Narrow band imaging for head and neck region and upper gastrointestinal tract

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Abstract

Endoscopy is essential for diagnosis and treatment of cancers derived from gastrointestinal tract. However, conventional white light image has technical limitation in detecting small or superficial lesions. Narrow band imaging, especially with magnification, allows visualize a microstructure pattern and microvascular patterns in the mucosal surface. These technical breakthroughs enable endoscopists to easily detect small pre-neoplastic and neoplastic lesions and to make differential diagnosis of these lesions. Appropriate diagnosis with NBI contributes to minimally invasive endoscopic resection.

Mini-abstract

Narrow-band imaging is discussed, which allows endoscopists to easily diagnose small lesions and to make differential diagnosis of these lesions. Appropriate diagnosis with NBI contributes to minimally invasive treatments.

Key words:
endoscopy, narrow band imaging, early detection, differential diagnosis

NARROW BAND IMAGING

Narrow band imaging (NBI) is an innovative optical technology that allows the distinct visualization of microsurface patterns and microvascular patterns on the mucosal surface (1-3). The NBI system uses narrow-band illumination created with optical interference filters that generate 415 nm and 540 nm wavelengths, corresponding to the peaks of absorption of hemoglobin. Therefore, thin blood vessels, such as capillaries, in the epithelium or mucosal layer can be seen more distinctly than in a conventional white-light image (WLI) (Figure 1).

Currently, two types of image reconstruction systems are used for endoscopic imaging: a red–green–blue (RGB) time sequential illumination system with a monochrome charge-coupled device (CCD) and white-light illumination with a color chip CCD. The NBI system is applicable to both systems by placing the narrow-band light filter in front of the light source. NBI can provide the same clinical benefits with both illumination systems (Table 1), although the color reproduction and the image resolution are somewhat different in the two systems (4).

HEAD AND NECK REGION

HEAD AND NECK CANCER

Lugol chromoendoscopy is the standard method for detecting early squamous cell carcinoma (SCC) of the esophagus. However, Lugol dye solution cannot be applied to the oropharynx or hypopharynx because of the risk of aspiration. Moreover, the image resolution of rhinolaryngoscopy does not effectively identify superficial neoplastic lesions in the head and neck region. Therefore, the early detection of cancers in the oropharynx and hypopharynx has been difficult. This is partly attributable to the technological limitations in mounting a high-resolution CCD on the tip of a rhinolaryngoscope.

Muto *et al*. first reported the utility of NBI combined with magnifying endoscopy (Q240Z, Olympus Medical Systems, Tokyo, Japan) in the identification of superficial SCCs in the head and neck region (5). Compared with WLI, NBI significantly improved the visualization of the cancerous lesions by enhancing the contrast between the cancerous lesion and the background nonneoplastic epithelium, and by the clear magnification of the microvascular architecture (6). Muto et al. reported that the well-demarcated brownish areas observed under NBI and the microvascular

irregularities visible under magnification with NBI were useful indicators of cancerous lesions in the head and neck region (1). In the multicenter prospective randomized study, NBI is revealed to be superior to WLI in the detection and differential diagnosis for superficial head and neck cancer (7).

Watanabe et al. reported that the NBI rhinolaryngoscope (ENF-V2, Olympus Medical Systems) with a color-chip light source (CLV-160B, Olympus Medical Systems) improved the diagnostic accuracy, and the negative predictive values for superficial lesions in the oropharynx and hypopharynx compared with those of conventional WLI (8, 9). However, there is still a critical difference in the image qualities of CCDs between the gastrointestinal endoscopy and that the rhinolaryngoscope.

Ugumori et al. prospectively compared the images taken with a color-chip-based rhinolaryngoscope and those taken with an RGB-sequential-system-based high-resolution gastrointestinal endoscope (10). Whereas the conventional white-light rhinolaryngoscope identified well-demarcated line between the neoplastic and nonneoplastic lesions in only 10% (5/51) of cases and microvascular irregularities in only 27% (14/51), the NBI rhinolaryngoscope identified these in 63% (32/51) and 94% (49/51) of cases, respectively. These results indicate that even with a rhinolaryngoscope, NBI can improve the visualization of epithelial neoplasms of the head and neck region.

