クリニカル・テクノロジー

Narrow Band Imaging of Oral Mucosa, Cancer and Pre-cancerous Lesions

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Abstract:

Narrow band imaging (NBI) enhances the diagnostic capability of endoscopy for tissue characterization. The procedure uses using narrow-bandwidth filters in a sequential red-green-blue illumination system. The blue filter corresponds to the peak absorption spectrum of hemoglobin and thus emphasizes images of capillary vessels on the surface mucosa. Here, we examined the applicability of the NBI system to evaluate oral mucosa, and the status of 6 patients with oral squamous cell carcinoma and 5 with oral pre-cancerous lesions. Regular, orderly, thin-caliber vessels in the tongue, floor of the mouth, buccal mucosa, soft palate and lip were clearly distinguished by NBI. However, small vessel branches are difficult to evaluate in the gingival and hard palate mucosa. Adding the patterns of capillary branches to find mucosal patterns appeared to improve the diagnostic value for detecting the borders of oral cancer or pre-cancerous lesions by NBI. The vascular pattern revealed by NBI defined the margin of hyperkeratotic lesions. Although appropriate criteria for oral cancer lesions remain to be established, the NBI system should be useful in the diagnosis of patients with oral cancer and pre-cancerous lesions.

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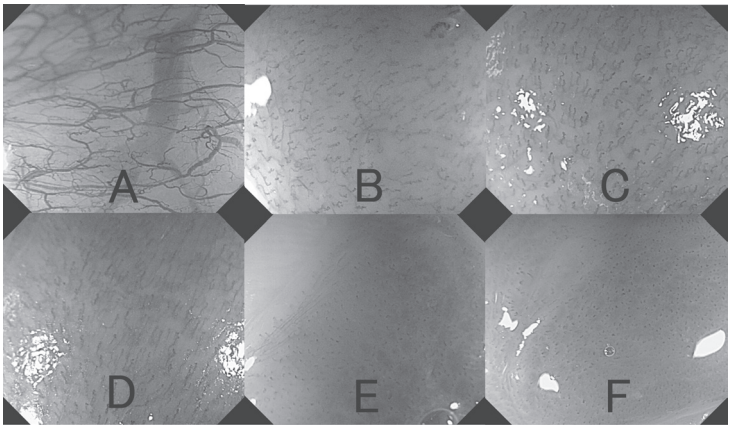


Fig. 2

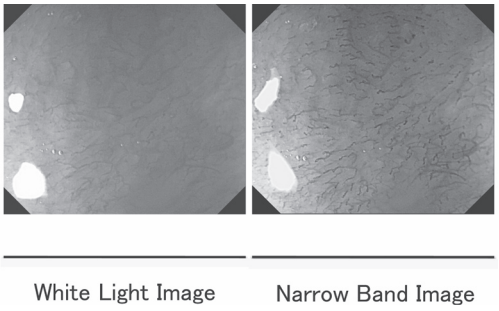
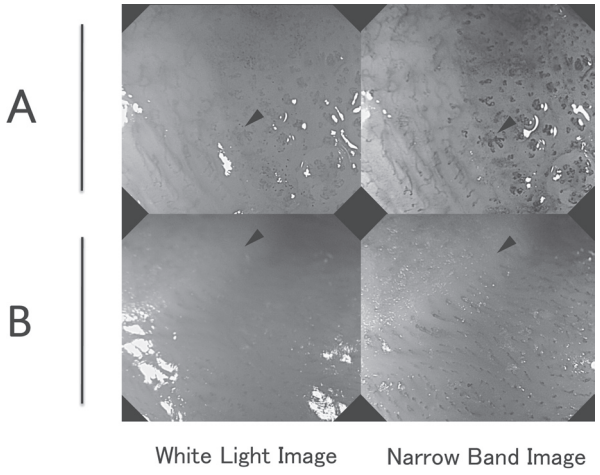


