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A new CT dynamic maneuver "Mouth Opened with Tongue Extended" can improve the clinical TNM staging of oral cavity and oropharynx squamous cell carcinomas

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ABSTRACT

Objectives: Cross sectional imaging is mandatory for oral cavity and oropharynx head and neck squamous cell carcinoma's (ooSCC) local extension and TNM staging. However a complex anatomy and frequent dental metallic artifacts make it difficult. This study assesses the clinical benefit of "Mouth Open with Tongue Extended" dynamic maneuver at CT (CTmote) as compared to the conventional CT (CTconv) and MRI.

Material: Retrospectively, 58 patients with histologically proven ooSCC (oral cavity: 34; oropharynx: 24) were included in the study. All had endoscopy with biopsies, MRI, CTconv and an CTmote acquisitions. Data were splitted in 3 datasets and 2 independent radiologists performed readings blindly. Gold standard was pTNM in 31% of cases; otherwise cTNM obtained at multidisciplinary team meeting with endoscopy and mapping biopsies were used.

Results: CTmote was feasible for all patients including those already treated by surgery or radiotherapy. Exact TNM staging was obtained in 68%, 83%, 83% for CTconv, CTmote and MRI respectively. The best exam ratings at paired wise comparisons were 3%, 47%, 50% for CTconv, CTmote and MRI respectively. CTmote and MRI observer agreements, image quality and confidence ratings, were comparable and higher compared to CTconv ($p < 0.001$).

Conclusions: CTmote improves oral cavity and oropharynx tumour stage assessment compared to CTconv with performances close to those of MRI examination. In clinical practice, combining both CT with MOTE maneuver and MRI seems to be the optimal imaging strategy for local staging.

Abbreviations: AIDR, Adaptative Iterative Dose Reconstruction (Toshiba); CNR, Contrast to Noise Ratio; CT, Computed tomography; DLP, Dose Length Product; FOV, Field Of View; Gy, Gray; HNSCC, Head and Neck Squamous Cell Carcinoma; ooSCC, Oropharyngeal an Oral cavity Squamous Cell Carcinoma; HPV, Human Papilloma Virus; IRSN, Institute de Radioprotection et de Sureté Nucléaire; CTmote, CT acquisition with Mouth Opened with Tongue Extended; CTconv, CT acquisition without dynamic maneuver; MRI, Magnetic Resonance Imaging; PACS, Picture Archiving and Communication System; RECIST, Response Evaluation Criteria In Solid Tumors; ROI, Region Of Interest; SPSS, Statistical Package for the Social Sciences (IBM); TNM, Tumor Node Metastasis (classification), cTNM (clinical), pTNM (pathological); TE, Time of Echo (milliseconds); TR, Time of Repetition (milliseconds); TSE, Turbo Spin Echo; UH, Hounsfield Unit; VIBE, Volumetric Interpolated Breath-hold Examination (Siemens)

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Introduction

Head and neck cancers are the sixth commonest cancer worldwide. Among them, 90%are squamous cell carcinomas (HNSCC) [1]. Oral cavity is the HNSCC localisation in 20–25%, and oropharynx in 8–34% [2]. While tobacco and alcohol are still considered as the main risk factors, an increased incidence has been reported for Human Papilloma Virus related cancers [3].

Therapeutic options for oral cavity and oropharynx head and neck squamous cell carcinoma's (ooSCC) include surgery, radiotherapy, chemotherapy or a combination of these treatments. The treatment plan for a given patient is related to a number of factors including age and health status and TNM staging. This staging is commonly performed based on clinical examination, endoscopy and cross sectional imaging. In addition, assessment and staging of deep submucosal extension is achieved using palpation under endoscopy combined to computed tomography (CT) and/or magnetic resonance imaging (MRI). The diagnosis is challenged by the head and neck anatomical complexity and the presence of imaging artifacts. The TNM classification of these cancers takes into account the size of the lesion together with the potential invasion of several deep anatomic structures such as cortical bone or extrinsic tongue muscles (genioglossus or palatoglossus) [4]. MRI plays a key role for such a classification [5,6].