When combined with a high-definition television camera (HDTV), the effectiveness of NBI is improved in terms of both its sensitivity and specificity.(11)

NBI is also reportedly useful in detecting metachronous SCC after treatment for esophageal SCC (chemoradiotherapy, radiation therapy, or surgery), and unknown primary SCC of the neck, and adenoid hypertrophy (12-18) (Table 1).

The early detection of cancer in this region increases the possibility of minimally invasive surgery, including endoscopic mucosal resection and endoscopic submucosal dissection methods (19, 20). The potential advantages to patients resulting from an early diagnosis, with the preservation of organ and tissue functions, are obvious.

Esophagus

ESOPHAGEAL SQUAMOUS CELL CARCINOMA

Although the early detection of cancer offers the best prognosis, many esophageal SCCs (ESCCs) are still detected at a late stage, with a consequently poor prognosis. One reason is that the early detection of ESCC is difficult using conventional WLI endoscopy because it cannot identify the morphological changes of superficial ESCC. Although Lugol chromoendoscopy is the sanistive method for the detection of early

superficial ESCC (Figure1 A, B), iodine is an irritant and causes unpleasant reactions, such as pain, discomfort and sometimes allergic reaction. In contrast, NBI is less invasive than Lugol chromoendoscopy and enhances the clarity of the intrapapillary capillary loop (IPCL) patterns beneath the epithelium (5, 21, 22), so it is expected to replace Lugol chromoendoscopy in this role (Figure1 C,D).

Using an ultrathin endoscope (5 mm in diameter at the distal end; XP260N, Olympus Medical Systems), Lee et al. reported the utility of NBI in the detection and accurate diagnosis of ESCC (23). The sensitivity of NBI was significantly better than that of conventional WLI. The specificity and positive predictive value of NBI were also better than those of Lugol chromoendoscopy, whereas their diagnostic accuracy and negative predictive value were similar. These results suggest that, even when an ultrathin endoscope is used, NBI is the best tool for screening for superficial esophageal neoplasms, as in the head and neck region.

In a multicenter prospective randomized study (7), NBI with a standard-diameter endoscope showed approximately twofold greater sensitivity than WLI. Furthermore, most of the Lugol-voiding lesions overlooked by NBI endoscopy were low grade intraepithelial neoplasia or lesions without atypical findings (24).

In 2011, a new classification of magnified endoscopy for superficial ESCC was

proposed by Japan Esophageal Society (2d5), which allows the differential diagnosis of ESCC, intraepithelial neoplasia, and inflammation. This classification is expected to simplify the diagnosis and evaluation of the depth of invasion of superficial ESCCs.

GASTROESOPHAGEAL REFLUX DISEASE (GERD)

GERD is defined by the presence of reflux esophagitis. When it causes reflux symptoms (chest pain, heartburn, discomfort, etc.), the patient's quality of life is adversely affected (26). Moreover, a significant number of patients with GERD symptoms show no endoscopic signs of esophagitis. This condition is described as "nonerosive reflux disease" (NERD). Many NERD patients show minimal endoscopic findings, such as a whitish or reddish edematous change or erosion that is not regarded as a mucosal break (27). These minimal changes are potentially related to various GERD symptoms (28). However, the interobserver agreement when NERD is diagnosed with conventional WLI is reportedly too low to support the clinical significance of this technique (29). In contrast, NBI is expected to overcome this limitation, because it allows the visualization of the superficial and slight findings attributable to NERD, which cannot be seen with conventional WLI.

Lee et al. reported that the intraobserver and interobserver consistencies in grading

esophagitis improved when NBI was used instead of WLI (30). Sharma et al. reported a feasibility study of magnified endoscopy with NBI in patients with GERD (31). They showed that increased numbers and the dilatation of IPCLs were the best predictors of a diagnosis of GERD, with moderate to high interobserver agreement.

BARRETT'S ESOPHAGUS AND CANCER

The incidence of esophageal adenocarcinoma is increasing in Western countries (32) and Barrett's esophagus (BE) is a precursor lesion of this malignancy. Surveillance of BE using WLI with random four-quadrant biopsies is the accepted practice and is recommended by the American Gastroenterological Association statement (33). Sharma et al. (34) showed in a randomized, controlled, international, crossover trial that the success of NBI in detecting intestinal metaplasia did not differ from that of the currently accepted practice of random biopsies, but required significantly fewer biopsies.

