



A narrative review: narrow-band imaging endoscopic classifications

Qingya Yang^{1#}, Zhimei Liu^{2#}, Hui Sun¹, Fangdong Jiao¹, Bing Zhang¹, Jun Chen³

¹Department of Urology, Qilu Hospital (Qingdao), Cheeloo College of Medicine, Shandong University, Qingdao, China; ²Department of Clinical Medicine, Qingdao Medical College, Qingdao University, Qingdao, China; ³Department of Urology, Qilu Hospital, Cheeloo College of Medicine, Shandong University, Jinan, China

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[#]These authors contributed equally to this work.

Correspondence to: Jun Chen. Department of Urology, Qilu Hospital, Cheeloo College of Medicine, Shandong University, 107 Wenhua West Street, Jinan 250000, China. Email: chenjunxinxiang@163.com.

Background and Objective: With the development of endoscopic techniques, narrow-band imaging (NBI) has been widely used in the diagnosis of various types of diseases. NBI can detect mucosal lesions at an early stage and different classification strategies have been established to help clinicians in disease diagnosis. However, there is currently no consensus for the classification criteria. This report summarizes the current classifications of diseases using NBI, so as to provide a comprehensive understanding of the various manifestations of mucosal lesions under NBI, and to promote the development of more practical NBI classifications.

Methods: The PubMed database was searched for English language articles published between January 1994 and November 2021 using the keywords ‘narrow band imaging’, ‘NBI’, and ‘classification’.

Key Content and Findings: We systematically summarized the NBI classifications and manifestations of different diseases. The morphology of the mucosa and vessels was used as the basis of most classifications. These classifications are mainly helpful to distinguish benign and malignant tumors and to detect early neoplastic lesions.

Conclusions: This review summarized existing NBI classifications for different systems. These classifications will be updated as the understanding of diseases increases and new optical techniques become available to better assist doctors in making clinical decisions.

Keywords: Narrow-band imaging (NBI); classifications; cancer; endoscopy; diagnosis

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Introduction

Cancer is a major cause of death worldwide and remains a major public health threat (1-3), with a predicted 34 million annual global cases by 2070 (1). It has been widely accepted that the early detection and effective

treatment of cancer can decrease the mortality rate (4-6). Therefore, different guidelines have been established to efficiently and effectively detect cancer (7).

A variety of diagnostic methods have been used in clinical practice, including advanced endoscopic

imaging technology, which is a minimally invasive and intuitive diagnostic method used for early detection and identification of various types of cancer (8-11). Narrow band imaging (NBI) is a powerful tool for the diagnosis of disease as it enables clear visualization of the surface of the capillary vessels. Indeed, numerous studies have shown that NBI can improve the precision of tumor diagnosis (12-17).

With increasing research, multiple NBI endoscopic classifications have been established based on different organs. These classifications show differences as well as similarities between organs. Comparing different classifications can provide a reference for diseases that have no NBI classification, such as bladder tumors; it can also provide clues for further improving the existing classifications. Since all classifications are based on the same NBI technique, it may be possible to identify a general classification feature. However, until now, there has been no comprehensive review on this topic. Herein, we present a detailed review of the current NBI endoscopic classifications, so as to provide a useful guidance for precise diagnosis. We also present several possible advancements of other diseases which will be explored further. Moreover, we have proposed some improvements on the classification and diagnosis of several types of diseases, which are still currently under research. We present the following article in accordance with the Narrative Review reporting checklist (available at <https://qims.amegroups.com/article/view/10.21037/qims-22-728/rc>).

Methods

A systematic literature search was conducted in the PubMed database using the keywords “narrow band imaging”, “NBI”, and “classification”. Articles published from 1 January 1994 to 10 November 2021 were included. Two investigators independently checked each identified article according to the inclusion criteria. A total of 75 English articles were selected. *Table 1* shows the detailed search strategy.

The mechanism of NBI

NBI is one of the advanced endoscopic imaging technologies. Since the first pilot study reported by Sano *et al.* in 2001, it has been applied for decades (18,19). NBI can improve the resolution and contrast of an image by using a superior method of visualizing the mucosal and submucosal vasculature (20). When the instrument is in NBI mode, the optical filters only allow 2 specific

wavelengths to pass through, namely, 415 nm (blue light) and 540 nm (green light). The blue light and green light are absorbed by hemoglobin (21). The wavelength of blue light is relatively short and can clearly detect the appearance of superficial mucosal vessels with brown color. In contrast, the green light can be used to show the appearance of the blood vessels in the submucosa with cyan color.

The application value of NBI in the detection of early cancer is that it can identify the intrapapillary capillary loops (IPCLs) (21-23). In stratified epithelium, IPCLs are single loops originating from the arborescent vascular network, which is connected to the submucosal vessels (24). The structure of the vessels changes dynamically to ensure metabolic exchanges. The IPCLs initially elongate and dilate, and when tumors invade the submucosa, they are destroyed and replaced by irregular neo-tumor vasculature (24,25).

NBI can therefore be used as a powerful tool to observe endoscopic features and make classifications for better diagnosis. As such, we will present literature reviews for the existing NBI classifications of different organs.

Head and neck tumors

NBI, to date, has been used in the diagnosis and classification of lesions located in the head and neck, including oral, pharyngeal, laryngeal, and sinonasal diseases. Using NBI, the surface and the capillaries can be seen clearly, and thus, classifications are always based on their morphology.

The classifications of laryngeal lesions

NBI is valuable in detecting early laryngeal cancer (26,27) and currently, 4 types of classifications are available, including Ni Classification 2011, Ni Classification 2019, the European Laryngological Society (ELS) Classification, and Puxeddu Classification (*Table 2*).

Ni Classification was initially reported in 2011, and updated in 2019 with an additional classification of the vocal cord leukoplakia. In Ni Classification 2011, Ni classified IPCL changes into 5 groups (I to V). Type I to IV are considered benign. Type V, which is regarded as malignant is subdivided into types Va, Vb, and Vc according to shape, regularity, and distribution of vessels (28).

In Ni Classification 2011, the vocal cord leukoplakia was assigned to type III lesions. However, different researchers have reached different conclusions when they observed the images. Therefore, Ni *et al.* updated the Ni Classification in 2019 to resolve the inconsistencies. The 2019 version

Table 1 Summary of the literature search strategy

| Items | Specification |
|-------------------------------------|--|
| Date of search | Nov 10, 2021 |
| Database and other sources searched | PubMed |
| Search terms used | “narrow band imaging”, “NBI”, and “classification” |
| Timeframe | January 1994 to November 2021 |
| Inclusion and exclusion criteria | Inclusion criteria: articles which describe the classification of NBI Exclusion criteria: articles which describe the features of diseases but with no classification |
| Selection process | Z Liu and Q Yang conducted the selection, all authors attended a meeting to discuss the literature selection and a consensus was reached. |

NBI, narrow-band imaging.

divided vocal cord leukoplakia into 6 types (*Figure 1*) (29).

ELS Classification was reported by Christoph Arens, and divides the vocal fold diseases into 2 groups, namely, benign and premalignant or malignant lesions. They specified that the benign conditions include longitudinal vascular changes, such as ectasia, meandering vessels, increasing number and density of blood vessels, and vessel branches or direction changes. However, indicator vessels are not specific a symptom of benign lesions as they can also occur in malignant lesions. Therefore, when clinicians observe this kind of change, they need to examine the pathology of the vocal fold. Moreover, the premalignant lesions are featured by perpendicular vascular changes, indicating dilated IPLs. The spiral shape with wide-or narrow-angled turning points indicate recurrent respiratory papillomatosis (RRP) or precancerous or cancer lesions, and further attention is warranted when clinicians observe this change (30).

The Puxeddu Classification, developed by Puxeddu *et al.*, is used to detect neoangiogenesis in tumors. It is divided into 5 types (0 to IV) based on the enhanced contact endoscopy vascular patterns. Each type represents normal mucosa, inflammation, hyperplasia, mid-moderate dysplasia, and high-grade dysplasia (HGD)/carcinoma in situ (CIS)/invasive carcinoma, respectively (31).

Some researchers have compared the previous 3 classifications, and set up a vocal fold leukoplakia (VFL) management algorithm (32). Indeed, a deeper understanding of these classifications may help clinicians to better manage diseases.

The classification of sinonasal lesions

Bruno *et al.* introduced the sinonasal mucosa (SN) patterns,

which are classified into five groups (SN1 to SN5), to assist the diagnosis of sinonasal diseases.