Although dynamic maneuvers in the course of CT assessments have been described in the late 1980's [7], the corresponding clinical benefits have been very scarcely reported. Several maneuvers have been described so far including the *"eee" phonation* for glottis carcinomas [8], the modified *Valsalva* for hypopharyngeal carcinomas [9,10], the *puffed cheeks* for the lips and internal cheek surfaces [9,11–14] and the *open mouth* for the oral cavity and the oropharynx [9,13]. The corresponding rationale was to stretch both the mucosa and the deep spaces at the vicinity in order to improve tumor delineation and in some cases, avoid metallic dental artifacts. To the best of our knowledge, the added value of these maneuvers for the TNM staging of cancer lesions has not been evaluated so far.

The aim of this study was to assess the "Mouth Open with Tongue Extended" (MOTE) dynamic maneuver for tumor staging of ooSCC using conventional CT and MRI. Image quality, inter- and intra-observer reproducibility were also assessed.

Material and methods

Patients

This retrospective clinical study was approved by the institutional ethics committee (CIL APHM n°2017-32) in accordance with the guidelines of Helsinki III declaration. From september 2015 to december 2016, 64 patients with histologically proven oral or oropharyngeal carcinomas were retrospectively included. Patient consents were waived and clinical examination was performed by an expert surgeon. Each patient had endoscopic biopsies, cervical MRI and head and neck conventional CT (CTconv). An additional head and neck CT was acquired with the MOTE maneuver (CTmote). Patients were excluded because of cheek lesions (3), non-HNSCC carcinoma (2) and allergic risk (1). A total of 58 consecutive patients were included.

Imaging technique

Prior to the CT examination, patient practiced the MOTE maneuver with a trained radiology nurse. They were asked to keep their mouth wide opened and their tongue extended for a 5 s period while breathing with their nose.

The whole set of CT imaging was performed using a multi-detector CT scanner (Aquilion Prime Toshiba Medical Systems, Otawara, Japan) and a cranio-caudal helical acquisition. Fixed parameters were used according to the industrial recommandations i.e. 80 × 0.5 mm detectors, 40 mm collimation, 0.5 s rotation time, pitch of 0.813 mm/rotation, 120 kV tube voltage, auto-exposure for mAs intensity, FC08 soft filter, AIDR-3D enhanced reconstruction.

A single-phase bolus injection of 120 mL iodinated contrast media (Iobitridol Xenetix® 350 mg/mL, Guerbet, France) was performed at a flow rate of 1.5 mL/s. The CTconv acquisition was performed from the orbital apex to the base of the neck and started 52 s after the injection (total duration: 10 s, Field Of View: 18 cm). Then, the CTmote acquisition was performed from the orbital floor to the cricoid cartilage and started 75 s after the injection (duration: 3.2 s, Field Of View: 15 cm).

Multiplanar reconstructions were performed using the dedicated CT workstation. Axial slices parallel to the hard palate (1 mm thickness) were generated with a 0.8 mm increment.

MRI were performed at 1.5 Tesla (Amira Siemens, Erlangen, Germany) with a 16-channel phased array head and neck coil. The following sequences were used. Axial and coronal T2W (TSE) without fat saturation (TE = 107 ms, TR = 5570 ms, slice thickness = 4 mm, Gap = 0, FOV = 20 cm), Axial T1W (SE) without fat saturation (TE = 8.4 ms, TR = 560 ms, slice thickness = 3 mm, gap factor = 0, FOV = 20 cm) and post contrast 3D gradient recall T1 with fat saturation (Vibe, 3D Ultra Fast Gradient Echo, TE = 3.98 ms, TR = 9.75 ms, slice thickness = 0.6 mm, gap factor = 0, FOV = 20 cm, bandwidth = 157 Hz/Px, matrix = 333 × 448). A 0.2 mL/kg gadolinium injection (Dotarem® gadotrial acid, Guerbet France) was performed for that sequence.

Data analysis

Demographic data, treatments, tumor location, tumor size (RECIST 1.1 criteria) and radiation dose for each acquisition (DLPhead) were collected for each patient.

Images were splitted in 3 independent data sets (CTconv, CTmote and MRI) and were blindly assessed twice by each of the 2 radiologists (GB and AV with 4 and 15-year experience respectively). The purpose was to stage the tumor (T) according to the AJCC 7th Edition TNM system [4] but the N and M status were beyond the scope of the present study. Based on clinical data, CTconv, CTmote, MRI and 18FDG-TEP/CT, the pathological Tumor-Node-Metastasis stage (pTNM) was assessed in operated patients while the clinical Tumor-Node-Metastasis stage (cTNM) was defined for patients who did not have a surgery.

