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Evaluating Laryngopharyngeal Tumor Extension Using Narrow Band Imaging Versus Conventional White Light Imaging

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Bernard F. A. M. van der Laan, MD, PhD ; Boudewijn E. C. Plaat, MD, PhD

Objective/Hypothesis: Comparing detection and extension of malignant tumors by flexible laryngoscopy in the outpatient setting with laryngoscopy under general anesthesia using both White Light Imaging (WLI) and Narrow Band Imaging (NBI).

Study Design: Prospective study.

Methods: Two hundred and thirty-three patients with laryngeal and pharyngeal lesions underwent flexible and rigid laryngoscopy, with both WLI and NBI. Extension of malignant lesions ($n = 132$) was compared between both techniques in detail.

Results: Sensitivity of NBI during flexible endoscopy (92%), was comparable with that of WLI during rigid endoscopy (91%). The correlation of tumor extension between flexible and rigid laryngoscopy was high ($r_s = 0.852-0.893$). The observed tumor extension was significantly larger when using NBI in both settings. The use of NBI during flexible laryngoscopy leads to upstaging (12%) and downstaging (2%) of the T classification.

Conclusions: NBI during flexible laryngoscopy could be an alternative to WLI rigid endoscopy. NBI improves visualization of tumor extension and accuracy of T staging.

Key Words: Head and neck cancer, narrow band imaging, laryngoscopy, tumor extension, white light imaging.

Level of Evidence: 3

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INTRODUCTION

Endoscopy is essential in the diagnosis of mucosal lesions of the larynx and pharynx. To increase the diagnostic accuracy more advanced endoscopic techniques have been developed over the recent years, such as narrow band imaging (NBI). NBI uses a narrow bandwidth filter to filter blue (415 nm) and green light (540 nm) corresponding with the absorption peak of hemoglobin, which, therefore, highlights the vascular patterns of the superficial mucosa.¹⁻³ The specific vascular patterns are significantly related to malignancy.⁴ Several studies showed that NBI is a promising technique for detection of malignancies in the larynx and pharynx.^{1,5-8}

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Exact tumor extension determination is essential for adequate staging and treatment. Previous studies showed that intraoperative use of NBI makes it easier to determine tumor margins and identify surrounding dysplasia in early glottic tumors and oropharyngeal tumors.⁹⁻¹² A traditional work up consists usually of a computed tomography (CT) scan and a direct laryngoscopy under general anesthesia with biopsy taking. The last years the possibilities for office-based biopsies have increased. A procedure under general anesthesia is, therefore, not always necessary.¹³⁻¹⁵ Another reason to perform a direct laryngoscopy is the presumed superior image quality of rigid endoscopy. However, the introduction of High Definition (HD) image quality techniques has led to much better quality of the images obtained with flexible scopes.

The primary goal of this prospective study was two-fold: first, to determine the diagnostic value of WLI and NBI for detecting carcinoma in situ (CIS) and invasive carcinoma (CA), and second, to reveal differences in the assessment of mucosal extension of neoplastic lesions between flexible laryngoscopy in the outpatient setting versus rigid laryngoscopy under general anesthesia when using conventional white light imaging (WLI) and NBI and its influence on Tumor (T) classification.

MATERIALS AND METHODS

Between March 2015 and January 2018, 302 patients with a lesion in the pharynx or larynx were included. In all patients, both flexible laryngoscopy and rigid laryngoscopy were carried out. Data were collected prospectively after institutional review board approval (NL53152.042.15). In the outpatient clinic,