SN1 is regarded as the normal mucosa and the images vary along with the subsite of the nasal cavity: head of turbinate: a dotted pattern composed of small and close dark dots; body of turbinate: a simple network of loosely arborescent vessels oriented in a parallel manner and in posterior-anterior direction; and nasal septum: small and thin dark-blue vessels which are crowded and densely branched.

SN1 is only represented in normal mucosa, whereas SN2–5 can be observed in various diseases. SN2 represents the irregular speckles with a background of edematous mucosa; it shows diffuse and thin vessels compared to SN1, which can be found in allergic rhinitis, atrophic rhinitis, chronic rhinosinusitis without nasal polyps (CRSsNP), and normal mucosa.

The image of SN3 is green/blue oblique vessels sparsely distributed in a “broken apart” fashion, while an underlying vascular background is not clearly visible. SN3 can be found in sinonasal papilloma, eosinophilic granulomatosis with polyangiitis (formerly, Churg-Strauss syndrome), chronic rhinosinusitis with nasal polyps (CRSwNP), CRSwNP in cystic fibrosis, allergic rhinitis, synechia, and squamous cell carcinoma.

SN4 is described as large elongating and congested vessels with thinner anastomoses joining the individual branches. It can be observed in different pathology pictures of sinonasal disease, including sinonasal papilloma, eosinophilic granulomatosis with polyangiitis, Schwannoma, intestinal-type adenocarcinoma (ITAC), septal perforation, CRSsNP, granulomatosis with polyangiitis (formerly, Wegener’s granulomatosis), CRSwNP in cystic fibrosis,

Table 2 The classifications of laryngeal lesions

| Classification | Lesion manifestations |
|--|--|
| Ni Classification [2011] | <p>I: IPCLs are almost invisible, while oblique and arborescent vessels of small diameter can be seen</p> <p>II: IPCLs are almost invisible, but the vessels that can be seen have a larger diameter</p> <p>III: the mucosa is white and the IPCLs are invisible, and whether oblique and tree-like-vessels can be seen is dependent on the thickness of the white patch</p> <p>IV: mucosal IPCLs are arranged comparatively regularly and are low in density. There are bifurcations or slight dilations of the capillary terminals, and IPCLs appear to be scattered, tiny, dark brown spots. Oblique and arborescent vessels are usually invisible</p> <p>Va: with their high density and prominent dilation, IPCLs can appear solid or hollow, brownish, speckled, and shaped in various ways</p> <p>Vb: as IPCL destructs, its remnants look like snakes, earthworms, tadpoles, or branches. Additionally, the micro-vessels dilate, elongate, and appear woven</p> <p>Vc: necrotic tissue covers the lesion surface, and the tumor surface is irregularly covered with IPCLs which appear as brownish speckles or tortuous shapes with uneven density</p> |
| Ni Classification of the vocal cord leukoplakia [2019] | <p>I: in contrast to IPCLs, white plaque is observed, with obliquely running vessels and branching vessels under it</p> <p>II: white patches appear, but IPCLs, obliquely running vessels, or branches cannot be seen</p> <p>III: on the surface of the vocal cord mucosa without leukoplakia, IPCLs appear as small brown spots with a relatively regular arrangement without boundaries. There are no obliquely running or branching vessels</p> <p>IV: IPCLs can be observed, showing large brown spots and embedded at the surface of white plaques</p> <p>V: IPCLs can be seen, shown as large brown spots, which appear at the surface of the vocal cord mucosa outside the leukoplakia with obvious boundaries</p> <p>VI: IPCLs are visible, characterized by large brown spots or twisted earthworm-like vessels distributed at the surface of the leukoplakia and also at the surface of the vocal cord epithelium outside the leukoplakia</p> |
| ELS Classification [2016] | <p>Benign lesions: longitudinal vascular changes</p> <p>Premalignant lesions: perpendicular vascular changes</p> |
| Puxeddu Classification [2015] | <p>0 (normal mucosa): thin-end regular subepithelial vessels connecting with a thicker and deeper arborescent vascular network running parallel to the epithelium</p> <p>I (inflammation): the subepithelial vessels are increased in number and size, with irregular and sometimes crossing directions.</p> <p>II (hyperplasia):</p> <p>(i) Initial stage: intra-CLs are visible running toward the surface. CLs are generally still very thin and short, arising from the underlying inflammatory vasculature, with a scattered distribution;</p> <p>(ii) Mature hyperplasia: the deeper inflammatory vascular network is not visible, and only the elongated CLs can be easily seen;</p> <p>(iii) Vegetating keratosis: the deeper inflammatory vascular network is often not visible, and the elongated CLs are difficult to see. A particular type of “bobby-pin” which is encased by typical papilloma can be seen in laryngeal papillomatosis.</p> <p>III (mild-moderate dysplasia): vascular changes become more consistent, with elongated small vessels in the typical “bobby-pin” shape, but some arborescence appears at the end of the CLs</p> <p>IV (high-grade dysplasia/carcinoma in situ/invasive carcinoma): the vascularity of the chorion is more evident, and CLs appear significantly dilated, with various shapes and a wide range of vascular architectural changes such as corkscrews or tree-like patterns</p> |

IPCLs, intrapapillary capillary loops; CLs, capillary loops.

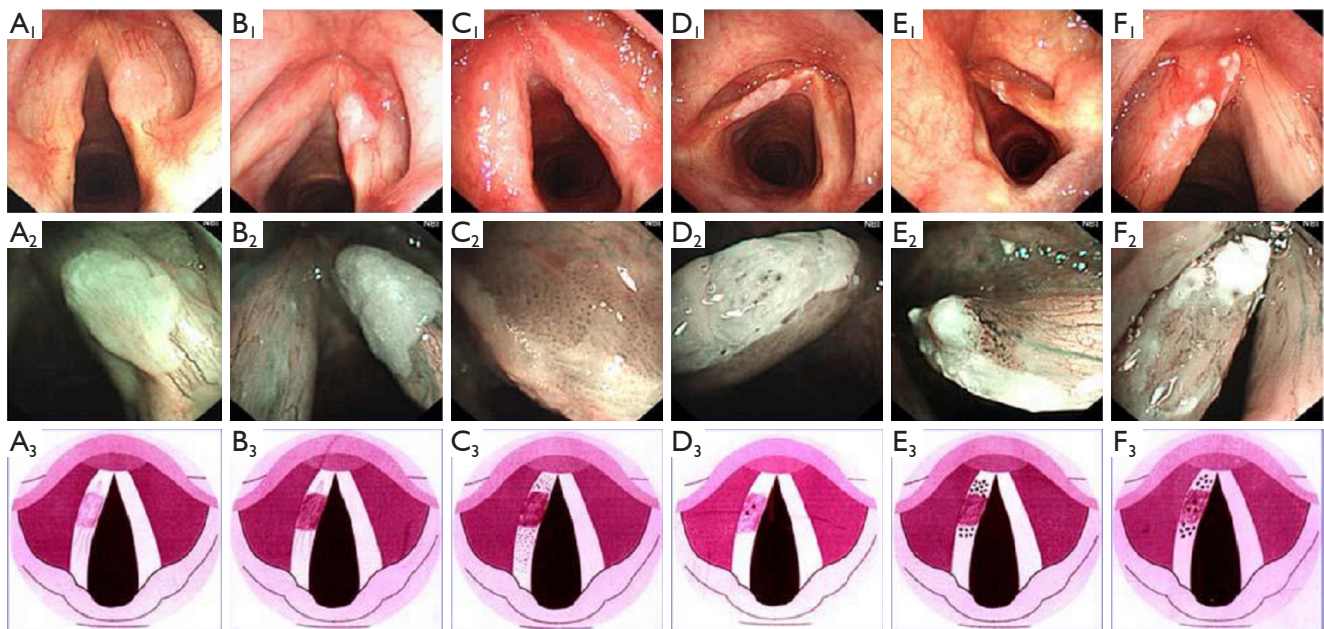


Figure 1 The Ni Classification 2019. Classification of vocal cord leukoplakia according to IPCL patterns. (A1-3) Type I IPCL pattern; (B1-3) type II IPCL pattern; (C1-3) type III IPCL pattern; (D1-3) type IV IPCL pattern; (E1-3) type V IPCL pattern; and (F1-3) type VI IPCL pattern. This figure is licensed by John Wiley and Sons. IPCL, intraepithelial papillary capillary loop.

plasmacytoma, mucosal melanoma, and synechia.

In SN5, IPCLs are clearly visible with a relatively smooth arrangement. It often shows up in granulation, mucosal melanoma, ITAC, and squamous cell carcinoma (33).