Tumour invasion was assessed for each anatomical structure specified by the 2009 TNM classification [4] i.e. epiglottal lingual surface, larynx, cortical bone, mandible, hard palate, maxillary sinus, extrinsic tongue muscles, skin, masticatory space, pterygoid apophysis, medial pterygoid muscle, lateral pterygoid muscle, lateral nasopharynx, internal carotid artery, and skull base. Structural invasion was ranked using a 5-point Likert scale (1 = no invasion, 2 = unlikely invasion, 3 = unclear invasion, 4 = highly probable invasion and 5 = obvious invasion).

A confidence score was calculated as follows: 100% for strong confidence (Likert 1 or 5), 50% for intermediate confidence (Likert 2 or 4), 0% for weak confidence (Likert 3).

With respect to potential metal and motion artifacts, the quality of each examination was defined using a 3-point Likert scale (1 = poor interpretation value, 2 = intermediate interpretation value but valuable diagnostic contribution, 3 = optimal). Once the blind status was uncovered, the overall quality was assessed by pairwise comparison [15] according to the overall lesion's conspicuity (best, intermediate, low).

The "Mouth Opened with Tongue Extended" maneuver suitability was assessed on the basis of the inter-alveolar distance in sagittal sections and the protraction quality according to a 3-point Likert scale (1 poor: within the dental arches, 2 intermediate, 3 optimal: opening the epiglottic vallecula).

The contrast-to-noise ratio (CNR) was measured in 2 regions of interest (ROI) in order to assess the quality of the tumor enhancement.

CNR = (ROI mean tumor density − ROI mean muscle density / ROI muscle standard deviation).

The 10 mm^2 ellipsoidal ROI were positioned within the tumor and the left masseter muscle on 1 mm reconstructions thereby avoiding areas of excessive density variations [16].

Statistical analysis

Statistical analyses were performed using SPSS (IBM Chicago USA, version 20). The TNM staging agreement, and rater agreements was assessed using the intraclass correlation (ICC) and interpreted using the Koo and Li guideline [17] as follows: 0–0.5: poor agreement; 0.51–0.75: moderate agreement; 0.76–0.90: good agreement; 0.91–1: excellent agreement.

Pearson Chi2 tests and exact Fisher tests were performed in order to compare the TNM confidence score and the quality of the tests. Student's T-tests were used in order to assess the CNR difference. Reproducibility, intra and inter-observers variability of the TNM stage was assessed using the Cohen's Kappa index. A *p value* lower than 0.05 was considered as significant.

Results

Population

A total of 58 tumors were assessed in 58 patients (12 women, 21%). Mean age of patients was 63.6 ± 11.1. Among the tumors, 34 (59%) were in the oral cavity and 24 (41%) in the oropharynx while 15 were post-therapeutic recurrences (26%). The mean tumor size was 32.2 ± 14.8 mm. Tumor characteristics are summarized in Table 1. Eighteen patients had a surgery and their pTNM was staged. For all of them, the pTNM stage was identical to the corresponding cTNM. The mean time between radiological examinations was 5.2 ± 8.9 days. The CTmote induced a 33.7% over-irradiation (96.14 mGy cm ± 12.6) of the DPL.

Tumor stage agreement (T)

As detailed in Table 2, exact T stage was obtained for 68%, 83%, and 83% for CTconv, CTmote, and MRI respectively (mean of the readings). A significant agreement ($p < 0.001$) was obtained for the three readings and was moderate for CTconv (ICC = 0.66 ± 0.03) and good for both CTmote (ICC = 0.86 ± 0.06) and MRI (ICC = 0.84 ± 0.06). The same trend was observed comparing primary and recurrent tumor subsets (Table 2). Poorer agreement were observed in recurrent subsets (Table2).

Detail of anatomical structures

Confidence scores for delineation of anatomical structures were significantly ($p < 0.001$) larger for both CTmote (92% ± 8%) and MRI (91% ± 7%) as compared to CTconv (86% ± 11%) (Table 2).

