Role of dynamic multidetector computed tomography using 'eee' phonation in the diagnosis of various laryngeal lesions

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Objective
The aim of the study was to determine the effectiveness of dynamic multidetector computed tomography (MDCT) using 'eee' phonation in the detection and delineation of extension of various laryngeal lesions in comparison with conventional nonfunctional MDCT.

Patients and methods
The study included 60 patients with suspected laryngeal pathology who underwent precontrast and both prephonation and during-phonation contrast-enhanced MDCT. Each imaging study was evaluated for pyriform sinus and ventricle involvement, vocal cord mobility, and local tumor staging of malignant laryngeal lesions. All patients subsequently underwent direct laryngoscopy. Detailed endoscopic findings were reported and compared with MDCT findings.

Results
Dynamic MDCT using 'eee' phonation is effective in the assessment of pyriform sinus and ventricle involvement with high sensitivity (100% for both), high specificity (97.83 and 97.44%, respectively), and high accuracy (98.3% for both), compared with lower accuracy of conventional nonfunctional MDCT, which is 78.3% and 93.3%, respectively. It is also highly accurate in the assessment of vocal cord mobility (94.6%) and it increases the accuracy of MDCT in local tumor staging of malignant laryngeal lesions to 80.4% compared with 76.1% accuracy of conventional nonfunctional MDCT.

Conclusion
Dynamic MDCT using 'eee' phonation is effective in the detection and delineation of extension of various laryngeal lesions and is more accurate than conventional nonfunctional MDCT.

Keywords:
dynamic maneuver, larynx, multidetector computed tomography, phonation

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Introduction

Laryngeal lesions require precise assessment and good evaluation to determine the best treatment for each lesion [1]. The principal diagnostic tools for the evaluation of laryngeal diseases include otolaryngologic examination, laryngeal endoscopy, computed tomography (CT), MRI, and biopsy with histological examination [2].

Multidetector computed tomography (MDCT) is one of the most advanced techniques that are crucial for the assessment of laryngeal and extralaryngeal structures [3]. Its greatest advantages are speed and improved detector efficiency, which overcome the limitations of single-slice CT [4].

Phonation is one of several dynamic breathing maneuvers that have been used for supplemental CT imaging of the neck. Other dynamic maneuvers include 'the puffed-cheek' maneuver and a modified Valsalva technique. The modified Valsalva technique and phonation are more applicable to mucosal lesions within the pharynx and larynx. Both create air contrast for better tumor detection [5].

The advent of MDCT scanners has enabled the acquisition of images of the larynx during phonation as one-volume images without motion artifacts, as with a 64-detector MDCT scanner the entire neck can be imaged in less than 8 s [6]. The coronal reconstruction of the volume images makes it possible to see changes in the vocal cords during phonation [7]. Moreover, it is useful in determining the type and amount of materials needed for injection laryngoplasty, which is used to manage vocal cord paralysis [8].

The aim of the study was to determine the effectiveness of dynamic neck MDCT using 'eee' phonation in

the detection and delineation of extension of various laryngeal lesions in comparison with conventional nonfunctional MDCT.

Patients and methods

Study population

This is a prospective study carried out during the period from August 2011 to April 2015. It included 60 patients (48 male and 12 female patients with ages ranging from 8 to 79 years and mean of 56.09 years) who were suspected to have laryngeal lesions on the basis of clinical examination and data from indirect (fiberoptic) laryngoscopy. Patients were referred from the ENT clinic and Phoniatric unit to the Radiology Department of Assiut University Hospital for MDCT examination of the larynx. The study was carried out after obtaining the permission of the Ethics Committee of Scientific Research, Faculty of Medicine, Assiut University, with informed consent of the patients.

Each patient was subjected to the following

(1) Detailed history as regards the onset, course, and duration of symptoms, associated symptoms, previous operations, and other medical problems.
(2) Clinical examination of patients by fiberoptic endoscopy either in the ENT clinic or Phoniatric Unit.
(3) Precontrast and both prephonation and during-phonation contrast-enhanced MDCT examination of the larynx.
(4) Direct laryngoscopy under general anesthesia with a detailed endoscopic evaluation report and pathological study for comparison.