Because esophageal adenocarcinoma has a poor prognosis when detected at an advanced stage, endoscopic surveillance is recommended to detect high-grade dysplasia and mucosal neoplasia in patients with BE. However, it is difficult to identify these lesions with conventional WLI. NBI with magnifying endoscopy allows us to visualize the details of the mucosal microsurface pattern and the microvascular pattern without

additional equipment or dye solutions (35).

Hamamoto et al. first reported that NBI could better visualize the esophagogastric junction, net-like capillary vessels, and columnar-lined esophagus (seen in BE) than conventional WLI (36). Kara et al. reported that indigo carmine chromoendoscopy and NBI were similarly effective in the diagnosis of high-grade dysplasia or early cancer in BE (37). Wolfsen et al. (38) reported that high-resolution NBI can detect dysplastic lesions more efficiently, with fewer biopsy samples, than standard-resolution WLI. Singh et al. (39) reported that NBI with magnification is superior to WLI with magnification in the prediction of histology in BE.

A recent meta-analysis (40) that included 446 patients with 2194 lesions reported that NBI with magnification shows high diagnostic precision in detecting high-grade dysplasia, with a sensitivity and specificity of 96% and 94%, respectively.

Stomach

DETECTION OF GASTRIC NEOPLASM BY NBI

In the stomach, NBI has been considered to be used with magnification for detailed examinations. Because the light intensity under the NBI filter is low, a non-magnified image becomes dark compared with that produced under WLI. Furthermore, because

the image becomes noisy with the electrical enhancement used to keep the endoscopic image bright, it is insufficient to observe the wide area of the stomach. There is also, as yet, no evidence that NBI is superior to WLI in detecting early gastric neoplasms. To overcome these limitations, much brighter NBI system with higher resolution will be commercially available when this review is published. Then, the evidence of other clinical benefit of NBI such as detection will be expected in future.

DIFFERENTIAL DIAGNOSIS OF GASTRIC CANCER

Yao et al. originally reported unique magnifying endoscopic findings of gastric cancer in 2002 (41). This marked the beginning of the era of using magnifying endoscopy for the diagnosis of gastric cancer. The utility of magnifying endoscopic observations combined with WLI for the differential diagnosis of flat or slightly depressed gastric cancers and nonneoplastic lesions, such as gastritis, has been reported. NBI combined with magnifying endoscopy (magnifying NBI) provides better visualization of the mucosal surface and microvascular architecture than magnifying WLI (42). Several reports have compared the diagnostic yield of magnifying NBI with that of magnifying or nonmagnifying WLI in distinguishing small gastric cancers from the flat or depressed benign lesions caused by chronic gastritis (43-45). However, all those reports had some

limitations: they were performed at only one institution, evaluated stored images and did not involve real-time assessment, or included gastric lesions with a definite pathological diagnosis. To overcome these limitations, Ezoe et al. performed a multicenter, prospective, randomized, controlled trial that targeted newly detected, undiagnosed lesions to compare and evaluate the diagnostic yields of magnifying NBI and conventional WLI. The trial revealed that magnifying NBI, especially after nonmagnifying WLI, showed an extremely high diagnostic performance (46).

These lines of evidence suggest that magnifying NBI is currently one of the standard endoscopic modalities in the differential diagnosis of gastric cancers.

DETERMINATION OF THE LATERAL EXTENT OF GASTRIC CANCER

To achieve the complete resection of a mucosal gastric cancer with endoscopic resection, an accurate diagnosis of the extent of the tumor is required. By clearly visualizing the microvascular architecture and the microsurface structure inside and outside the lesion, magnifying NBI can distinguish the cancer margins from the surrounding benign mucosa, so it is expected to be useful for delineating the extent of a gastric tumor. In 2004, Sumiyama et al. retrospectively described the feasibility of NBI for the guidance of *en bloc* endoscopic resection when combined with a multibending endoscope, but did

