Narrow Band Imaging in Gastroenterology

Nitin Aherrao*, Deepak Ahire**

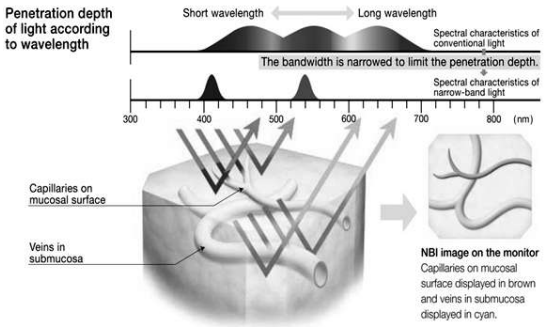
Introduction

Advanced endoscopic imaging techniques (AEITs) are imaging embedded in gastrointestinal scopes that allow changing the white-light (WL) image in order to enhance visualisation of the mucosal surface architecture and microvascular pattern, potentially improving endoscopic diagnosis.[1,2]

Narrow-band imaging (NBI) was initially developed by Sano et al. under the supervision of Dr Shigeaki Yoshida at the National Cancer Center Hospital East in 1999.[3,4] A prototype short-wavelength narrow-band red/green/blue (RGB) filter was successfully created in 2001 (monochrome NBI).[3,4] The microvascular architecture of the gastrointestinal tract and tumour surface structure were successfully visualised in colour using 415- and 540-nm short and medium-wavelength filters in 2003.[5] Subsequently, various improvements, such as noise reduction, light amount adjustment and colour adjustment, were made, and OLYMPUSEVIS LUCERA SPECTRUM (Olympus Medical Systems Corp., Tokyo, Japan) was launched in the market as the final mass production model in 2006. Yasushi Sano, Gastrointestinal Center, Sano Hospital, 2-5-1 Shimizugaoka, Tarumi-ku, Kobe, Hyogo 655-003. NBI provides enhanced images of vessels and surface patterns of lesions and has greatly contributed to detection and diagnosis of colorectal tumours. It has changed the role of ordinary diagnostic methods such as WL imaging and chromoendoscopy.

This study will highlight the application of NBI colonoscopy with or without optical zoom magnification for the detection and diagnosis of dysplasia, cancer in oesophagus and stomach, duodenal atrophy, colorectal lesions, and discuss the education and training of practitioners, and future perspective in Indian patients. Accurate in vivo prediction of polyp histology may prevent the removal of insignificant hyperplastic polyps detected in the distal colon (discard strategy) or the need for histologic assessment of diminutive polyps (resect and discard strategy), which decreases the duration, cost, and risks of colonoscopy.[6]

Based on the fact that light penetration is wave length dependant, shorter the wavelength, the shallower the penetration. NBI system consist of a filter with narrow band which increased blue light (WL 415 nm) & decreased red light (WL 630nm) contribution, real time endoscopic technique that enhances



*Gastroenterologist and Endoscopist, **Resident, Bombay Hospital and Medical Research Centre, 12 New Marine Lines, Mumbai - 400 020.

visibility of mucosal surface structure without use of dye (mucosal pattern). Integrated system with HRE mode & possibility of switching between both modes

Oesophagus

In the oesophagus, WLE provides little detail of the mucosal surface and is not able to accurately differentiate intestinal metaplasia from normal gastric mucosa or dysplastic epithelia. NBI allows a better evaluation of mucosal and vascular patterns that are associated with Barrett Oesophagus (BO), dysplasia, and oesophageal cancer .[1,7]

Magnification endoscopy with NBI (ME-NBI) also allows a better visualisation of normal capillary mucosal vessels (intraepithelial papillary capillary loops [IPCLs]) and submucosal vascularity (branching vessels).[1, 8] Normal IPCLs are observed as brown loops originating from a branching vessel, running perpendicularly in the lamina propria and finally reaching the intraepithelial papillae (Fig. 1a).[10] On the other hand, in neoplastic lesions the abnormal mucosal and capillary patterns have characteristic features. In squamous neoplastic lesions, IPCLs exhibit characteristic morphological changes, being dilated, tortuous, and irregular in dysplastic lesions, and destructed and replaced by tumour vessels in squamous cell carcinomas (SCCs).[1,8,9] Likewise, in BE a circular and "ridged/ villous" pattern with regular vessels is predictive of specialised intestinal metaplasia, and irregular mucosal and vessel patterns are predictive of dysplasia.[1,7]

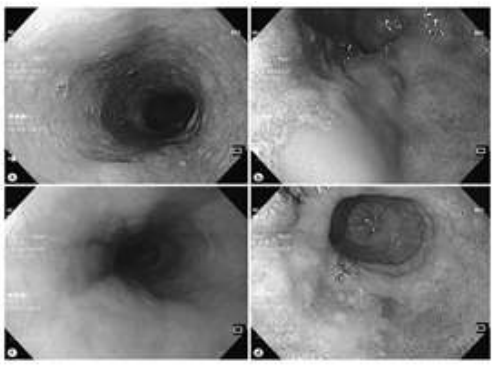


Fig. 1 a -Narrow-band imaging features in normal mucosa of the oesophagus (a), in squamous cell dysplasia (b), and in cancer (d). c White-light features in cancer.