Inclusion criteria

All patients with a provisional diagnosis of laryngeal lesions by fiberoptic endoscopy examination with no age or sex predilection.

Exclusion criteria

All patients with a fixed tracheostomy tube, poor diagnostic quality images, pregnant women (especially in early pregnancy), and those with contraindication to contrast media, such as hypersensitivity and impaired renal function.

Patient preparation

No specific preparation is needed, but any metallic objects in the head and neck region must be removed before examination to avoid artifacts, and the patient must be given sufficient practice on how to perform the dynamic 'eee' phonation maneuver.

The standard MDCT protocol performed for all patients was as follows

CT examination was performed using a 64-channel Multidetector CT scanner (Toshiba, Japan) Aquilion machine. All patients underwent both standard acquisition of neck and dynamic maneuver using 'eee' phonation.

First, we performed noncontrast standard acquisition of the neck. Then a postcontrast examination was carried out by giving an amount of 2 ml/kg of nonionic contrast agent (Ominpaque 370 mg iodine concentration) using an automatic injector at a rate of 3 ml/s, with a 50-s delay (arterial phase) and another scan was taken. In both scans, patients were instructed to breathe quietly and not to swallow. A lateral scanogram and axial planes were acquired perpendicular to the long axis of the neck (parallel to the hyoid bone). Scanning was performed in a craniocaudal direction from the skull base (1 cm above sella) to the thoracic inlet (aortic arch) under the following parameters: 120–140 kVp, tube current 150–280 mA, and a 512 × 512 pixel matrix. The FOV was 16–18 cm. The data were reconstructed into 0.625-mm-slice images resulting in a total of 120–180 axial slices.

Seventy seconds after the start of the contrast injection, another functional dynamic study was conducted by instructing patients to perform 'eee' phonation. This was done from the base of the tongue to the upper third of the trachea including the complete laryngeal and hypopharyngeal areas.

Postprocessing

The acquired images were transferred to a Vitrea Vital Image (VPMC – Revision C) with manufacturer software that allows generation of two-dimensional multiplanar reconstruction in the sagittal and coronal planes. Axial CT images as well as coronal and sagittal reformatted multiplanar images were reviewed with both soft tissue and bone windows.

Data analysis and image interpretation

Image analysis and interpretation was done on combined axial, coronal, and sagittal views. Thereafter, these data were compared with conventional laryngoscopic data.

The following data were recorded at each examination

(1) Prephonation and during-phonation assessment of pyriform sinus and ventricle involvement.
(2) During-phonation assessment of vocal cord mobility.
(3) Prephonation and during-phonation local tumor staging of malignant laryngeal lesions: local

staging was based on the criteria for Head and Neck cancer staging according to the TNM scale of the American Joint Committee on Cancer (AJCC) (2010).

Statistical analysis

Data were checked, coded, entered, and analyzed using statistical program for social science, version 19 (SPSS Inc., Chicago, Illinois, USA) as follows: description of quantitative variables as mean, SD and range; description of qualitative variables as number and percentage; Sensitivity,specificity ,accuracy,predictive values of positivity and negativity of Dynamic Phonation MDCT study were recorded.

Results

Sixty patients (48 male and 12 female patients with ages ranging from 8 to 79 years and mean of 56.09 years) were included in our study.

Among the 60 patients enrolled in the study, eight had benign (13.33%) and 52 had malignant (86.67%) lesions. Among the patients with benign lesions four were male and four were female, with ages ranging from 8 to 70 years (mean age 44.17 years), whereas among those with malignant lesions 47 were male and five were female, with ages ranging from 40 to 79 years (mean age 60.2 years).

Among the eight benign lesions, three were cases of vocal cord paralysis (37.5%) (Fig. 1), two cases were hemangiomas (25%), one was a laryngeal cyst (12.5%), one was a vocal cord polyp (12.5%), and the last case was diffuse inflammatory laryngeal edema (12.5%) (Table 1). Among the 52 malignant lesions 49 cases were squamous cell carcinoma (94.3%), two were non-Hodgkin's lymphoma (3.8%), and one case was multiple myeloma (1.9%) (Table 2).