not perform a formal evaluation (47). Kadowaki et al. compared the utility of magnifying NBI and magnifying WLI in recognizing gastric cancer demarcation. They also reported that magnifying NBI is more useful when it is combined with acetic acid (48). Kiyotoki et al. (49) and Nagahama et al. (50) reported the superiority of magnifying NBI to chromoendoscopy for determining the lateral extent of early gastric cancer. These lines of evidence suggest that magnifying NBI can be a useful modality for determining the lateral extent of gastric cancer. However, it must be emphasized that it is still difficult to accurately define the tumor margin in undifferentiated gastric cancers; the successful delineation rate was 0% for undifferentiated cancers in one study (50). Because undifferentiated gastric cancers often spread subepithelially and are covered with nonneoplastic foveolar epithelium, observation of the mucosal surface by NBI is not useful for determining the tumor margin of this type of gastric cancer. Therefore, it is necessary to take biopsy specimens of the surrounding mucosa to define the extent of an otherwise undetectable tumor in undifferentiated gastric cancers.

PREDICTION OF THE HISTOLOGICAL TYPE OF GASTRIC CANCER

Nakayoshi et al. reported that the different microvascular patterns detected with magnifying NBI images are useful in predicting the histological type of a superficial

gastric cancer (51). Differentiated adenocarcinomas display a “fine network pattern,” and undifferentiated adenocarcinomas display a “corkscrew pattern” in their microvascular structures (Figure 2). Yoshida et al. reported that a “nonstructural pattern” appeared to be a useful marker of undifferentiated superficial gastric cancers (52).

Although these studies have indicated the utility of magnifying NBI in the prediction of the histopathological type of a gastric cancer, its reliability must be validated in a large-scale prospective study. Moreover, even if magnifying NBI can predict the histological type of a cancerous lesion, histological confirmation by biopsy is required at this time. However, the prediction of histological type could be useful to the endoscopists when selecting the site of a biopsy in a lesion because gastric cancers are usually heterogeneous.

DIAGNOSIS OF THE TUMOR DEPTH OF GASTRIC CANCER

In contrast to ESCC, there is no evidence that NBI, with or without magnifying endoscopy, can predict the depth of tumor invasion in a patient with gastric cancer.

DIAGNOSIS OF GASTRIC ADENOMA

Because most gastric adenomas form protruded lesions, the differential diagnosis of

protruded gastric cancer and protruded adenoma is sometimes difficult (53, 54). Yao et al. reported that the characteristic finding of magnifying NBI, a white opaque substance (Figure 3), is a relevant sign for differentiating protruded adenomas from protruded cancers (55). Tsuji et al. also reported that the presence of an irregular microvascular pattern or irregular microsurface pattern with a demarcation line between the lesion and the surrounding area under magnifying NBI is useful in distinguishing cancers from adenomas (56). Maki et al. reported that magnifying NBI appears to be useful in differentiating between cancerous and adenomatous superficial elevated lesions of the stomach with significantly higher sensitivity and accuracy (57). In contrast, depressed-type adenoma is rare, although it is clinically important because it has greater malignant potential than protruded adenoma (58). Tamai et al. reported that depressed-type adenomas display a regular ultrafine pattern, in which the network of microvessels is composed of small and regular circles, which differs from the irregular fine network pattern of well-differentiated gastric cancers (59).

These reports indicate that magnifying NBI should be a useful modality for the accurate diagnosis of gastric adenoma.

Duodenum

Small duodenal ampullary tumors are treated by surgical resection or endoscopic resection. However, the lateral margin must be precisely assessed before curative endoscopic resection. Uchiyama et al. reported that magnifying NBI with a direct frontal-view magnifying endoscope can predict the histological characteristics of ampullary lesions by detecting abnormal vessels and microsurface patterns (60). Itoi et al. reported that NBI with a conventional duodenoscope, with no magnifying capacity, allowed better visualization of the tumor margin than indigo carmine chromoendoscopy (61). However, these studies included only a small number of cases, so further studies with a sufficient number of patients are required to evaluate the usefulness of NBI for duodenal tumors.

Conclusion

NBI is now useful endoscopic modality for head and neck region and the upper gastrointestinal tract. It helps the endoscopists to do early detection and accurate diagnosis for the head and neck neoplasia and disease in the upper gastrointestinal diseases. Furthermore, it provides the many chance to do minimally invasive treatment and improves the patients' survival and quality of life. Then, standard education

program of NBI in clinical practice will be needed.

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Table1 Advantage of NBI in contrast to WLI or CE in the clinical practice in the head and neck region and the upper gastrointestinal tract.

