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Horizon Scanning Technology

Prioritising Summary

Narrow Band Imaging for the improved detection of precancerous lesions during colonoscopy

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AHTA

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PRIORITISING SUMMARY (UPDATE 2009)

REGISTER ID:	**000414**
NAME OF TECHNOLOGY:	**NARROW BAND IMAGING**
PURPOSE AND TARGET GROUP:	**IMAGING MODALITY FOR THE IMPROVED DETECTION OF PRECANCEROUS LESIONS DURING COLONOSCOPY**

2009 SAFETY AND EFFECTIVENESS ISSUES

A large amount of literature was published on NBI since the original prioritising summary was written in 2008. The highest quality evidence and larger studies are reviewed below.

Two systematic reviews were published in 2009; one was focussed on NBI in the upper gastrointestinal tract and the other on NBI during colonoscopy.

The first systematic review was based on thirteen papers for a variety of oesophageal conditions: squamous cell carcinoma (n =2), gastroesophageal reflux disease (GERD, n = 2) or Barrett's oesophagus (BO, n = 9) and seven studies on stomach conditions. For early squamous cell carcinoma diagnosis, the review concluded that although NBI looks promising there is a lack of published information to date for this application. For GERD, NBI showed a significant increase in sensitivity compared to standard endoscopy, which performs poorly in the diagnosis of GERD. This may reduce the need for the tests routinely performed subsequent to standard endoscopy to confirm diagnosis. BO diagnosis is not a focus of this summary but the systematic review found that there were conflicting results published for this condition, some studies showing better and some showing worse performance compared to standard methods. The studies on stomach conditions either suffered from poor quality or did not show a clear benefit of NBI over normal endoscopy for diagnosis of these conditions. The authors conclude that NBI shows promise for some of the conditions but larger randomised studies are required to allow conclusions to be drawn about its effectiveness (Curvers et al 2009) (Level I Diagnostic evidence).

A systematic review on NBI use during colonoscopy identified 16 studies: one on the detection of polyps, five on neoplasia detection, and 10 on lesion differentiation. The review of detection studies did not show an improvement in detection rates using NBI, with only one of the three large randomised studies showing a significant increase in detection when using NBI versus standard whitelight endoscopy (WLE). The authors note that the study showing a positive outcome for NBI was flawed in design. The authors conclude that there was no benefit shown in the current literature regarding the use of NBI for the detection of neoplasia. The second part of the review focussed on the use of NBI to differentiate lesions detected with WLE. The authors pooled the results of the reviewed studies and found that the overall sensitivity was

92% (95% CI [89, 94]) and overall specificity was 86% (95% CI [80, 91]). The pooled results of a comparator technique called chromoendoscopy[1] found similar differentiation results with a sensitivity of 91% (95% CI [83, 96]) and a specificity of 89% (95% CI [83, 93]). The review also looked at four studies which reported on inter-operator agreement using NBI. The results showed good to perfect agreement between operators in four studies (κ values ranging from 0.64 to 1.0, with three of the four studies reporting very high κ values). Overall the review shows that NBI is unproven for the detection of neoplasia but comparable to established techniques for the differentiation of lesions (van den Broek et al 2009) (Level I Diagnostic evidence).

A study of 47 consecutive patients compared the ability of NBI to detect colorectal lesions versus WLE. Patients confirmed to have neoplastic lesions were then blindly assessed using NBI at a separate institute. The procedure at the second institute consisted of analysing a segment of colon with only NBI then reviewing the results from the first institute. If it was confirmed that a lesion was missed then the colonoscope was switched to WLE mode and the operator attempted to investigate the discrepant lesions. Although NBI detected more neoplasia overall (NBI: 134/153 vs WLE: 116/153; $p = 0.02$), 12 per cent of the lesions detected by WLE were missed using NBI. WLE missed 24 per cent of lesions detected by NBI (Uraoka et al 2009) (Level III-2 Diagnostic evidence).

The ability of NBI to detect oesophageal lesions in a population with known lesions was compared to WLE and WLE plus iodine staining. The population consisted of 90 subjects with a mean age of 57 years. Lesions were confirmed with pathology. The results showed that iodine staining detected 100% (138/138) of the lesions, with NBI and WLE detecting 87.0% (120/138) and 75.4% (104/138) of the lesions, respectively (Huang et al 2009) (Level III-2 Diagnostic evidence).

