

Narrow band imaging for Barrett's oesophagus

Medtech innovation briefing

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Summary

- The **technology** described in this briefing is narrow band imaging (NBI). It is used for identifying neoplastic and dysplastic tissue during endoscopy in people with known or suspected Barrett's oesophagus.
- The **innovative aspects** are that NBI provides real-time optical enhancement of the endoscopy procedure, allowing the endoscopist to identify areas for targeted biopsy.
- The intended **place in therapy** would be as well as white-light endoscopy in people with Barrett's oesophagus either during initial diagnostic endoscopy or for surveillance of people with Barrett's oesophagus. It is intended to reduce or remove the need to take random biopsies.
- The **main points from the evidence** summarised in this briefing are from 3 studies: 1 randomised crossover trial, 1 feasibility study and 1 report on the development and validation of diagnostic criteria for NBI, including a total of 1,185 adults and 330 images. They show that NBI is at least as effective as white-light endoscopy in people with Barrett's oesophagus and suspected dysplasia and neoplasia.

- **Key uncertainties** around the evidence or technology are that current evidence for NBI was done in highly specialised centres, therefore it is unclear how generalisable this is to routine NHS practice.
- The **cost** of NBI would be as well as standard care and is estimated by the company to be £1,120 per NBI endoscopy. The increased **resource impact** may be offset if there is a reduced need for histopathology testing.

The technology

Narrow band imaging (NBI, Olympus) is an optical imaging technology that improves the visibility of vessels and other tissues on mucosal surfaces. It can be applied as part of a standard endoscopic examination. NBI is a part of the Evis Lucera Spectrum and Evis Lucera Elite endoscopy systems. It works by filtering the white light for specific light wavelengths that are absorbed by haemoglobin for maximum contrast. Using NBI, capillaries on the mucosal surface and veins in the submucosa are displayed in different colours on the endoscopist's monitor.

NBI can be used in several conditions, but this medtech innovation briefing focuses only on its use during both initial diagnostic endoscopy for people with suspected Barrett's oesophagus and as a monitoring tool for surveillance of patients with Barrett's oesophagus. Compared with white-light endoscopy, the images of capillaries seen when using NBI are more defined. This may reduce the possibility of missing an area of abnormal cells during endoscopy. During white-light endoscopy, random biopsies are taken to increase the diagnostic yield of neoplastic and dysplastic lesions. Using NBI allows areas to be identified for targeted biopsy and areas of normal tissue to be excluded by the endoscopist. The company claims the use of the technology could improve the real-time distinction between neoplastic or dysplasia lesions and surrounding non-neoplastic or non-dysplastic Barrett's tissue, reducing the need for histopathology because fewer biopsy samples are being taken.

Innovations

NBI uses an optical filter that limits light from 415 nm to 540 nm, matching the absorption spectrum of haemoglobin. While other technologies mainly focus on post-processing adjustments using software, NBI is an optical enhancement. There are other systems available that allow real-time assessment during endoscopy.

Current care pathway

Currently, people with suspected or known Barrett's oesophagus will have white-light endoscopy done by a doctor or specialist nurse. The current [British Society of Gastroenterology guideline](#) recommends the Seattle biopsy protocol, which includes 4-quadrant random biopsies every 2 cm as well as targeted biopsies on macroscopically-visible lesions at the time of diagnosis and at subsequent surveillance. It is reported that there is only slight discomfort and pain associated with this kind of biopsy. A variety of other imaging techniques may also be used to enhance visualisation of Barrett's oesophagus such as magnification, high-definition endoscopy and chromoendoscopy. However, expert advice suggests that these techniques are not routinely used in the NHS. Biopsies taken during an endoscopy are sent to histopathology where they are examined under a microscope to see if any abnormal cells are present, and to grade the extent of any abnormality.

When areas of abnormality are identified during an endoscopy, surveillance endoscopies can be recommended to monitor for further changes. In some cases, treatments to destroy or remove the abnormal cells and prevent them from progressing into cancer may be offered. NICE's guideline on [Barrett's oesophagus](#) describes the use of ablative therapy in people with high-grade dysplasia or intramucosal cancer. NICE has also published guidance on [endoscopic radiofrequency ablation for Barrett's oesophagus with low-grade dysplasia or no dysplasia](#). Other treatment options include endoscopic mucosal resection, photodynamic therapy or surgical resection.