Site	Category	Study aim	Evidence	Magnification	Study design	Diagnosis	Reference
Head and neck	Squamous cell carcinoma	Detection	NBI >WLI (accuracy: 86.7 vs. 62.9%)	+	Prospective RCT	On site	7
		Differential diagnosis	NBI > WLI	+	Prospective RCT	On site	7
Esophagus	Squamous cell carcinoma	Detection	NBI > WLI (accuracy: 88.9 vs. 56.5%)	+	Prospective RCT	On site	7
			NBI = iodine CE (accuracy: 95.1 vs. 85.9 %)	+	Prospective non-RCT	On site	24
		Differential diagnosis	NBI > WLI	+	Prospective RCT	On site	7
	Adenocarcinoma	Detection of HGD/early cancer	NBI = WLI + indicocalmine CE	+	Prospective non-RCT	On site	37
		Differential diagnosis	M-NBI > M-WLI	+	Prospective non-RCT	Review	39
		Grade of dysplasia	NBI > WLI	−	Prospective non-RCT	On site	38
	Barrett's esophagus	Detection of SIM	NBI = indigocalmine CE > WLI (Sn.: 56 vs. 55 vs. 24%, Sp.: 90 vs. 100 vs. 40%)	+	Prospective non-RCT	Review	36
Stomach	Adenocarcinoma	Detection	No literature				
		Differential diagnosis of small depressive lesions	C-WLI + M-NBI > M-NBI > C-WLI (accuracy: 96.6 vs. 90.4 vs. 64.8%)	+	Prospective RCT	On site	46
		Differential diagnosis of superficial elevated lesions	M-NBI > C-WLI (accuracy: 92 vs. 74%)	+	Retrospective	Review	57
		Detection of lateral extent of early gastric cancer	M-NBI > indigocalmine CE	+	Prospective RCT	On site	49
		Diagnosis of tumour depth	No pivotal study				
	Adenoma	Detection	No pivotal study				
Duodenum	Adenocarcinoma	Detection	No pivotal study				
		Differential diagnosis	No pivotal study				
	Ampullary tumour	Visualization of tumour margin	NBI > indigocalmine CE	−	Prospective non-RCT	Review	61

NBI: narrow-band imaging; WLI: white light imaging; PPV: positive predictive value; NPV: negative predictive value; SIM: specialized intestinal metaplasia; HGD: high grade dysplasia; Sn.:sensitivity; Sp.: specificity; M-NBI: magnifying NBI; M-WLI: magnifying WLI; CE: chromoendoscopy; C-WLI: conventional nonmagnifying WLI

Figure Legends

Figure 1. Superficial squamous cell carcinoma in the lower thoracic esophagus.

(A) WLI shows scattered reddish spots in the slightly reddish area.

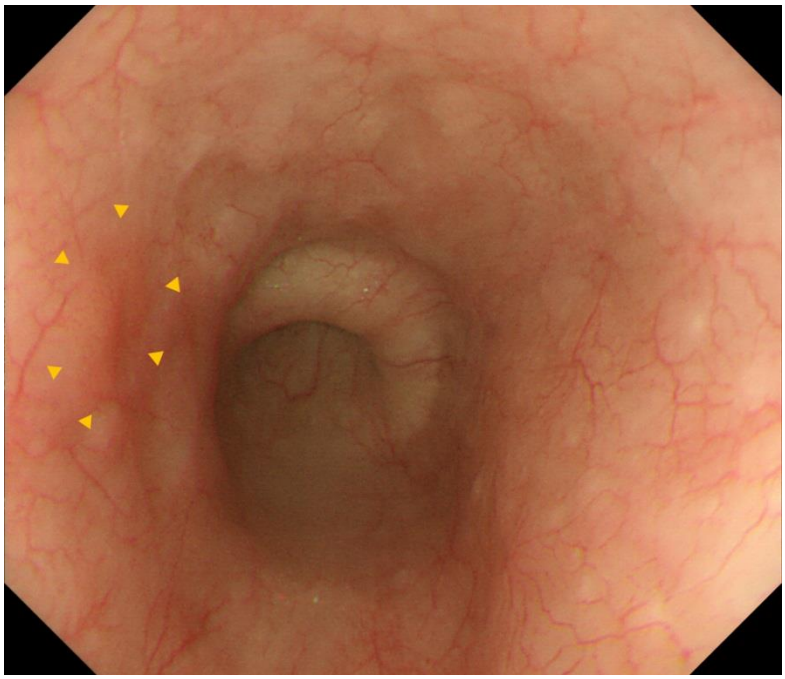
(B) Lugol chromoendoscopy shows unstained area.