Using histology as the gold standard, NBI and lugol chomoendoscopy[2] were compared for the detection of lesions in a patient population of 142 with head and neck squamous cell carcinoma (SCC). Sixteen patients were found to have oesophageal lesions by NBI (21 lesions total, 15 clinically important). Nineteen additional patients were found to have additional lesions by lugol chomoendoscopy (22 lesions total, 1 clinically important). Compared to the gold standard of histology NBI showed a sensitivity of 90.9% (95 % CI [58.7, 99.8]) and a specificity of 95.4% (95 % CI [90.3, 98.3]) for the detection of clinically important lesions (Takenaka et al 2009) (Level III-2 Diagnostic evidence).

Watanabe et al (2009) used WLE to detect laryngeal lesions in a patient population[3] undergoing laryngoscopy at a Japanese clinic. WLE detected 35 suspected lesions in

[1] Chromoendoscopy is endoscopy using dyes to increase contrast of target lesions.
[2] Lugol's Iodine is a stain that helps discriminate between lesions and normal tissue.
[3] The total number of patients assessed was not reported

34 patients. NBI was used to differentiate the lesions between malignant or non-malignant. The gold standard used was histopathology. NBI detected 21/23 malignant lesions (sensitivity 91.3%) and correctly diagnosed 11/12 non-malignant lesions (specificity 91.6%) (Watanabe et al 2009) (Level III-2 Diagnostic evidence).

Two systematic reviews and four primary studies are included in this update. The reported sensitivity and specificity of NBI is high compared to other techniques and/or standard techniques. Despite this, the value of this information is questionable as the populations examined are either very high risk for, or patients with, malignancies. The conclusions of the two systematic reviews show that NBI may be useful for differentiating clinically significant from non-significant lesions. Other uses of NBI are not supported by evidence or are at a preliminary stage of investigation. Long term follow up studies are needed to determine the effectiveness of NBI for detection and differentiation.

2009 Cost Impact

No cost effectiveness information was found during the preparation of this update. Olympus, the manufacturer of the CF-Q180 AL colonoscope used in several studies in this prioritising summary, was contacted regarding the cost of a NBI capable colonoscope system but at the time of publication no reply was forthcoming.
The high definition model of this endoscope (CF-H180 AL) is quoted as having a cost of $US 70,500 ($36,000 for endoscope, $22,000 for processor (Evis Exera II), and $12,500 for the light source (Evis Exera II)) (Kwon et al 2009).

2009 Summary of findings

The studies reviewed in this update support the use of NBI for the differentiation of malignant from non-malignant lesions of the colon. Based on current evidence, NBI alone is not a significant improvement over standard methods. Higher quality studies in appropriate patient groups are needed to determine the effectiveness of NBI

HealthPACT action:

NBI may be of limited use for the differentiation of benign or malignant polyps associated with Barrett's Oesophagus as general practice is to remove all polyps regardless. In addition, the majority of scopes available and in use in Australia have the capacity for NBI. HealthPACT have therefore recommended that further assessment of this technology is no longer warranted.

Number of included Studies

Total number of studies	
Level I diagnostic evidence	2
Level III-2 diagnostic evidence	4

2009 REFERENCES:

Curvers, W. L., van den Broek, F. J. et al (2009). 'Systematic review of narrow-band imaging for the detection and differentiation of abnormalities in the esophagus and stomach (with video)', *Gastrointest Endosc*, 69 (2), 307-317.

Huang, L. Y., Cui, J. et al (2009). 'Narrow-band imaging in the diagnosis of early esophageal cancer and precancerous lesions', *Chin Med J (Engl)*, 122 (7), 776-780.

Kwon, R. S., Adler, D. G. et al (2009). 'High-resolution and high-magnification endoscopes', Gastrointestinal Endoscopy, 69 (3, Part 1), 399-407.Takenaka, R.,

Kawahara, Y. et al (2009). 'Narrow-Band Imaging Provides Reliable Screening for Esophageal Malignancy in Patients With Head and Neck Cancers', *Am J Gastroenterol*.

Takenaka, R., Kawahara, Y. et al (2009). 'Narrow-Band Imaging Provides Reliable Screening for Esophageal Malignancy in Patients With Head and Neck Cancers', *Am J Gastroenterol*.

Uraoka, T., Sano, Y. et al (2009). 'Narrow-band imaging for improving colorectal adenoma detection: appropriate system function settings are required', *Gut*, 58 (4), 604-605.

van den Broek, F. J., Reitsma, J. B. et al (2009). 'Systematic review of narrow-band imaging for the detection and differentiation of neoplastic and nonneoplastic lesions in the colon (with videos)', *Gastrointest Endosc*, 69 (1), 124-135.

Watanabe, A., Taniguchi, M. et al (2009). 'The value of narrow band imaging for early detection of laryngeal cancer', *Eur Arch Otorhinolaryngol*, 266 (7), 1017-1023.