The classifications of pharyngeal lesions

NBI is highly powerful, not only in differentiating nonmalignant from malignant lesions (34), but also in detecting precancerous lesions and predicting the invasive depth and thickness of pharyngeal tumors (35-37). To date, the classifications include IPCL Pattern Classification, namely, the Japan Esophageal Society Classification (JES Classification), and the NBI Classification of nasopharyngeal mucosal microvessel patterns.

The squamous epithelium which covers the pharynx is the same as the one on the esophagus. The invasive depth can be determined based on the pattern of the IPCLs, as detected by magnifying endoscopy with narrow-band imaging (ME-NBI) (38). Therefore, the classification criteria for these vascular patterns, such as IPCL Pattern Classification and JES Classification, can also be applied in the differentiation of pharyngeal diseases. In contrast, the JES Classification is used more frequently in routine

practice. These 2 classifications will be described as part of esophageal diseases.

The Ni Classification has been used for the early diagnosis of head and neck squamous cell carcinomas (HNSCCs) and this classification also shares some common criteria with the JES Classification. Eguchi found that Va and Vb of the Ni Classification corresponded to the B1 and B2 Classification, respectively (28,36,39-41).

Ni *et al.* introduced the NBI Classification of nasopharyngeal mucosal microvessel patterns, which can be classified into the following 5 types (I to V) based on the morphology of the IPCL (Table 3). They also studied the relationship between histopathological diagnosis and endoscopic findings. The conclusion was that normal nasopharyngeal mucosa showed as type I, lymphoid hyperplasia often appeared as type II, nasopharyngeal radiation-induced inflammation showed as type III or IV, and nasopharyngeal carcinoma (NPC) mainly exhibited type V (42).

The classifications of oral lesions

Takano summarized a new IPCL classification of oral mucosa on the basis of Inoue's classification (40), and

Table 3 NBI classification of nasopharyngeal mucosal microvessel patterns

| Type | IPCLs | Microvascular network | The submucosal veins |
|----------|--|---|--|
| Type I | Invisible | Oblique and arborescent vessels and can be observed as thin, short brownish line shapes | Indistinct, dark-green stump shapes |
| Type II | Invisible | Oblique and arborescent vessels can be observed indistinctly and nearly disappear | Invisible |
| Type III | Invisible | Oblique and arborescent vessels which are engorged and can be seen clearly as fine brownish lines | Enlarged and can be seen clearly as thick, twisted, dark-green line shapes |
| Type IV | Visible, with a relatively regular arrangement and high density, appear as scattered, small, dark-brown dots. | Nearly invisible | Nearly invisible |
| Type V | Dilated, elongated, and distorted, and appear clearly as irregular, twisted, brownish line shapes; have snake-like, earthworm-like, or branch-like shapes. | Nearly invisible | Nearly invisible |

NBI, narrow-band imaging; IPCLs, Intrapapillary capillary loops.

divided it into 4 types (I to IV). The morphology of the IPCL varies in each type.

Type I appears as a wavy line with both wavy arms. Type II is dilated and is similar to type I, but has a much larger caliber than those far from the lesion. Type III displays generally elongated IPCLs that are accompanied by dilation. They can appear as long lines or as tangled lines due to a severe increase in length. Type IV is in the progression of carcinogenesis, the terminal branch loops dilate, elongate, and eventually destruct. Considering the histology, type I occurs in the normal mucosa, types II and III occur in non-neoplastic lesions with predominance of the latter, and types III and IV occur in neoplastic lesions (15).

Although previous studies have only focused on the histology, Tirelli holds a different opinion. He suggested that it is necessary to consider the different epithelial structures (43,44). On the basis of both the epithelial structure in the different oral subsites and the different tissue, he proposed the following 6 vascular patterns on NBI: normal 1, 2a, 2b, dysplastic 1–2a, and 2b. The appearance of malignant lesions was also described (*Figure 2*).

The classification of the epithelium was raised by Lin *et al.* in 2012, which helps us understand why different sites of the same organ show different images. In this classification, 4 types of epithelia were described, including type 1 or keratinized thick stratified squamous; type 2a or nonkeratinized thin stratified squamous; type 2b or nonkeratinized very thick stratified squamous; and type 3 or

pseudo-stratified ciliated columnar epithelium (44) (*Table 4*).

Upper gastrointestinal lesions

The first pilot study by Sano *et al.* showed that NBI can be used to diagnose gastric, esophageal, and colorectal lesions by examining the surface structure and capillaries (18). A large number of studies have since been published regarding NBI (45–52) and several classifications have been developed for the diagnosis of various lesions.

The classifications of esophageal lesions

Superficial esophageal squamous cell carcinoma

Microvascular (MV) patterns of IPCLs, first identified under white light, were up until recently, the only reliable indicator of tissue atypia (22,53). Later, research demonstrated that NBI can detect superficial cancer more frequently than white light imaging in the esophagus, since it can better recognize IPCLs. Based on these findings, the IPCL classifications were first established in 2001 and continue to be updated. This 5-tier classification (type 1 to 5) is well-matched to histological characterization with normal tissue, esophagitis, mild dysplasia, severe dysplasia, and cancer (54).

Considering the clinical relevance and convenience of reference to the general user, a novel categorization of the original IPCL classification was put forward in 2015. In this classification, the categories of IPCL classification