"Mouth Opened with Tongue Extended" maneuver

Mouth opening was 47.1 ± 12 mm. The quality of the lingual protraction was of paramount importance for an optimal score in 40% (n = 23), intermediate in 41% (n = 24), and poor in 19% (n = 11). No significant difference was observed in mouth opening (p = 0.312) and lingual protraction (p = 0.736) between patients with primary tumors or post-therapeutic recurrences.

Image quality

MRI exams were classified as the optimal solution in 50% of the cases. The CTmote was rated as the best examination in 47% of cases (Fig. 1) and in 3% for the CTconv. Due to metallic artifacts, 13 (22%) CTconv examinations, 3 (5%) CTmote, and 4 (7%) MRI could not be analyzed. Regarding the motion artifacts, 3 MRI exams could not be analysed whereas CTmote and CTconv were all interpreted. The examination's quality was significantly better using the CTmote as compared to CTconv both regarding overall quality ($p < 0.001$, Fig. 2) and metallic artifacts ($p < 0.001$, Fig. 2). Motion artifacts were not different between the two modalities (p = 0.34).

Contrast to noise ratio (CNR)

The mean tumor enhancement, assessed by CNR was significantly larger (p = 0.004) with CTmote (3.14 ± 2.7) as compared to CTconv acquisitions (2.29 ± 3).

Reproducibility

Agreements evaluated for the TNM were significant ($p < 0.001$) for the 3 readings of the 3 exams. The intra-observer agreement was excellent for MRI (ICC = 0.92) and CTmote (ICC = 0.91), and moderate for the CTconv (ICC = 0.67). The inter-observer agreement was good for both MRI (ICC = 0.83) and CTmote (ICC = 0.81), moderate for CTconv (ICC = 0.66). The same trend was observed while comparing primary and recurrent tumor subsets, especially poor agreements were observed in intra-observer agreements in recurrences (ICC = 0.43).

Table 1
Patients and tumor characteristics.

	Overall	Primary	Recurrence
Cases	58 (100%)	43 (74%)	15 (26%)
Previous Surgery			3 (5%)
Previous Radiotherapy			5 (9%)
Previous Surgery + Radiotherapy			7 (12%)
Location			
Oral cavity	34 (59%)	24 (41%)	10 (17%)
Oropharynx	24 (41%)	19 (33%)	5 (9%)
Sub-location			
Oral cavity			
Vestibule	4 (7%)	2 (3%)	2 (3%)
Anterior floor	11 (19%)	9 (16%)	2 (3%)
Mobile tongue	13 (22%)	9 (16%)	4 (7%)
Junctional area	2 (3%)	2 (3%)	0 (0%)
Palate	1 (2%)	0 (0%)	1 (2%)
Retromolar trigone	1 (2%)	1 (2%)	0 (0%)
Oropharynx			
Tongue base	5 (9%)	3 (5%)	2 (3%)
Glossotonsillar sulcus	7 (12%)	5 (9%)	2 (3%)
Tonsil	9 (16%)	8 (14%)	1 (2%)
Soft palate	3 (5%)	2 (3%)	1 (2%)
Pharyngeal wall	2 (3%)	2 (3%)	0 (0%)
cTNM MTM*			
T1	5 (9%)	5 (9%)	0 (0%)
T2	11 (19%)	10 (17%)	1 (2%)
T3	2 (3%)	2 (3%)	0 (0%)
T4a	35 (60%)	22 (38%)	13 (22%)
T4b	5 (9%)	4 (7%)	1 (2%)
pTNM post-surgery**			
T1	3 (5%)	3 (5%)	0 (0%)
T2	7 (12%)	7 (12%)	0 (0%)
T3	0 (0%)	0 (0%)	0 (0%)
T4a	8 (14%)	8 (14%)	0 (0%)
T4b	0 (0%)	0 (0%)	0 (0%)
Total	18 (31%)	18 (31%)	0 (0%)

* Clinical Tumor Node Metastasis staging during multidisciplinary team meeting.

** Pathological Tumor Node Metastasis staging stage given by histopathologic examination of a surgical specimen.

Table 2
Results.