PRIORITISING SUMMARY (2008)

REGISTER ID: **000414**

NAME OF TECHNOLOGY: **NARROW BAND IMAGING**

PURPOSE AND TARGET GROUP: **IMAGING MODALITY FOR THE IMPROVED DETECTION OF PRECANCEROUS LESIONS DURING COLONOSCOPY**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

☐	Yet to emerge	☐	Established
☐	Experimental	☒	Established *but* changed indication or modification of technique
☐	Investigational	☐	Should be taken out of use
☐	Nearly established		

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☐	Yes	ARTG number
☐	No	
☒	Not applicable	

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Germany	✓		
United States	✓		
Japan	✓		

IMPACT SUMMARY:

Companies that produce standard imaging equipment such as Olympus provide high resolution endoscopes capable of performing narrow band imaging. Although narrow band imaging is a relatively new imaging modality, it has been in use in Australia, mainly for patients with Barrett's oesophagus. This prioritising summary examines the use of narrow band imaging for the new indication of the detection of precancerous gastric and colorectal lesions. The technology would be made available through specialist hospitals for patients undergoing a conventional bronchoscopy or endoscopy.

2008 BACKGROUND

Narrow band imaging (NBI) is an imaging technique that exploits the specific transmissibility and absorption characteristics of specific wavelengths of light. Longer

wavelengths of light penetrate further into tissue and different wavelengths are absorbed differently by structures within the tissue. Specifically, blue light (415nm) allows the visualisation of the superficial capillary network as it does not penetrate the tissue to a great extent. Green light (540nm) penetrates further into the tissue allowing the visualisation of deeper structures such as sub-epithelial vessels. When images from the two light sources are combined a high contrast image of the tissue surface is generated.

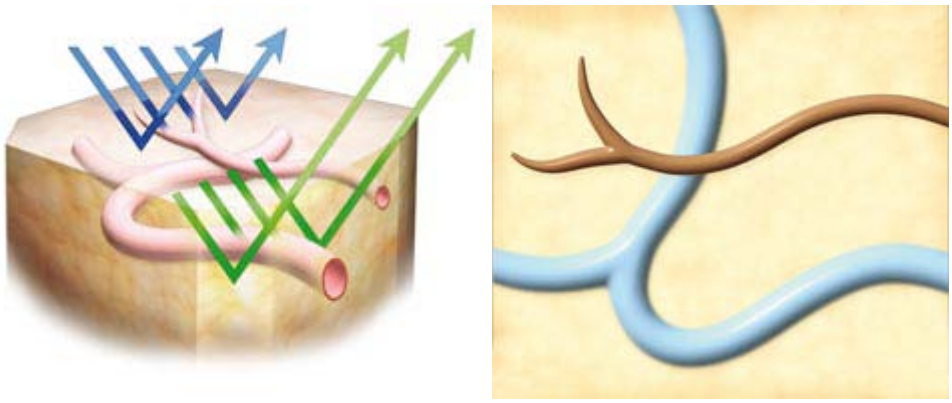

Figure 1 NBI image acquisition.
Blue light only penetrates the near surface, whereas green light penetrates to deeper structures (left). The combined image shows the capillaries in brown and the underlying veins in blue (right).

Lesions visualised with NBI can be categorised using two different techniques. One method involves the analysis of microvasculature, with neoplastic lesions displaying increased or abnormal microvessel density. A second method developed by Kudo et al (1994) involves analysis of the "pit pattern" of a lesion which results from the surface structures and superficial mucosal capillaries. The Kudo pit pattern allows the lesion to be graded on a scale from nonadenomatous to adenomatous[4]. These methods are applicable to a variety of tissue types, including the colon.

2008 Clinical Need and Burden of Disease

In 2004 there were 12,977 new cases of colorectal cancer diagnosed within Australia. According to the AIHW there are no national prevalence data available for colorectal cancer (AIHW 2007). In 2006-07 there were a total of 230,911 separations for colonoscopy as recorded under 4 categories (G43Z Complex Colonoscopy, G44A Other Colonoscopy W Catastrophic or Severe CC, G44B Other Colonoscopy W/O Catastrophic or Severe CC, G44C Other Colonoscopy Sameday) (AIHW 2008). It is not clear how many of these separations are related to colorectal cancer diagnosis.

[4] Adenomatous lesions are not necessarily cancerous but have the risk of progression to malignancy.