flexible laryngoscopy was performed by using an Olympus HD ENF-VH video laryngoscope attached to an HD monitor (Olympus Nederland BV, Zoeterwoude, The Netherlands), and during the inspection, both conventional WLI and NBI were used. In the operating room, a rigid laryngoscope (0° 5.4-mm wide-angle Storz telescope, and in selected cases a 90° Storz telescope) and camera system (Olympus OTV-S7ProH-HD-12E HD autoclavable camera head, Olympus EVIS EXERA CLV-180 light source, 300 W xenon with NBI filter; Olympus EVIS EXERA CV-180 processor, HD television; Olympus Nederland BV, Zoeterwoude, The Netherlands) were used while inspection was performed with both WLI and NBI by four experienced head and neck oncologic surgeons who received instructions to record both WLI and NBI images in a structured manner. Real-time videos of the procedures were saved in the electronic patient records. Lesions concerned both benign and malignant lesions: data of all lesions was used to calculate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy. Only the lesions with a definitive histopathological diagnosis of carcinoma (in situ) ($n = 132$) were included for further analyses in this study. Patient and lesion characteristics are presented in Table I. Two of the investigators (MZ and BP), both experienced with NBI, evaluated all videos in a structured setting: evaluation of WLI images of each patient had to be completed before the NBI evaluation took place. The tumor extension was documented by dividing the official TNM sites and subsites further into “detailed subsites.” The true vocal folds, for example, were divided into an anterior third part, middle third part, and posterior third part. An overview of all detailed subsites is attached in a Supporting Table 1. For all NBI evaluations, the additional value of NBI for tumor surface assessment was decided by consensus between the two investigators. The investigators were not blinded for the patient’s medical history and intoxications, to resemble the real clinical situation, but they were blinded for histopathology results. The histopathological diagnosis and the final T classification after rigid endoscopy in combination with additional CT or Magnetic Resonance Imaging (MRI) was used as the gold standard.

SPSS version 23 statistical software (IBM Corp., Armonk, NY) was used for performing statistical analysis. Correlation plots were modified by using the jitter function. Spearman rank correlation analyses and matched-pairs Wilcoxon non-parametric analyses were performed. Significance levels of $P < 0.05$ were considered statistical significant. A Bonferroni correction was applied for all P values, to correct for multiple testing.

RESULTS

The sensitivity, specificity, PPV, NPV, and accuracy of WLI and NBI for diagnosing CIS or CA in the total group of included patients ($n = 233$), are presented in Table II. During flexible laryngoscopy, 19 tumors were missed with WLI: eight of these tumors were correctly identified by using NBI. During rigid laryngoscopy, 11 tumors were missed with WLI: five of these tumors were detected with NBI of which one was a second primary tumor.

As shown in Table III, the average number of involved detailed subsites per lesion during flexible laryngoscopy was 4.38 with WLI evaluation and 4.84 when using NBI ($P < .001$). During rigid endoscopy, the observed tumor extension was also significantly larger with NBI ($P = .004$). Laryngeal tumors were significantly larger with NBI, both during flexible laryngoscopy and rigid laryngoscopy. Pharyngeal tumors were significantly

TABLE I.
Patient and Lesion Characteristics.

All Lesions	n	%
Total	233	100
Male	165	71
Female	68	29
Median age in years $\pm$ SD (range)	62 $\pm$ 14 (10–90)	
Lesion localization		
Glottis	139	59
Supraglottis	32	14
Hypopharynx	25	11
Oropharynx	34	14
Subglottis	1	1
Nasopharynx	2	1
Malignant Lesions	n	%
Total	132	100
Gender		
Male	107	81
Female	25	19
Median age in years $\pm$ SD (range)	66 $\pm$ 11 (27–90)	
Lesion localization		
Glottis	67	51
Supraglottis	22	17
Hypopharynx	22	17
Oropharynx	20	15
Subglottis	1	1
Nasopharynx	-	-
Tumor classification		
Tcis	15	11
T1	9	7
T1a	25	19
T1b	6	5
T2	22	17
T3	33	25
T4	22	17
Treatment		
CO ₂ laser resection	34	26
Radiotherapy	53	40
Chemoradiation	30	23
Total laryngectomy	5	4
No treatment	10	8

larger with NBI during flexible laryngoscopy ($P = .03$), but during rigid laryngoscopy, the difference between tumor extension with WLI and NBI was not significant. Figure 1 shows the correlation between tumor extension observed with WLI versus NBI. Evaluation of oropharyngeal tumors during rigid laryngoscopy showed a fair correlation¹⁶ ($r_s = 0.597$) between evaluation with WLI and NBI. Correlations between WLI and NBI for all other TNM subsites were very strong (r_s varying from 0.856 to 0.999). A subgroup analysis was performed for p16 positive and negative oropharyngeal tumors. In our study