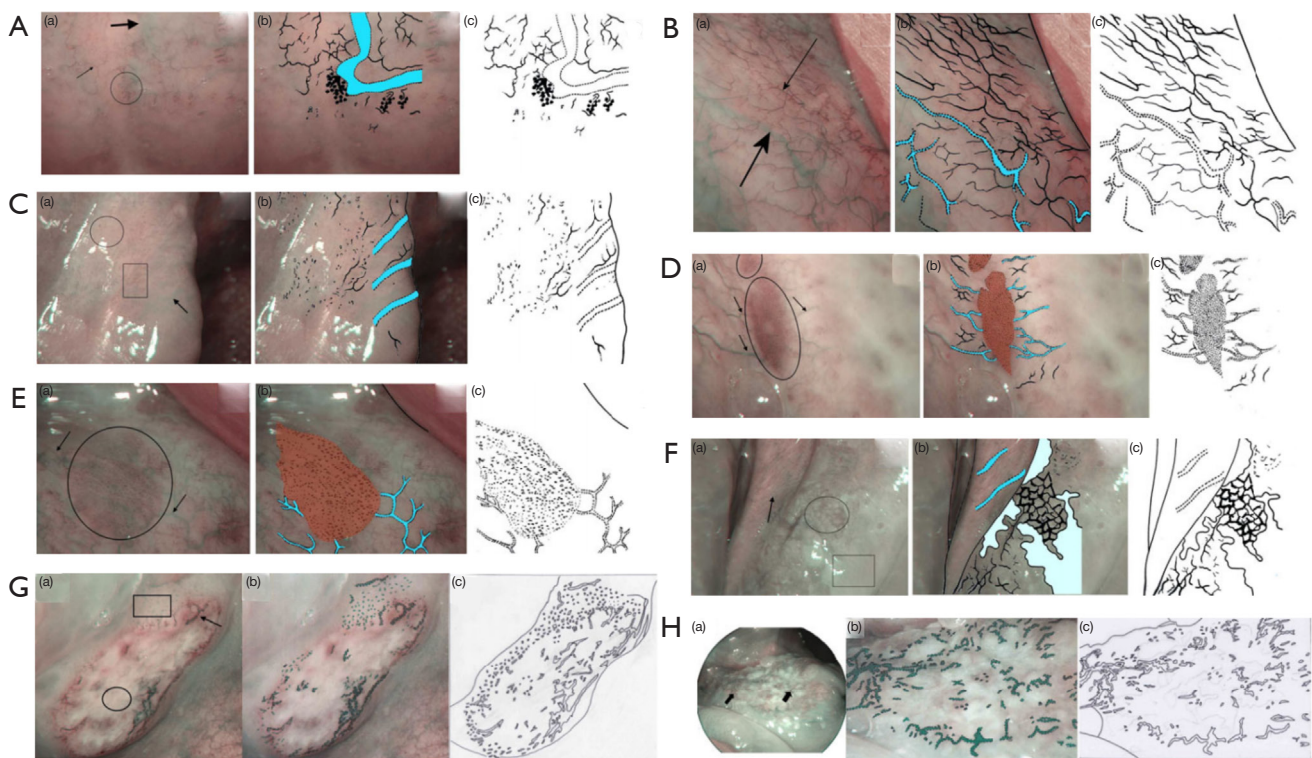


Figure 2 The classification raised by Tirelli. (A) Normal pattern in type 1 epithelium: (a) posterior hard palate appearance on NBI endoscopy. Superficial mucosal capillaries (thin arrow), submucosal veins (thick arrow), and flower-like structures (circle); (b) superficial mucosal capillaries, submucosal veins (in cyan), and flower-like structures; (c) schematic drawing. (B) Normal pattern in type 2a epithelium: (a) floor of mouth appearance on NBI endoscopy. Superficial mucosal capillaries (thin arrow), submucosal veins (thick arrow); (b) superficial mucosal capillaries and submucosal veins (in cyan); (c) schematic drawing. (C) Normal pattern in type 2b epithelium: (a) inferior trigone appearance on NBI endoscopy. Superficial mucosal capillaries (circle, rectangle), submucosal veins (arrow); (b) superficial mucosal capillaries and submucosal veins (in cyan); (c) schematic drawing. (D) Dysplastic pattern in type 1 epithelium: (a) severe dysplasia of the hard palate on NBI endoscopy. A well-demarcated brownish/purple area with thick dark spots is visible (circle); it is perpendicularly reached by dilated light blue vessels (arrows); (b) the well-demarcated brownish/purple area perpendicularly reached by dilated light blue vessels (in cyan); (c) schematic drawing. (E) Dysplastic pattern in type 2a epithelium: (a) severe dysplasia of the floor of mouth on NBI endoscopy. A well-demarcated brownish/purple area with thick dark spots is visible (circle); it is perpendicularly reached by dilated light blue vessels (arrows); (b) the well-demarcated brownish/purple area perpendicularly reached by dilated light blue vessels (in cyan); (c) schematic drawing. (F) Dysplastic pattern in type 2b epithelium: (a) severe dysplasia of an inferior trigone on NBI endoscopy. Mesh (circle), leukoplakia (rectangle) and the submucosal vessels (arrow); (b) the image resembles a mesh, leukoplakia, and the submucosal vessels (in cyan); (c) schematic drawing. (G) Neoplastic pattern in an ulcerated cancerous lesion: (a) ulcerated cancer of the hard palate on NBI endoscopy. Necrosis in the center of the lesion (circle), dark green spots (rectangle), dilated winding vessels or bobby-pin (arrow); (b) dark green spots, dilated winding vessels, or bobby-pin; (c) schematic drawing. (H) Neoplastic pattern in a vegetating cancerous lesion: (a) vegetating cancer of the floor of mouth on NBI. Unstructured vessels appearing as dark green spots, dilated winding vessels or as bobby-pin (arrow); (b) dark green spots, dilated winding vessels, or bobby-pin; (c) schematic drawing. This figure is licensed by John Wiley and Sons. NBI, narrow-band imaging.

were redistributed into 3 groups: Group 1 (non-neoplastic: IPCL I and II), Group 2 (borderline: IPCL III and IV), and Group 3 (cancer: IPCL V) (14).

In 2005, Arima *et al.* also put forward an endoscopy classification of MV patterns (types 1 to 4) to help diagnose

and assess the extent and depth of tumor invasion (55). However, this study was conducted with magnifying endoscopy (ME), namely optical magnifying video endoscope.

For the sake of convenience and efficacy, researchers used

Table 4 Vascular patterns and corresponding epithelium classification on NBI of oral lesions

| Type | Morphology | The type of epithelium |
|-----------------|---|------------------------|
| Normal 1 | Superficial mucosal capillaries: thin dark green/brown vessels with small branches arising at an acute angle in the posterior hard palate, punctuations along the palatine crests in the anterior-lateral part of the hard palate and mucosa of gingiva Submucosal veins: some large light blue vessels could be glimpsed Minor salivary glands: some of the branching vessels ended with a “flower-like” configuration with a thin vessel acting as a “stem” and several points all around as the “petals” | Type1 epithelium |
| Normal 2a | Superficial mucosal capillaries: thin dark green/brown vessels with small branches arising at an acute angle Submucosal veins: large light blue vessels were clearly visible | Type2a epithelium |
| Normal 2b | Superficial mucosal capillaries: regular and equidistant dark green/brown small punctuations or short dashes if the vessels were visualized perpendicularly, or thin parallel vessels if they were longitudinal to the mucosa Submucosal veins: some large light blue vessels could be glimpsed | Type2b epithelium |
| Dysplastic 1-2a | Mucosa: a well-demarcated brownish/purple area with thick dark spots Submucosal veins: large light blue vessels are invisible in the brownish/purple area, and the dilated light blue vessels can perpendicularly reach the lesion | Type1 and 2a epithelia |
| Dysplastic 2b | Mucosa: a honeycomb mesh made up of multiple polygonal areas. Submucosal veins: large light blue vessels are invisible, but can sometimes be seen in the surrounding areas | Type 2b |
| Neoplastic | Dark green spots, dilated winding vessels or a bobby-pin can be seen over the whole cancer surface, in the case of ulcerated lesions, the presence of a necrotic core prevents visualization of the vasculature | - |

NBI, narrow-band imaging.

ME-NBI to integrate the classifications mentioned above into 1 simplified classification, the JES Classification (56). The JES Classification system consists of the following 2 types: type A microvessels are associated with noncancerous lesions and lack severe irregularity, whereas type B microvessels are associated with cancerous lesions with severe irregularity. According to the indications for endoscopic resection (ER), type B vessels can be subdivided into B1, B2, and B3, which correspond to an absolute indication type, a relative indication type, and a contraindication type, respectively.

As for the morphology, type A was described as normal IPCL or abnormal microvessels without severe irregularity. The characteristic of type B is abnormal microvessels with severe irregularity or highly dilated abnormal vessels. B1 is defined as type B vessels with a loop-like formation with dot-like microvessels. B2 is defined as type B vessels without a loop-like formation, a stretched and markedly elongated transformation with a multilayered arrangement or an irregularly branched/running pattern are typical feature. B3 is defined as highly dilated abnormal vessels appearing

green in color. In addition, the diameter of B3 is 3 times more than that of the B2 vessels.

Barrett's esophagus (BE)

NBI is a promising tool for identifying specialized intestinal metaplasia (SIM), dysplasia, and early cancer in patients with BE. Moreover, it has been shown to accurately diagnose disease according to histology findings (57-63).

On the basis of correlation with histology, in 2006, Sharma *et al.* established the Classification of mucosal and vascular patterns according to NBI endoscopy. Also known as the Kansas Classification, it describes 3 specific mucosal patterns and 2 distinct vascular patterns (59).

In the same year, Kara *et al.* noted the mucosal morphology and vascular patterns and recommended a hierarchical classification and a risk stratification of mucosal morphology, called the Amsterdam Classification (58).

Since the first 2 preliminary descriptive studies showed a strong correlation between NBI findings and histology, investigators moved to validate a simplified mucosal

morphology classification called Nottingham Classification in 2008. Singh *et al.* (60) classified the mucosal morphology into 4 types (type A to D): columnar mucosa without intestinal metaplasia, intestinal metaplasia, low-grade dysplasia (LGD), and HGD in BE.

To further validate the 3 classifications, a specific study was performed. It was found that the 3 classifications could be used in the clinical environment. However, there was no adequate interobserver agreement (64). In addition, due to the complexity involved, a simplified classification of mucosal morphology merely focusing on capillary pattern (CP) was established in 2015, namely, the Classification of Capillary and Pit Pattern (CP Classification) (65). This classification categorized the images into 2 types: type I and type II.

Prior to the introduction of CP Classification, there was another classification which also referred to the morphology of mucosa and vessels. Anagnostopoulos *et al.* used high resolution magnification endoscopy (HRME) and NBI to identify SIM and dysplasia in BE in 2007 (66) (Figure 3A,3B).

Until 2015, none of the classifications mentioned above were accepted widely. Therefore, Barrett's International NBI Group (BING) developed a consensus-driven NBI Classification called the BING Criteria. It was aimed at helping clinicians better identify intestinal metaplasia/nondysplastic Barrett's esophagus (NDBE) and HGD/esophageal adenocarcinoma (EAC) (67). According to this classification, mucosal and vascular patterns are both categorized as regular or irregular.

Additionally, the JES also developed a consensus-based and more simplified classification in 2018, called the JES-BE classification. It was used to recognize superficial BE-related neoplasms with high-definition magnification NBI (HM-NBI). Compared with other classifications, this was easy to understand by integrating the diagnostic criteria for early gastric cancer with novel diagnostic criteria, resulting in a modified flat pattern corresponding to non-dysplastic histology (39).

The mucosal morphology in the classification systems mentioned above is described in Table 5.