IPCL (intra papillary capillary loop)- Brown loop originating from branching vessel which running perpendicularly in lamina propia and finally reaching the intraepithelial papillae. Examine IPCL carefully in the area with colour changes - dilatation, branching and irregular shape and calibre

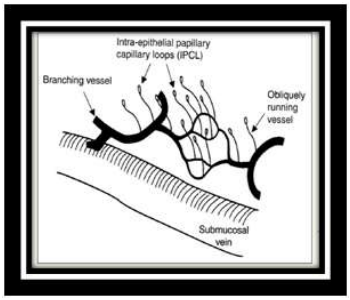


Fig. 1 b

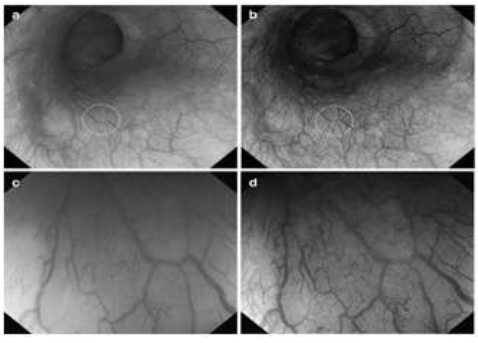


Fig. 1 C

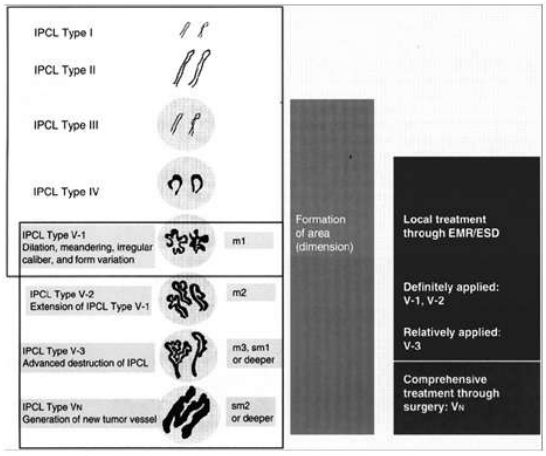
Fig. 1 C Showing

- No pits- surface appears flat
- Deeper mucosal vessels- branches (green)
- Superficial mucosal vessels- loops (intra papillary capillary loop, brown)

ME NBI Classification

This classification use for estimate invasion depth in SCC

- A) IPCL Pattern classification(INOUE Classification)
- B) Novel Classification - simpler to use in clinical practice
- IPCL-Described IN 2001 (Five pattern of IPCL) distinction between- normal mucosa, atypia, and cancer



The IPCL pattern classification includes two sets of diagnostic criteria.

IPCL pattern classification from IPCL type I to type V-1 is used for the tissue characterisation of flat lesions. IPCL type V-1 to type VN reflects cancer infiltration depth. IPCL type III corresponds to borderline lesions which potentially include oesophagitis or low-grade intraepithelial neoplasia. IPCL type III should be considered for endoscopic follow up. In IPCL type IV, high-grade intraepithelial neoplasia appears, and then further treatment with endoscopic mucosal resection (EMR) / endoscopic submucosal dissection (ESD) is recommended. EMR/ESD for IPCL types V-1 and V-2 should be also considered as they are definite M1 or M2 lesion with no risk of lymph node metastasis. IPCL type V3 corresponds to an M3 lesion, and diagnostic EMR/ESD should be applied as a "complete biopsy" to decide on a final treatment strategy. IPCL type VN corresponds to a "new tumour vessel", often associated with sm2 invasion with significantly increased risk of lymph node metastasis. Surgical treatment should be recommended.