Fig. 1



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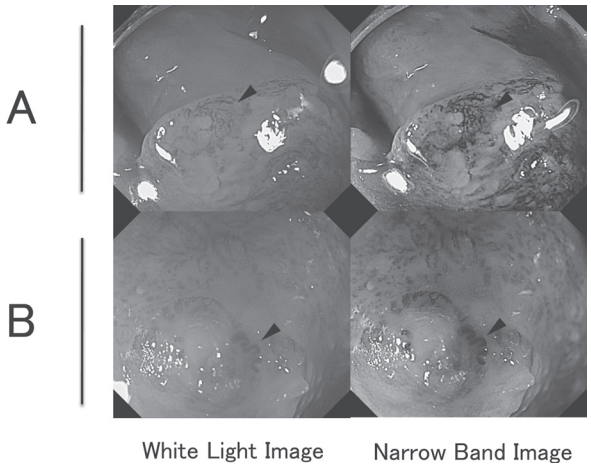

Fig. 4

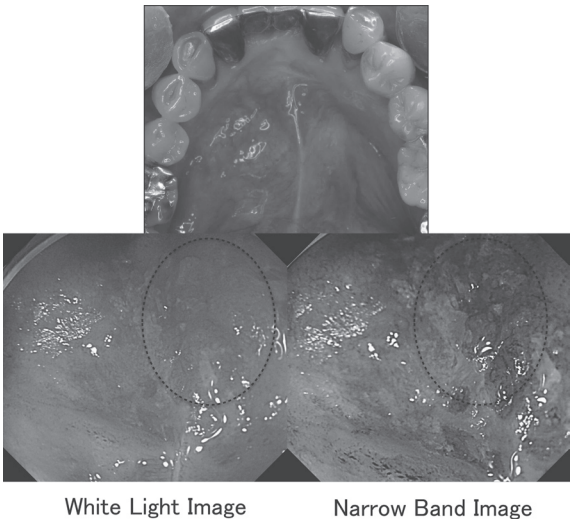

Fig. 5

Introduction

Endoscopy identifies lesions as changes in color tone and irregularities of the surface mucosa. Examining surface microstructure using a magnifying endoscopy can reveal the characteristics of the lesion. Narrow band imaging (NBI) is a novel method of image processing that uses filters to dissociate bands of the light spectrum, which highlights specific features such as capillary and mucosal patterns.[6] Narrow band imaging is a video endoscopic imaging technique that enhances images of the mucosal microstructure and capillaries of the superficial mucosal layer using novel narrow-band filters (wavelength ranges of the new RGB filters: red [R], 485–515 nm; green [G], 430–460 nm and blue [B], 400–430 nm) that differ from the RGB of a plain sequential endoscope, and changes the spectral features of the observation light relative to that of the narrow band filters.[3] Combining the narrow band imaging system with a magnifying endoscope allows simple and clear visualization of fine mucosal appearance and capillaries of the superficial mucosal layer simply by switching the lighting system, without the need for dyes or acetic acid.

Over 300,000 patients worldwide are annually diagnosed with oral squamous cell carcinoma (OSCC). This aggressive epithelial malignancy is associated with high mortality and severe morbidity among long-term survivors.[1] Pre-cancerous lesions of the oral cavity are defined as morphologically altered tissue in which cancer is more likely to occur than in its apparently normal counterpart. The prognosis of patients with malignancies of the oral cavity depends strictly on early detection of premalignant and malignant lesions. Both leukoplakia and erythroplakia might have malignant potential and are categorized as oral precancerous lesions.

The present study examines whether or not the NBI system is useful for examining the oral mucosa, oral precancerous lesions and OSCC.

Materials and Methods

Subjects

Eleven subjects with oral precancerous lesions (n = 5) and with oral cancer (n = 6) and 2 healthy non-smokers (controls) were admitted to the Oral and Maxillofacial Surgery, Showa University Dental Hospital during the period from April to December 2007.

The Medical Ethics Committee of Showa University School of Dentistry approved the study protocol and we obtained written informed consent from the volunteers and patients to participate in this study.

The study protocol complied with the Declaration of Helsinki, as adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964, amended by the 29th World Medical Assembly, Tokyo, Japan, October 1975, the 35th World Medical Assembly, Venice, Italy, October 1983, and the 41st World Medical Assembly, Hong Kong, September 1989.