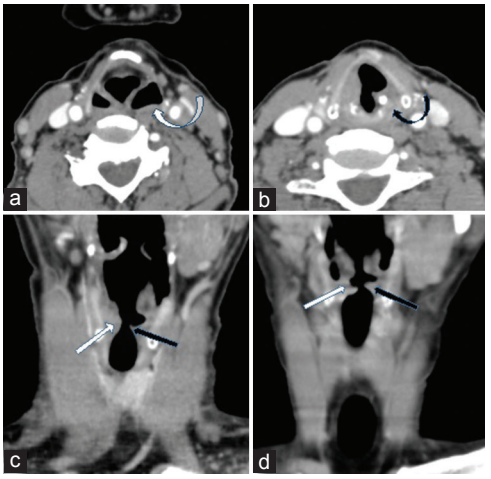
Assessment of involvement of pyriform sinus by prephonation and during-phonation MDCT in comparison with direct laryngoscopy

Of the 14 cases that showed pyriform involvement by direct laryngoscopy, nine cases could not be assessed by prephonation MDCT but the other five cases correctly showed involvement, whereas by phonation all 14 cases correctly showed involvement. Of the 46 cases that showed no pyriform sinus involvement by direct laryngoscopy, four cases could not be assessed by prephonation study but the other 42 cases correctly showed no involvement, whereas by phonation study 45 cases correctly showed no involvement and one case incorrectly showed involvement. This means that phonation MDCT study is more accurate than prephonation study in the assessment of pyriform involvement as the accuracy of prephonation study is 78.3%, whereas the accuracy of phonation study is 98.3%, sensitivity is 100%, specificity is 97.83%, positive predictive value is 93.3%, and negative predictive value is 100% (Tables 3 and 4, Fig. 2).

Assessment of involvement of ventricle by prephonation and during-phonation MDCT in comparison with direct laryngoscopy

Of the 21 cases that showed ventricle involvement by

Figure 1



A female patient, aged 50 years, presented with hoarsness of voice. (a, b) Postcontrast axial MDCT images showing left vocal cord paralysis in terms of dilatation of the left pyriform sinus with medial deviation of the aryepiglottic fold (curved white arrow) and prominent left true vocal cord and anteromedial deviation of the left aryetenoid cartilage (curved black arrow, with no focal enhanced mass.). (d) Coronal image during phonation showing free mobile right vocal cord as it shows complete adduction towards midline (white arrows), with fixed left vocal cord (black arrows) compared with prephonation coronal image (c). Diagnosis: idiopathic left vocal cord paralysis. MDCT, multidetector computed tomography.

Table 1 Pathology of benign lesions

Benign lesions	*N*=8 (*n* (%))
Vocal cord paralysis	3 (37.5)
Hemangioma	2 (25)
Laryngeal cyst	1 (12.5)
Vocal cord polyp	1 (12.5)
Diffuse inflammatory laryngeal edema	1 (12.5)

Table 2 Pathology of Malignant lesions

Malignant lesions	No. (*n*=52)	%
Squamous cell carcinoma	49	94.23
New cases	41	
Post-cricoid carcinoma with laryngeal extension	3	
Follow-up (with recurrent mass)	3	
Follow-up (no recurrent mass)	2	
Non Hodgkin lymphoma (B-cell)	2	3.8
Multiple myeloma	1	1.9

Table 3 Pyriform sinus involvement by prephonation and during-phonation MDCT in comparison with direct laryngoscopy

Endoscopy (*n*=60)	MDCT prephonation			MDCT during-phonation		Total	%
	Involved	Not involved	Cannot be assessed	Involved	Not involved		
Involved	5	0	9	14	0	14	23.33
Not involved	0	42	4	1	45	46	76.66

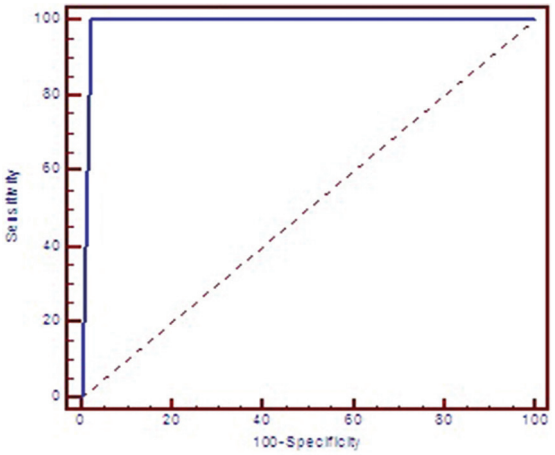
MDCT, multidetector computed tomography.