TABLE II.
The Diagnostic Value of WLI and NBI During Flexible Laryngoscopy in the Outpatient Setting and Rigid Laryngoscopy Under General Anesthesia (n = 233).

	Flexible Laryngoscopy (Outpatient Setting)		Rigid Laryngoscopy (Operating Room)	
	WLI (%)	NBI (%)	WLI (%)	NBI (%)
Sensitivity	86	92	91	95
Specificity	87	85	86	82
PPV	90	89	90	87
NPV	82	89	88	92
Accuracy	86	89	89	89

NBI = narrow band imaging; NPV = negative predictive value; PPV = positive predictive value; WLI = white light imaging.

population, 10 tumors were p16 negative, seven were p16 positive, and of three tumors the HPV status was not assessed. In all p16 negative tumors, clear malignant vascular patterns were visible, although in two cases obscured by mucus, ulceration, and debris during flexible laryngoscopy. Of the p16 negative tumors, seven tumors were judged to be of equal size with WLI and NBI, and three were larger with NBI. Three out of seven p16 positive tumors showed clear malignant vessels and these tumors were judged to be of equal size with WLI and NBI. Three out of seven tumors were missed with WLI during flexible laryngoscopy but were detected with NBI and one tumor was missed during flexible laryngoscopy with both WLI and NBI (but was detected during rigid laryngoscopy and assessed as larger with NBI).

As shown in Figure 2, there is a significant correlation between the tumor extension observed during flexible and rigid laryngoscopy. This correlation was statistically significant ($P < .001$) and (moderately) strong¹⁶ (r_s varying from 0.769 to 0.935) for all TNM subsites separately, except for oropharyngeal tumors observed with NBI ($r_s = 0.586$, $P = .07$). Tumors were observed as smaller during flexible laryngoscopy than observed during rigid laryngoscopy ($P < .01$), for both WLI and NBI.

Figure 3 shows whether clinical T classifications with WLI and NBI were equal in different settings: flexible laryngoscopy, rigid laryngoscopy and after final staging. In 21/132 (16%) tumors, the T classification differed between WLI and NBI in the outpatient clinic: T upstaging using NBI was found in 18 cases, of which 17 confirmed during rigid laryngoscopy (three tumors were even further upstaged, and 16 were confirmed after final staging). The T stage was downstaged by NBI in three cases: In two cases the stage changed from T1b to T1a glottis laryngeal cancer, which was confirmed during rigid laryngoscopy (after biopsies it was known the tumor concerned CIS instead of invasive CA, and the tumor extension was correct with NBI) and in one case, the hypopharyngeal tumor was incorrectly downstaged with NBI because the caudal tumor extension was not visible due to an insufficient overview of the piriform sinus.

In 50/132 cases (38%) histology or imaging changed the diagnosis or T classification: upstaging based on CT or MRI (n = 36), lesion concerned CIS instead of CA (n = 6), lesion was visually suspect for benign leukoplakia, but CIS or CA was found (n = 3), lesion was visually suspect for papilloma, but CIS was found (n = 2), the lesion was visually suspect for CIS, but pathology showed

TABLE III.
Number of Affected Detailed Subsites* per Lesion.

