throughout the study duration and the capsule was easily ingested by 99.1% of patients (1 patient was unable to swallow the capsule). There were 2 incidences of technical problems where the frames obtained had large gaps within the sequence of frames captured, as a result of this, 3 patients (including the patient who was not able to swallow the capsule) were excluded from the efficacy analysis. Meanwhile, the case series (n = 28) conducted by Sánchez-Yagüe et al. (2006) to assess the feasibility, accuracy, safety and acceptability of OCE for the study of GORD and oesophageal varices reported no capsule-related complications; with the exception of one technical problem where a capsule did not record any images. Similarly, Lapalus et al. (2006) and Eisen et al. (2006) did not observe any capsule-related adverse events when the device was utilised to evaluate oesophageal varices.

Physical tolerance scores revealed that OCE examination was associated with significant reduction in overall discomfort, pain, nausea and belching compared to conventional endoscopy but was not associated with a significant reduction in difficulty with swallowing (Lapalus et al. 2006). In fact, patients deemed the capsule to be very difficult to swallow (scoring 9 out of 10) by 10% of patients while there were no such complaints for conventional endoscopy. Most patients (20/21, 95%) in this cohort preferred OCE over conventional endoscopy, with the exception of the one patient who could not swallow the capsule (Lapalus et al. 2006). Similarly, Eliakim et al. (2004) reported that most patients (11/15, 73%) preferred OCE and three patients were undecided. The patient satisfaction assessment by Eliakim et al. (2005) rated OCE significantly higher compared to conventional endoscopy in pain during/after procedure, discomfort during/after procedure, overall convenience and missed time from work (all $p < 0.0001$). In contrast to Lapalus et al. (2006), Eliakim et al. (2005) reported that patients found the capsule to be significantly easier to swallow compared to the insertion of an endoscope ($p < 0.0001$).

Overall, OCE with the PillCam ESO appears to be well tolerated and safe in all the studies included in this assessment. No severe side effects were reported and the capsules were excreted uneventfully in all patients who managed to swallow it.

Effectiveness

a) Gastro-oesophageal reflux disease

The comparative case series study by Eliakim et al. (2005) reported that in the group of patients diagnosed with Barrett's oesophagus by conventional endoscopy, OCE (median recording time: 245 [range 6 – 1678 seconds] seconds; median number of oesophageal frames: 980 [range 24 – 6712 frames]) demonstrated a sensitivity of 97% and a negative predictive value (NPV) of 97% while specificity and positive predictive value (PPV) were estimated to be 99% for both these parameters. When 'intention to treat' analysis was utilised, the sensitivity and specificity demonstrated was to be 92% and 99% respectively. Meanwhile in patients diagnosed with oesophagitis utilising endoscopy, the intention to treat analysis showed that OCE achieved a sensitivity of 85%, negative predictive value (NPV) of 92%, specificity of 99% and PPV of 97%. Overall, intention to treat analysis for the diagnosis of 'any oesophageal findings' achieved a sensitivity of 90%, specificity of 95%, PPV of 97% and NPV of 85%. Post-adjudication committee decision, the sensitivity of OCE for diagnosing any oesophageal abnormalities was 92%, NPV was 88%, specificity was 95% and PPV was 97%. These results indicate that OCE was capable of acquiring satisfactory images with a high degree of accuracy and was comparable to conventional endoscopy in diagnosing oesophageal mucosal pathology. Comparable results were reported in the pilot study conducted by Eliakim et al. (2004) earlier, where the sensitivity and specificity achieved was 100% and 80% respectively, with PPV of 92% and NPV of 100%. In this pilot study, OCE identified oesophageal pathology in all 12 patients where pathological confirmation was previously obtained via conventional endoscopy. In addition, OCE managed to identify an additional pathology in one patient which was not evident from previous endoscopy (Eliakim et al. 2004).

When the PillCam ESO, which captures images at 14 frames per second (fps), was compared to another capsule that has a rate of 4 fps in 42 patients with GERD (Kolowsky et al. 2006), it was shown that the PillCam was more sensitive in diagnosing oesophageal erosions or ulcers (100% sensitivity) and Barrett's oesophagus (100% sensitivity). In contrast, the 4 fps capsule was only capable of diagnosing 16/19 cases of ulcers (84% sensitivity) and 6/8 cases of Barrett's oesophagus (75% sensitivity). In addition, the PillCam ESO had significantly superior visualisation of the upper oesophageal sphincter (80% vs 24%, $p < 0.01$) and the entire oesophagus (76% vs 12%, $p < 0.01$) when compared to the 4 fps capsule (Kolowsky et al. 2006). Although not stated by the authors of this study, it is possible that the 4 fps capsule utilised was the PillCam SB, predecessor of the PillCam ESO.