Table 4 Pyriform sinus assessment by phonation MDCT study compared with direct laryngoscopy

Sensitivity	Specificity	PPV	NPV	Accuracy	AUC
100.00	97.83	93.3	100.0	98.3	0.989

AUC, area under the curve; MDCT, multidetector computed tomography; NPV, negative predictive value; PPV, positive predictive value.

Figure 2



Receiver-operating characteristic (ROC) curve showing sensitivity, specificity and area under the curve for Phonation MDCT study in assessment of pyriform sinus involvement.

direct laryngoscopy, one case could not be assessed by prephonation MDCT but the other 20 cases correctly showed involvement, whereas by phonation study all 21 cases correctly showed involvement. Of the 39 cases that showed no ventricle involvement by direct laryngoscopy, 36 cases correctly showed no involvement and three cases incorrectly showed involvement by prephonation study, whereas by phonation study 38 cases correctly showed no involvement and only one case showed involvement incorrectly. This means that phonation MDCT is more accurate than prephonation study in the assessment of ventricle involvement as the accuracy of prephonation study is 93.3%, whereas the accuracy of phonation study is 98.3%, sensitivity is 100%, specificity is 97.44%, positive predictive value is 95.5%, and negative predictive value is 100% (Tables 5 and 6, Fig. 3).

Assessment of involvement of vocal cord mobility by phonation MDCT study in comparison with direct laryngoscopy

After exclusion of four cases as they could not be assessed by endoscopy, phonation MDCT could correctly detect vocal cord mobility in 53 cases out of 56, compared with endoscopy. Therefore, the accuracy of phonation MDCT in the assessment of vocal cord mobility is 94.6% (Table 7).

Local tumor staging of the 46 cases with laryngeal squamous cell carcinoma (according to AJCC) by prephonation and during-phonation MDCT and endoscopy compared with combined local tumor staging by both MDCT and direct laryngoscopy

The combined preoperative local tumor staging by both MDCT and direct laryngoscopy showed that two cases are T_0 (4.3%), nine cases are T_1 (19.6%), nine cases are T_2 (19.6%), 18 cases are T_3 (39.1%), and eight cases are T_4 (17.4%) (Table 8).

Regarding local tumor staging by endoscopy alone

Of the 18 cases diagnosed as T_3, nine cases were correct, where eight were diagnosed as T_2 and one case was diagnosed as T_1. From the eight cases diagnosed as T_4, one case was diagnosed correctly as T_4, four were diagnosed as T_3, and three cases were diagnosed as T_2. However, all two cases diagnosed as T_0, the nine cases diagnosed as T_1, and the nine cases diagnosed as T_2were correctly diagnosed (Table 8). Thus, the accuracy of endoscopy alone in local tumor staging was 65.2%.

Local tumor staging by prephonation MDCT

Of the 18 cases diagnosed as T_3, 13 cases were correct, whereas five cases were diagnosed as T_2. Of the eight cases diagnosed as T_2, four cases were diagnosed correctly, whereas four cases were diagnosed as T_1. Of the nine cases diagnosed as T_1, eight cases were diagnosed correctly as T_1, whereas one case was diagnosed as T_0. All two cases diagnosed as T_0 and the eight cases diagnosed as T_4 were correct (Table 8). Thus, the accuracy of prephonation MDCT in local tumor staging was 76.1%.

Local tumor staging by phonation MDCT

Of the nine cases diagnosed as T_1, eight cases were correct, whereas one case was diagnosed as T_0. From the 18 cases diagnosed as T_3, 16 cases were correct, whereas two cases were diagnosed as T_2. All nine cases diagnosed as T_2 and the two cases diagnosed as T_0 were correct (Table 8). Thus, the accuracy of phonation MDCT in local tumor staging was 93.5% (Figs. 4 and 5).

