Evaluating lingual carcinoma for surgical management: what does volumetric measurement with MRI offer?

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ABSTRACT. MRI plays a crucial but under utilized role in the surgical management of lingual squamous cell carcinoma (SCC). Measurement of three-dimensional tumour volume (TV) has the potential to guide management of clinically negative cervical lymph nodes and address deficiencies in current TNM staging criteria. This work studied the value of MRI-measured TV as a predictor of 2 year disease-related survival (DRS) and disease-free survival (DFS), as well as occult cervical lymph node metastasis (OM) in lingual cancer. TV was determined by manually segmenting the tumour contour in each image slice and using the resulting pixel value to calculate the three-dimensional extent of disease. TV was also compared with the more established measure of tumour thickness (TT). Significant differences in DRS ($\chi^2(1) = 7.7$, Hazard ratio (HR) = 7.3, $p = 0.005$) and DFS ($\chi^2(1) = 5.6$, HR = 4.3, $p = 0.02$) at two years were found using a cut-off of 8 cm³. Similarly, a significant relationship between TV and occult cervical lymph node metastasis was discovered using a 3 cm³ cut-off (OR = 6.7, $p = 0.02$, Fisher's Exact Test).

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Introduction

Oral cancer is the 12th most common cancer globally and the 8th most common in developing countries, affecting 270 000 people worldwide each year [1]. Together, pre-disposing factors of alcohol and tobacco are associated with more than 75% of oral cancers [2]. Oral cancer also has a propensity to metastasise to cervical lymph nodes but lymphadenopathy remains occult, evading clinical detection, in the majority of cases. Accordingly, a large number of patients who undergo elective neck dissection are found to have no evidence of cervical node metastasis on pathological examination and might have been spared this additional procedure.

The staging of oral cavity squamous cell carcinoma (SCC) is currently based on clinical measurement of tumour surface dimensions as outlined by American Joint Committee on Cancer (AJCC) criteria [3]. MRI is used in a supplemental role to evaluate tumour thickness and invasion into adjacent structures, which might not be readily apparent on clinical examination. This information is used to determine the treatment approach to the primary lesion and cervical lymph nodes, and to indicate prognosis.

Criticism of the current TNM (tumour, node, metastasis) staging criteria has resulted from several studies showing that the size-based T criteria fail to demonstrate a significant relationship with patient survival [4, 5]. Lenz et al [6] found that clinical T stage (cT) of oral cancer predicted the pathology T stage (pT) only 47% of

the time. There are several reasons for this first, clinical measurement of oral cancers is difficult and limited by poor access, patient discomfort and the gag reflex. Second, superficial tumour size is not necessarily related to prognosis. Large superficial tumours can be managed well whereas small deep tumours may evade locoregional control. Third, the majority of oral and pharyngeal cancers fall in the T2 category (20–40 mm). Tumours beyond 40 mm usually invade surrounding structures and are designated T4, leaving a paucity of T3 tumours [7]. Finally, surgical planning depends on tumour invasion: the surgeon needs to know the extent of tumour invasion to achieve adequate surgical clearance.

Recent work has focused on alternative measurements, including tumour thickness (T_T), depth of invasion (T_D) and volume (T_V), which may better reflect the natural history of the tumour. In particular, depth of invasion is regarded as a highly significant predictor of cervical node metastasis, local recurrence and survival [8]. The majority of this recent work has evaluated post-surgical specimens.

T_D is the extent of cancer growth into the tissue beneath an epithelial surface, which can be an existing surface or a reconstructed surface, for example in the case of an exophytic growth. The T_D is not equivalent to the T_T , which is defined as the distance from the deepest point of invasion to the tumour surface. There has been no attempt to define the epithelial surface.