(C) (D) NBI shows clearly defined brownish spots indicating dilated intrapapillary capillary loops.

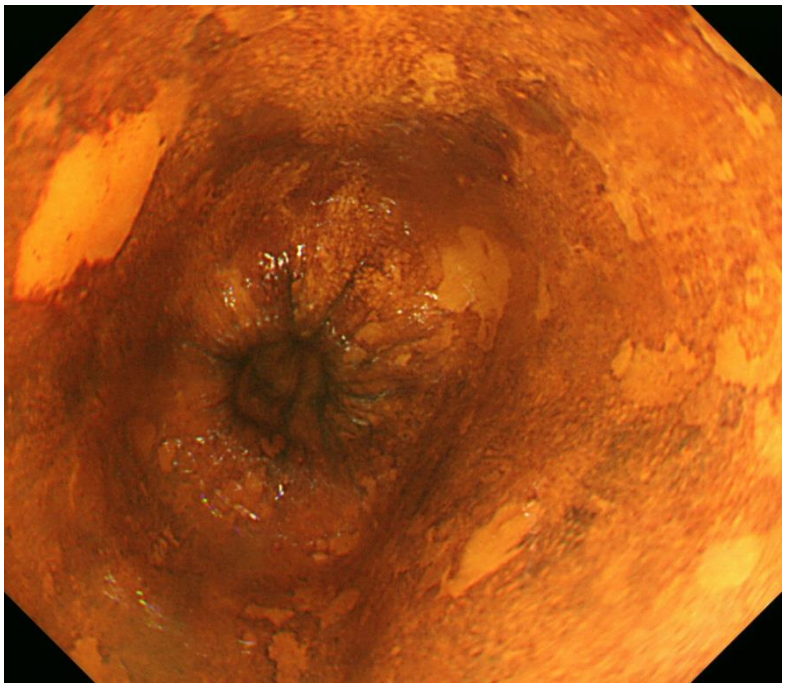
Figure 2. Microvascular patterns of gastric cancer. (A) Fine network pattern indicates differentiated adenocarcinoma. (B) Corkscrew pattern indicates undifferentiated adenocarcinoma.

Figure 3. White opaque substance (WOS) within an elevated adenoma and well-differentiated adenocarcinoma. (A) The regular distribution of WOS indicates adenoma. (B) The irregular distribution of WOS indicates adenocarcinoma.

Figure 1 (A)



(B)



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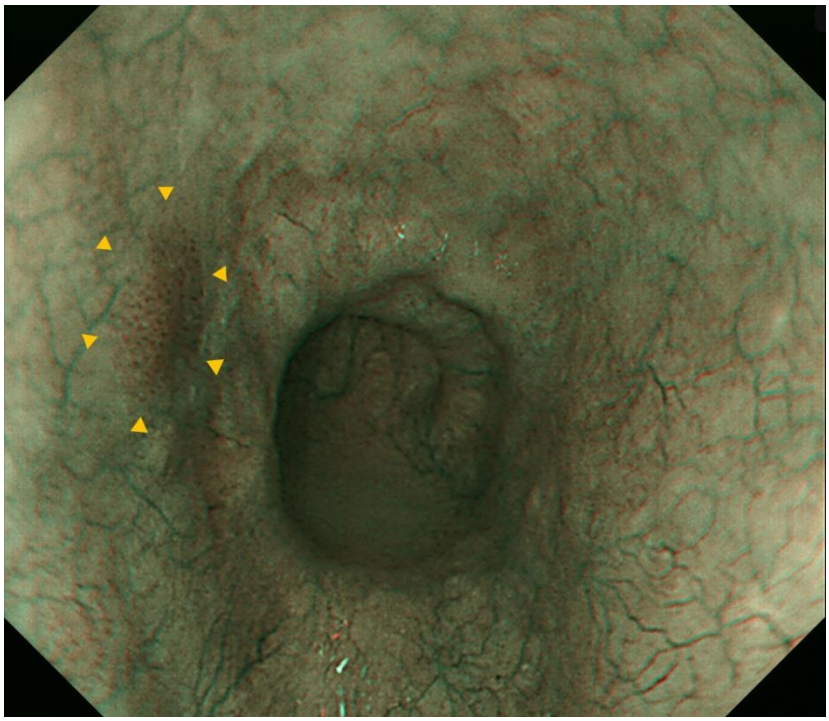