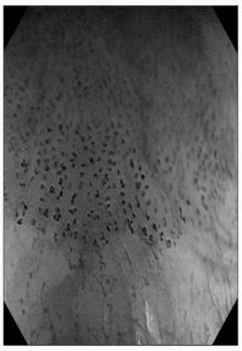
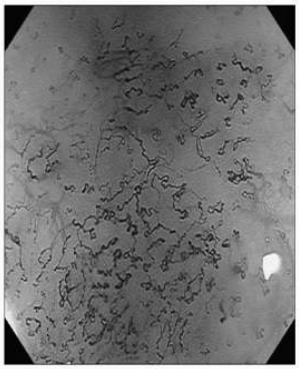


Fig. 1 d

- IPCL V1-Superficial Oesophageal cancer



IPCL V3- Cancer Involving Deeper Mucosa or Submucosa

The overall accuracy of pattern IPCL IV or greater was 80.0% (sensitivity 58.5% and specificity 96%). The sensitivity and specificity of IPCL type V1-2, type V3, and type Vn were 89.5 and 79.6%, 58.7 and 83.8%, and 55.8 and 98.6%, respectively. However, a small study compared diagnoses of the invasion depth of SCC between ME-NBI and WL and showed no additional benefit .

Barrett Oesophagus

Current guidelines recommend endoscopic surveillance in BE, with random 4-quadrant biopsy specimens obtained every 1-2 cm to detect dysplasia (Seattle protocol), in addition to targeted biopsies of suspicious lesions under WLE.[10]

Two studies showed that NBI with targeted biopsies improves the diagnosis of dysplasia when compared to HDWL examination with the Seattle protocol.[7,11] Additionally, three recent meta-analyses showed that NBI is an accurate test to diagnose dysplasia in BE, with a sensitivity of 94.2%, a specificity of 94.4%,and a negative predictive value of 97.5% in the most recent meta-analysis.[10,12]

Consensus-Driven Classification of Barrett's Epithelium

Morphologic characteristics	Classicifation
Mucosal pattern	
Circular, ridged/villous, or tubular pattern	Regular
Absent or irregular patterns	Irregular
Vascular pattern	
Blood vessels situated regularly along or between mucosal ridges and/or those showing normal, long, branching patterns	Regular
Focally or diffusely distributed vessels not following normal architecture of the mucosa	Irregular

Non dysplastic BE - Circular, tubular or villous mucosal pattern with regular vessel

Dysplasia - Irregular or absent mucosal pattern, vessel not following normal glandular architecture

For ME-NBI in BE, four classification systems have been proposed: from Kansas, Amsterdam, Nottingham, and the Barrett's International NBI Group (BING),1. The BING system is a simplified NBI classification proposed with the objective of integrating multiple classifications of NBI surface patterns in BE. In this classification, nondysplastic BE has a circular, tubular, or villous mucosal pattern with regular vessels, while dysplasia is characterised by an irregular or absent mucosal pattern and vessels not following the normal glandular architecture. Validation studies of this classification using MENBI showed that the BING classification can predict the presence or absence of dysplasia with a high level of accuracy (> 90 %) and very high interobserver agreement.[1,13,14] However, without magnification this classification seems less useful, based on a recent study evaluating HD-NBI without magnification in the diagnosis of dysplasia. The specificity and negative predictive value for dysplasia were high (>85%).

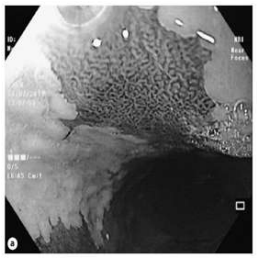


Fig. 1 e- Nondysplastic BE

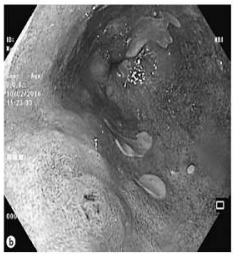


Fig. 1 f- Dysplastic BE

Stomach

Endoscopic evaluation of the gastric mucosa with WL correlates poorly with histological findings, while NBI can improve the correlation with histology.[1,15] Several NBI patterns, sometimes different patterns, have been associated with several gastric pathologies, namely, Helicobacter pylori (Hp) gastritis, intestinal metaplasia, dysplasia, intramucosal cancer, and submucosal cancer.

