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Narrow Band Imaging (NBI) — Endoscopic Method for Detection of Head and Neck Cancer

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1. Introduction

The most common head and neck malignancy is squamous cell carcinoma (SCC). It is well recognized that these tumours may arise in multiple sites, either synchronously or metachronously [1]. The surgical and oncological treatment of large tumours leads to a significant mutilation of the affected individual. The results are not only cosmetic, but also functional defects, such as swallowing, chewing, breathing disorders and voice production deterioration. Early detection of these tumours is therefore one of the most important factors of treatment success [2].

Efforts to achieve the earliest detection of malignant disease have led to the development of new endoscopic examination methods. Lesions few millimetres in diameter are in most cases impossible to detect using conventional white light endoscopy. This led to the introduction of special endoscopic methods that allow detection of lesions of millimetre dimensions. New techniques such as autofluorescence [3], contact endoscopy and optical coherence tomography (OCT) [4] are increasingly used in ENT practice. In the last few years, NBI (Narrow Band Imaging) method has been introduced [5]. This diagnostic tool was already proved as a useful screening method in other endoscopic fields (e.g. gastroenterology) [6]. Superficial mucosal lesions that would be missed by regular white light endoscopy, can be identified, in view of their neoangiogenetic pattern of vasculature, using the narrow-band imaging in head and neck mucosa.

2. The principles of NBI endoscopy

The best case scenario for early detection of mucosal SCC would be at the stage of dysplasia or carcinoma in situ (CIS). These early lesions are difficult to detect in white light endoscopy, if they are less than 1 cm in diameter [7]. In the oesophagus, these lesions can be easily detected by Lugol chromoendoscopy, where squamous dysplasia and CIS appear as Lugol voiding lesions [8]. This is not suitable for investigation of upper aerodigestive tract due to severe mucosal irritation caused by Lugol solution [7]. Chromoendoscopy is able to show differences in epithelium quality. NBI shows differences in epithelium quality and changes of mucosal vascularization. NBI is an optical image enhancement technology that enhances vessels in the mucosal surface and patterns of the mucosa using the characteristics of light spectrum [6]. It is a non-invasive technique that can be carried out in the outpatient clinic without need of general anaesthesia. NBI system consists of the same components as conventional videoendoscopic systems - light source, camera unit and camera head or chip equipped videoendoscope. In addition, NBI system contains a special image processor and a lighting unit with special filters that narrow frequency range of emitted light to 400-430 nm (centered at 415 nm) and 525-555 nm (centered at 540 nm) bands. It relies on the principle of depth of light penetration. In contrast to red light, 415 nm wavelength light has less penetration and less scattering thus enhancing image resolution. The blue filter is designed to correspond to the peak absorption spectrum of haemoglobin to enhance the image of capillary vessels (IPCL - Intraepithelial Papillary Capillary Loops) on mucosal surface. 540 nm wavelength light penetrates deeper and highlights the submucosal vascular plexus. The reflection is captured by a charge coupled device chip (CCD), and an image processor creates a composite pseudo-colour image, which is displayed on a monitor, enabling NBI to enhance mucosal contrast without the use of dyes [9] (Figure 1). In the resulting image the mucosal microvascularization is displayed brown and submucosal vessels cyan (Figure 2). Vascular structures are displayed with greater contrast to the epithelium than in white light illumination [10]. In detection of surface mucosal changes characteristic for neoplastic lesions (e.g. dysplasia, ca in-situ, carcinoma) epithelial abnormalities (thickening, changes in the surface layer) and vascular changes can be better observed in NBI. In developing neoangiogenesis IPCL changes occur (expansion, extension and changes of course). These changed IPCL are noticeable in the NBI as brown dots irregularly distributed in the demarcated area of altered epithelium [6]. It is possible to detect lesions measuring a few millimetres in diameter.

3. The use of NBI endoscopy in ENT

Typical suspect finding in NBI image is defined as well demarcated brownish area, exhibiting scattered brown dots within this area on close view [11] (Figure 3). Brown dots are caused by expansion of IPCL, which is due to neoangiogenesis in tumour growth. The finding of brown dots, spread freely in the mucosa of e.g. post-irradiation oedema, without boundary line of altered epithelium, must be carefully distinguished. Such image can not be judged as suspect for neoplasia (Figure 4).