Population, setting and intended user

Barrett's oesophagus is a condition where the cells of the oesophagus grow abnormally and can develop into cancer over time. The most common cause of Barrett's oesophagus is acid reflux, which can inflame the oesophagus and may lead to a condition called gastro-oesophageal reflux disease (GORD). Around 3% to 10% of people with acid reflux will develop Barrett's oesophagus.

NBI can be used for first-time diagnosis of Barrett's oesophagus or for surveillance endoscopies in people with Barrett's oesophagus. The endoscopy will be done in a hospital by a doctor or specialist nurse. Additional training may be needed to make optical diagnoses and target biopsies with NBI.

Costs

Technology costs

The cost for NBI endoscopy is additional to the cost of white-light endoscopy, however the company estimates that costs for histopathology will be decreased if NBI is used.

The company states that the average cost per person for NBI endoscopy is £1,120, this includes histopathology costs of £348 per person.

Costs of standard care

The company states that the average cost per person for standard white-light endoscopy is £1,340, this includes histopathology costs of £623 per person.

Resource consequences

The Evis Lucera Spectrum and Evis Lucera Elite endoscopy systems are used in about 84% of endoscopy units in the UK, these devices all have NBI capability. Adopting NBI will need no change for units already using Evis Lucera endoscopy devices.

Regulatory information

Narrow band imaging is included in the Evis Lucera Spectrum and Elite endoscopy systems; these devices are CE-marked class I medical devices. To examine the oesophagus a flexible endoscope is needed; this is a class IIa medical device.

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected

characteristics under the Equality Act 2010).

No equality issues were identified.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the [interim process and methods statement](#). This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Three studies are summarised in this briefing including 1,185 people with confirmed or suspected Barrett's oesophagus and a further 330 images obtained with narrow band imaging (NBI).

There are also 2 meta-analyses that are applicable to NBI. [Thosani et al. \(2016\)](#) reported pooled sensitivity, negative predictive value, and specificity for NBI of 94.2% (95% confidence interval [CI], 82.6 to 98.2), 97.5% (95% CI, 95.1 to 98.7), and 94.4% (95% CI, 80.5 to 98.6), respectively (reference standard not reported). [Qumseya et al. \(2013\)](#) reported that advanced imaging techniques (such as NBI) increased the diagnostic yield for detection of dysplasia or cancer by 34% (95% CI, 20% to 56%; $p < 0.0001$) in comparison with non-advanced endoscopy.

[Table 1](#) summarises the clinical evidence as well as its strengths and limitations.

Overall assessment of the evidence

The evidence for NBI is of good quality and provides useful information as to how NBI could be used in the NHS. The evidence includes a randomised crossover trial comparing NBI (targeted biopsy) with standard white-light endoscopy (random biopsy), a feasibility study that reports diagnostic accuracy and a report on the development and validation of a new criteria for optical diagnosis of dysplasia intended for use with NBI. The research was done in specialist centres and endoscopies were done by highly trained endoscopists so may not be reproducible in all NHS settings.

Table 1 Summary of selected studies

<u>Beg et al. (2018)</u>	
Study size, design and location	1,022 people with Barrett's oesophagus in a before-and-after study. Location: UK.
Intervention and comparator(s)	NBI. Comparators: acetic acid chromatography and white-light endoscopy. During the prospective period data were obtained for 560 gastroscopies. Endoscopies happening after April 2011 were done using white-light endoscopy and NBI. If the length of Barrett's epithelium was greater than 3 cm, acetic acid chromatography was also used.
Key outcomes	During 2007 to 2010 dysplasia was detected in 11.0% of patients, low-grade dysplasia in 7.7% and high-grade dysplasia or cancer in 3.3%. During 2011 to 2014 dysplasia was detected in 11.3% of patients, low-grade dysplasia in 9.4% and high-grade dysplasia or cancer in 1.9%.
Strengths and limitations	This study showed that using NBI and acetic acid chromatography did not result in an increased detection rate of dysplasia. This study has a before-and-after design and introduces a change in practice between the prospective period and the study period, which may have confounded results.
<u>Nogales et al. (2017)</u>	
Study size, design and location	Evaluation of 100 images of Barrett's oesophagus taken using NBI. Location: Spain.
Intervention and comparator(s)	Images obtained using non-magnifying NBI in the Evis Exera III endoscope. Interpretation of images compared with clinical assessment using white-light endoscopy and histopathology.