It is important to recognise that the normal gastric body and antral mucosa have a slightly different appearance with NBI .[16]

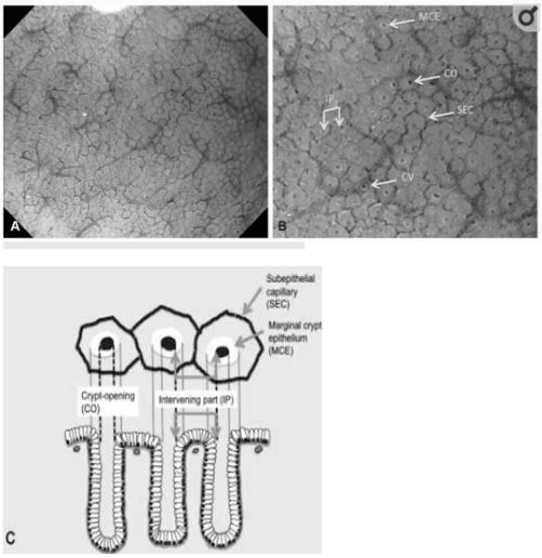


Fig. 2 a-Body and fundus of stomach

Fig. showing- Round pits, Microvessel arranged honeycomb pattern (SECN), Regular collecting venules (CV), Circular marginal crypt epithelium (MCE)

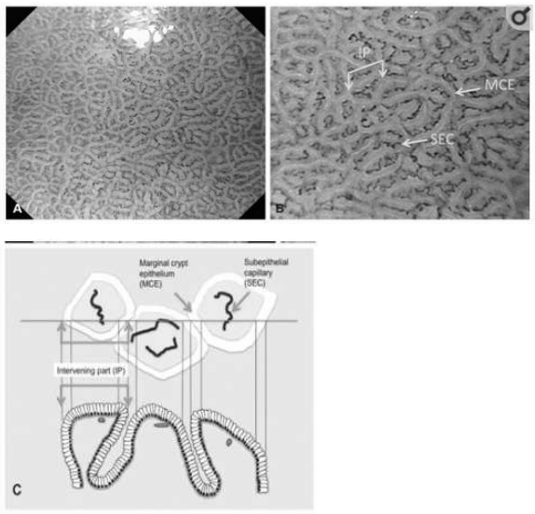


Fig. 2 b- Antrum of stomach

Fig. showing-Reticular pits, Regular coil subepithelial capillary, Absent collecting venules, Regular polygonal or Curved MCE

Gastric Intestinal Metaplasia, Dysplasia, and Early Gastric Cancer

With NBI, the presence of regular mucosal and vascular patterns excludes dysplasia, being that ridged or villous patterns are suggestive of intestinal metaplasia.[10,31,33,34] Other features besides pits and vascular patterns were associated with histological findings. For example, areas of intestinal metaplasia can present as a"light-blue crest," which is defined as a fine, blue line on crests of epithelial surfaces/gyri, being highly specific for the diagnosis of intestinal metaplasia.[38] On the other hand, dysplasia or cancer may present as a "white opaque substance," which, as the name implies, is

characterised by white material above the mucosa.[8,16,17] However, a white opaque substance has also been associated with intestinal metaplasia, so it is not a specific marker

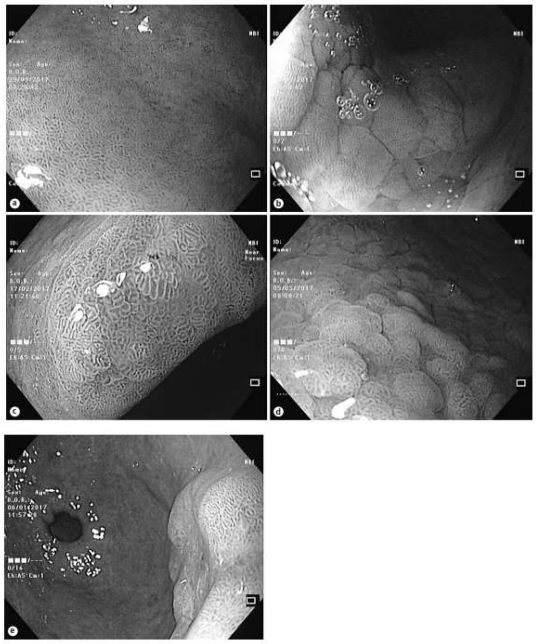


Fig 2c

Narrow-band imaging simplified classification for gastric lesions.

a Pattern Aa (normal antrum, with regular oval/circular mucosa and regular vessels in the centre of the gland). b Pattern Ab (normal gastric body, with regular circular mucosa and the gland surrounded by regular vessels). c, d Pattern B corresponds to intestinal metaplasia of the antrum and of the gastric body (regular, ridge, or tubulovillous mucosal patterns with regular vessels; presence of a light-blue crest). e Pattern C is associated with dysplasia/cancer (absent or irregular mucosal patterns with architectural distortion and irregular vascular patterns).