The classifications of gastric lesions

Yao *et al.* performed a series of studies for the diagnosis of gastric lesions based on MV architecture and density (68-70). In 2009, they established the Yao vessel plus surface (VS) Classification System which is based on MV patterns and microsurface (MS) patterns. Both of these consist of

3 types of manifestations: regular, irregular, and absent. Yao *et al.* also described the hallmarks of early gastric cancer, which is an irregular MV pattern and/or an irregular MS pattern together with a clear demarcation line (71).

The classification raised by Nakayoshi *et al.* was based on classifying the MV patterns into the following 3 groups: A, fine-network pattern (FNP); B, corkscrew pattern (CSP); and C, unclassified pattern which was not mentioned concretely in the previous research (72). However, Yokoyama *et al.* held the opinion that neither FNP nor CSP are applicable to early gastric lesions. As such, they further worked on an unclear pattern which is described as 'unclassified pattern' in the classification raised by Nakayoshi *et al.*, leading to the definition of a new category, the intra-lobular loop pattern (ILL). They also raised a novel classification based on abnormal MV pattern and irregularity of superficial glandular structure which divided the NBI images into 4 categories: FNP, ILL-1, ILL-2, and CSP. They concluded that differentiated-type of adenocarcinomas show abundant vascular patterns, such as "FNP" or "ILL"; whereas the undifferentiated-type of adenocarcinomas show poor vascular patterns, for example, "CSP" or "ILL-2" (73). These classifications were similar those outlined in the study by Inoue *et al.* (74).

To classify gastrointestinal superficial neoplastic lesions and predict the presence of submucosal invasion, the Paris Classification, which is based on white light, was put forward in 2002. This is an international standard classification, developed from the Japanese macroscopic classification for gastric cancer (75,76). The classification divided the lesions into 3 categories: protruding lesions, non-protruding lesions, and excavated lesions. Each of them can be subdivided with different occurrence. Several studies were performed to differentiate between adenomas (ADs) (Vienna classification category 3) and carcinomas (Vienna classification category 4 or 5) (77-79), as both belonged to 0-II lesions according to the Paris classification (80). However, there remain several difficulties in distinguishing between ADs and carcinomas through evaluating the vascular patterns of lesions. Nakamura *et al.* established another classification on the basis of superficial structures (SSs) and irregular microvascular patterns (IMVPs) (81). Subsequently, Kobayashi *et al.* established A-B classification which is useful for differentiating gastric carcinomas from ADs (82). They found that A type and AB type lesions were associated with carcinomas, whereas B type lesions were ADs and carcinomas.

In addition, due to the inconsistent reliability and

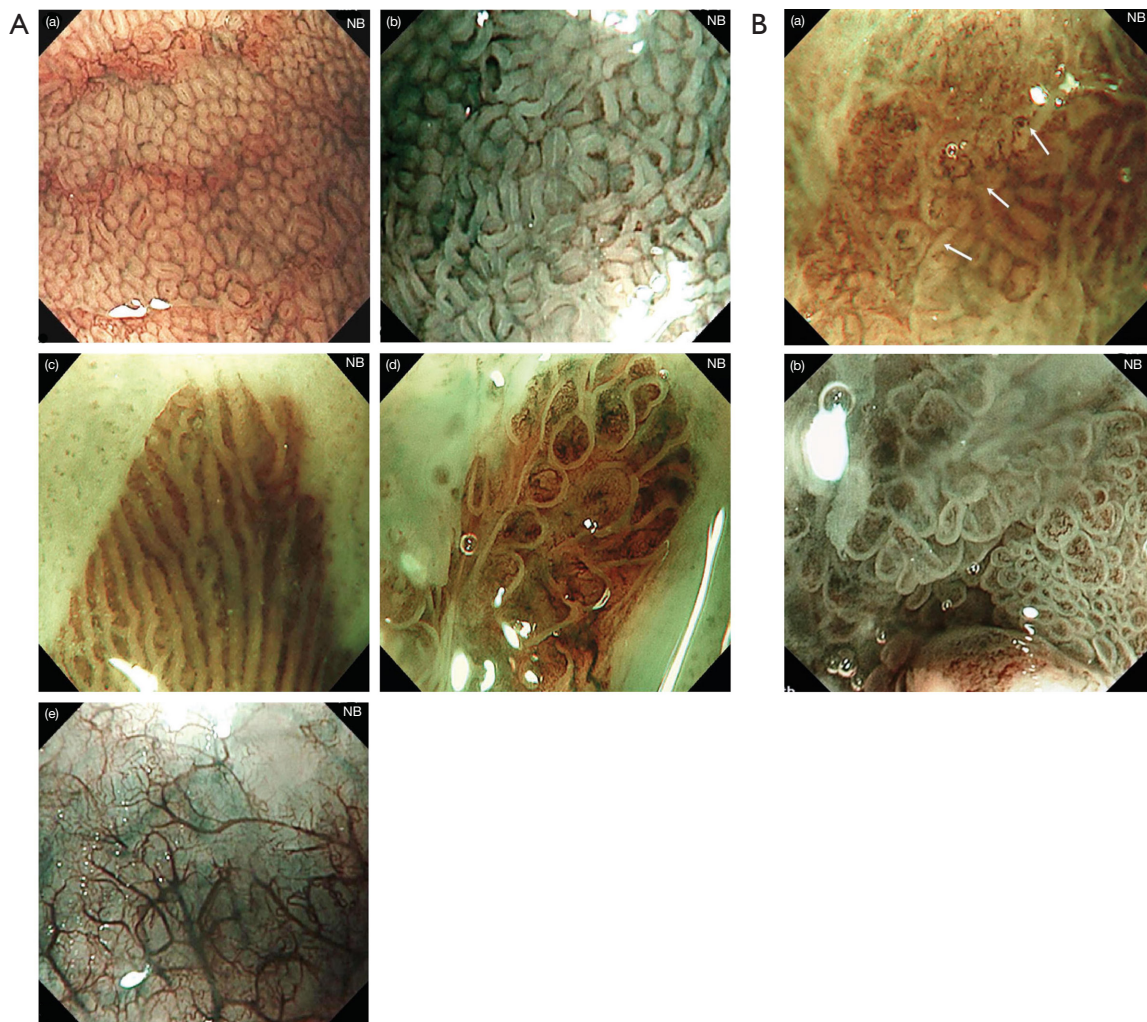


Figure 3 High resolution magnification endoscopy plus NBI findings of Barrett's epithelium. (A) Narrow-band endoscopic imaging of in non-dysplastic Barrett's esophagus shows microstructural and microvascular changes: (a) RMSP with round pattern; (b) RMSP with tubular pattern; (c) RMSP with linear pattern, (d) RMSP with villous pattern; (e) absent microstructural pattern. (B) Narrow-band endoscopic imaging of in neoplastic Barrett's esophagus shows microstructural and microvascular changes: (a) figure shows a clear demarcation line (white arrows) between the neoplastic mucosa with irregular microvessels (left part) and the non-neoplastic mucosa with regular microstructural pattern (right part); (b) figure shows IMSP with irregular microvascular pattern. This figure is licensed by John Wiley and Sons. NBI, narrow-band imaging; IMSP, irregular microstructural pattern; RMSP, regular microstructural pattern.

external validity of NBI in the stomach, Pimentel-Nunes *et al.* proposed a simplified classification. This classification was associated with the different patterns and different histology conditions: “regular vessels with circular mucosa” (pattern A), “tubulo-villous mucosa” (pattern B), and “irregular vessels and mucosa” (pattern C). The 3 types are associated with normal histology, intestinal metaplasia, and dysplasia, respectively (83).

