



Narrow band imaging in the intra-operative definition of resection margins in oral cavity and oropharyngeal cancer



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SUMMARY

Objectives: In oncological surgery, a three-dimensional resection 1.5–2 cm from the gross tumour edge is currently considered appropriate, and the status of resection margins is the most reliable indicator of radicality. Awareness of “field cancerization” calls for a re-evaluation of the benchmarks of tumour resection; however, its identification is not simple because the dysplastic areas may be far from the main lesion and difficult to recognize macroscopically. New technologies such as narrow band imaging (NBI) could improve the detection of neoplastic and pre-neoplastic areas, ensuring more precise resections. The main purpose of this study was to investigate the value of NBI in detecting pre-cancerous areas and/or cancer around the tumour bulk intra-operatively, to achieve adequate resection of the tumour.

Materials and Methods: The resection margins of 8 oral cavity and 8 oropharyngeal cancers were first drawn by macroscopic evaluation and then re-defined using NBI. Resections were performed following the NBI-drawing if extemporaneous histological examinations of the NBI-defined enlargements were positive for dysplasia or cancer. The number of clear margins was evaluated.

Results: Resections margins were free of tumour or dysplasia at extemporaneous examination; on definitive histology, two patients had a margin positive for cancer and dysplasia, respectively. Among the NBI-defined enlargements, 25% were positive for dysplasia and 75% for cancer. The sensitivity, specificity, positive and negative predictive values were 100%, 88.9%, 100% and 87.5%, respectively.

Conclusion: The method we propose could be useful for obtaining free surgical margins and reducing the potential development of tumour foci resulting from incomplete resection.

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Introduction

The main goal of oncologic surgery remains the excision of the tumour, with macroscopically adequate surgical margins [1]. The current surgical standard in the oral cavity and pharynx implies a resection with a macroscopic margin of 1 cm [2–4], 1.5 cm [5] or 2 cm [6–8] in the three dimensions, both superficially and deeply, assuming that the tumour is as wide on the surface as in depth. Obtaining uninvolved margins at final histological examination is therefore currently the gold standard for surgeons, because the presence of dysplasia or carcinoma following resection of carcinoma of the head and neck, has been shown to be associated with a higher incidence of local recurrence events [9]. However, this appears particularly difficult in consideration of the peculiar frequent growth pattern of oral squamous cell carcinomas (OSCC),

defined as the “field cancerization” phenomenon. This concept assumes that multiple, unrelated, precancerous lesions may exist adjacent to the original tumour mass, each one bearing the potential to develop into a new tumour [10–12]. Although in practice the identification of these proves very challenging by routine examination, substantial progress has been made in the last ten years with the development and optimization of innovative imaging techniques allowing improved visualization of the superficial extension of the tumour [13–15].

Among these diagnostic tools, narrow band imaging (NBI) has widely demonstrated its effectiveness in helping to detect superficial mucosal lesions of the oral and pharyngeal mucosa [13,14].

The main purpose of this pilot study was to investigate the value of NBI in detecting intraoperatively pre-cancerous areas (dysplasias) and/or cancer around the clinically visible tumour bulk, in order to achieve adequate resection of the entire local tumour and maximize the number of free resection margins at definitive histological examination.

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Materials and methods

This pilot prospective study was conducted at the ENT Department of Cattinara Hospital in Trieste (Italy) in accordance with the Declaration of Helsinki, and approved by the local ethics committee.

NBI is a video endoscopic system with narrow band filters that allows for the passage of only two specific bands of the visible spectrum which correspond to the absorption peak of haemoglobin. The filtered wavelengths enhance the microvascular abnormalities associated with the preneoplastic and neoplastic changes of the mucosal lining of the upper aerodigestive tract [16]. In our study NBI was used for the intra-operative definition of resection margins in patients with oral cavity and oropharyngeal cancer to evaluate whether it could help in detecting pre-cancerous areas (dysplasias) and/or cancer around the tumour bulk intraoperatively.

Among candidates for surgery, established by a multidisciplinary panel, we decided to focus on a subset of patients who met the following inclusion criteria: age between 18 and 90 years, no previous surgery, radiotherapy or chemotherapy for head and neck cancers, no cancers located in the hypopharynx or larynx. During the first 6 months of intraoperative use of NBI, 37 patients with squamous cell carcinoma (SCC) came to our attention; among the 11 patients with a tumour located in the oral cavity, 3 were excluded because of previous surgery; among the 11 patients with oropharyngeal tumour, 3 were excluded because of previous surgery; 15 patients were excluded because the cancer was located in the hypopharynx ($n = 6$) or in the larynx ($n = 9$). Therefore, 16 patients with SCC of the oral cavity ($n = 8$) and oropharynx ($n = 8$) were finally included in the study; all of them had a biopsy-proven diagnosis of SCC and clinical staging (cTNM) obtained with computed tomography (CT) and magnetic resonance imaging (MRI), in accordance with the NCCN guidelines (National Comprehensive Cancer Network). The tumour sites and subsites and clinical staging are summarized in Table 1.