	Overall			Primary			Recurrence		
	CTconv	CTmote	MRI	CTconv	CTmote	MRI	CTconv	CTmote	MRI
n	58	58	58	43	43	43	15	15	15
Accuracy									
Exact staging (%)*	68% ± 4%	83% ± 5%	83% ± 6%	67% ± 6%	83% ± 6%	84% ± 6%	71% ± 4%	82% ± 8%	80% ± 7%
Overall agreement (κ)**	0.66 ± 0.03	0.86 ± 0.06	0.84 ± 0.06	0.66 ± 0.03	0.86 ± 0.06	0.84 ± 0.06	0.25 ± 0.22	0.59 ± 0.16	0.48 ± 0.07
Intra-observer agreement (κ)	0.67	0.91	0.92	0.7	0.89	0.94	0.43	1	0.83
Inter-observer agreement (κ)	0.66	0.81	0.83	0.64	0.8	0.86	0.58	0.8	0.69
Confidence (score%)***	86% ± 11%	92% ± 8%	91% ± 7%	86% ± 12%	92% ± 8%	91% ± 7%	86% ± 9%	92% ± 7%	91% ± 6%
Quality									
Overall quality£	2.3 ± 0.7	2.5 ± 0.6	2.4 ± 0.6	2.2 ± 0.7	2.4 ± 0.7	2.5 ± 0.7	2.5 ± 0.9	2.7 ± 0.8	2.2 ± 0.8
Metal artifacts£	2.2 ± 0.8	2.5 ± 0.6	2.8 ± 0.6	2.1 ± 0.8	2.4 ± 0.7	2.7 ± 0.7	2.4 ± 0.9	2.6 ± 0.8	2.8 ± 0.9
Kinetic artifacts£	3 ± 0.2	3 ± 0.1	2.4 ± 0.6	3 ± 0.5	3 ± 0.5	2.5 ± 0.7	3 ± 0.8	3 ± 0.8	2.2 ± 0.8
Best exam$	3%	47%	50%	0%	47%	53%	13%	47%	40%
Worst exam$	84%	3%	12%	86%	2%	12%	80%	7%	13%

* Exactitude of TNM staging compared to gold standard. Results are presented as means ± sd unless otherwise specified.
** Overall agreement refers to concordance between observer. Values are expressed as ICC's kappa.
*** Confidence score in detailed structure mentioned in TNM staging.
£ Quality score based on 3-points Likert (mean ± sd).
$ Quality based on pairwise comparison.