For the evaluation of gastric lesions with NBI, three classifications were proposed: a simplified classification system for NBI in the diagnosis of gastric lesions, the vessels plus surface classification, and the classification of gastric lesions proposed by Li.[1,15,16,19,20] To our knowledge, for the diagnosis of gastric atrophy there is no validated NBI endoscopic pattern or classification

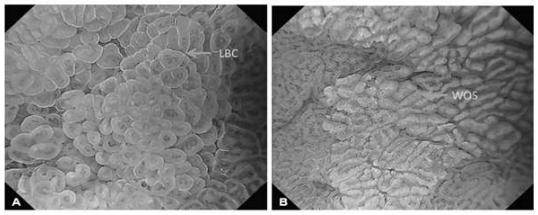
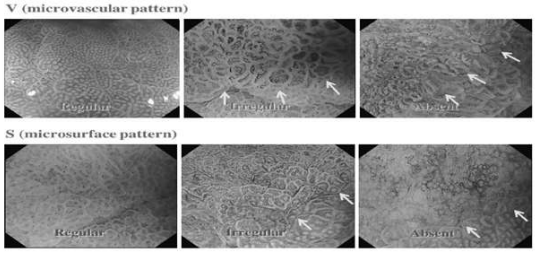


Fig. 2 d

Intestinal metaplasia - Light blue crest (epithelial margin), "Ridge and villous pattern"

Dysplasia or cancer - White opaque substance (WOS) visualised by reflections/strong scattering of whole projected lights located in the surface epithelium of the intervening part.

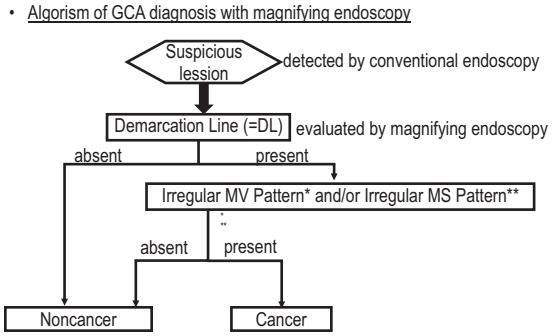
Gastric Cancer - VS Classification



ME-NBI has also been proven useful in the diagnosis of early gastric cancer, and the magnifying endoscopy simple diagnostic algorithm for early gastric cancer (MESDA-G) was recommended for the evaluation of a suspicious gastric lesion.[21] It applies the Vessels plus Surface Classification and suggests evaluation with NBI if a clear border between the suspicious lesion and the background mucosa (demarcation line) exists: if absent, it excludes cancer; if present, microvascular and microsurface patterns

should be evaluated.

Magnifying Endoscopy Simple Diagnostic Algorithm for Early Gastric Cancer (MESDA-G)



Propossed-Endoscopic grading of gastric intestinal metaplasia with NBI

This classification considers five different gastric areas: two areas in the antrum, two in the body, and one in the incisura. Each area may have a score of 0 (no intestinal metaplasia), 1 (focal intestinal metaplasia, ≤30% of the area), or 2 points (extensive intestinal metaplasia in that area, >30% of the area), resulting in a possible total of 10 points. The total score will vary from 0 (normal endoscopy with no areas suggestive of intestinal metaplasia) to 10 (diffuse metaplasia). The letter a or c is added to the score if metaplasia is more evident in the antrum (a) or in the corpus/body (c), suggesting environmental or autoimmune gastritis, respectively.[15] An endoscopic grade of gastric intestinal metaplasia of 5 was identified as the optimal cutoff value to identify patients with extensive intestinal metaplasia deserving surveillance, with a sensitivity of 94.2% and a specificity of 95.2%.[15] This classification showed a high correlation with histology and is thus a promising tool, although validation studies are still needed.

Fig 2 f-

	Proposed classification				
	A	B		Hp+	C
Mucosal pattern	Regular Circular	Regular ridge/tubulo-villous	Light blue crest	Regular	Irregular/absent White oapque substance
Vascular pattern	Regular Thin/peripheric (body (b) or thick/central (a) vessels	Regular		Regular with variable vascular density	Irregular
Expected outcome	Normal	Intestinal metaplasia		H.pylori infection	Dysplasia

Subtype= Aa- normal antrum, Ab- normal body

+ > Hp gastritis , Aa + Hp gastritis in normal antral mucosa

Duodenum

Duodenal mucosal lesion are frequent cause of malabsorption and, in these patients, conventional white light endoscopy (WLE) does not show any mucosal abnormality.[22] Hence, biopsy of abnormal-appearing areas on WLE would miss the diagnosis in many patients. Advances in endoscopic technology have facilitated visualisation of the mucosal surface in greater detail and enabled the detection of lesions not apparent on conventional WLE.[23] Magnification narrow band imaging (NBI) endoscopy allows clear visualisation of duodenal villi and assessment of their morphology.[24] This technique helps identify villous atrophy prior to biopsy as well as recognise patchy lesions that may help obtain a targeted biopsy, thereby increasing the diagnostic yield of the biopsy specimen.[1,25,26] The current practice of obtaining random duodenal mucosal biopsies from normal appearing areas in all patients with

suspected malabsorption is not optimal as the histology may be normal in a large number of patients which adds to the cost of treatment. NBI, by virtue of being able to identify normal microsurface and microvascularity may enable us to avoid unnecessary biopsies from normal-appearing areas.[24,27] We aimed to assess the sensitivity and specificity of NBI compared to histology in the diagnostic evaluation of patients suspected to have disorders causing malabsorption.