Table 5 Ventricle involvement by prephonation and during-phonation MDCT in comparison with direct laryngoscopy

Endoscopy (*n*=60)	MDCT prephonation			MDCT during-phonation		Total	%
	Involved	Not involved	Cannot be assessed	Involved	Not involved		
Involved	20	0	1	21	0	21	35
Not involved	3	36	0	1	38	39	65

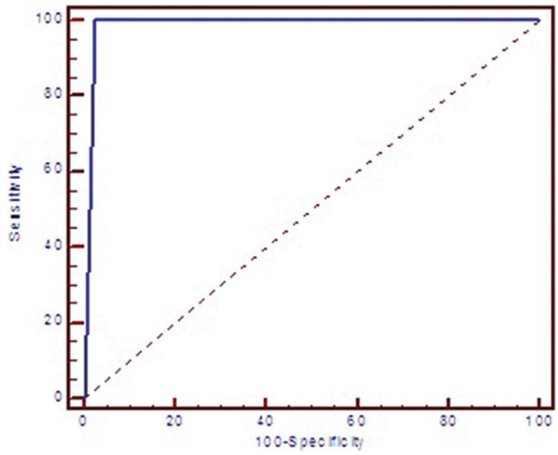
MDCT, multidetector computed tomography.

Table 6 Ventricle assessment by phonation MDCT study compared with direct laryngoscopy

Sensitivity	Specificity	PPV	NPV	Accuracy	AUC
100.00	97.44	95.5	100.0	98.3	0.987

AUC, area under the curve; MDCT, multidetector computed tomography; NPV, negative predictive value; PPV, positive predictive value.

Figure 3



Receiver-operating characteristic (ROC) curve showing sensitivity, specificity and area under the curve (AUC) for Phonation MDCT study in assessment of ventricle involvement.

Discussion

Neck MDCT with dynamic maneuvers is of considerable importance as it can improve the visualization of particular anatomic structures. During prolonged phonation of [eee], the distention of the pyriform sinuses allows better delineation and detection of early invasion of pyriform sinuses. Moreover, a better visualization of the laryngeal ventricle can be achieved [9]. The advent of MDCT scanners has enabled the acquisition of images of the larynx during phonation as a one-volume image that makes it possible for direct evaluation of vocal cord mobility and paralysis [7].

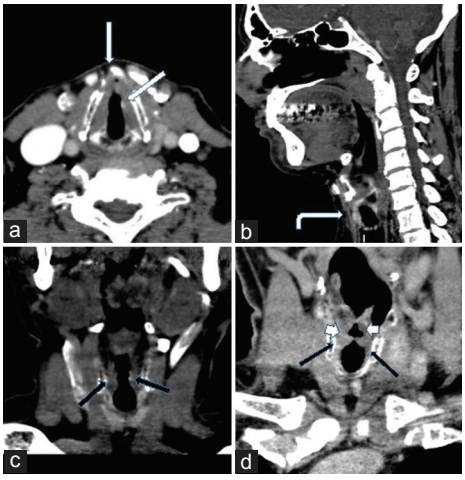
The success rate of these dynamic maneuvers is variable, especially when an incremental CT technique is used, and is strongly dependent on patient cooperation. These problems are largely overcome by MDCT, as the patient has to perform the maneuver only once during one rapid acquisition [9], and it can be performed without increased patient motion. This is because of the speed of a 64-detector MDCT that allows an entire scan to be acquired in less than 8 s [6].

Our study illustrates that the dynamic MDCT using 'eee' phonation is more accurate than conventional nonfunctional MDCT for assessment of pyriform sinus with high accuracy 98.3% compared with accuracy 78.3% with conventional MDCT. This agrees with the results of Stadler and colleagues [10,11]. It is also more useful in the delineation of the laryngeal ventricle with an accuracy of 98.3% compared with an accuracy of 93.3% with conventional MDCT. This closely agrees with the results of Latif *et al.* [12], who reported that accuracy of CT to evaluate the laryngeal ventricle is 100%. The slight difference between the two studies may be because Latif *et al.* [12] compared CT results with pathological postoperative data and not with endoscopic data as in our study. This information is very important as the laryngeal ventricle is considered the transition zone between supraglottic and glottic regions and hence its infiltration can affect preoperative staging and therapeutic strategy and it is not always obtainable with direct laryngoscopy. This agrees with the results of Lell *et al.* [9], who reported that functional MDCT is more accurate than nonfunctional MDCT in the evaluation of the laryngeal ventricle.

