RESEARCH COMMUNICATION

When should MRI be Recommended for the Accurate Clinical Staging of Base of Tongue Carcinoma?

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Abstract

  <u>Background and Purpose</u>: According to the American Joint Committee on Cancer (AJCC) cancer staging criteria (6th edition), cross-sectional imaging for base of tongue carcinoma is recommended when the deep tissue extent of a primary tumor is in question. The aim of this study was to establish which group of patients MRI might most benefit from accurate clinical staging of base of tongue carcinomas. <u>Patients and Methods</u>: The clinical stagings of 33 patients with pathologically proven squamous cell carcinomas of the base of tongue were performed by two otorhinolaryngologic surgeons. Their results were compared with the results from MRI interpreted by a neuroradiologist and the numbers of patients being upstaged, downstaged or with an unchanged stage were recorded and analyzed. <u>Results</u>: The tumor stages were changed in 13 of 33 patients (39.4%, 95% CI: 23.9-57.87%) and the overall stage groupings were changed in 10 (30.3 %, 95%CI: 15.6-48.7%) after performing MRI. Mis-staging by clinical examination in the overall stage grouping was as high as 83.3% (95%CI: 35.9-99.6%) in stages II and III and 85.7% (95% CI: 42.1-99.6%) in T3. <u>Conclusion</u>: MRI should be recommended in base of tongue carcinoma whenever clinical examination suggests overall stage groupings II, III or tumor stage T3.

Key Words: Base of tongue carcinoma - neoplasm staging - MRI

Introduction

The accuracy of pre-therapeutic staging is an important factor in the treatment planning of head and neck carcinomas and pre-therapeutic cross-sectional imaging assessment of the tumor and nodal extents should be part of standard care for most head and neck carcinomas nowsaday. However, pre-therapeutic imaging assessment for orophyarngeal carcinoma patients is still not as widely performed as it should be, especially in institutes which use 2D- planning radiation therapy or concomitant chemoradiotherapy instead of surgery as the primary treatment modality. The reasons may be due to its high cost and the belief that the TNM-classification may not be altered or only slightly altered after performing imaging.

According to the AJCC Cancer Staging Manual, 6th edition (American Joint Committee on Cancer, 2002), cross-sectional imaging in oropharyngeal carcinoma (including base of tongue carcinoma) is recommended when the deep tissue extent of the primary tumor is in question. CT or MRI may be employed. The problem with this recommendation is that it is frequently not easy to assess the primary tumor extension in question with a good degree of confidence by clinicians since base of tongue

carcinoma tends to grow silently and deeply beyond the reach of accurate assessment by clinical examination. A related problem with the recommendation is that even though either MRI or CT can be used for the clinical staging of base of tongue carcinoma, MRI is widely believed to be superior to CT in the assessment of tumor extension in most oral and oropharyngeal carcinomas (Larsson,1988; Lufkin and Hanafee,1988; O'Reilly et al., 1989; Kassel et al.,1989; O'Reilly et al., 1989; Kassel et al.,1989; Mukherji et al.,1997; Becker,2005), and should be used as the first choice whenever available and no contraindications. Most of the published literature to date has reported only on the overall staging accuracy of CT or MRI for oral or oropharyngeal cavity cancer (Larsson et al., 1987; Vogl et al., 1988; Lenz and Hermans ,1996; Kosling et al., 2000; Becker,2005), but until now there has yet to be a single study mainly devoted to the influence of MRI upon the clinical staging of base of tongue carcinoma.

We therefore compared TNM stagings based solely on clinical examinations with or without imaging findings in an effort to establish which groups of patients might benefit most from an MRI, and who should be recommended for the accurate clinical staging according to the AJCC recommendations.