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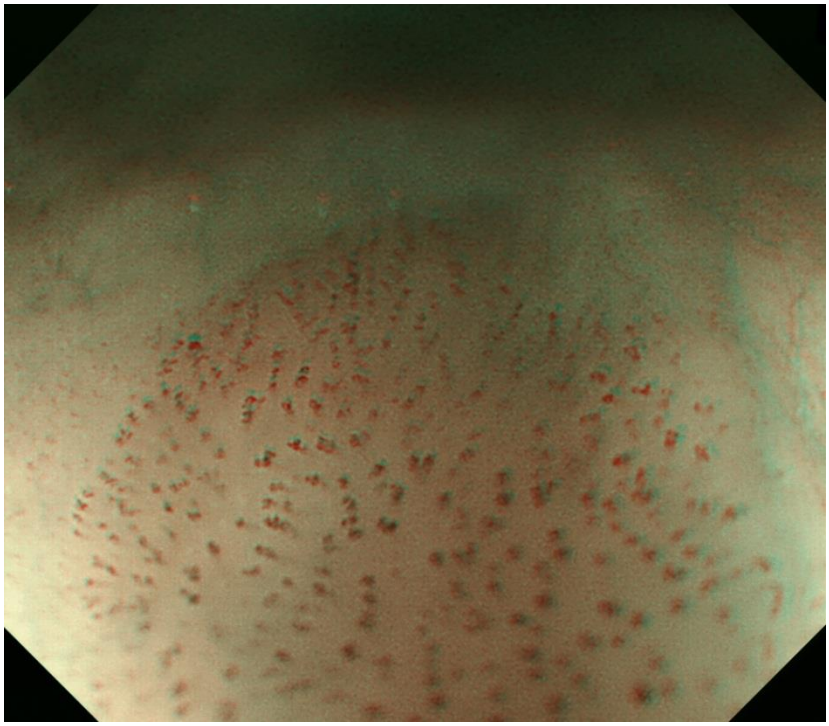
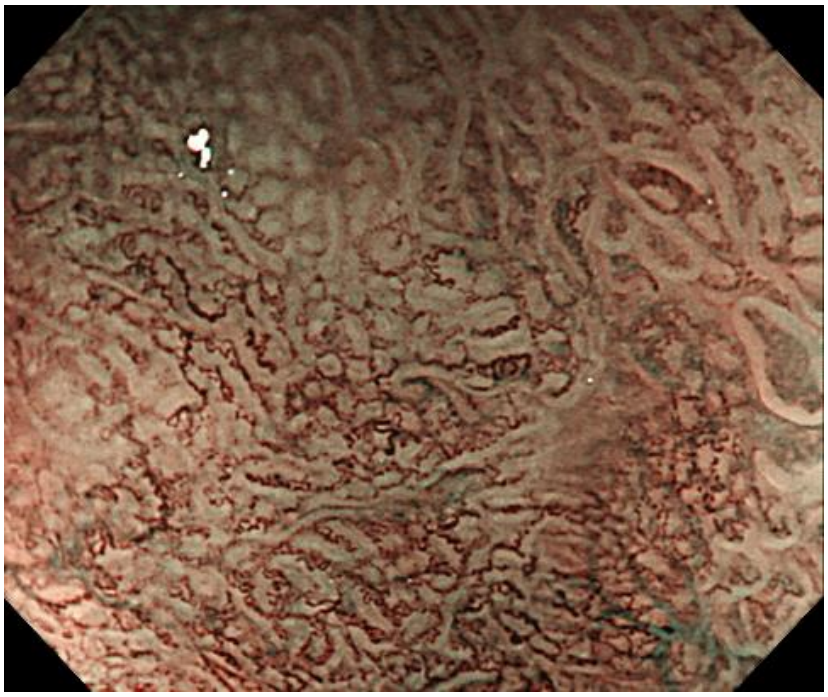