	Outpatient Clinic: Flexible Laryngoscopy			General Anesthesia: Rigid Laryngoscopy		
	Detailed Subsites WLI Mean $\pm$ SD [Range]	Detailed Subsites NBI Mean $\pm$ SD [Range]	P Value	Detailed Subsites WLI Mean $\pm$ SD [Range]	Detailed Subsites NBI Mean $\pm$ SD [Range]	P Value
Total group (n = 132)	4.38 $\pm$ 3.58 [0–19]	4.84 $\pm$ 3.87 [0–20]	<.001	5.71 $\pm$ 4.29 [1–19]	5.90 $\pm$ 4.56 [0–16]	.004
Laryngeal (n = 89): Glottis and supraglottis	4.54 $\pm$ 3.49 [1–18]	4.96 $\pm$ 3.70 [1–20]	.003	5.60 $\pm$ 4.04 [1–17]	5.92 $\pm$ 4.39 [1–22]	.002
Glottis (n = 67)	3.82 $\pm$ 3.01 [1–16]	4.16 $\pm$ 3.19 [1–16]	.03	4.66 $\pm$ 3.64 [1–16]	4.90 $\pm$ 3.78 [1–16]	.004
Supraglottis (n = 22)	6.73 $\pm$ 3.98 [1–18]	7.36 $\pm$ 4.14 [1–20]	NS	8.45 $\pm$ 3.93 [1–17]	9.05 $\pm$ 4.72 [2–22]	NS
Pharyngeal (n = 42): Hypopharynx and oropharynx	4.07 $\pm$ 3.84 [0–19]	4.64 $\pm$ 4.28 [0–19]	.03	6.05 $\pm$ 4.83 [1–19]	5.95 $\pm$ 4.96 [0–19]	NS
Hypopharynx (n = 22)	3.95 $\pm$ 4.28 [0–19]	4.32 $\pm$ 4.40 [0–19]	NS	6.14 $\pm$ 4.94 [1–19]	6.27 $\pm$ 5.09 [1–19]	NS
Oropharynx (n = 20)	4.20 $\pm$ 3.40 [0–11]	5.00 $\pm$ 4.23 [0–17]	NS	5.95 $\pm$ 4.84 [1–16]	5.60 $\pm$ 4.91 [0–16]	NS
Subglottis (n = 1)	3	3	NS	2	2	NS

*Detailed subsites are TNM tumor subsites further divided into smaller areas which allowed more precise evaluation of the tumor extension.

NS = not significant.

Flexible laryngoscopy in the outpatient clinic

Rigid laryngoscopy under general anesthesia

Fig. 1. Correlation between tumor extension observed with White Light Imaging (WLI) versus Narrow Band Imaging (NBI): Flexible laryngoscopy versus rigid laryngoscopy. X-axes show the number of affected detailed subsites when using WLI and Y-axes show the number of affected detailed subsites when using NBI.

CA (n = 2), and the lesion was visually suspect for chronic laryngitis, but CA was found (n = 1).

In 42 of the 132 lesions (32%), the complete tumor was visible during flexible laryngoscopy, that is, all tumor margins were visible, including the most distal margin: these lesions concerned 27/67 (40%) glottic tumors (of which 7 CIS, 14 T1a, 3 T1b, 2 T2, and 1 T3 tumor), 4/22 (18%) supraglottic tumors, 3/22 (14%) hypopharyngeal tumors, and 8/20 (40%) oropharyngeal tumors. T WLI and T NBI were equal in 34/42 cases (81%). Thirty out of these 34 T classifications did not change during rigid laryngoscopy.

Figure 4 shows three examples of the additional value of NBI. Table IV shows the subjective evaluation of the observers, about whether or not the use of NBI was useful.

DISCUSSION

To the best of our knowledge, this is the first prospective study evaluating the exact tumor extension of malignant lesions in the larynx and pharynx and determining differences in tumor staging between WLI and NBI during both flexible laryngoscopy in the outpatient setting and rigid laryngoscopy under general anesthesia.