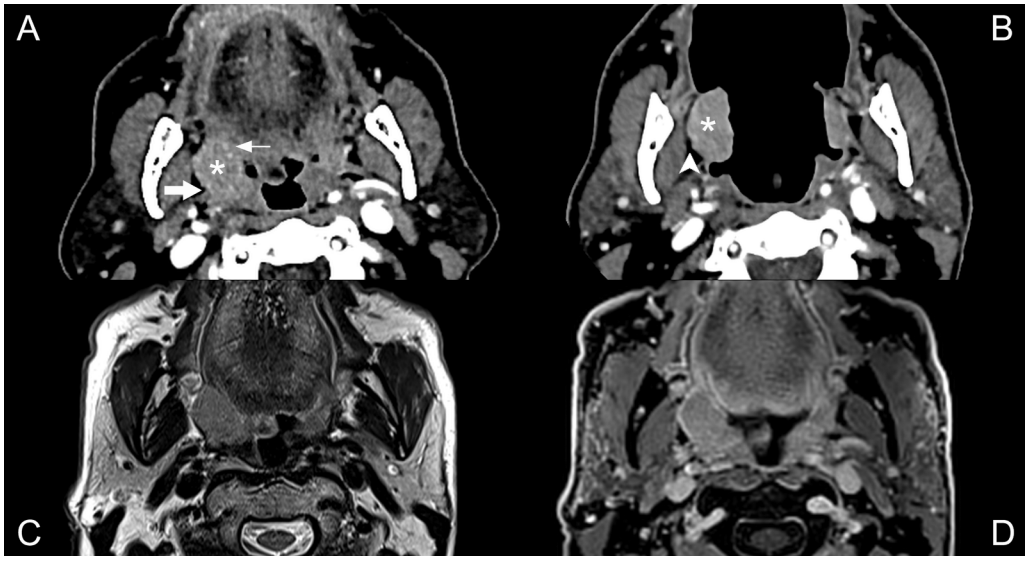

Fig. 1. T2 staged tonsillar carcinoma with typical concordant aspect in CTconv, CTmote, and MRI. CT with injection in axial section centered on the oropharynx, conventional closed mouth (A), in MOTE maneuver (B). MRI in T2 (C) and T1 weighted axial section with gadolinium injection and fat saturation (D). A 73-year-old male, former smoker with squamous cell carcinoma cT2N0M0 (pT2) of the right tonsil. In image A, an asymmetry of the tonsils is distinguished with a nodular contrast enhancement of the right tonsil (*). The edges are not very well limited with the glosso-tonsillar sulcus in front (fine arrow); the lateral pharyngeal wall and the styloglossus muscle behind (broad arrow). In image B the lingual protraction stretches the structures of the oropharynx and distends the glosso-tonsillar sulcus path. The tonsillar compartment is isolated and the absence of invasion of the tongue base and the styloglossus muscle appears certain. The fatty border separating the medial pterygoid muscle from the tumor is better visualized (arrowhead) than in image A. The tumor enhancement is greater with CTmote (CNR = 4.3) than in CTconv (CNR = 2 4). MRI images (C, D) appear to be of good quality on both sequences.

Discussion

This study clearly disclosed that the "mouth opened with tongue extended" dynamic maneuver performed as part of a post contrast CT could decrease metallic artefacts and increase clinical benefits for ooSCC staging. As compared to CTconv, CTmote was more accurate and specific for the local oral cavity and oropharynx cancer staging. Tumour visualization and image quality scores were similar between CTmote and MRI. However the nature and rate of artifacts were different between CTmote and MRI.

Advantages offered by the MOTE maneuver could be accounted for by the fact that x-ray beam could better penetrate the oral cavity with no obstacles related to dental amalgams [9,13,18]. Alternative solutions such as the gantry tilt along the dental arch plana have been proposed [9,19].

Tumor delineation

During the MOTE maneuver, one could observe that dental arches drew back while the lingual protraction unfolded the extrinsic tongue muscle and mucosa and more particularly the glossotonsillar sulcus. These changes might account for the better visualization of the tumor as illustrated by the 47% better conspicuity in CTmote as compared to CTconv (3%). The displacement of initially contiguous structures also unraised potential doubts about an invasion within the vicinity of the tumour (Fig. 1).

Reproducibility

Tumor extension assessment was more reproducible using the CTmote as compared to the CTconv. To the best of our knowledge, the readings reproducibility associated to a dynamic maneuver of the oral cavity and oropharynx has not been studied so far. This larger