Figure 1. NBI principles (with permission of OLYMPUS CZECH GROUP).

Figure 2. Healthy nasopharyngeal mucosa in white light (A) and NBI (B), mucosal blood vessels displayed in brown and submucosal vessels in cyan.

Recently, NBI was used for diagnosis of oral [12], oropharyngeal [13], hypopharyngeal [14], nasopharyngeal [15] and laryngeal [16] pathologies. NBI is used for screening and for follow-up after chemo- and/or radiotherapy treatment of head and neck SCC [17]. Some authors also used NBI intraoperatively to perform targeted biopsies of most suspect areas and also to determine the safe limits of resection margins [17] (Figure 5).

Figure 3. Mucosal spread of squamous cell carcinoma in vallecula in white light (A) and NBI (B). Clear boundary line between tumour and healthy mucosa and scattered brown dots are well visible in NBI.

Figure 4. Post-radiotherapy mucosal oedema of the arytenoids in white light (A) and NBI (B). Non-suspect image of brown dots.

For NBI endoscopy both flexible and rigid videoendoscopic systems are used in ENT. For outpatient practice ultra-thin flexible videoendoscopes were developed with distal end diameter of 3-4 mm, and also ultra-thin bronchoscopes or gastroscopes with the diameter of the distal end of less than 5 mm are used. These scopes are suitable for transnasal insertion and therefore allow to examine the nasal sinuses, nasopharynx, oropharynx, hypopharynx, oesophagus, larynx, trachea and bronchi and provides better results than conventional transoral examination. Transnasal examination can be performed under local anaesthesia of the nasal mucosa and throat or without any anaesthesia [18]. Improved contrast between mucosal epithelium and blood vessels helps to visualize mucosal lesions few millimetres in

Figure 5. Bilateral carcinoma of the vocal folds in white-light (A) and NBI (B). Supraglottic spread of the cancer is clearly visible on NBI image.

diameter (Figure 6). The sensitivity and specificity of flexible NBI endoscopy in follow-up of head and neck SCC patients were reported 91,3 - 100% and 91,6 - 98% respectively [17,11].

Rigid telescopes are also used in the outpatient service during the examination of the nasal cavities, nasopharynx, oropharynx and oral cavity. Rigid angled telescopes (0°, 30° and 70°) yielded significant improvement in the diagnostic possibilities of direct laryngoscopy under general anaesthesia [19,20]. They allow a thorough examination of all areas of the larynx and even the front commissure and subglottic area. Sensitivity and specificity of NBI examination can be significantly increased in combination with high definition (HDTV) magnifying endoscopy [21].

4. Magnifying endoscopy and endoscopy with high-definition (HDTV)

Development of mucosal malignancies is accompanied by changes of IPCL in terms of their extension, expansion, irregularities of calibre, loss of regular arrangement and in the last stage of tumourigenesis complete loss of vascular microarchitecture [22]. Standard endoscopes, however, does not permit a more accurate display of these changes. They are displayed as irregularly dispersed brown dots in NBI endoscopy. Certain magnification and image resolution is needed to obtain better visibility of IPCL changes [9]. Recent development in endoscopic techniques has led to the introduction of so-called magnifying endoscopy, which, combined with high-definition television (HDTV) allows to display the vascular microarchitecture in vivo. Till now, malignant lesions were determined only on the basis of histological examination. Rigid magnifying telescopes, which allow observing the surface of the mucosa from a distance of few millimetres (e.g. combined with direct laryngoscopy) in combination with HDTV camera head, allow diagnosing the malignancy with high probability prior the conclusion of histology examination. Different classifications of IPCL changes were proposed

Figure 6. Larynx - the left vocal cord dysplasia in white light (A) and NBI (B), arrows point demarcated area of altered epithelium with the presence of brown dots. Another dysplastic lesion in the same patient in the posterior part of the vocal cord in white light (C) and NBI (D).

for oesophagus and pharynx [23], oral cavity [12] and larynx [16]. In oesophagus and pharynx the IPCL changes are graded as Type I (normal IPCL) to Type V (cancer IPCL). Type V is further subdivided into 4 sublevels. According to these levels, the depth of cancer invasion into the mucosa and submucosal tissue can be evaluated [23]. For oral cavity just Type I (normal IPCL) to Type IV (cancer IPCL) grades are proposed [12] (Figure 7, 8).