Diagnostic Value of NBI

Results of this study show that NBI is of additional value to WLI alone, for diagnosing CIS or CA. This is in line with previous studies.^{1,2, 6–8, 17–23} The sensitivity of NBI in the outpatient setting (92%) is comparable with the sensitivity of WLI during rigid endoscopy (91%), which supports our hypothesis that many of the rigid endoscopies under general anesthesia can be avoided by performing flexible endoscopy with NBI combined with biopsy taking.

Tumor Extension and Tumor Classification

Our study shows that NBI reveals malignancies, which are missed by WLI, both during flexible and rigid endoscopy. NBI led to accurate T upstaging in 12% and T downstaging in 2% of the patients during flexible laryngoscopy, which implies that tumor classifications and the choice of treatment are actually influenced by NBI. For instance, in this study, five tumors were upstaged from T1a to T1b or T2 tumors by using NBI during flexible laryngoscopy. This changed our choice of treatment. This study shows as well the difficulties to differentiate benign from malignant purely on images. Six tumors were not recognized correctly as malignant based on clinical evaluation (complaints and images), even after rigid endoscopy; the clinical diagnoses of these lesions were papilloma, benign leukoplakia, and chronic laryngitis, which are all well-known pitfalls in evaluation of lesions in the larynx and pharynx, both with WLI and NBI.^{1,24–27} These findings emphasize that a biopsy is the golden standard. The main limitation of this study was that the exact tumor extension had not been biopsy confirmed. Multiple studies, however, showed that NBI-guided resection of small

laryngeal carcinoma and oral cavity carcinoma, reduced the number of positive superficial margins and recurrence rate, confirming reliable assessment of tumor extension with NBI.^{9,23,28,29} To support these findings, we have conducted a study in which biopsies of NBI suspicious tumor margins were taken. We hope to report these results soon.

This study showed the value of CT and MRI. CT and MRI enable evaluation of the deep submucosal structures, cartilage invasion, and invasion in the pre-epiglottic and paraglottic spaces, which cannot be reliably assessed with endoscopy alone.^{30–33} In 36 cases (27%), the final T classification was changed by CT or MRI. In a study by Charlin et al. T upstaging based on CT, was found in 22.7% of the cases.³⁴ On the other hand, it is known that small tumors cannot be visualized properly and are missed by CT, MRI, or fluorodeoxyglucose-positron emission tomography scan.^{23,35,36} Charlin et al. showed that 10.6% of the laryngeal cancers were understaged when staging was based on CT scan alone, due to superficial mucosal tumor growth.³⁴ Multiple studies showed a low T staging accuracy of laryngeal and hypopharyngeal tumors, ranging from 52.9% to 58.8%, based on laryngoscopy alone and a significant improved staging accuracy (85%–88.2%) was found, when laryngoscopy was combined with radiology.^{37–39} Therefore, the use of cross-sectional imaging and clinical staging based on endoscopy is recommended.

Recommendations. Based on the performed correlation analyses and our findings of alteration of T classification, we recommend to perform flexible endoscopy alone (without rigid endoscopy), in combination with CT or MRI, in case all tumor margins are clearly visible during flexible endoscopy. This is true for all T stages and subsites. In this study, however, in only 32% of the cases all tumor margins were visible during flexible laryngoscopy. For glottic tumors, flexible endoscopy combined with NBI is advised for tumor staging, based on the significant ($P < .001$), high correlation ($r_s > 0.9$) we found when comparing flexible and rigid endoscopy with WLI, and even more pronounced when using NBI. It must be mentioned that patients with T1a glottic laryngeal carcinoma need to undergo rigid endoscopy under general anesthesia for treatment purposes and not only for diagnostic purposes. Although, a very high correlation was found between flexible and rigid endoscopy, glottic tumors were staged significantly larger after rigid endoscopy evaluation. This implies that apparently not all tumor margins were assessed accurately during flexible laryngoscopy. In this study, in 18/67 glottic tumors, the T classification found during flexible endoscopy was not equal to the T classification found during rigid endoscopy (or T NBI differed from T WLI). In 13 of these 18 cases, a CT was performed, and the final T stage was equal to the T classification based on the CT scan alone in 10 out of 13 cases. In two cases, the T classification could not be reliably assessed on the CT scan and in one case the radiological T stage was T1a, but pathology showed CIS instead of CA. Moreover, in seven glottic tumors the T classification of flexible and rigid endoscopy was equal, but the tumor was further upstaged based on the CT