2008 DIFFUSION

While NBI is currently in use in Australia for Barrett's oesophagus, no evidence was found indicating NBI is used during colonoscopy for colorectal cancer diagnosis. However, a recent demonstration (August 2008) of the technique was conducted at the Royal Brisbane and Women's Hospital, by Dr Omori, a gastrointestinal surgeon from Kawasaki Hospital, Japan.

2008 COMPARATORS

Colonoscopy is the gold standard for diagnosis of potentially cancerous polyps. Being the gold standard, it is difficult to assess the accuracy of colonoscopy. As newer techniques emerge it is evident that colonoscopy is lacking in some areas such as amount of surface area of the colon able to be visualised (East et al 2007), the difficulty of detecting flat lesions with conventional colonoscopy (Dekker & Fockens 2005), and the estimated polyp miss rate of 10-20 per cent (Bensen et al 1999; Robertson et al 2005).

2008 SAFETY AND EFFECTIVENESS ISSUES

Several studies have investigated the diagnostic ability of NBI for colorectal lesions compared to conventional white light colonoscopy and histology. Adler investigated NBI in a trial where patients presenting for routine colonoscopy diagnosis were randomly assigned to either conventional or NBI colonoscopy. The study involved 401 eligible patients (200 NBI, 201 conventional colonoscopy) and found that the detection rate of adenomas was higher in the NBI group (23%) than the conventional group (17%), although this did not reach significance (p= 0.129). There was an apparent training effect involving the conventional method, where the first 100 patients showed a 26.5 per cent adenoma detection rate for NBI and eight per cent for conventional colonoscopy, however the last 100 patients had an adenoma detection rate of 25.5 and 26.5 per cent for NBI and conventional colonoscopy, respectively. The authors speculated that the improved polyp detection using NBI may increase the ability of the clinicians to recognise polyps using conventional colonoscopy (Adler et al 2008) (Level III-2 diagnostic evidence).

A second study randomised 276 patients presenting for routine colonoscopy to NBI or conventional colonoscopy. After either NBI or conventional colonoscopy was carried out a subsequent examination with conventional colonoscopy was performed as the reference standard. The neoplasm miss rate was calculated against the reference standard and was similar for both techniques (NBI = 17/135 (12.6%) vs conventional colonoscopy = 17/141 (12.1%). The miss rate for *advanced adenomas* was less than one per cent (Kaltenbach et al 2008) (Level III-2 diagnostic evidence).

Inoue et al investigated NBI versus conventional colonoscopy in a prospectively recruited population of 243 patients who were randomly assigned to either NBI or conventional colonoscopy. The procedure times for either NBI or conventional

colonoscopy were not significantly different. The NBI procedure (127 polyps, 62%) detected significantly more polyps versus conventional colonoscopy (78 polyps, 38%) ($p=0.014$). When the polyps were analysed by histology, 169 of 205 were found to be neoplastic. The NBI group had 103 neoplasms (60.9%) and the conventional colonoscopy group had 66 neoplasms (39.1%). The NBI technique detected more small adenomas compared to conventional colonoscopy ($p<0.05$). There were no significant adverse effects for either procedure reported at a two week follow up (Inoue et al 2008) (Level III-2 diagnostic evidence).

A comparison of conventional colonoscopy and NBI was performed in 302 prospectively recruited patients. The patients were analysed in a sequential manner with polyps found by conventional colonoscopy re-analysed by NBI. The polyp's histology grades were predicted with both techniques and this was compared to the actual histology determined at a later date. The diagnostic accuracy of conventional colonoscopy and NBI versus histology were not different (77% versus 80%, $p=0.35$). However, there was an apparent learning curve associated with the NBI technique as its accuracy improved from 74 per cent to 87 per cent over the course of the trial. The sequential design only allowed the testing of the diagnostic accuracy of polyps known by conventional colonoscopy and did not allow for the potential for different rates of polyp detection with NBI that may have occurred if it was used in isolation (Rogart et al 2008) (Level III-2 diagnostic evidence).

Sikka et al compared NBI versus conventional colonoscopy with regard to correct prediction of histology status as determined later. The population consisted of 63 patients and these were analysed with both techniques sequentially. NBI showed a sensitivity of 95 per cent (correctly identified 93/98 neoplastic polyps) and a specificity of 90 per cent (correctly identified 56/62 non-neoplastic polyps). Conventional colonoscopy had a sensitivity of 59 per cent (correctly identified 58/98 neoplastic polyps) and a specificity of 76 per cent (correctly identified 47/62 non-neoplastic polyps). The overall diagnostic accuracy of NBI was 93 per cent and for conventional colonoscopy was 66 per cent ($p<0.0001$) (Sikka et al 2008) (Level III-2 diagnostic evidence).