Figure 2 (A)



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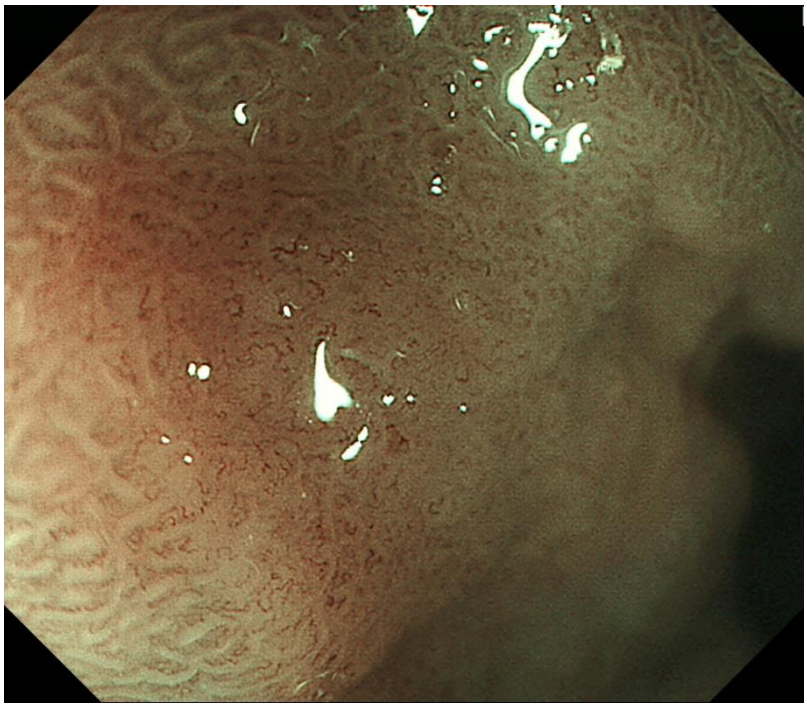
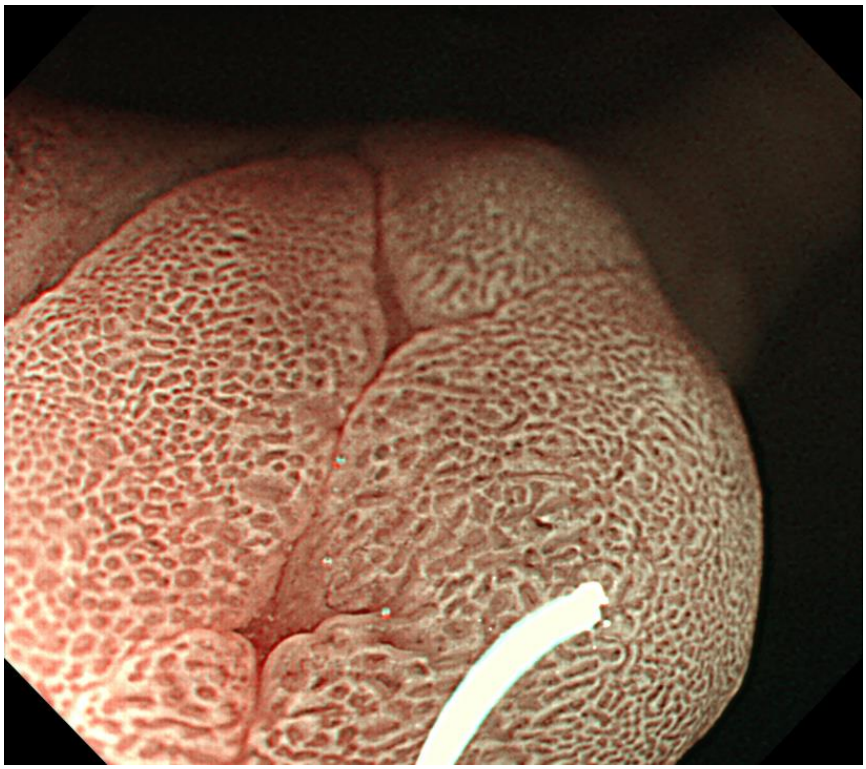


Figure 3 (A)



(B)