Fig. 2. Correlation plots: determining tumor extension with flexible versus rigid laryngoscopy (WLI and NBI). X-axes show the number of affected detailed subsites when performing flexible laryngoscopy (FL) and Y-axes show the number of affected detailed subsites when performing rigid laryngoscopy (RL).

Fig. 3. Flow diagram showing if Tumor (T) classifications with NBI are equal to T classifications with WLI, during flexible laryngoscopy, rigid laryngoscopy, and after final staging.

scan. This emphasizes our statement that for glottic tumors flexible laryngoscopy in combination with a CT scan is a very reliable T classification method and rigid endoscopy under general anesthesia can be prevented, if the clinic has the possibility to perform office-based biopsies. For oropharyngeal tumors flexible endoscopy is found to be accurate as well, since the most caudal tumor margin often is visible and subtle malignant vessel patterns are clearly visible. The correlation between flexible and rigid endoscopy is high ($r_s = 0.935$). Especially when

combined with NBI, flexible laryngoscopy of oropharyngeal tumors is accurate: three p16 positive tumors, which were missed with WLI alone, were detected with NBI. Oropharyngeal tumors were often bleeding during rigid endoscopy, which complicated assessment under rigid endoscopy, especially with NBI. It is known that blood causes unreliable NBI assessments, due to absorption of the light by hemoglobin.^{2,24} Therefore, rigid endoscopy will not be the first choice to determine oropharyngeal tumor extension. We noticed that tumor extension of

Fig. 4. Three examples of the additional value of NBI in three different TNM subsites: glottic, hypopharyngeal, and oropharyngeal. (A1) WLI shows a T1a tumor of the left vocal fold. (A2) NBI shows involvement of the anterior part of the right vocal fold (upstaging to T1b tumor, confirmed by histopathology). (B1) Mild hyperemia of the right piriform sinus. (B2) Malignant vascular pattern in a clearly demarcated area, histopathology showed squamous cell carcinoma. (C1) No malignant lesion is visible. (C2) A malignant vascular pattern is visible at the left pharyngeal arch. Pathology showed carcinoma in situ. The arrows point toward the malignant blood vessel patterns.

oropharyngeal tumors was even smaller with NBI compared with WLI evaluation during rigid endoscopy. This difference can be explained by these bleeding tumors, which caused inaccessible (and therefore) less affected detailed subsites in NBI evaluation. In the evaluation of the tumor extension of the 18 “not-bleeding” oropharyngeal tumors, tumor extension was equal to or larger with NBI, compared to WLI evaluation. For large supraglottic tumors rigid endoscopy is recommended, since the caudal tumor extension often is incompletely visible due to bulky tumor covering the vocal folds beneath. For

hypopharyngeal tumors rigid endoscopy is recommended too, since the caudal tumor extension often is incompletely visible, due to inability to assess both the medial and lateral wall of the piriform sinus completely. It should be emphasized that visualization of the esophagus and the inlet by performing an esophagoscopy is important in patients with hypopharyngeal cancer, since head and neck second primary tumors often coexist, especially hypopharyngeal and esophageal tumors and NBI seems to be an accurate technique for detection of these second primary tumors.^{21,40} Office based gas insufflation may

TABLE IV.
Additional Value of NBI During Flexible Laryngoscopy in the Outpatient Clinic versus Rigid Endoscopy Under General Anesthesia.

