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Original Research

## A study on the intrapapillary capillary loop detected by narrow band imaging system in early oral squamous cell carcinoma

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## ABSTRACT

**Objective:** The purpose of this study is to determine the effectiveness of narrow band imaging (NBI) by analyzing three-dimensional (3D) images of intrapapillary capillary loop (IPCL) and recording changes over time.

**Methods:** This study was conducted between April 2007 and October 2011 at the Department of Oral and Maxillofacial Surgery of Tokyo Dental College Chiba Hospital. A total of 119 cases and 40 healthy volunteers were observed with NBI. Within a total of 119 cases oral squamous cell carcinoma (OSCC) was diagnosed in 48 cases (40%), leukoplakia in 26 cases (22%), oral lichen planus in 18 cases (15%), gingivitis in 5 cases (4%), aphtha in 4 cases (3.5%), ulcer in 4 cases (3.5%), erythroplakia in 3 cases (2.5%), pigmentation in 3 cases (2.5%), and other diseases in 8 cases (7%). The 40 healthy volunteers were medically examined at the regions of the gingiva, lower lip, buccal mucosa, oral floor, lateral border of the tongue, and dorsal surface of the tongue.

**Results:** Morphological changes of IPCL were analyzed through the construction of 3D images. The dimension, volume and density of vascular vessel were compared between OSCC, dysplasia and normal mucosa. Abnormal vascular vessels were apparent in cases of dysplasia and OSCC when examined through magnifying endoscopy with NBI. Morphological changes of IPCL such as dilation, aggregation and thickness increasing observed by NBI were certified through 3D imaging.

**Conclusions:** These results suggest that NBI is an effective method for the early detection of OSCC.

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### 1. Objective

Narrow band imaging (NBI) system is a novel endoscopic method [1]. This technology was developed by the Division of Endoscopy and Gastrointestinal Oncology, National Cancer Center Hospital East and Olympus Medical Systems in 2003 [2].

NBI uses special optical filters that narrow light bandwidth to enhance the visualization of mucosa surface and microvasculature [3]. Wavelengths of light in the visible spectrum are filtered from the illumination source, with the exception of narrow bands in the blue and green spectra centered at 415 and 540 nm, respectively, coinciding with the peak absorption spectrum of oxyhemoglobin,

making vascular vessels more prominent when viewed in NBI mode [4]. NBI is widely used for the examination of esophageal and pharyngeal mucosa. NBI combined with magnifying endoscopy to examine the condition of intrapapillary capillary loop (IPCL) is useful for the early detection of early carcinoma within the esophagus [5], oropharynx, and hypopharynx regions [6,7]. The oral cavity and esophagus are covered with squamous epithelium with similar vascular structures; therefore the authors screened the oral mucosa and found similar vascular changes since 2009. The effectiveness of NBI in the diagnosis of early oral squamous cell carcinoma (OSCC) is due to the ability to study and contrast IPCL and its vascular architecture [3]. Several studies have suggested that capillaries penetrate the epithelium in case of early mucosal carcinoma [8,9], however no histological microvascular images have been described yet. In order to investigate the changes associated with IPCL in various lesions, we constructed three-dimensional images (3D) of IPCL on a personal computer (PC), and compared the dimension, volume, and density of vascular vessels between normal mucosa, dysplasia and OSCC and recorded observations over time.

\* Asian AOMS: Asian Association of Oral and Maxillofacial Surgeons; ASOMP: Asian Society of Oral and Maxillofacial Pathology; JSOP: Japanese Society of Oral Pathology; JSOMS: Japanese Society of Oral and Maxillofacial Surgeons; JSOM: Japanese Society of Oral Medicine; JAMI: Japanese Academy of Maxillofacial Implants.

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The purpose of this study is to analyze the clinical features of early OSCC using NBI in order to determine the effectiveness of NBI by analyzing 3D images of IPCL and recording changes over time.

## 2. Materials and methods

### 2.1. Subjects

This study was conducted between April 2007 and October 2011 at the Department of Oral and Maxillofacial Surgery in Tokyo Dental College Chiba Hospital. A total of 119 cases were studied and those that were diagnosed as non-OSCC or OSCC underwent observations with NBI to detect pathological lesions and its surrounding mucosa. OSCC cases were limited only to T1 and T2 cases. As controls, 40 healthy volunteers with normal mucosa underwent observation with NBI to the gingiva, lower lip, buccal mucosa, oral floor, lateral border of the tongue, and dorsal surface of the tongue. This study was approved by the Ethics Committee of Tokyo Dental College (Approval No. 235) and undertaken according to the Declaration of Helsinki. All patients and volunteers gave written informed consent before the procedures.