5. Limits of NBI endoscopy

In some cases even NBI endoscopy examination does not bring the expected results. Since NBI is an optical method based on observation of the mucosal surface, conditions that prevent a direct view of the clear mucous membrane may limit or completely baffle the examination. Most often this is due to stagnant saliva or sticky mucus, especially in patients with a history of oncology treatment. Also, lesions that are characterized by a high layer of hyperkeratosis prevent visualization of mucosal vascularization – eg. verrucous carcinomas [24].

Figure 7. HDTV NBI magnifying endoscopy, the buccal mucosa. Normal (Type I) intraepithelial papillary capillary loops - IPCL (A), enlarged and irregular dysplastic IPCL (Type III) (B).

Figure 8. Advanced tumour of apex of tongue – HDTV NBI, complete collapse of IPCL microarchitecture (Type IV) is visible.

NBI endoscopy brings great results in case of clear observable mucosa. Benign findings such as vocal cord polyps, nodules or granulomas are clearly recognizable. Blood vessels run parallelly to the mucosal surface and do not form brown dots (Figure 9), in contrast to malignant changes that typically show presence of these dots.

Nevertheless, most false positive results of NBI endoscopy were reported in case of laryngeal papillomatosis [11]. In these cases, demarcated lesions with scattered brown dots are often found. The discrimination from cancerous lesions could be very difficult using non-magnifying NBI endoscopy (Figure 10).

Figure 9. Benign polyp of vocal cord in white-light (A) and NBI (B). Blood vessels run paralelly to the mucosal surface. No brown dots are visible.

Figure 10. Laryngeal papilloma in white-light (A) and NBI (B). Verrucous cancer of the vocal fold in white-light (C) and NBI (D). Discrimination of these lesions can be very difficult

Utilization of HDTV NBI magnifying endoscopy can improve the diagnostic accuracy. The papillomas are characterised by forming multiple papillae covered by squamous epithelium with a central axis vessel in each papilla [25]. The microarchitecture of these lesions is often rather regular. On the other hand, the cancerous lesions are characterised by lost of regularity of IPCL shape and also by disruption of the microarchitecture regularity [26] (Figure 11, 12).

Figure 11. Laryngeal papilloma in HDTV NBI magnifying endoscopy(A, B). Multiple regular papillae covered by squamous epithelium with a central axis vessel are typical for papillomas.

Figure 12. Spinocellular carcinoma of the vocal cord in HDTV magnifying endoscopy in white light (C) and NBI (D). Complete disruption of vascular microarchitecture and IPCL irregularities are clear signs of carcinoma.

6. Conclusions

NBI is an advanced endoscopic imaging technique that allows early detection of small superficial mucosal lesions that are undetectable using the conventional white-light endoscopy. NBI is increasingly used in otorhinolaryngology as a convenient screening method for detection of new diseases, but also for follow-up of patients after treatment for head and neck malignant tumours, when early detection of possible recurrence is crucial. Intraoperatively, it can be used as a helpful tool for targeting biopsies, determining the tumour spread and safe resection margins. Using magnifying HDTV endoscopy in combination with NBI dramatically improves the sensitivity and specificity of endoscopic examination. The main advantage is its use particularly in direct laryngoscopy under general anaesthesia in combination with rigid angled telescopes that allow determining the malignancy with high probability during the operation as well as the exact extent of disease.

NBI endoscopy investigation can be limited in cases of stagnant saliva, sticky mucus or high layer of hyperkeratosis. In these situations the clear mucosal surface can be impossible to observe, therefore the advantages of NBI method could be lost. NBI endoscopy achieves high sensitivity and specificity, yet can lead to false positive findings, most frequently in the case of laryngeal papillomatosis. Finding of brown dots there may be mistakenly interpreted as tumour neovasculation. Utilization of HDTV NBI magnifying endoscopy contributes to better differentiation of these lesions.

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