NBI endoscopy

Subjects and healthy volunteers were evaluated using a standard magnification endoscope (Olympus

Fig. 1 Comparison of white light and narrow band images of normal tongue. Magnified high-resolution white light image (left); NBI endoscopic photographs (right). Regular, orderly, thin-caliber vessels are more obvious in NBI image of tongue mucosa.

Fig. 2 NBI evaluation of normal oral mucosa. Normal oral mucosa (A, floor of mouth; B, soft palate; C, buccal mucosa; D, lip; E, gingiva; F, hard palate) of healthy volunteers. Regular, orderly, thin-caliber vessels in floor of mouth, soft palate, buccal mucosa, and lip. Orderly dots are located on top of intrapapillary capillary loops (IPCLs) in gingival and hard palate mucosa.

Fig. 3 NBI findings of oral precancerous lesion (leukoplakia). Small vessels are evident. Vessels display corkscrewed tortuosity in area of leukoplakia (A). Magnified high-resolution white light image of same lesion (B) could not emphasize mucosal abnormality or margin of the hyperkeratotic lesion, whereas NBI defined lesion margin with normal vascularity or IPCLs and invisible vascular area.

Fig. 4 NBI and white light evaluation of OSCC of the tongue. A, OSCC in Patient 1. Vascularity is increased and irregular at tumor mass of tongue on NBI image. B, OSCC in Patient 2. Dilated and twisted vessels (triangle) are obvious at tumor mass of tongue on NBI image.

Fig. 5 NBI observations of early cancer from lower gingival mucosa to the floor of the mouth. Normal and magnified high-resolution white light images clearly visualize mucosal abnormality, whereas NBI highlights rough surface findings of OSCC with irregular vascularity.

GIF Q240Z; Olympus Inc., Tokyo, Japan) with an NBI light source. The sequential lighting method in video endoscopes has a rotating disc with red, green, blue (RGB) optical filters positioned in front of a white light source. The NBI uses spectral narrow band optical filters instead of the full spectrum of white light. The penetration depth of light depends on wavelength; that is, the shorter the wavelength, the more superficial the penetration. Blue light typically reaches into shallow surfaces (mucosal imaging) because it has the shortest wavelength. Therefore, blue light with special narrow band filters (415, 445 and 500 nm) enhances images of superficial tissue structures. The main chromophore in mucosal tissues in the visible wavelength range is hemoglobin, which has a maximal absorptive wavelength near 415 nm, which enables NBI to detect vascular structures and patterns more accurately than conventional endoscopy. A transparent cap fitted onto the distal tip of the endoscope maintained the distance between the endoscope and oral mucosa.

Evaluation

We examined the applicability of the NBI system to evaluate oral mucosa, and the status of 6 patients with oral squamous cell carcinoma and 5 with oral pre-cancerous lesions whether or not the NBI system is useful for early detection of oral cancer or pre-cancerous lesions. Regular, orderly, thin-caliber vessels in the tongue, floor of the mouth, buccal mucosa, soft palate and lip were clearly distinguished by NBI.

Results

NBI observations of normal oral mucosa

We evaluated 7 areas of the oral mucosa (tongue, gingival, floor of the mouth, buccal mucosa, hard palate, soft palate and lip) of healthy volunteers. Figure 1 shows magnified high-resolution white light images and photographs of NBI endoscopic images.

Regular, orderly, thin-caliber vessels were more obvious in the tongue (Fig. 1), floor of the mouth, buccal mucosa, soft palate and lip (Fig. 2A～D) on NBI images. The tops of intrapapillary capillary loops (IPCLs) were apparent as well-ordered dots, but to evaluate the branching pattern of small vessels in the gingival and hard palate mucosa was difficult (Fig. 2E and F).

Observations of oral precancerous lesions (leukoplakia) using NBI

Figure 3A shows that NBI emphasized the nature of small vessels in leukoplakia of the tongue (Patient 1) as a corkscrewing tortuosity with a clear margin. Figure 3B shows that a magnified high-resolution white light image could not define a mucosal abnormality or the margin of the hyperkeratotic lesion in leukoplakia of the tongue (Patient 2), whereas NBI delineated the margin of the lesion with normal vascularity or IPCLs and the vascular pattern.