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Table 1. Scan parameters for MRI

Scan orientation	Axial SE T1w	Axial FSE T2w	Post Gd-DTPA Axial SE T1w with fat suppression	Coronal FSE T2w	Post Gd-DTPA coronal SE T1w with fat suppression	Sagittal SE T1w	Sagittal FSE T2w
Repetition time/ echo time(ms)	874/15	8257/112	1265/15	6821-8257/112	1045-1265/15	722-874/15	6821-8257/112
Echo train length	none	15	non	15	non	non	15

Materials and Methods

Between June 2004 and August 2006, 33 newly diagnosed and pathologically proven squamous cell carcinoma of the base of tongue patients (31 male, 2 female; mean age 64.5 years; age range 35-83 years) were included in the prospective study. Before performing MRI, the primary tumor and neck nodes were clinically staged by two otorhinolaryngologic surgeons using the AJCC Cancer Staging Criteria (6th edition), based on a careful examination through inspection, palpation, indirect mirror examination and complete endoscopy. In the event of any disagreement, the final decision was made through consensus. Patients were excluded from the study if distant metastases were found, since MRI would not add other useful information about the overall clinical staging.

All the patients then underwent an MRI examination on a 1.5 T MR unit (Siemens, Magnetom Vision, Erlangen, Germany) with a phased-array neck coil from the skull base to the thoracic inlet before any further treatment. The images were obtained in three planes with four millimetre thick sections, a one milimetre intersection gap, a field of view of 20 cm and acquisition matrix of 256x192. Other scan parameters are summarised in Table 1. The average interval between completion of the clinical and MRI examinations was 8.2 days.

The MRI images were reviewed by a neuroradiologist, who was blinded to the tumor and nodal extent, for the size, the extent of invasion of the primary lesion and the cervical lymph nodes to determine a precise TMN stage according to the AJCC cancer staging criteria (6th edition). Special attention was directed to the size (greatest dimension) and the involvement of deep surrounding tissues (i.e. deep/extrinsic tongue muscles, larynx, etc.) of the primary tumor mass. The appropriate nodal stage was assessed from the MRI, using the two major imaging criteria of nodal size (maximum diameter) and the presence of central non-homogeneity (Som and Brandwein, 2003). Afterwards we compared the T stage, N stage, and overall stage grouping by both clinical examination and MRI. The number of patients being upstaged, downstaged or unchanged was recorded and analysed.

Results

We found that between the clinical examination and the MRI, the allocated tumor stages disagreed in 14 of 33 patients (42.4%, 95%CI: 25.5-60.8%); 13 of them (92.9%, 95% CI: 66.1-99.8%) were upstaged after performing MRI (Table 2). One patient who had a small mucosal lesion about 0.5x1 cm in size observed only by clinical examination but not by MRI was downstaged (3%, 95% CI: 0.1-15.8%). The tumor stages were therefore changed in 13 of 33 patients (39.4%, 95% CI: 23.9-57.9%) after performing MRI. A high prevalence of mis-stagings by clinical examination was seen in T2 and T3 stages by as much as 50.0% (95% CI: 21.09-78.91%) and 85.7% (95% CI: 42.1-99.6%). Not a single case of mis-staging in T4a and T4b was found. The clinical details of each patient were summarized in Table 3.

The nodal stages were changed in 18 of 33 patients (54.5%, 95% CI: 36.4-76.9%); the majority (16 patients, 88.9%, 95% CI: 65.3-98.6%) were upstaged with two patients (11.1%, 95% CI: 1.4-34.7%) were downstaged (Table 4).

MRI upstaged the overall stage groupings in 10 out of 33 patients (30.3%, 95%CI: 15.6-48.7%) but did not alter the overall stage groupings in 23 of the 33 patients (69.7%, 95%CI: 56.3-84.4%) (Table 5). There was a high prevalence of mis-stagings after performing MRI in both stages II and III at 83.3% (95%CI: 35.9-99.6%).

The numbers of the overall stage groupings by clinical examination and after performing the MRI were summarized in Table 6.

Discussion

We found that both clinical examination and MRI are

Table 2. Comparison Between the Tumor Stagings by Clinical Examination and by MRI.