In normal subject the villi have greater length than breadth which gives them a leaf or finger like appearance the Light Blue Crest present - at the edge of villi and intravillous capillary loop network. Atrophy of villi alter this ratio and makes them appear shortened or convoluted or stubbed or even absent in patient with villous atrophy.

A villous crypt ratio of >3:1 was considered normal; a ratio of 1-3:1 denoted the presence of mild to moderate atrophy and a ratio <1:1 signified severe villous atrophy.[28] In addition to villous morphology, crypt architecture and presence of other lesions and parasites were also assessed.

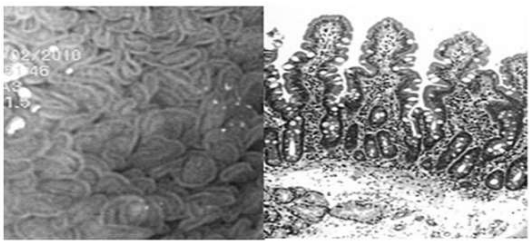


Fig 3 a

Appearance of normal duodenal villi on magnification narrow band imaging (Left) and histology (Right, 20× magnification

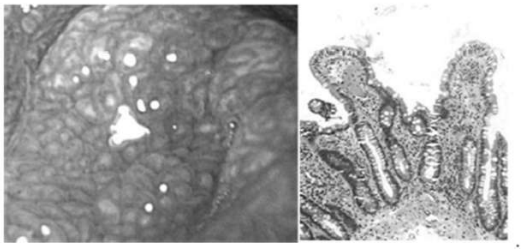


Fig 3b

Mild duodenal villous atrophy

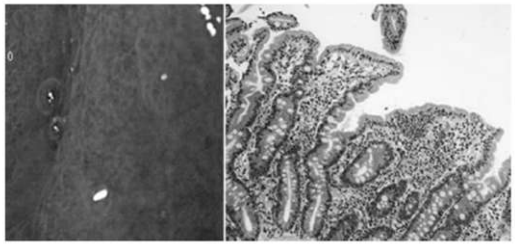


Fig 3 c

Severe duodenal villous atrophy

Colon

Normal colonic mucosa presents a circular and regular gland and vessel pattern on NBI. Colon inflammation maintains the same pattern, but with thicker vessels and variable vascular density, which confer a reddish appearance of the mucosa. When this pattern is seen in a polyp or lesion, it suggests a mucosal or inflammatory polyp.

Polyps/Flat Lesions

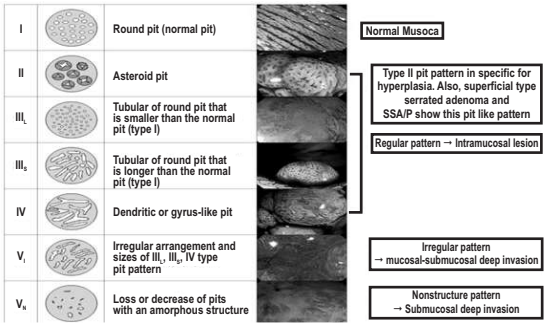
Most colorectal polyps/superficial lesions are histologically classified into adenomas and serrated polyps (hyperplastic polyps [HPs], sessile serrated adenomas/polyps [SSA/Ps], and traditional serrated adenomas).[29]

NBI provides enhanced vessel and surface patterns of lesions and contributes to the detection and characterisation of colorectal polyps. It is helpful for the

prediction of histology (real-time optical biopsy) and for estimating the depth of invasion of a colorectal cancer.[8,30] The use of validated scales allows an improvement of the diagnostic accuracy of in vivo optical diagnosis and decreases interobserver variability.[31]

The Kudo classification characterises the mucosal pit pattern, and the Sano classification assesses the capillary pattern. Both of them were the mainstay of polyp assessment, and the remaining systems were derived from the former ones.[31,33]