Key outcomes	Dysplasia prediction accuracy for NBI was 81.1%, sensitivity 48.4%, specificity 91%, positive predictive value 61.4% and negative predictive value 85.5%. Intraobserver concordance for dysplasia was weak, K=0.4.
Strengths and limitations	This study used the BING classification system to assess images. Diagnosis was made using a photographic image taken during endoscopy, which may have confounded results.
<u>Sharma et al. (2016)</u>	
Study size, design and location	Development and validation of a classification system to identify high-grade dysplasia and oesophageal adenocarcinoma with NBI. 230 images were reviewed during the development and validation process. Location: international (Barrett's international NBI group, BING).
Intervention and comparator(s)	NBI. No comparator.
Key outcomes	The classification system was developed and agreed during a meeting of the BING. The classification system was then independently validated by experts. The BING criteria identified patients with dysplasia at 85% overall accuracy, 80% sensitivity, 88% specificity, 81% positive predictive value, and 88% negative predictive value, compared with histology results. When dysplasia was identified with a high level of confidence, these values were 92%, 91%, 93%, 89%, and 95%, respectively, compared with histology results. Agreement between validating experts was high (K=0.681).
Strengths and limitations	Although this study does not compare NBI with any other method of endoscopy it provides useful guidance on how to classify images obtained by NBI. This study was funded by the company.
<u>Sharma et al. (2013)</u>	

Study size, design and location	123 people with Barrett's oesophagus in a randomised crossover trial. Location: international.
Intervention and comparator(s)	NBI and high-definition white-light endoscopy. During high-definition white-light endoscopy biopsies were taken every 2 cm as well as additional biopsies in areas with visible lesions. During NBI endoscopy only targeted biopsies were obtained. All patients received both endoscopy methods.
Key outcomes	Both high-definition white-light endoscopy and NBI detected intestinal metaplasia in 92% of patients. Use of NBI resulted in significantly fewer biopsies compared with high-definition white-light endoscopy (3.6 compared with 7.6 per person, $p < 0.0001$). NBI detected a higher proportion of areas with dysplasia (30% compared with 21%, $p = 0.01$). Endoscopists performing the procedures noted that irregular mucosal and vascular patterns were present in all areas of high-grade dysplasia and that non-dysplastic tissue appeared normal.
Strengths and limitations	The study is of good quality and is published in a leading journal. The study was done in 3 centres, 2 in the US and 1 in Netherlands, and therefore may not be representative of NHS practice. In this study results were analysed per lesion rather than by patient. This suggests NBI is able to detect more lesions but not necessarily more people with high-grade dysplasia.
<u>Singh et al. (2013)</u>	
Study size, design and location	40 people with Barrett's oesophagus in a preliminary feasibility study. Location: Australia.
Intervention and comparator(s)	Optical diagnosis using NBI with biopsy of target lesions, NBI dual focus mode (magnification up to 70 times) was also used. NBI optical diagnosis results were compared with final histopathological diagnosis.

Key outcomes	NBI: sensitivity 100%, specificity 93.8%, positive predictive value 68.6%, negative predictive value 100%. NBI dual focus: sensitivity 100%, specificity 86.2%, positive predictive value 73.6%, negative predictive value 100%.
Strengths and limitations	The authors specified that the dual focus mode was used in areas that appeared normal after NBI examination. It is not clear if this mode is available in all endoscope models.
Abbreviations: NBI, narrow band imaging.	