The classifications of duodenal lesions

Ampullary tumors

In 2006, Uchiyama *et al.* attempted to establish a classification with ME-NBI to differentiate benign and malignant ampullary tumors based on the vessel patterns and surface structures of the ampullary lesions (84). They classified the images into 3 groups: I, oval-shaped

Table 5 NBI classification systems of Barrett's esophagus

| Classification system | Manifestation |
|--|---|
| Amsterdam Classification | Mucosal pattern: regular (flat, villous/gyrus, other), irregular/disrupted Vascular pattern: regular, irregular, normal-appearing long branching vessels |
| Kansas Classification | Mucosal pattern: ridge/villous, circular, irregular/distorted Vascular pattern: normal (presence of thin vessels with a uniform branching pattern), abnormal (dilated, corkscrew vessels with increased vascularity and abnormal, non-uniform branching pattern) |
| Anagnostopoulos' Classification | Mucosal pattern: regular microstructural pattern, irregular microstructural pattern, absent microstructural pattern Vascular pattern: regular microvascular pattern, irregular microvascular pattern |
| Barrett's International NBI Group (BING) Criteria | Mucosal pattern: regular (circular, ridged/villous, tubular), absent, irregular Vascular pattern: regular (blood vessels situated regularly along or between mucosal ridges and/or those showing normal, long, branching patterns), irregular (focally or diffusely distributed vessels not following normal architecture of the mucosa) |
| Japan Esophageal Society Barrett's esophagus (JES-BE) Classification | Mucosal pattern: invisible (flat), visible (pit, non-pit) Vascular pattern: invisible (flat), visible (net, non-net) |
| Nottingham Classification | Type A: round pits with regular microvasculature Type B: villous/ridge pits with regular microvasculature Type C: absent pits with regular microvasculature Type D: distorted pits with irregular microvasculature |
| Classification of Capillary and Pit Pattern (CP Classification) | Type I: uniform branches or vine-like pattern with a clear shape that can be traced smoothly Type II: coiled or spiral pattern with a nonuniform shape that cannot be traced sufficiently and with increased vascularity |

NBI, narrow-band imaging.

villi; II, pinecone/leaf-shaped villi; and III, irregular/nonstructured. In addition, they also set up the definition of abnormal vessels: dilated, tortuous, or network-like vessels. By integration of the observation and histological confirmation, they found that type I surface structure occurred in inflammation or hyperplastic lesions, whereas type II and/or III occurred in ADs and adenocarcinomas. Additionally, they can be used to differentiate ampullary ADs from adenocarcinomas since abnormal vessels only appear in adenocarcinomas. However, the limitation of this study is that there were only a few cases, which indicates that further studies are still needed.

Until 2015, Park *et al.* put forward 4 types of meaningful irregular villous patterns: irregular villous arrangement, irregular villous size, disappearance of ridge, and demarcation with normal villi. Abnormal microvasculature was defined as dotted or significantly dilated vessels. Through multivariate

analysis, they concluded that ampullary tumors (adenoma and adenocarcinoma) had irregular villous arrangement and abnormal microvasculature. Unlike previous research, abnormal microvasculature was the only significant factor associated with adenoma but not adenocarcinoma. As for the other types, it was not used for tumor identification (85).

Non-ampullary duodenal lesions

Recently, it has been confirmed that NBI can be used in the detection of non-ampullary duodenal tumors (86-88). Accordingly, several classifications were proposed.

In 2014, Kikuchi *et al.* developed a classification focusing on surface pattern and vascular patterns with ME-NBI in order to detect superficial non-ampullary duodenal epithelial tumors (SNADETs) (89). They also discovered the relationship between the patterns and pathology according to the revised Vienna classification (90): all

mixed-type lesions correlated with category 4/5 tumors; monotype lesions, absent pattern, and network pattern lesions correlated with category 3 tumors; unclassified pattern lesions correlated with category 4 tumors; and further validation is needed for intrastructural vascular (ISV) pattern lesions.

In 2015, Tsuji *et al.* used the VS classification system to detect early gastric cancer to evaluate SNADETs (71,91). They found that an irregular MS pattern is more frequent in Category 4, whereas a MV pattern shows no prominent difference between category 3 and category 4.

In 2017, Mizumoto *et al.* further enriched the Hiroshima classification, which is used to detect colic lesions to classify non-ampullary duodenal tumors. It revealed the relationship between NBI findings (type B or C) and Vienna classification (category 3 or 4) (90,92). Category 4 lesions are larger than category 3 lesions, and in category 4, type C lesions are more common than type B lesions (93).

Additionally, in 2019, Kakushima *et al.* reconsidered the limitations which existed in previous studies. The ME-NBI patterns were applied to differentiate low-grade adenoma (Vienna category 3, C3) and high-grade adenoma/carcinoma (C4/5) among SNADETs (88,89,91,94). Considering the surface structure and vasculature, 4 ME-NBI patterns were categorized: surface villous structure with intrastructural vessels; surface tubular structure with network vessels (network); surface villous structure with white opaque substance (WOS); and surface disappeared structure with irregular vessels (disappeared-irregular). It revealed that disappeared pattern should be considered as a specific feature to detect category 4/5 lesions. Some findings supported previous research by Kikuchi *et al.*, namely, that WOS is similar to a monotype of surface pattern suggestive of category 3, and disappeared-irregular is similar to a monotype of surface pattern with vascular unclassified pattern (89).

Lower gastrointestinal lesions

Colorectal lesions

Many studies have suggested that NBI plays an important role in the diagnosis of colorectal lesions (95-97). As such, many researchers have made great efforts to simplify and unify the classifications.

In 2011, Tanaka *et al.* summarized the classifications of early gastric carcinoma (98), such as the Sano classification (99) (Figure 4A), Hiroshima classification (100,101) (Figure 4B), Showa classification (102) (Figure 4C),

vascular/surface classification (71), evaluation method of Kurume University, and the evaluation method of the Cancer Institute Hospital of Japanese Foundation for Cancer Research. Afterwards, they established an international classification called the Narrow Band Imaging International Colorectal Endoscopic (NICE) classification. Validation studies of NICE classification have shown that this classification is useful in diagnosis of colorectal lesions (103,104).

The pit pattern mentioned in the table was created by Kudo *et al.* Although it was not applied with NBI, it still plays an important role in the diagnosis of colorectal lesions (105,106). In 2007, Hirata *et al.* concluded that NBI magnification is useful for the assessment of pit patterns even without chromoendoscopy (107). However, in 2013, Hayashi *et al.* studied the relationship between NBI magnifying observation using Hiroshima classification and pit pattern for the diagnosis of colorectal tumors (108). They found that the effects of both methods were similar in detecting lesions with regular structure, whereas the pit pattern diagnosis was more detailed than NBI magnifying observation in lesions with irregular structures.

Although the classifications mentioned above have been reported useful in detecting colorectal lesions, there are still some clinical problems that cannot be resolved. Therefore, the Japan NBI Expert Team (JNET) classification was developed in 2016 by integrating 4 precious magnifying NBI classifications (the Sano, Hiroshima, Showa, and Jikei classifications). Based on vessel pattern and surface pattern, the endoscopic images can be divided into 3 types: type 1, type 2A, type 2B, and type 3 (109,110) (Figure 5). In the same year, considering that current classifications did not include neoplastic sessile serrated adenomas/polyps (SSA/Ps), the Workgroup Serrated Polyps and Polyposis (WASP) classification was proposed (111). This classification combined both NICE classification and criteria for differentiation of SSA/Ps, namely, the Hazewinkel criteria, to differentiate ADs, hyperplastic polyps (HPs), and SSA/Ps in a stepwise method (112).

In 2017, Sumimoto *et al.* evaluated the diagnostic ability of each type of JNET classification, and found that type 2B was the unreliable one. Thus, they proposed JNET classification and type 2B sub classification to improve the diagnostic performance and to choose better treatment methods (113). Type 2B was further divided into type 2B-low and type 2B-high according to the level of irregularity in surface and vessel patterns. The vessel pattern of type 2B-low is that the thickness and distribution