A surgeon explained to the patient that during the surgery, NBI, a new type of imaging tool, would be used to define the real extension of the lesion beyond the macroscopic margins defined both visually and by palpation, that the resection would be performed following the NBI-guided drawing if extemporaneous histological examinations of the area between the two tattoos were positive for dysplasia or cancer, and that this procedure carried no additional risks and required no specific preparation. The patients signed a detailed informed consent form, with the privacy policy agreement.

A few days before surgery, two physicians experienced in the use of NBI carried out a preliminary evaluation focusing on the

clinically negative areas around the tumour that had a suspicious appearance on NBI: this step served only the practical purpose of reducing the intraoperative time required for defining the resection margins. NBI was performed using a Visera Elite system (OTV-S190 video processor and CLV-190 light source, OTV-S7Pro-10E HDTV camera; Olympus Medical Systems Corp, Tokyo, Japan) with rigid endoscopes with a viewing angle of 70° for the oropharynx or an angle of 0° for the oral cavity. Patients were examined in a seated position; no specific patient preparation was necessary; local anaesthesia was achieved with lidocaine spray 10 g/100 ml only if necessary. During the examination, particular care was taken to avoid bleeding, which alters the penetration of light into tissue and precludes NBI evaluation. In the event that the preoperative evaluation could not be completed because of poor patient compliance or difficulty reaching the tumour with the endoscope tip, the NBI evaluation was carried out only intraoperatively. All procedures were recorded on video.

In the operating room on the day of surgery, after general anaesthesia and preparation of the surgical field, and before any surgical action involving bleeding which negatively affects NBI evaluation, a first definition of the resection margins was obtained with an electric scalpel, using a ruler to help maintain a distance of 1.5 cm from the macroscopic lesion boundaries defined visually and by palpation. Then, the two NBI experts made an additional assessment and re-defined the resection margins using the same instrument as used preoperatively. The apparently healthy mucosa surrounding the main tumour mass was considered positive at NBI evaluation if it displayed the known alterations of the intrapapillary capillary loop (IPCL), such as dilatation and crossing, elongation and meandering or pattern destruction and angiogenesis, which can underlie histological changes (Fig. 1) [17–19]. This evaluation increased the operating time by an average of 5 min. The different steps were video recorded (Fig. 2).

The two templates were then compared and the distance between them measured; if a difference between them was found, several biopsies were obtained from the area between the white-light (WL) and NBI tattoos which showed the most suspicious vascular changes (Fig. 3), and they were sent to a dedicated pathologist for extemporaneous histological examination. We decided to use a combination of NBI positivity and positive result of frozen sections collected in these areas to guide the resection margins because this was a pilot study and defining the margins on NBI appearance alone would not have been ethical given the

Table 1
Patients and tumours' characteristics.

Id	Site	Subsite	cTNM
1	Oral cavity	Floor of mouth	T2N0M0
2	Oropharynx	Tonsil, base of tongue	T3N2bM0
3	Oropharynx	Tonsil	T2N1M0
4	Oral cavity	Floor of mouth	T2N1M0
5	Oral cavity	Floor of mouth	T2N2cM0
6	Oropharynx	Tonsil, soft palate	T3N1M0
7	Oral cavity	Anterior tongue	T1N0M0
8	Oral cavity	Floor of mouth, anterior tongue	T3N0M0
9	Oropharynx	Tonsil, soft palate	T3N1M0
10	Oral cavity	Floor of mouth, anterior tongue	T4aN2bM0
11	Oropharynx	Tonsil, soft palate	T1NxM0
12	Oral cavity	Floor of mouth	T2N0M0
13	Oropharynx	Tonsil	T4aN2bM0
14	Oropharynx	Retromolar trigone	T3N2aM0
15	Oropharynx	Soft palate	T2N2bM0
16	Oral cavity	Anterior tongue	T3N0M0

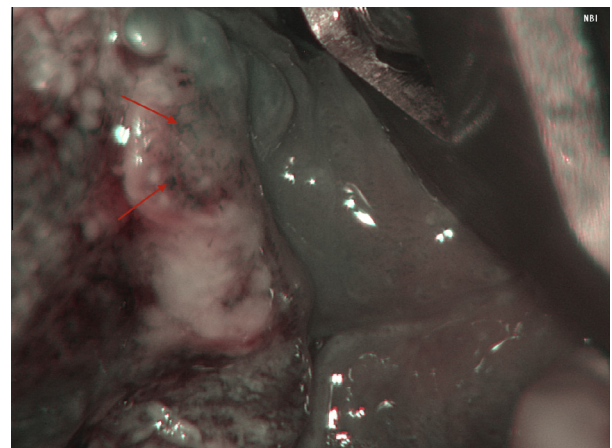


Fig. 1. Vegetating lesion of the posterior left tongue margin: arrows indicate altered intra-papillary capillary loops (IPCL) (capillary meandering) defined as positive at NBI evaluation. The histological examination confirmed the presence of squamous cell carcinoma.

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