Vocal cord mobility is one of the most important TNM staging criteria by the AJCC classification; hence its assessment is very important to avoid understaging or overstaging [13]. CT is mainly used to identify only the cause of paralysis. This is because conventional axial CT could not capture dynamic changes in the vocal cords, although these changes are crucial to the diagnosis of vocal cord paralysis. However, the advent of MDCT has enabled the acquisition of images of the larynx during phonation as a one-volume image, and coronal reconstruction of the volume images makes it possible to see changes in the vocal cords during phonation [7].

Kim *et al.* [14] reported that dynamic MDCT with 'eee' phonation is accurate in the assessment of vocal cord mobility with an accuracy of 95% and that coronal reconstructed images are more useful than conventional axial CT images in the assessment. This agrees with our study, which reported that the

Figure 4



A male patient, aged 66 years, presented with hoarseness of voice. (a) Postcontrast axial MDCT image showing mild focal thickening of the anterior third of the left vocal cord extended to the anterior commissure with enhancement of its medial surface (white arrows). (b) Sagittal image confirms anterior comissure extension (curved arrow). (c) Prephonation coronal image confirms the presence of focal thickening of left vocal cord and enhancement of its medial surface. (d) Coronal image during phonation showing free mobility of both vocal cords as they are seen totally adducted at midline compared with the prephonation image (c) (black arrows), also it is showing distension of both ventricles, which are seen totally free (short white arrows), excluding the supraglottic extension. Diagnosis: malignant left glottic carcinoma *in situ* with submucosal microinvasion (stage T_1No). MDCT, multidetector computed tomography.

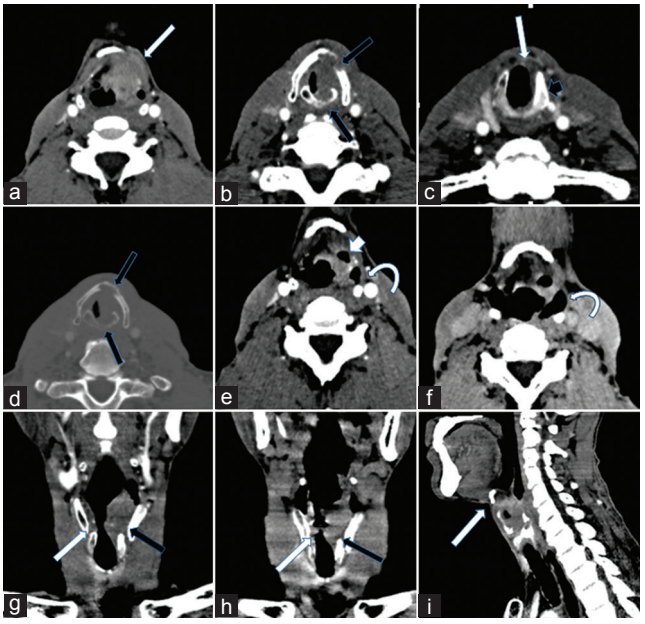
accuracy of MDCT using 'eee' phonation was 94.6%; we also reported that coronal reconstructed images are better than axial images in the diagnosis of vocal cord paralysis.

Our study also reported that the accuracy of MDCT in local TNM staging of laryngeal cancer is improved by adding dynamic maneuver using 'eee' phonation (accuracy of 93.5%) compared with nonfunctional conventional MDCT (accuracy of 76.1%).

Our observations disagree with the results of Gilbert *et al*. [13], who reported that the overall accuracy of MDCT in TNM staging for laryngeal cancer does not improve by adding the dynamic maneuver. This may be because their study compared CT staging results with pathological postoperative data, whereas in our study we compared MDCT staging results with combined endoscopic and MDCT staging data.