T_D and T_T , like surface diameter, do not reflect the three-dimensional (3D) and sometimes irregular growth of tumours. T_V reflects growth in any plane and thus has the potential to play a role in patient management. Further, T_V is amenable to measurement during pre-operative MRI studies and may be a suitable adjunct to surgical planning. The soft-tissue discrimination of MRI

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readily reveals tumour invasion and spread to surrounding structures. T_2 weighted images demonstrate superior contrast and are sensitive to the presence of tumour tissue, which is usually hyperintense when compared with surrounding muscle [9]. The alternative sectional technique, CT, may be less useful in the oral cavity because of the lower contrast resolution in soft tissues and the beam hardening artefact caused by dental amalgam.

Some studies have supported volumetric analysis of head and neck cancers for the prediction of survival [10, 11]; whereas other studies have failed to find a significant relationship between tumour volume and survival [12, 13]. The present study further evaluates T_V , as measured by MRI, as a prognostic indicator of disease-free survival (DFS) and disease-related survival (DRS), and as a predictor of occult cervical lymph node metastasis (OM).

Materials and methods

Patients diagnosed with histologically proven SCC of the tongue presenting at the John Radcliffe Hospital, Oxford between 1998 and 2006 were studied retrospectively. All patients undergoing staging MRI, and in whom the primary treatment was surgical resection, were included in the study. No patients underwent pre-operative chemo- or radiotherapy. Patients were excluded if their MRI studies could not be recovered or were incomplete, if they underwent tumour biopsy ten days prior to MRI (to avoid false-positive findings from inflammatory response to biopsy), or if tumours were obscured by a motion or susceptibility artefact. In the majority of cases, at our institution, the neck is treated with an ipsilateral or bilateral modified radical neck dissection (MRND). Supraomohyoid neck dissection, with or without extension to level 4, may be employed for elective neck dissection at the surgeon's discretion.

Because of the retrospective nature of the data analysis, the MRI parameters varied slightly. All coronal and axial studies were carried out on a 1.5T scanner (General Electric Healthcare Medical Systems, Milwaukee, WI), with a 512×512 pixel matrix in all but two patients for whom a 256×256 matrix was used. T_2 weighted fast spin-echo images with fat suppression were used in all studies with echo train lengths ranging from 10 to 16. Field of view ranged from $16 \text{ cm} \times 16 \text{ cm}$ to $26 \text{ cm} \times 26 \text{ cm}$ except in one patient where $48 \text{ cm} \times 48 \text{ cm}$ was used. Slice thickness ranged from 3.5 mm to 6.0 mm, and interslice spacing ranged from 0.0 mm to 1.0 mm except in one instance where 5.0 mm spacing was used.

Tumour volume was calculated using a manual segmentation technique. All segmentation was performed in duplicate by the first author on studies obtained in the coronal or axial plane. A choice was made between the axial and coronal studies based on image quality and tumour orientation. In cases where it was difficult to define all tumour margins, images were reviewed by a radiologist specialising in oral radiology (SJG). Using a graphics tablet, the contour of the tumour was segmented in each slice of the MRI study and the T_V was obtained as a quantity of voxels using software

developed in house (KP). The number of voxels representing the tumour was multiplied by the voxel volume to obtain the tumour volume in cm^3 . In cases where biopsy-proven SCC was not visible on MRI, the lesion was given a volume of 0.0 cm^3 . An example is shown in Figure 1.

T_T measurements were made perpendicular from the tumour surface to the deepest extent of tumour invasion on coronal or axial T_2 weighted MRI studies. In cases where it was difficult to define all tumour margins, images were reviewed by a radiologist specialising in oral radiology (SJG). In cases where biopsy-proven SCC of the tongue was not visible, the lesion was given a tumour thickness of 0.0 mm.

DRS was defined as the interval between the date of surgical resection and lingual disease-related death. Patients were censored at the end of the two-year follow-up period or at last documented follow-up. DFS was defined as the time interval between the date of surgical resection and the documented return of malignant disease (as local or regional recurrence, distant metastasis or second primary tumour of the upper aerodigestive tract) in patients who were considered disease-free following primary surgical treatment. Patients were censored if they were disease-free at the end of the two-year follow-up period or at the last documented follow-up.