MRI Clinical Examination	Agreed Stage	Up/Down Stage	Changed to	Mis-staging % (95% CI) * Binomial Exact
T1	4	1*	T0	16.7% (0.4% - 64.1%)
		1	T4a	16.7% (0.4% - 64.1%)
T2	6	6	T4a	50.0% (21.1% - 78.9%)
T3	1	6	T4a	85.7% (42.1% - 99.6%)
T4a	7	-		0.0% (0.0% - 41.0%) * one-sided
T4b	1	-		0.0% (0.0% - 97.5%) * one-sided

One patient had a tiny ulcerated mucosal base lesion at the mid part of the base of the tongue about 0.5x1 cm in size, missed by MRI. The tumor staging was therefore T1 according to the clinical examination

Table 3. Summarized Clinical Details of Each Patient

No	Gender	Age	Size (maximum diameter, cm)		T-stage		N-stage		Overall stage		Compared T-stage	N-stage	Results OSG
			CE	MR	CE	MR	CE	MR	CE	MR			
1	m	50	5	4.5	T4a	T4a	N0	N1	IVA	IVA	-	↑	-
2	m	61	6	6.5	T4b	T4b	N3	N3	IVB	IVB	-	-	-
3	m	70	3	2.6	T2	T2	N1	N2c	III	IVA	-	↑	↑
4	m	74	5	5	T3	T4a	N0	N0	III	IVA	↑	-	↑
5	m	68	2	2	T1	T1	N2a	N2a	IVA	IVA	-	-	-
6	m	76	4	2.3	T2	T2	N2b	N2c	IVA	IVA	-	↑	-
7	m	67	3.5	3.2	T2	T4a	N0	N0	II	IVA	↑	-	↑
8	m	76	3	4.8	T3	T4a	N2b	N2b	IVA	IVA	↑	-	-
9	m	54	2.5	2.8	T2	T2	N1	N1	III	III	-	-	-
10	m	70	3	2.2	T2	T4a	N2c	N2c	IVA	IVA	↑	-	-
11	m	48	4	5	T2	T4a	N2c	N2c	IVA	IVA	↑	-	-
12	m	86	1	* ND	T1	T0	N0	N0	I	I	↓	-	-
13	m	76	3	2.5	T2	T2	N0	N0	II	II	-	-	-
14	m	53	4	5.5	T4a	T4a	N1	N2c	IVA	IVA	-	↑	-
15	m	46	1.5	1.4	T1	T1	N2a	N2a	IVA	IVA	-	-	-
16	m	55	2	1.2	T1	T1	N1	N2b	III	IVA	-	↑	↑
17	m	70	5	4.5	T3	T4a	N2c	N2c	IVA	IVA	↑	-	-
18	m	56	4	6	T4a	T4a	N1	N2b	IVA	IVA	-	↑	-
19	m	67	3	3.4	T2	T2	N2a	N2c	IVA	IVA	-	↑	-
20	f	45	4.5	5	T2	T4a	N0	N2c	II	IVA	↑	↑	↑
21	m	78	5	3.5	T3	T4a	N2b	N2c	IVA	IVA	↑	↑	-
22	m	82	2	2	T1	T1	N0	N0	I	I	-	-	-
23	m	78	4	3.2	T2	T4a	N0	N1	II	IVA	↑	↑	↑
24	m	60	4	2.7	T1	T4a	N1	N2c	III	IVA	↑	↑	↑
25	m	65	5	4.7	T4a	T4a	N1	N2c	IVA	IVA	-	↑	-
26	m	67	5	4.3	T3	T4a	N2c	N2b	IVA	IVA	↑	↓	-
27	m	83	6	5.7	T3	T4a	N1	N0	III	IVA	↑	↓	↑
28	m	35	6	5	T4a	T4a	N1	N2c	IVA	IVA	-	↑	-
29	m	76	4	4	T2	T4a	N0	N0	II	IVA	↑	-	↑
30	f	62	3	7.4	T4a	T4a	N1	N2c	IVA	IVA	-	↑	-
31	m	74	6	5.8	T4a	T4a	N1	N2c	IVA	IVA	-	↑	-
32	m	76	2.5	2.7	T2	T2	N0	N2b	II	IVA	-	↑	↑
33	m	58	5	4.8	T3	T3	N2c	N2c	IVA	IVA	-	-	-