Observations of OSCC using NBI

Figure 4 shows a white light image and NBI findings of OSCC. Figure 4A (OSCC; Patient 1), shows increased and irregular vascularity at the tumor mass of the tongue and Fig. 4B (OSCC; Patient 2) shows dilated and twisted vessels at the tumor mass of the tongue on NBI. Figure 5 shows early stage cancer from the mandibular gingival mucosa to the floor of the mouth. Normal observation and magnified high-resolution white light imaging could not define any mucosal abnormalities, whereas NBI emphasized the rough surface of OSCC with irregular vascularity.

Discussion

Although the oral cavity can be easily accessed and observed, normal mucosa and oral precancerous lesions can be difficult to be distinguished. Precancerous lesions have been defined as morphologically altered tissue in which cancer is more likely to occur than in its apparently normal counterpart. Clinically, leukoplakia and erythroplakia might have malignant potential and are categorized as oral precancerous lesions.[8, 10)]

Oral, esophageal and gastric precancerous lesions or early cancer have historically been evaluated by staining with Lugol's solution (LS).[2)] This iodine-based compound has affinity for glycogen in non-keratinized

squamous epithelium, which assumes a dark greenish-brown color when stained. Glycogen-depleted areas, such as inflammation, squamous dysplasia and neoplastic lesions, remain unstained or weakly stained. The LS stain is easy to apply for mucosal examination, but it is contraindicated for patients who are allergic to iodine.

Within the past decade, advances in biomedical optics have overcome the limitations of conventional endoscopy for diagnosing intestinal metaplasia, dysplasia, and carcinoma.[5] The novel NBI high-resolution endoscopic imaging uses the optical characteristics of light to detect mucosal and vascular details. Narrow band imaging has several advantages compared with other methods with respect to observing esophageal, gastric and intestinal mucosa, and it enables detailed inspection of the mucosal and vascular surface without staining agents.

Although NBI has the potential to evaluate oral mucosa, definite NBI findings of this tissue have not been described. Figures 1 and 2 show obvious regular, orderly, thin-caliber vessels in the tongue, floor of the mouth, buccal mucosa, soft palate and lip on NBI images. Small vessels branching in areas of gingival and hard palate mucosa were not so easy to evaluate, although IPCLs appeared as orderly dots (Fig. 2E and F). Thus, we proved that NBI can evaluate the vascular appearance of the oral mucosa.

Tipoe et al. described increased vascularity and angiogenesis in proliferating and transforming oral lesions including hyperplasia, dysplasia and squamous cell carcinoma of the cheek mucosa,[9] but vessel patterns in precancerous or squamous cell carcinoma of the oral mucosa have not yet been described. Here, NBI highlighted small vessels and vessels with corkscrewed tortuosities in areas of leukoplakia with a clear margin (Fig. 3A). Hirata et al.[4] identified invisible microvessels that are a significantly frequent feature of hyperkeratotic lesions of colorectal tumors, and the microvascular features determined by NBI magnification corresponded with immunohistochemical features of microvessels. In the present study, NBI defined the margin of leukoplakia of the tongue as an invisible vascular area, whereas magnified high-resolution white light could not depict the margin (Fig. 3B).

Gono et al.[3] reported that NBI enhances epithelial microvascular patterns, and that small colonic polyps of adenomas or cancers can be visualized as brown staining in NBI images, which facilitates diagnosis. Muto et al.[7] have described the value of the NBI system using a gastrointestinal endoscope to detect superficial lesions of the head and neck mucosa. In the present study, NBI imaging revealed increased and irregular vascularity, and highlighted the rough and irregular surface of OSCC. These results showed that the NBI findings of oral leukoplakia and OSCC were significantly improved compared with those acquired using conventional white light.

Changes in the epithelial microvessels of the oral mucosa were recognizable using NBI because its optical properties enhance the contrast of epithelial microvessels. If oral cancers can be detected with NBI in the epithelium *in situ*, the risk of metastasis would be decreased and the rates of a favorable prognosis should be improved. Although further investigation is required to determine the applicability of NBI to detecting pre-malignant oral lesions, the NBI system will be useful for managing patients with oral cancer and pre-cancerous lesions.

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