The clinical case series by Sánchez-Yagüe et al. (2006) reported that the PillCam ESO revealed oesophageal erosion in 58.33% (14/24 patients) of examinations carried out in patients with GORD ($n = 23$). Meanwhile, 64.3% (9/14 patients) presented with grade I oesophagitis and 35.7% (5/14 patients) presented with grade II oesophagitis. The PillCam ESO revealed an oesophageal tumour in one patient (which was diagnosed earlier), and a follow-up capsule was utilised to confirm evolution of the mucosectomy at 3 months. Of the 5 patients who underwent OCE for the study of oesophageal varices, 4/5 had varices (1 case of small varices, 3 cases of enlarged tortuous varices) and stomach imaging revealed images that were compatible with portal hypertension gastropathy. Proper examination of the Z-line is particularly important in OCE due to the fact that lesion characteristics of oesophagitis are usually found at this level in GORD patients. Complete visualisation was achieved in 79.3% (23/29 studies) of examinations, with 5 (5/29; 17%) cases of blind spots lesser than 90° and one case (3.7%) where 180° of the Z-line was not visualized. The authors stated that a total of 10/29 (34.5%) examinations revealed images compatible with Barrett's oesophagus (Sánchez-Yagüe et al. 2006).

Overall, these studies suggest that OCE with the PillCam ESO is a convenient and sensitive method for visualisation of oesophageal mucosal pathology and is comparable to conventional endoscopy.

b) Oesophageal varices

Lapalus et al. (2006) evaluated the feasibility, tolerability, and accuracy of the PillCam ESO for evaluating oesophageal varices (as well as other lesions associated with portal hypertension) in patients suffering from cirrhosis. All patients (n = 21) underwent endoscopy on the same day as OCE, OCE was conducted first. Both conventional endoscopy and OCE was feasible in 95% (20/21) of patients; however the overall quality¹ of OCE was lower compared to endoscopy (6.7 ± 2.1 vs 8.1 ± 1.1 ; mean \pm SEM). No varices were identified in 4 patients with conventional endoscopy. In regards to diagnostic accuracy of OCE, there was complete diagnostic agreement with conventional endoscopy regarding the absence or presence of oesophageal varices in 17/20 patients (85%). In the three patients where there was a discrepancy between the two procedures, they were diagnosed with grade I varices with conventional endoscopy and no varices with OCE. Overall, the sensitivity of OCE for detecting oesophageal varices in comparison to conventional endoscopy as the gold standard was 81% with a 100% PPV, a specificity of 100% and NPV of 57%. In addition to this, all patients were adequately classified utilising OCE for the indication of beta-blocker treatment or band ligation. In the stomach, the mean recording time with OCE was 616 (range 251 – 1200 seconds) seconds. One patient had gastric varices that were diagnosed with both conventional endoscopy and OCE. Portal hypertension gastropathy was diagnosed in 16/21 patients with conventional endoscopy and 13/20 patients with OCE. In the 4 patients where there was a discrepancy, conventional endoscopy diagnosed them as having gastropathy in 3 cases but not on OCE; while the final patient was diagnosed with gastropathy with OCE but not with conventional endoscopy (Lapalus et al. 2006).

In another case series (Eisen et al. 2006) where the PillCam ESO was to diagnose oesophageal varices, it achieved a sensitivity of 100%, a specificity of 77%, a positive likelihood ratio of 4.3, and a negative likelihood ratio of 0.0 compared to conventional endoscopy. However despite these encouraging results, the authors highlighted that one key disadvantage of capsule endoscopy was the lack of insufflation to better appreciate the true size of the varices in the oesophagus. The lack of power in this clinical study did not allow the authors to access the accuracy of grading, however, variceal grading appeared to be fairly accurate based on the impression of variceal size on the fraction of circumference of the capsule view involved (Eisen et al. 2006).

The sensitivity and specificity achieved for OCE in both studies on oesophageal varices were quite inconsistent and may have been due to the variation in oesophageal transit times or disruptive incidences (e.g. bubbles, secretions etc.) in individual patients. However, the result from both studies suggests that OCE is feasible and accurate for the diagnosis of oesophageal varices without the need for conscious sedation and its associated costs.

COST IMPACT

The Given Workstation (which includes a dedicated computer, printer and LCD screen) loaded with the RAPID software application costs AUD\$30,000 while the DR2 DataRecorder kit costs AU\$16,700. The single use PillCam ESO capsule is supplied in packs of 10 which costs AUD\$8950 (AUD\$895 per capsule). Given Imaging Inc., has stated that the Given Workstation, DataRecorders and the RAPID software are designed to be compatible with the PillCam family of capsules and therefore medical centres that are currently utilising the

¹ The global quality of the procedure was rated by two independent endoscopists using a 10cm visual analogue scale (0 bad, 10 very good).