Recent and ongoing studies

- [Assessment of a consensus driven narrow band imaging \(NBI\) pattern classification system in Barrett's oesophagus](#). ClinicalTrials.gov identifier: NCT01580631. Status: suspended. Indication: Barrett's oesophagus. Devices: NBI.
- [A multicentre study evaluating the impact of NBI on patients with Barrett's oesophagus associated neoplasia undergoing endoscopic eradication therapy \(EET\)](#). ClinicalTrials.gov identifier: NCT03191604. Status: recruiting. Indication: Barrett's oesophagus. Devices: NBI, video intervention.
- [Cap assisted upper endoscopy versus high definition white light endoscopy and narrow band imaging alone in the detection of visible lesions Barrett's oesophagus: a randomised tandem study](#). ClinicalTrials.gov identifier: NCT03417570. Status: recruiting. Indication: Barrett's oesophagus. Devices: NBI, cap assisted upper endoscopy.
- [Endoscopic detection of early neoplasia in patients with Barrett's oesophagus](#). ClinicalTrials.gov identifier: NCT00590239. Status: recruiting. Indication: Barrett's oesophagus. Devices: not stated.

Specialist commentator comments

Comments on this technology were invited from clinical specialists working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

All 5 specialists were familiar with this technology and use it regularly.

Level of innovation

All specialists stated that narrow band imaging (NBI) is innovative (despite being first introduced to the NHS in 2006) and that it has not been superseded or replaced by other technologies. One specialist noted that the image produced by NBI is substantially different to images produced by other endoscopy methods, such as white-light endoscopy. Another specialist noted that NBI has inline filter manipulation, which differentiates it from other advanced endoscopy techniques and involves post-imaging manipulation.

One specialist noted that using NBI would need a novel protocol for optical assessment only without random biopsies.

Potential patient impact

All specialists suggested that if NBI allows earlier detection of dysplasia and early cancer, it could allow for earlier treatment and better health outcomes for patients. One specialist noted that if early neoplastic change is detected, radiofrequency ablation can be used to prevent any further changes to the tissue. Another specialist noted that use of NBI may lead to a slight reduction in endoscopy time because of fewer biopsy samples being collected.

All specialists noted that NBI is most useful in people with Barrett's oesophagus who have suspected dysplasia or unusual lesions. These people will have had a previous white-light endoscopy and will have been referred for further investigation at an endoscopy unit.

One specialist noted that if NBI reduces the number of biopsies needed it may be particularly beneficial to people who are not able to tolerate repeat biopsies, such as people on antithrombotic medication.

Potential system impact

Two specialists agreed that if NBI were used widely there would be a reduction in biopsies and associated costs. Earlier detection of cancer may also lead to reduced treatment costs. One specialist noted that NBI was likely to cost the same as white-light endoscopy

and that there was not enough evidence to support a reduction in histopathology costs.

One specialist estimated that two-thirds of endoscopy units in the UK use an Olympus endoscope with NBI functionality, another estimated that around 80% of units had NBI available.

All specialists highlighted the need for training for endoscopists in how to use NBI and on how to implement visual assessment technique over random biopsy.

General comments

Most endoscopy units in the NHS will have equipment that is capable of using NBI, however, most endoscopists have not been trained or evaluated in their use of this technology.

The evidence for NBI shows that it can be used to improve detection of high-grade dysplasia, however there is no evidence to show that it can be used to detect low-grade dysplasia. If low-grade dysplasia is detected the patient may be referred for ablation treatment because there is evidence to show that this can help prevent the disease from progressing.

The evidence for NBI compares its use with standard definition white-light endoscopy, however, specialist commentators note that high-definition white-light endoscopy with targeted biopsy is used in some endoscopy units in the NHS.

Specialist commentators

The following clinicians contributed to this briefing:

- Professor John de Caestecker, consultant gastroenterologist, University Hospitals of Leicester, no conflicts declared.
- Massimiliano di Pietro, senior clinical investigator scientist and honorary gastroenterology consultant, Medical Research Council Cancer Unit University of Cambridge and Cambridge University Hospitals, no conflicts declared.

- Professor Krish Ragnath, professor of gastrointestinal endoscopy and consultant gastroenterologist, Nottingham University Hospital, has declared receipt of consultancy, educational and research grants from Olympus.
- Ian Beales, consultant gastroenterologist, Norfolk and Norwich University Hospital, no conflicts declared.
- Dr Ben Collepriest, consultant gastroenterologist and endoscopy lead clinician, Royal United Hospital, Bath, no conflicts declared.

Development of this briefing

This briefing was developed by NICE. The [interim process and methods statement](#) sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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