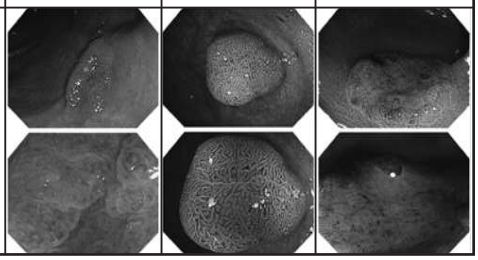
Fig 4 a



The NBI International Colorectal Endoscopic (NICE) (Fig.4b) and the Japan NBI Expert Team (JNET) classifications simultaneously evaluate surface and capillary patterns.[1,34] The NICE classification was proposed in 2012 by an international expert group for the diagnosis of colonic lesions.[35,36] An advantage of this Western validated classification is that it can be applied using NBI with or without optical magnification.[1,35] It categorises three types of lesions: type 1 (HP), type 2 (adenoma), and type 3 (deep submucosal invasive colorectal carcinoma).[8,35,36]

Fig 4 b-

NBI International Colorectal Endoscopic (NICE) Classification*

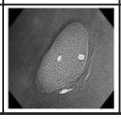
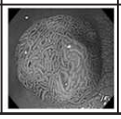
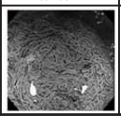
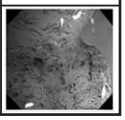
	Type 1	Type 2	Type 3
Color	Same or lighter than background	Browner relative to background (verify color arises from vessels)	Brown to dark brown relative to background; sometimes patchy whiter areas
Vessels	None, or isolated lacy vessels coursing across the lesion	Browner vessels surrounding white structures**	Has area(s) of disrupted or missing vessels
Surface Pattern	Dark or white spots of uniform size, or homogeneous absence of pattern	Oval, tubular or branched white structure surrounded by brown vessels**	Amorphous or absent surface pattern
Most likely pathology	Hyperplastic	Adenoma***	Deep submucosal invasive cancer
Examples			

* Can be applied using colonoscopes with or without optical (zoom) magnification
** These structures (regular or irregular) may represent the pits and the epithelium of the crypt opening.
*** Type 2 consists of Vienna classification types 3, 4 and superficial 5 (all adenomas with either low or high grade dysplasia, or with superficial submucosal carcinoma). The presence of high grade dysplasia or superficial submucosal carcinoma may be suggested by an irregular vessel or surface pattern, and is often associated wtih atypical morphology (e.g. depressed area).

The NICE classification with unmagnified NBI distinguishes neoplastic from nonneoplastic lesions as accurately as does ME-NBI (with a sensitivity, specificity, and negative predictive value of 97.5, 83.3, and 92.6% for unmagnified NBI vs. 97.5, 85.1, and 95.2% for ME-NBI, respectively).[37] However, with ME-NBI the rate of optical diagnoses of diminutive and small colorectal polyps is significantly improved.[38] The NICE classification is also clinically useful to predict deep submucosal invasive carcinoma (with a sensitivity of 94.9% and a negative predictive value of 95.9%).[36]

The JNET classification was proposed in 2014 The JNET classification was proposed in 2014,[39] aiming to unify previous classifications into one universal ME-NBI classification of colorectal tumours.[39] Lesions are classified into four types.[39]

Fig 4 c-

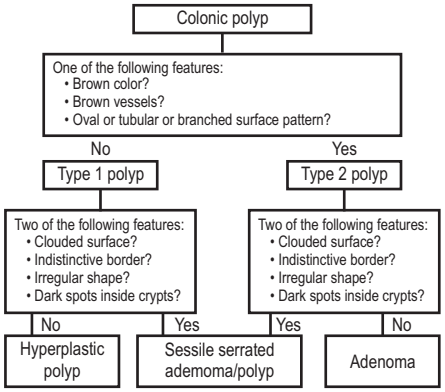
	Type 1	Type 2A	Type 2B	Type 3
Vessel pattern	• Invasible*1	• Regular caliber • Regular distribution (meshed/spiral pattern)*2	• Variable caliber • Irregular distribution	• Loose vessel areas • Interuption of thick vessels
Surface pattern	• Regular dark or white spots • Similar to surrounding normal mucosa	• Regular (tublar/branched/ papillary)	• Irregular or obscure	• Amorphous areas
Most likely histology	Hyperplastic polyp/ Sessile serrated polyp	Low grade intramucosal neoplasia	High grade intramucosal neoplasia/Shallow submucosal invasive cancer *3	Deep submucosal invasive cancer
Endoscopic image				

*1. If visible, the caliber in the lesion is similar to surrounding normal mucosa.
*2. Micro-vessels are often distributed in a punctate and well-ordered reticular or spiral vessels may not be observed in depressed lesions.
*3. Deep submucosal invasive cancer may be included.