### 2.2. Observation of oral mucosa with NBI

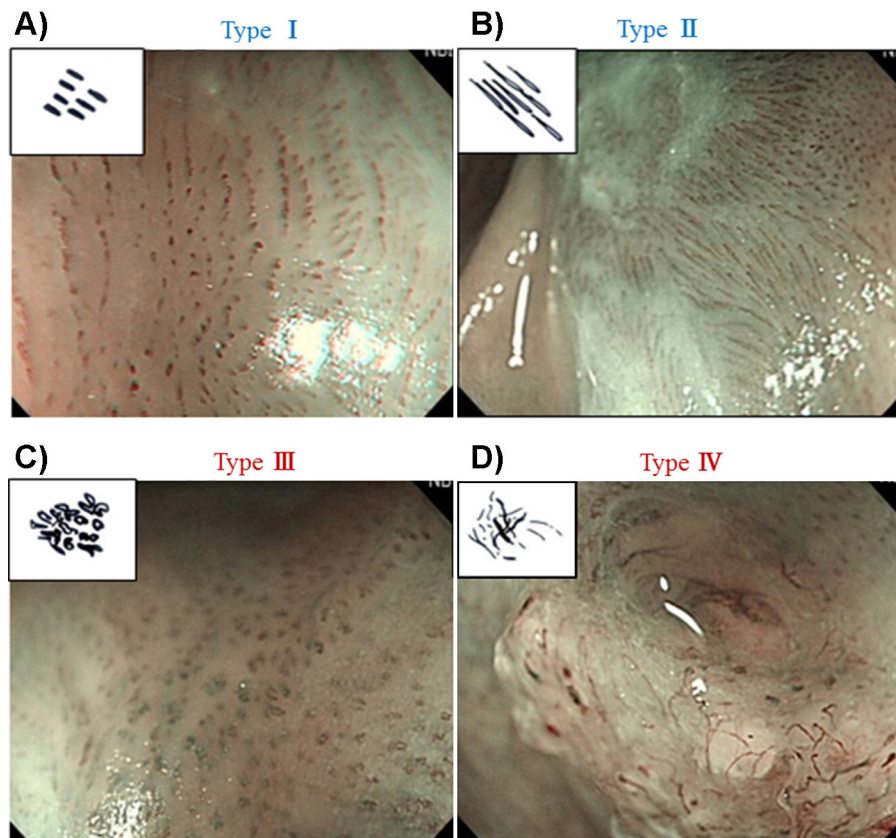
Observation of the oral mucosa with NBI was carried out with the Evis Lucera Spectrum Video Imaging System (CV-260SL processor and CLV-260SL light source, Olympus Medical System Corp., Tokyo, Japan). NBI shows vascular vessels by irradiating two narrow band wavelengths (390–445 nm/530–550 nm) which corresponds

to the hemoglobin absorption band. Thin vascular vessels such as capillaries in the mucosal surface can be observed as good contrast.

IPCL images of 119 patients (OSCC 48, non-OSCC 71) and 40 healthy volunteers were classified by Takano's classification [3] (Fig. 1): Type I, regular brown dots; Type II, IPCL pattern dilation and crossing; Type III, IPCL pattern elongation and meandering; Type IV, IPCL pattern destruction and angiogenesis as a consequence of carcinogenesis progression [3]. According to the results from the IPCL classification, 159 cases of IPCL patterns were divided into two groups Type I, II and Type III, IV. The specificity and sensitivity of the 2 groups were calculated to detect OSCC.

### 2.3. 3D imaging construction and measurement of vascular vessels

Within the 119 cases that were observed with NBI, serial sections were obtained from 16 cases that underwent resection. 3D images were constructed from these 16 cases after immunohistochemical staining and 8 were diagnosed as OSCC, the other 8 cases were diagnosed as dysplasia (1 mild, 4 moderate, 3 severe). Normal mucosa specimens 3 cases were obtained from the surrounding regions of dysplasia cases. From the OSCC cases 5 were tongue lesions and 3 were buccal mucosa lesions. From the dysplasia cases 6 were tongue lesions, 1 buccal mucosa lesion, and 1 gingiva lesion. Normal cases were all tongue lesions. All of these lesions were diagnosed by an oral pathologist. To distinguish the endothelial cells of vascular vessels, paraffin-embedded specimens were sliced along the lesion into 60 serial sections each 4  $\mu\text{m}$  in length and stained with the automatic immunohistochemistry system (DISCOVERY;



**Fig. 1.** IPCL classification: A) normal IPCL (Type I) appears with both waved arms together, as a waved line. Type I image is showing oral floor. B) At dilation, IPCL (Type II) has a similar shape to Type I, but their caliber is notably increased compared with others far from the lesion. Type II image is showing gingiva. C) Elongation (IPCL Type III) can be visualized as a simple increase in length or as tangled lines due to the severe increase in length. Generally, elongated IPCL is accompanied by dilation. Type III is showing buccal mucosa. D) IPCL Type IV is characterized by large vessels with no loops at the terminal branches due to the progression of carcinogenesis which leads to dilation and elongation of the loops and finally their destruction. Type IV is showing tongue.

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