Flexible Laryngoscopy in the Outpatient Clinic		Rigid Endoscopy Under General Anesthesia	
NBI useful n=90 (68%)	Reasons (n.): <ul style="list-style-type: none"> • Determining exact tumor extension, clear malignant vessels (13%) • Larger tumor extension (36%) • With NBI more suspect for malignancy (6%) • Clear malignant vessels in between or around leukoplakia/granulation tissue (6%) • Smaller tumor extension (4%) • Extra lesion detected (3%) 	NBI useful n=86 (65%)	Reasons (n.): <ul style="list-style-type: none"> • Larger tumor extension (34%) • Determining exact tumor extension, clear malignant vessels (19%) • Clear malignant vessels in between or around leukoplakia/granulation tissue (4%) • With NBI more suspect for malignancy (3%) • Smaller tumor extension (3%) • Extra lesion detected (3%) • Same tumor extension, confirmation of what was seen with WLI (1%)
NBI not useful n = 42 (32%)	Reasons (n.): <ul style="list-style-type: none"> • Same tumor extension. NBI offers no further insights (18%) • Insufficient zooming (5%) • Thick leukoplakia/ granulation tissue (3%) • Tumor extension seems larger although this was not confirmed under general anesthesia (2%) • The mucosa was covered with thick mucus (2%) • No malignant vessels visible (2%) • Large diffuse area with malignant vessels. Differentiation between chronic laryngitis and malignancy is impossible (1%) • Submucosal lesion (1%) 	NBI not useful 46 (35%)	Reasons (n.): <ul style="list-style-type: none"> • Same tumor extension. NBI offers no further insights (14%) • Bloody tumor (8%) • Tumor seems larger, though not histologically confirmed (7%) • Thick leukoplakia/ granulation tissue (2%) • No malignant vessels visible (3%) • No perpendicular approach (1%) • Under exposure due to technical problem (1%) • Large diffuse area with malignant vessels. Differentiation between chronic laryngitis and malignancy is impossible (1%)

The percentages in parentheses are rounded up to whole numbers.

play a role in evaluation of the depth of the piriform sinus and esophagus⁴¹; however, we cannot give recommendations on this issue as it is not performed in our clinic. Future studies can show whether or not flexible laryngoscopy in combination with CT or MRI is as reliable for tumor staging as rigid endoscopy in combination with CT or MRI, for supraglottic and hypopharyngeal tumors. It can be speculated that flexible endoscopy in combination with CT or MRI for these tumors, will at least approach or might even equal tumor staging with rigid endoscopy with CT or MRI, since often the T classification is determined by paraglottic space, pre-epiglottic space or thyroid cartilage invasion. However, a previous study showed that it is difficult to determine the exact tumor extension in the piriform sinus on the lateral and medial walls by CT scan alone.³²

It is known that NBI endoscopy has a learning curve: training improves the quality of NBI endoscopy, including the interpretation of the images.²⁴ Ishihara et al. described a six-month learning period for evaluation of NBI images.⁴² Endoscopists performing the NBI endoscopies in this study were experienced clinicians; however, the results of this study can be translated to less experience clinicians, since we previously found that the intra-observer agreement for less experienced observers improved remarkably when WLI was combined with NBI

and less-experienced observers were able to recognize malignant vessel patterns even better.⁴³

CONCLUSION

The sensitivity for diagnosing CIS or invasive CA with NBI during flexible laryngoscopy is high (92%) and is comparable with the sensitivity of WLI during rigid endoscopy. The observed tumor extension is significantly larger when using NBI, both during flexible and rigid laryngoscopy. The use of NBI during flexible laryngoscopy, leads to accurate T upstaging (12%) and T downstaging (2%). To achieve a reliable T classification during flexible laryngoscopy, it is important that all tumor margins are visible. For the diagnostic process, for glottic and oropharyngeal tumors flexible endoscopy in combination with CT or MRI is advised (without rigid laryngoscopy). For hypopharyngeal and large supraglottic tumors it is advised to perform rigid endoscopy under general anesthesia.

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