However, we agree with Gilbert *et al*. [13] that the accuracy of laryngeal cancer staging using endoscopy alone is 64%, which in our study is 65.2%. We also agree that combination of endoscopic and MDCT staging will improve the overall staging.

Figure 5



A male patient, aged 62 years, presented with hoarsness of voice and dysphagia. (a–d) Axial postcontrast MDCT images of the left transglottic mass showing the following: (a) supraglottic extension in terms of infiltration into the left side of the pre-epiglottic space, left paraglottic space, and left aryepiglottic fold (white arrow); (b) glottic extension in terms of infiltration into the left vocal cord, anterior and posterior comissures with erosion of the left lamina of the thyroid cartilage and left arytenoid cartilage (black arrows), confirmed in bone window image (d); (c) mild left subglottic extension (white arrow) with sclerosis of the left side of the cricoid cartilage (short black arrow). (e) Prephonation axial image showing infiltration into the left aryepiglottic fold and suspicious infiltration into the left pyriform sinus (curved white arrow) with secondary laryngocele (short white arrow). (f) Axial image during phonation showing distension of the left pyriform sinus and excluding its infiltration (curved white arrow). (h) Coronal image during phonation showing free mobile right vocal cord as it shows complete adduction towards midline (white arrows), with fixed left vocal cord (black arrows) compared with prephonation coronal image (g). (i) Sagittal image confirming extension to the pre-epiglottic fat but excluding infiltration into the epiglottis and valleculae (white arrow). Diagnosis: malignant left transglottic well-differentiated squamous cell carcinoma (stage T_4N_0). MDCT, multidetector computed tomography.

One of the limitations of the MDCT protocol with dynamic maneuver in our study is that it is dependent on patient compliance, and so when the vocal cords showed no adduction in the images acquired during phonation it was unclear whether the cords fixed or whether the patient did not follow instructions. Also the dynamic protocol cannot be followed in patients with a fixed tracheostomy tube and in some children; in these cases the assessment of vocal cord mobility can be done more efficiently and reliably with a clinical mirror or endoscopy than with CT.

Conclusion

Dynamic neck MDCT using 'eee' phonation is effective and more accurate than conventional nonfunctional

Table 7 Assessment of vocal cord mobility by phonation MDCT study in comparison with conventional endoscopy

Endoscopy (*n*=56)	MDCT during-phonation				Total	%
	Fixed both vocal cords	Fixed left vocal cord	Fixed right vocal cord	Mobile both vocal cords		
Fixed both vocal cords	**3**	0	0	1	4	7.1
Fixed left vocal cord	0	**12**	0	0	12	21.4
Fixed right vocal cord	0	0	**10**	0	10	17.9
Mobile both vocal cords	0	1	1	**28**	30	53.6

MDCT, multidetector computed tomography.

Table 8 Local tumor staging of the 46 cases with laryngeal squamous cell carcinoma (according to AJCC) by prephonation and during-phonation MDCT and endoscopy compared with combined local tumor staging by both MDCT and direct laryngoscopy

Tumor staging by both MDCT and endoscopy (*n*=46)	Total	%	Tumor staging by endoscopy					Tumor staging by prephonation MDCT					Tumor staging by phonation MDCT study					
			T_0	T_1	T_2	T_3	T_4	T_0	T_1	T_2	T_3	T_4	T_0	T_1	T_2	T_3	T_4	Not done
T_0	2	4.3	**2**	0	0	0	0	**2**	0	0	0	0	**1**	0	0	0	0	1
T_1	9	19.6	0	**9**	0	0	0	1	**8**	0	0	0	1	**8**	0	0	0	0
T_2	9	19.6	0	0	**9**	0	0	0	4	**4**	1	0	0	0	**9**	0	0	0
T_3	18	39.1	0	1	8	**9**	0	0	0	5	**13**	0	0	0	0	**16**	0	2
T_4	8	17.4	0	0	3	4	**1**	0	0	0	0	**8**	0	0	0	0	**3**	5

MDCT, multidetector computed tomography.

MDCT in the detection and delineation of extension of various laryngeal lesions. It is also highly accurate in the evaluation of vocal cord mobility.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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