CE=Clinical Examination, *ND = Not detected, OSG=Overall Stage Grouping

valuable tools in the evaluation of base of tongue carcinoma. However, MRI added more information and significantly altered the overall stage grouping, tumor staging and nodal staging by 30.3% (95%CI: 15.6-48.7%), 39.4% (95%CI: 23.9-57.9%) and 54.5% (95% CI: 36.4-76.9%) respectively. For those patients examined clinically and placed in overall stage groupings II, III or tumor stage 3, pretherapeutic MRI should be performed to increase the accuracy of the pretherapeutic clinical staging assessment because of the high prevalence of mis-stagings found by clinical examination alone. MRI may not be necessary for the clinical staging of patients with overall stage groupings I and IV or tumor stages 1 and 4. Instead, CT may be more suitable and practically used in these groups since the primary concern is not mainly about the extent of the tumor but the nodal staging, and for such purposes there are no significant differences between CT and MR regarding the visualization of adenopathies (Hermans et al.,1994). In tumor stage 2 by clinical examination, which MRI altered the tumor staging by

50%, the use of pretherapeutic imagings should be mainly up to the judgment of the clinician in each patient. The extent of a tumor was often underestimated on clinical examination, leading to significant understagings of these primary tumors. Most base of tongue carcinomas tend to spread submucosally and the invasion of the deep extrinsic tongue muscles will significantly change the tumor less than 4 cm from T1, 2 or 3 to be T4a (Figs 1,2 & 3). We found that 16.7% of T1, 50% of T2 and 85.7% of T3 patients staged by clinical examination in our study were changed to tumor stage T4a after performing MRI. Most changes were due to the finding of invasion of the deep extrinsic tongue muscles, especially the genioglossus and hyoglossus muscles that could not be detected by the clinical examination.

Various tongue movements by the patients, commonly used to assess the presence or extent of invasion of deep extrinsic tongue muscles, are not sufficiently precise to determine definite tumor invasion. Invasion of the deep extrinsic tongue muscles can be better demonstrated by

multiplanar MRI, especially on SE T2w and post Gd-DTPA SE T1w with fat suppression sequences.

Another problem is indicated from the results of this study. Since the currently accepted clinical staging criteria were established based mainly on clinical examinations, now we must reconsider how the "imaging up-staging" may affect the prognosis, especially considering the slight invasions of the deep extrinsic tongue muscle criteria

which frequently can be detected only from imaging, and not by clinical examination. Should the AJCC staging system be revised to allow "minor" involvement of extrinsic tongue muscles seen only by imagings not to be upstaged to T4a, or should the guideline be revised to use the term that more practically used, such as "tongue fixation or limited tongue movement in various fashions by clinical examination" instead of "deep extrinsic tongue muscle invasion"? Or perhaps should cross-sectional imaging be recommended as mandatory in all patients with base of tongue carcinoma in a future TNM staging revision? Further study to assess imaging versus clinical

Table 4. Comparison Between the Nodal Stagings by Clinical Examination and by MRI

MRI Clinical Examination	Agreed Stage	Up/Down stage	Changed to	Mis-staging% (95%CI) * Binomial Exact
N0	6	2	N1	20.0% (2.5%-55.6%)
		1	N2b	10.0% (0.3%-44.5%)
		1	N2c	10.0% (0.3%-44.5%)
N1	1	1	N0	9.1% (0.2%-41.3%)
		2	N2b	18.2% (2.3%-51.8%)
		7	N2c	63.6% (30.8%-89.1%)
N2a	2	1	N2c	33.3% (0.8%-90.6%)
N2b	1	2	N2c	66.7% (9.4%-99.2%)
N2c	4	1	N2b	20.0% (0.5%-71.6%)
N3	1	-		0.0% (0.0%-97.5%) * one-sided

Table 5. Comparison Between the Overall Stage Grouping by Clinical Examination and by MRI.

MRI Clinical Examination	Agreed Stage	Up/Down Stage	Changed stage	Mis-staging % (95% CI) * Binomial Exact
Stage I	1	1	Stage 0*	50.0% (1.3% - 98.7%)
Stage II	1	5	Stage IVa	83.3% (35.9% - 99.6%)
Stage III	1	5	Stage IVa	83.3% (35.9% - 99.6%)
Stage IVa	18	-		0.0% (0.0% - 18.5%) * one-sided
Stage IVb	1	-		0.0% (0.0% - 97.5%) * one-sided

Table 6. Number of Overall Stage Groupings by Clinical Examination and after Performing MRI

	No. of patients By Clinical examination	No. of patients By Clinical examination plus MRI
Stage I	2	2
Stage II	6	1
Stage III	6	1
Stage IVa	18	28
Stage IVb	1	1