Most studies find that NBI performs at least equal to or better than conventional colonoscopy for the detection and prediction of the status of discovered polyps. Issues such as study design and learning curves were significant factors in some study outcomes.

2008 COST IMPACT

No studies reported on the relative costs of NBI versus conventional colonoscopy. Olympus, manufacturer of the CF-Q180 AL colonoscope used in several studies in this prioritising summary, was contacted regarding the cost of a NBI capable colonoscope system but at the time of publication no reply was forthcoming.

2008 Ethical, Cultural or Religious Considerations

No issues were identified/raised in the sources examined.

2008 Other Issues

No issues were identified/raised in the sources examined.

2008 Summary of findings

Based on the medium quality evidence presented in this prioritising summary, NBI seems to be an improvement over conventional colonoscopy. Evidence has been rapidly accumulating in recent times and a clear picture of the effectiveness of NBI may soon emerge.

2008 HealthPACT action:

The majority of colonoscopes manufactured have the capability of performing either conventional colonoscopy or narrow band imaging. There may be a learning curve involved in the use of narrow band imaging which may see the slow introduction of this technique. If the polyp detection rate is higher using narrow band imaging compared to conventional colonoscopy, then further investment in this technique would be warranted. Therefore HealthPACT have recommended that this technology be monitored in 12-months time for further information.

Number of included Studies

Total number of studies	
Level III-2 diagnostic evidence	5

References:

Adler, A., Pohl, H. et al (2008). 'A prospective randomised study on narrow-band imaging versus conventional colonoscopy for adenoma detection: does narrow-band imaging induce a learning effect?', *Gut*, 57 (1), 59-64.

AIHW (2007). *Incidence and prevalence of chronic diseases* [Internet]. Australian Institute of Health and Welfare. Available from: http://www.aihw.gov.au/cdarf/data_pages/incidence_prevalence/index.cfm#CRC [Accessed 15th October].

AIHW (2008). *Separation, patient day and average length of stay statistics by Australian Refined Diagnosis Related Group (AR-DRG) Version 5.0/5.1, Australia, 1998-99 to 2006-07* [Internet]. Australian Institute of Health and Welfare. Available from: http://www.aihw.gov.au/cognos/cgi-bin/ppdscgi.exe?DC=Q&E=/ahs/drgv5_9899-0607 [Accessed 15th October].

Bensen, S., Mott, L. A. et al (1999). 'The colonoscopic miss rate and true one-year recurrence of colorectal neoplastic polyps. Polyp Prevention Study Group', *Am J Gastroenterol*, 94 (1), 194-199.

Dekker, E. & Fockens, P. (2005). 'New imaging techniques at colonoscopy: tissue spectroscopy and narrow band imaging', *Gastrointest Endosc Clin N Am*, 15 (4), 703-714.

East, J. E., Saunders, B. P. et al (2007). 'Surface visualization at CT colonography simulated colonoscopy: effect of varying field of view and retrograde view', *Am J Gastroenterol,* 102 (11), 2529-2535.

Inoue, T., Murano, M. et al (2008). 'Comparative study of conventional colonoscopy and pan-colonic narrow-band imaging system in the detection of neoplastic colonic polyps: a randomized, controlled trial', *J Gastroenterol,* 43 (1), 45-50.

Kaltenbach, T., Friedland, S. & Soetikno, R. (2008). 'A Randomized Tandem Colonoscopy Trial of Narrow Band Imaging versus White Light Examination to compare Neoplasia Miss Rates', *Gut*.

Robertson, D. J., Greenberg, E. R. et al (2005). 'Colorectal cancer in patients under close colonoscopic surveillance', *Gastroenterology*, 129 (1), 34-41.

Rogart, J. N., Jain, D. et al (2008). 'Narrow-band imaging without high magnification to differentiate polyps during real-time colonoscopy: improvement with experience', *Gastrointest Endosc*.

Sikka, S., Ringold, D. A. et al (2008). 'Comparison of white light and narrow band high definition images in predicting colon polyp histology, using standard colonoscopes without optical magnification', *Endoscopy*.

SEARCH CRITERIA TO BE USED:

Colonic Polyps/*pathology
Colonoscopes
Colonoscopy/*methods
Diagnosis, Differential
Diagnostic Imaging/*instrumentation
Adenocarcinoma
Colorectal Neoplasms/*diagnosis/etiology
Colonic Neoplasms/diagnosis
Endoscopy, Gastrointestinal/*methods
Gastrointestinal Neoplasms/*diagnosis
Precancerous Conditions/diagnosis
Stomach Neoplasms/diagnosis