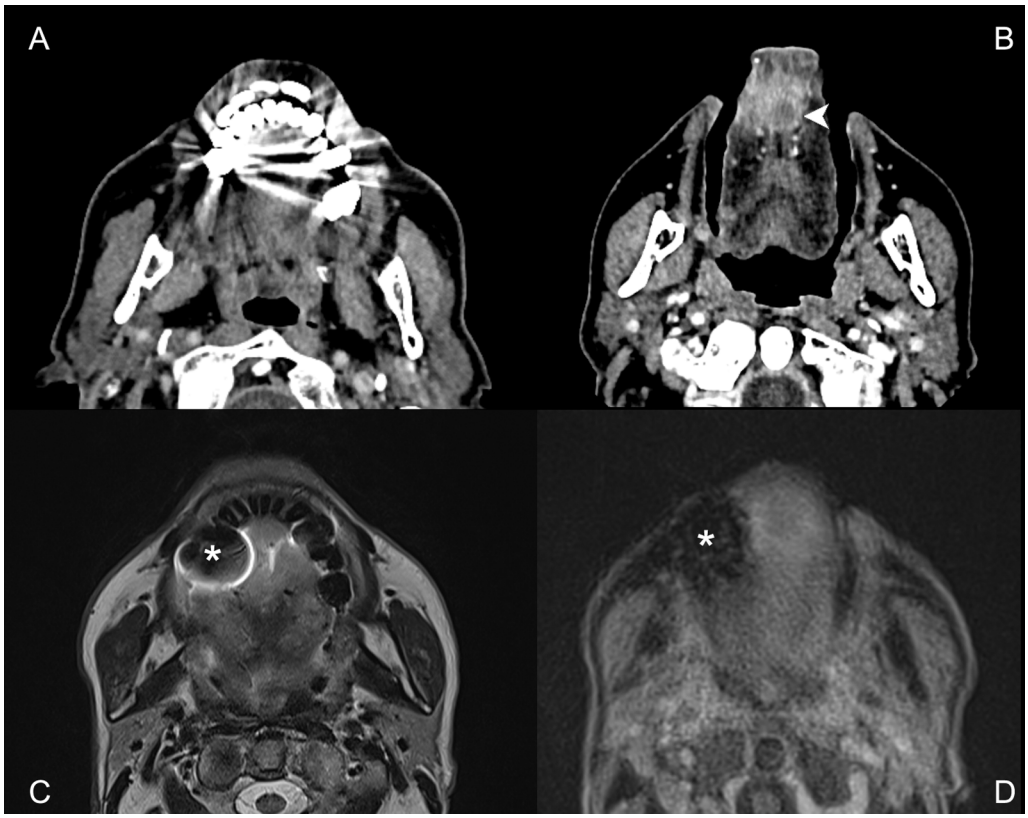

Fig. 2. T4a staged Tongue carcinoma: case of better conspicuity of the tumor with a CTmote compared to CTconv and MRI due to artifacts. CT with injection in axial section centered on oral cavity, conventional closed mouth (A), in MOTE maneuver (B). MRI in T2 (C) and T1 weighted axial section with gadolinium injection and fat saturation (D). A 58-year-old man, tobacco and alcohol consumer, with squamous cell carcinoma cT4aN2bM0 (pT4a) of the mobile tongue, found during a glossodynia assessment with dysphagia. In image A, important dental metal artifacts mask the tongue and prevent the tumor from being seen. In image B, the mouth opening removes the dental amalgams from the tumor and removes the metal artifacts at this level. A medial nodular contrast (arrow head) of the mobile tongue is then visualized. The invasion of the genio-glossus muscle is better visualized on the sagittal sections. The MRI sections (C, D) show an image distortion related to dental amalgam (*), barely distinguishable to the nodular contrast of the T1 images with gadolinium injection (D). The T1 sequence with injection of gadolinium (D) is also artefacted by the patient's movements.

reproducibility is likely related to the improved image quality allowing a more accurate assessment of tumor extensions. The reproducibility of the CTmote and MRI readings was comparable.

Metallic artifacts

Due to metallic artifacts, 22% of CTconv exams could not be analyzed (Fig. 2).

Movement artifacts

All the patients were able to stay still during the 3.2 s CTmote imaging session so that no movement artifacts were noticed. On the contrary, movement artifacts were observed for 22% of the MRI exams.

Enhancement

The CNR was significantly improved using the CTmote (3.14 ± 2.7) as compared to the CTconv (2.29 ± 3). According to Keberle [20], this improved CNR might be linked to the delayed enhancement of the ooSCC studied. However, no consensus has ever been reported regarding the injection protocol of a CT exam. Both a monophasic injection with a 2 mL/s flow rate [9,21,22] and a biphasic injection protocol [23] have been reported. Alternatively, acquisitions have been started 70–80 s post injection [9,16,18]. In fact, CNR enhancement for tumors, nodes, and vessels is patient dependent and related to multiple factors.

Radiation dose

As the additional CTmote acquisition induced a 33.7% increase in the DLP of the total cervical dose, one might consider this as a limit. However, one has to keep in mind that the total radiation dose remained below the 50th percentile (745 mGy cm) of the Diagnosis Reference Levels recommended by the IRSN (french nuclear safety and radioprotection institute) for the head CT exploration [24].

Limitations of the study

While the demographic details of our group were comparable to those from the literature in terms of sex, age [20] and initial location of the tumor [25], the proportion of T4a stages (60.3%) was larger than the relative amount reported in other series (Keberle: 31%, Auluck: 15–20%, Singh: 24%) [20,25,26]. This might be considered as a local recruitment bias. It could also be related to the extension of the extrinsic tongue muscles (especially the styloglossus and the palatoglossus muscles) which are difficult to assess both in terms of imaging and anatomopathology [27,28]. It is noteworthy that this stage has been recently excluded from the TNM classification.

Conclusion

Adding MOTE maneuver during CT acquisition can improve the assessment of local extension of HNSCC in oral cavity and oropharynx. The corresponding performance was comparable to what obtained with MRI examination. On that basis, the optimal imaging strategy in clinical practice could be to combine CT with MOTE maneuver and MRI.

Disclosure

The authors declare having no conflicts of interest

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.oraloncology.2019.04.023.

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