Figure 1. Sagittal SE T1-weighted MR Image. The lesion was upstaged to T4a from T1
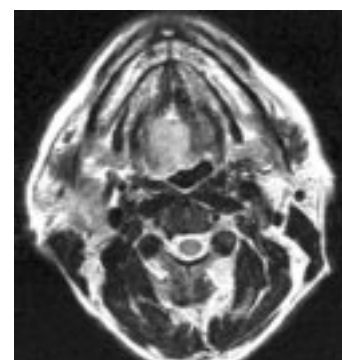

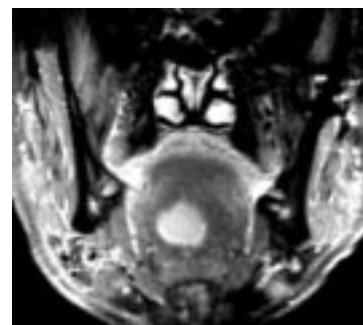**Figure 2. Axial SE T2-weighted MR Image**

Figure 3. Coronal post-Gd-DTPA SE T1-weighted MR Image

staging in a larger group of patients in whom outcomes can be correlated with non-imaging versus imaging-based staging may be needed.

It should be noted here again that MRI revealed less information than clinical examination in one patient who had a tiny ulcerated mucosal lesion at the mid-part of the base of the tongue about 0.5x1 cm in size, which could not be detected by MRI. Therefore, the tumor stage and stage grouping were determined according to the clinical examination. This was the only patient in whom MRI understaged the lesion due to its small size and the primarily mucosal involvement. Clinical examination was again revealed to be a very important component of accurate clinical staging, especially for the superficial mucosal lesion.

Our results also confirm again that squamous cell carcinoma tends to be diagnosed at a more advanced stage. Almost 90% of the patients in our study (87.9%, 95%CI: 71.8-96.6%) presented with an advanced disease (stage IVa or IVb) at the time of diagnosis.

Since the definite diagnosis of cancer is made primarily by biopsy, the role of imaging is to provide an accurate pre-therapeutic clinical staging and assist therapeutic planning. Carcinomas tend to have low signal intensity on T1-weighted images (Figure 1), which makes them difficult to differentiate from normal musculature. Tumors tend to have an intermdiate to high signal intensity on T2-weighted images, enhanced on post-Gd-DTPA SE T1w with fat suppression images, which allows sharp differentiation of the tumor from the low intensity surrounding musculature (Figures 2 & 3). The tumor size in its greatest dimension is important for T1-T3 tumor staging, while more severe invasions of adjacent structures such as the larynx, deep extrinsic muscle of the tongue, medial pterygoid muscles, hard palate, or mandible upstage the tumor staging to T4a, while further invasion of the lateral pterygoid muscles, pterygoid plates, nasopharynx or skull base will upstage the tumor staging to T4b.

Information that will directly affect the surgical approach is whether the tumor involves the ipsilateral neurovascular bundle, whether there is submucosal involvement in adjacent areas including the floor of the mouth, and wherther the tumor has crossed the midline. If the tumor crosses the midline, its relation to the contralateral lingual neurovascular bundle must be determined. The spread of a tumor across the midline and in proximity to the opposite lingual neurovascular bundle precludes a partial glossectomy and necessitates a total glossectomy (Mukherji et al.,1997; Becker,2005). Invasion of the epiglottis and preepiglottic space, which can be well demonstrated in the sagittal T1-weighted images, also indicates supraglottic or even total laryngectomy (Becker, 2005).

The risk of regional nodal spreading of base of tongue carcinoma is high, as had been already detected in 27 patients in our study (81.8%). Most of them involved level II and III nodes and (less commonly) level I nodes. Bilateral lymphatic drainage is also common and was seen in 16 patients (48.5%) in our study.

Mucosal lesions are better assessed by clinical examination, while the deeper submucosal extensions are better assessed by MRI. Information from both the clinical examination and MRI contribute equally as important tools for the staging assessments and MRI should be recommended as a part of the accurate staging assessment in base of tongue carcinoma whenever the clinical examination suggests an overall stage grouping II, III or tumor stage 3, due to the high prevalence of understagings.

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