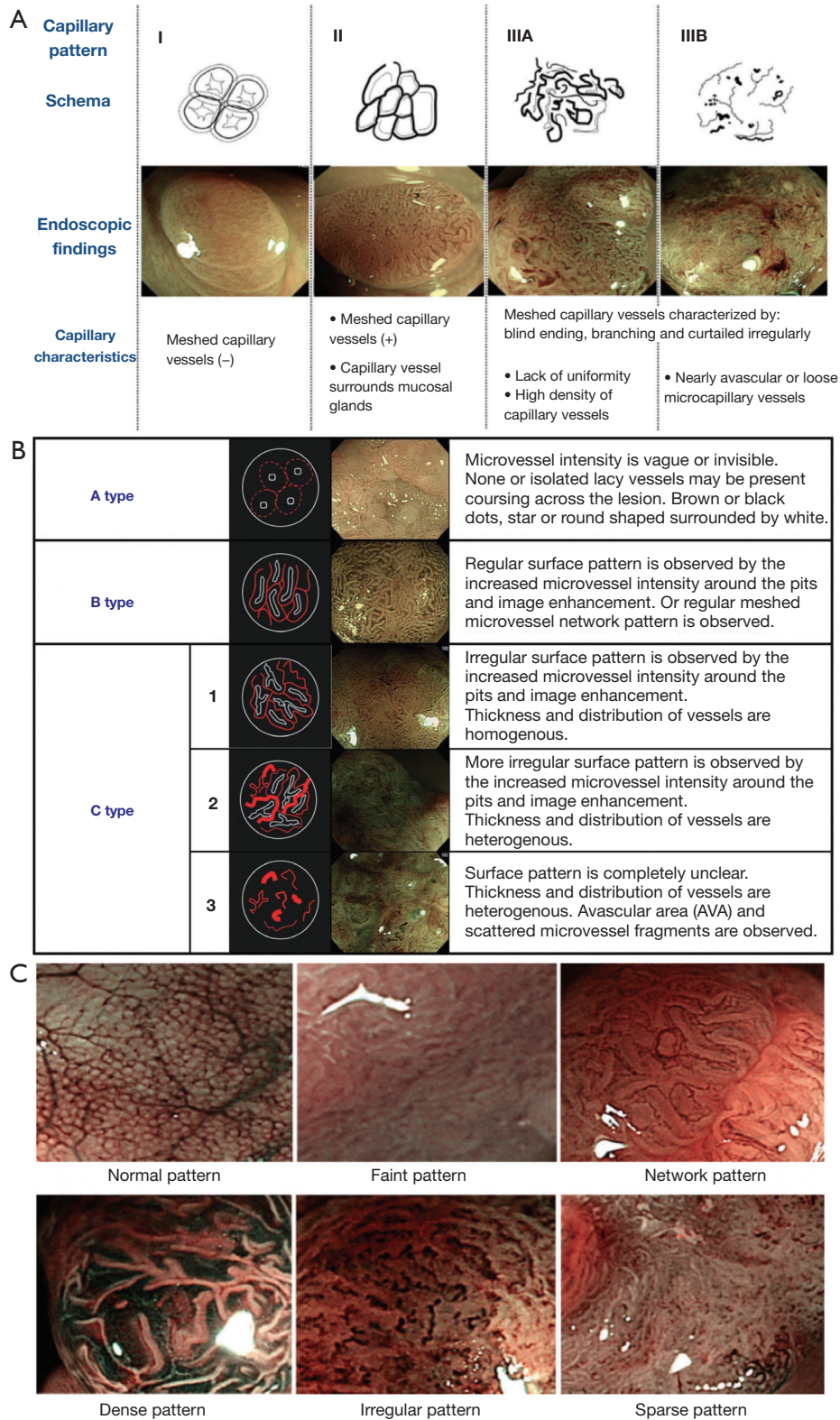


Figure 4 NBI magnifying observation classification proposed in Japan. (A) Sano classification. (B) Hiroshima classification. (C) Showa classification. This figure is licensed by John Wiley and Sons. NBI, narrow-band imaging.

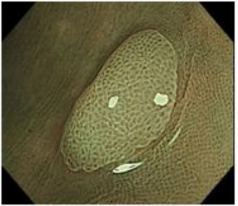
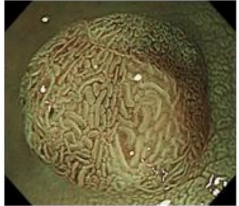
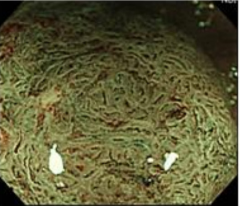
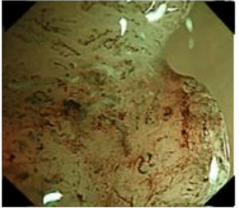
| | Type 1 | Type 2A | Type 2B | Type 3 |
|------------------------------|---|--|--|---|
| Vessel pattern | <ul style="list-style-type: none"> • Invisible^{*1} | <ul style="list-style-type: none"> • Regular caliber • Regular distribution (meshed/spiral pattern)^{*2} | <ul style="list-style-type: none"> • Variable caliber • Irregular distribution | <ul style="list-style-type: none"> • Loose vessel areas • Interruption of thick vessels |
| Surface pattern | <ul style="list-style-type: none"> • Regular dark or white spots • Similar to surrounding normal mucosa | <ul style="list-style-type: none"> • Regular (tubular/branched/papillary) | <ul style="list-style-type: none"> • Irregular or obscure | <ul style="list-style-type: none"> • 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 |  |  |  |  |

Figure 5 The Japan NBI Expert Team classification. ^{*1}, if visible, the caliber in the lesion is similar to surrounding normal mucosa; ^{*2}, microvessels are often distributed in a punctate pattern and well-ordered reticular or spiral vessels may not be observed in depressed lesions; ^{*3}, deep submucosal invasive cancer may be included. This figure is licensed by John Wiley and Sons. NBI, narrow-band imaging.

of irregular vessels are uniform, whereas type 2B-high is the diameter and/or distribution of irregular vessels are heterogeneous. As for the surface pattern, the characteristics of type 2B-low are as follows: (I) irregular in the pit-like pattern net-work; and (II) smooth pit-like structure margin without ravaging. The characteristics of type 2B-high are: (I) irregular and destroyed pit-like pattern; and (II) irregular, fluffing, and unclear pit-like structure margins. They found that type 2B-low can be considered a reliable indicator for ER, since a large majority were LGD, HGD, superficial submucosal invasive (SM-s) carcinoma. As for type 2B-high, further examination is needed to differentiate HGD and SM-s carcinoma from deep submucosal invasive (SM-d) carcinoma. Similarly, Kobayashi *et al.* also thought that if the lesion is diagnosed as JNET type 2B, it needed further evaluation. Instead of proposing a sub-classification, they used pit pattern as an additional method (12) (Table 6).

Pancreatic lesions

Before NBI was applied in the diagnosis of mucin-producing tumor of the pancreas (MPTP), namely, intraductal papillary-mucinous neoplasm (IPMN), many researchers tried to classify the pancreatic lesions according

to observations.

In 2000, Yamaguchi *et al.* classified the lesions based on the morphology and the inner color (114). The morphology was divided into 4 types: sessile, semipedunculated, villous, and vegetative tumors. The inner color can be divided into 2 types: white and red; and the red color can be observed as spotty or linear. However, this classification can only be used for pancreas mucinous lesions. In 2010, Miura *et al.* used this classification to categorize the images and found that NBI played an important role in the diagnosis of various lesions (115). Additionally, NBI can also be applied to the diagnosis of indeterminate pancreaticobiliary disease combined with per-oral video cholangiopancreatography (116). They described 9 types of images: tortuous/dilated vessels, infiltrative stricture, polypoid mass, fish-egg lesion, vegetative mass, ulceration, low-papillary mucosal lesion, and finger-like villiform lesion. The former 4 types were significantly associated with neoplasia.

Gynecologic lesions

The classifications of endometriotic lesions

NBI has been reported to be useful in detecting small endometriotic lesions (117,118). Several researchers made

Table 6 NBI classification methods of colorectal lesions

| Classifications | Evaluation method | Types |
|---|---|---|
| Sano classification | Capillary pattern | Type: meshed capillary vessels (-) Type II: meshed capillary vessels (+); capillary vessel surrounds mucosal glands Type III: occurs in deep SM invasive carcinomas Type IIIA: lake of uniformity; high density of capillary vessels Type IIIB: nearly avascular or loose micro-capillary vessels |
| Hiroshima classification | The pit pattern and microvessel features | Type A: normal or discolored lesion with invisible microvessels Type B: colorectal tumors with clear and regular pit-like pattern or regular meshed capillary network surrounding a pit Type C (C1–C3): colorectal tumors with unclear pit-like pattern, with avascular areas, and interspersed with irregular microvessels or fractured microvessels |
| Showa classification | Pit-like pattern and microvascular architecture | Normal pattern Faint pattern: the microvessels surrounding the pit are difficult to identify Network pattern: in tubular or tubulovillous adenomas Dense pattern: tubular adenoma Irregular pattern: deep SM invasive carcinoma Sparse pattern: deep SM invasive carcinoma |
| Jikei classification | Microvascular architecture and partially pit-like pattern | Type 1: vascular flow cannot be recognized Type 2: vascular diameter increases slightly Type 3: vascular diameter increases remarkably: 3V: regular vessel stream 3I: irregular vessel stream Type 4: microvessels are sparsely distributed |
| Evaluation method of the Fukuoka University Chikushi Hospital | Microvascular architecture and surface structure | Irregular: heterogeneous diversified and asymmetric Regular: homogeneous and symmetric |
| Evaluation method of the Cancer Institute Hospital of Japanese Foundation for Cancer Research | Microvessel pattern | Unclear: microvessels are uncertain Regular: microvessels on the tumor surface form a network Irregular: microvessels on the tumor surface don't form a network |
| Narrow band imaging international colorectal endoscopic (NICE) classification | Color; vessels; surface pattern | Type 1: Color: same or lighter than background. Vessels: None, or isolated lacy vessels might be present coursing across the lesion. Surface pattern: dark or white spots of uniform size, or homogenous absence of pattern. Most likely pathology: hyperplastic Type 2: Color: browner relative to background (verify color arises from vessels). Vessels: thick brown vessels surrounding white structures. Surface pattern: oval, tubular or branched white structures surrounded by brown vessels. Most likely pathology: adenoma Type 3: Color: brown to dark brown relative to background; sometimes patchy whiter areas. Vessels: has area(s) with markedly distorted or missing vessels. Surface pattern: areas of distortion or absence of pattern. Most likely pathology: deep SM invasive cancer |

NBI, narrow-band imaging; SM, submucosal.