PillCam SB may implement the PillCam ESO within the centre without incurring the cost of purchasing an entire new diagnostic system (Given Imaging Inc., personal communication, 2007).

To date, no cost-effectiveness studies have been conducted on the PillCam ESO. However, in conventional upper endoscopy, conscious sedation is routinely administered to assist with the procedure. Due to the fact that OCE with the PillCam ESO does not require the administration of conscious sedation, it is possible that direct costs related to peri- and post-procedural monitoring, medication costs, and complications/risks may be reduced.

The Medicare Benefits Schedule reimbursement fees for capsule and conventional endoscopy are listed in Table 1:

Table 1 Medical Benefits Schedule of fees for capsule and conventional endoscopy (Medicare Australia 2006)

Category	Item Number	Benefit (AUD)	Number of Claims (July 2005 to June 2006)
Capsule endoscopy to investigate an episode of obscure gastrointestinal bleeding, using a capsule endoscopy device approved by the Therapeutic Goods Administration	11820	\$1801.90	3613
Endoscopy with balloon dilatation of gastric or gastroduodenal stricture	30475	\$283.00	547
Oesophagoscopy (not being a service to which item 41816 or 41822 applies), Gastroscopy, Duodenoscopy or Panendoscopy (1 or more such procedures), with endoscopic sclerosing injection or banding of oesophageal or gastric varices	30476	\$217.00	1032

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified from the retrieved material.

OTHER ISSUES

Gralnek et al. (2006) reported that a new simplified ingestion procedure (SIP) significantly improved visualisation in comparison with the original ingestion procedure, with less interference due to bubbles/saliva observed at the gastro-oesophageal junction ($p = 0.002$) and improved visualisation at the Z-line ($p = 0.025$). Despite significantly faster oesophageal transit times ($p = 0.0001$), there were no significant differences in the amount of Z-line images captured by the PillCam ESO (Gralnek et al. 2006).

A non-randomised clinical trial which aims to recruit 150 patients is currently underway to evaluate the efficacy of OCE compared to conventional upper endoscopy. The expected date of completion is unknown (ClinicalTrials 2006).

HEALTHPACT CONCLUSION

The PillCam ESO appears to be a suitable alternative to conventional upper endoscopy for the examination of oesophageal pathologies, namely GORD and oesophageal varices. However, studies on cost-effectiveness and more comparative studies to conventional upper endoscopy are required. Based on the limited evidence available and the potential cost savings associated with the PillCam ESO, HealthPACT has recommended the technology be monitored.

- | | |
|--|--|
| <input type="checkbox"/> Horizon Scanning Report | <input type="checkbox"/> Full Health Technology Assessment |
| <input checked="" type="checkbox"/> Monitor | <input type="checkbox"/> Archive |
| <input type="checkbox"/> Refer | <input type="checkbox"/> Decision pending |

SOURCES OF FURTHER INFORMATION:

Given Imaging. Last updated 2006. http://www.givenimaging.com/Cultures/en-US/Given/English/Products/ESO_CE/ [Accessed December 2006].

LIST OF STUDIES INCLUDED

Total number of studies 6
Level III-2 and level IV Diagnosis evidence

SEARCH CRITERIA TO BE USED:

PillCam
Capsule endoscopy
?esophageal capsule
Gastroesophageal reflux

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Eliakim R, Sharma VK, Yassin K, Adler SN, Hacob H, Cave DR, Sachdev R, Mitty RD, Hartmann D, Schilling D, Riemann JF, Bar-Mier S, Bardan E, Fennerty B, Eisen G, Faigel D, Lewis BS, Fleischer DE. A prospective study of the diagnostic accuracy of PillCam ESO esophageal capsule endoscopy versus conventional upper endoscopy in patients with chronic gastroesophageal reflux diseases. *Journal of Clinical Gastroenterology* 2005; 39(7): 572-578.

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Lapalus M-G, Dumortier J, Fumex F, Roman S, Lot M, Prost B, Lion F, Ponchon T. Esophageal capsule endoscopy versus esophagogastroduodenoscopy for evaluating portal hypertension: a prospective comparative study of performance and tolerance. *Endoscopy* 2006; 38(1): 36-41.

Medicare Australia: Medicare benefits Schedule. Last update 2006. <http://www9.health.gov.au/mbs/> [Accessed December 2006].

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