A recent retrospective analysis concluded that types 1, 2A, and 3 of the JNET classification were very reliable indicators of a polyp histology (with a sensitivity, specificity, and accuracy of 87.5, 99.9, and 99.3% for type 1; 74.3, 92.7, and 77.1% for type 2A; and 55.4, 99.8, and 96.6% for type 3, respectively). However, the accuracy for type 2B lesions was lower (with a sensitivity, specificity, and accuracy of 61.9, 82.8, and 78.1%); for this type of lesions, chromoendoscopy with added indigo carmine improves diagnosis.[40] At present, large-scale validation studies of the JNET classification are needed to prove its utility in clinical practice.[39]

The current classification systems based on NBI do not include serrated adenomas (SSA/Ps and traditional serrated adenomas). These lesions are difficult to differentiate from HPs and sometimes from adenomas.[23] Recently, the workgroup serrated polyps and polyposis (WASP) classification was developed and validated to allow endoscopic differentiation between adenomas, HPs, and SSA/ Ps <10 mm in a stepwise approach (Fig. 4d).[29] First, colonic polyps are assessed for the presence of adenoma like features using the NICE criteria. The presence of at least one adenoma like feature is sufficient to diagnose a type 2 polyp. Subsequently, the diagnostic criteria are used to differentiate between SSA/Ps and HPs for type 1 polyps, and between SSA/Ps and adenomas for type 2 polyps. The presence of at least two SSA/P-like features is considered sufficient for a diagnosis. The introduction of the WASP classification significantly improved the accuracy of the optical diagnosis of serrated lesions, which showed to be sustainable after 6 months.[29] However more studies are needed before using this classification in clinical practice.

Fig- 4 d



Summary

1) **Squamous cell carcinoma of oesophagus-**

- NBI- better sensitivity for superficial oesophageal SCC when compared to WLE (97 % vs 55 % , p <0.001)
- NBI have increased accuracy and

specificity - as compared with Lugol (sensitivity similar)

- AS Low incidence of SCC in most countries, NBI used Routinely in pt with risk of SCC (with h/o head and neck ca, previous biopsy with dysplasia or caustic oesophagitis)
- In general population, value of NBI still to be determined, but probably it is only justified for improving characterisation, guiding biopsies and delimitation if any change in the oesophageal mucosa is seen with HDWL.

2) Barrett's Oesophagus

- NBI with targeted biopsies improves diagnosis of dysplasia when compare to HDWL examination with Seattle protocol
- NBI - accurate test to diagnosis Dysplasia in BE (Sensitivity- 94.2%, specificity- 94.4%, NPV-97.5%)
- Therefore, NBI is an important adjunctive tool that can help to target biopsies to suspicious areas and to delineate oesophageal lesions for endoscopic resection, and has a promising role in replacing the Seattle protocol in the future at least in reference centres, although more studies are needed before this recommendation can be made.

3) Stomach

In conclusion, NBI (with and without magnification) is accurate in the diagnosis of gastric intestinal metaplasia and dysplasia, and is superior to WL.[46,47] The use of NBI also improves the diagnosis of early gastric cancer[48-51] and is also helpful in the preoperative demarcation of cancer to prevent positive surgical margins postoperatively. NBI should be seen as a complement to WL, improving the diagnosis and detection of extensive intestinal metaplasia and superficial lesions with dysplasia and cancer.

4) Colon

- NBI may not significantly increase the rate of detection of colorectal neoplasia in average-risk populations . NBI could be an option for high-risk patients
- NBI is a useful tool for characterising lesions (predicting the risk of invasive cancer and defining margins of resection and residual neoplasia in piecemeal polypectomy scars)
- Helping to choose the best therapy (endoscopic mucosal resection, endoscopic submucosal dissection, or surgery).

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Atraumatic (pencil-point) versus conventional needles for lumbar puncture: a clinical practice guideline

Is the needle tip configuration important when performing a lumbar puncture for any indication? A systematic review published in the Lancet in December 2017 suggests that it is. The review found that using atraumatic (pencil-point) lumbar puncture needles instead of conventional lumbar puncture needles reduced the risk of post-dural-puncture headache and of return to hospital for additional pain control. This guideline recommendation aims to promptly and transparently translate this evidence to a clinical recommendation, following standards for GRADE methodology and trustworthy guidelines. The BMJ Rapid Recommendations panel makes a strong recommendation for the use of atruamatic needles for lumbar puncture in all patients regardless of age (adults and children) or indication instead of conventional needles.

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