Table 7 Cicinelli classification

| Types | Characteristics |
|----------------------------------|---|
| Normal proliferative endometrium | Flat endometrial mucosa with no evident vascular network |
| Polyp | New growth with a vascular axis |
| Atrophic polyp | new growth with vascular axis and subtle regular vascular network |
| Myoma | A regular branching of vessels on a whitish surface |
| Chronic endometritis | Inhomogeneous endometrium, blue, green, or brown colored depending on vascularization characteristics; dilatation of superficial and subepithelial vascular network; blue spots corresponding to intramucosal petechiae; micropolyps with a vascular axis |
| Low-risk hyperplasia | Thick endometrium with no evident or subtle vascular network |
| High-risk hyperplasia | Thick endometrium or irregular endometrial surface with irregular vessels |
| Endometrial cancer | Vegetations, profound alterations in mucosal architecture, cerebroid aspects, atypical aspects of vessels |

great efforts to establish classifications to help clinicians to better diagnose endometriotic lesions.

The classification of microhysteroscopic images without NBI was raised in 2003, which divided the images into 5 groups: normal hysteroscopy, benign lesion, low-risk hyperplasia, high-risk hyperplasia, and carcinoma (119). On the basis of the above classification, Cicinelli *et al.* proposed a criterion of NBI hysteroscopy, dividing the images into 8 groups: normal proliferative endometrium, polyp, atrophic polyp, myoma, chronic endometritis, low-risk hyperplasia, high-risk hyperplasia, and endometrial cancer (120). The characteristics of each type are listed in *Table 7*.

Using the criteria proposed by Cicinelli *et al.*, Tinelli conducted a multicenter study to validate the accuracy and efficacy of NBI for the diagnosis of endometrial cancer and hyperplasia (121). The result demonstrated that NBI with the criteria listed did in fact improve the recognition of lesions.

The classifications of cervical intraepithelial neoplasia (CIN)

In 2017, Nishiyama *et al.* explored a novel MV classification system to diagnose CIN with NBI using ME (122). The major factors in the study included vascular change, arrangement, and density. This classification categorized the images into 7 types: normal, CIN1, CIN2, CIN3, CIS, minimum invasive cancer (MIC), and invasive cancer (IC).

Meanwhile, 1 year later, Uchita *et al.* found other abnormal characteristics of CIN3 using ME-NBI: light white epithelium (l-WE), heavy white epithelium (h-WE),

and atypical IPCL (123). They found that atypical IPCL can correspond with IPCL classification (14).

Bronchus and lungs

Early in 2003, it was reported that NBI can be used in the differentiating precancerous and cancerous lesions of bronchial mucosa (124). In 2009, Herth *et al.* also reported that NBI can work as a powerful tool to detect early lung cancer (125). They presented a visual classification based on the vascular changes and classified the lesions into 4 grades: normal, abnormal but not suspicious, suspicious of intraepithelial neoplasia, and tumor. In the study, it was found that normal lesions showed normal mucosal vascularity. Suspicious lesions for intraepithelial neoplasia were characterized by ≥ 3 criteria: capillary loops, dotted vessels, complex vascular networks of tortuous vessels, and abrupt ending vessels. Abnormal but not suspicious lesions showed increased density and < 3 criteria mentioned above. Tumors under NBI were visible. This classification has been demonstrated to be useful in the detection of lung cancer (126,127).

Similarly, in 2010, Shibuya *et al.* classified the images into 5 groups: squamous dysplasia, angiogenic squamous dysplasia (ASD), CIS, micro invasive, and invasive. The vessel morphology can be classified into tortuous vessel networks, dotted vessels, and spiral and screw type vessels (128). Squamous dysplasia is characterized by tortuous vessel networks; ASD is characterized by tortuous vessel networks and dotted vessels; CIS, micro invasive, and invasive are observed with dotted vessels, spiral and screw

type vessels. Besides, the mean vessels diameter increased with the progression of lesions.

In 2021, Fukada *et al.* proposed a simple system to classify the bronchoscopic images of peripheral pulmonary tumor (PPT) (129). Based on the appearance of stenosis, the lesions were divided into stenotic type (ST) and non-stenotic type (NonST). According to the presence of epithelium and light blue line (LBL), the lesions were divided into exposed type (ET) and non-exposed type (NonET). They also correlated these types with pathological findings and found that most ST and NonET lesions are commonly shown in adenocarcinoma. Furthermore, ST and ET lesions can be observed in squamous cell carcinoma, whereas all NonST and NonET lesions are found in adenocarcinoma.

Bladder cancer

Studies have reported that NBI can improve the accuracy of the diagnosis of bladder cancer regardless of experience. It has been recommended by the European Association of Urology (EAU) guidelines for non-muscle-invasive urothelial carcinoma (130-136). However, there are few classifications for bladder cancer. In 2018, Dalgaard *et al.* used NBI flexible videoscopy (NBI-FV) to classify the lesions according to the characteristics of microvasculature (geometric pattern, dense, and tortuous and irregular) and mucosa (transparent, thick, and exophytic of papillary). The suspicion was scored from none (score 1) to high (score 5) on the Likert 5-score scale (LS) (137).

Scar

As guidelines recommended, targeted biopsies of resection site are necessary to exclude histopathological evidence of recurrence (138-140). However, with the development of the endoscopic system, it was demonstrated that the mucosal surface could be clearly observed using NBI. Many researchers have tried to set up classifications of scars to avoid unnecessary biopsies.

In 2017, Desomer *et al.* attempted to raise a standardized imaging protocol based on the Kudo's pit pattern and NICE classification used in colorectal lesions (103,105,106,141). Although the results suggested high sensitivity and accuracy, no official classification was raised. Therefore, some researchers developed the narrow-band imaging for scar (NBI-SCAR) classification in 2020 (142). By evacuating the scar with NBI, they described the key characteristics of both recurrent and non-recurrent disease. The features

of recurrence are dark brown color, elongated or branched pit pattern, and dense CP surrounding pits, whereas no recurrence is characterized by a whitish, pale appearance, round, and slightly larger pits compared with the surroundings, and irregular sparse vessels with no change in caliber.

Tips and tricks

As part of optical imaging, NBI uses light characteristics to acquire information on the mucosa and submucosa. Adequate light and a clear field of view are critical to imaging results. Light penetration may be altered by blood and bile, resulting in a black and red image, respectively, which interferes with the evaluation of NBI. To obtain a clear endoscopic view, it is extremely important to avoid bleeding during the examination and to wash the bile (143,144). NBI mainly assesses mucosal surface structures due to its light penetration characteristics. Therefore, all of the above classifications are based on mucosal and submucosal morphological manifestations, especially dynamic changes of IPCLs during tumor progression.

Future prospect and conclusions

With the rapid development of science and technology, artificial intelligence (AI) systems have been increasingly applied for endoscopic diagnosis (145-148). Moreover, studies have demonstrated that AI has a favorable performance with high sensitivity (149-151). Goda *et al.* also predicted that AI may be applied to improve diagnostic criteria for B2 vessels and modify the JES classification (152). At the same time, the combination of the emerging hyperspectral imaging (HSI) technology and AI in recent years has further improved the accuracy of early esophageal cancer detection (153-155). We believe that NBI combined with AI will be widely used in the diagnosis of diseases, and more simple classifications will be used in clinical practice to alleviate the workload of clinicians in the future.

Since the introduction of NBI, many studies have demonstrated its high value in detecting lesions in the early stage of diseases with high accuracy. To date, many studies have focused on NBI classifications in different systems. Most of these classifications share something in common, namely, they all use the characteristics of the vessels as a criterion of classifications. The lesions of different systems also presented unique features under NBI, which may be related to their different pathological changes. Therefore,

more clinical trial validations based on pathology as the gold standard can further promote the accuracy of NBI classification. Moreover, these classifications can also serve as the basis for research on AI diagnostic techniques.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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