Patients in the study sample with the clinical TNM classification N0, defined as the absence of lymphadenopathy on clinical examination and MRI imaging, were used to create a subsample for the study of OM. OM was defined as the histological confirmation of metastatic SCC in ipsilateral or contralateral cervical lymph nodes at the time of tumour excision.

For both OM and survival, patients were classified into high-risk and low-risk groups based on a series of integer cut-off values ranging from 2 to 8 cm^3 and 2 to 8 mm for T_V and T_T , respectively. All cut-off values with

Figure 1. Obtaining tumour volume. Coronal T_2 weighted image shows a large lingual squamous cell carcinoma as a well-defined area of high signal intensity in the otherwise low signal intensity substance of the tongue. The tumour has been outlined, demonstrating the process of manual segmentation.

statistically significant results were considered and the value with largest effect size was taken as the recommended cut-off.

Statistical analysis was carried out using SPSS (version 15.0; SPSS Chicago, IL). Survival analysis was carried out using the log-rank test and Cox proportional hazards model. In the OM study, dichotomous and ordinal variables were compared using the χ^2 test or Fisher's exact test as appropriate. The intraclass correlation coefficient was used to test the reliability of T_V and T_T measurements and the F statistic computed. All statistical tests were assessed at the 0.05 significance level.

Results

During data analysis, one patient had extreme values for both T_V (55.7 cm³, z-score 4.0) and T_T (47.0 mm, z-score 3.6) and was excluded. The 40 remaining patients (24 men, 16 women) had a mean age of 57 years (23–86 years). The mean follow-up duration was 30.4 months (8.7–57.0 months). The remaining demographic, clinical and pathological characteristics of the study population are summarised in Table 1.

17 patients (42.5%) received modified radical neck dissections (MRND), 8 patients (20%) supra-omohyoid dissections (SOHND), 8 patients (20%) SOHND with the addition of level IV (SOHND + IV), 3 patients (7.5%) bilateral neck dissections with ipsilateral MRND and contralateral SOHND + IV and 4 patients (10%) were managed with close follow-up.

cT was upstaged by pT in 1 case (3%) and downstaged in 20 cases (51%). Clinical N (cN) was increased by pathology N (pN) in 14 cases (36%) and downstaged in 3 cases (8%). Clinical stage (cStage) was increased by pathology stage (pStage) in 8 cases (20.5%) and downstaged in 12 cases (31%). The cT and pT of the patient sample are compared in Table 2.

The intraclass correlation coefficient for the duplicate T_V measurements made by the single observer was 0.98 (95% CI 0.96–0.99, $F = 102.1$, $p < 0.001$). Similarly, the intraclass correlation coefficient for the duplicate T_T measurements made by the single observer was 0.99 (95% CI 0.98–0.99, $F = 169.7$, $p < 0.001$).

Survival

11 of the 40 (25%) patients died, 8 because of complications of their disease and 3 because of an unrelated pathology. 7 out of the 8 disease-related deaths occurred within the 24 months following surgical resection. In this group the median T_V was 24.0 cm³ (1st quartile (Q1) 3.3 cm³, 3rd quartile (Q3) 32.0 cm³), whereas in the censored group, the median T_V was 2.0 cm³ (Q1 0.0 cm³, Q3 5.9 cm³). When grouped using a cut-off value of 8.0 cm³, T_V was a predictor of DRS ($\chi^2(1) = 7.7$, $p = 0.005$). DRS was predicted by cT ($\chi^2(1) = 7.8$, $p = 0.05$), cN ($\chi^2(1) = 13.2$, $p < 0.001$) and cStage ($\chi^2(1) = 7.9$, $p = 0.05$) but not by tumour grade ($\chi^2(1) = 1.1$, $p = 0.58$). T_T did not predict DRS at any cut-off value. The DRS results are summarised in Tables 3 and 4. A Kaplan–Meier plot is shown in Figure 2a.

Table 1. Demographic, clinical and pathological information for the study sample

	n (%)
Sex	
Male	24 (60)
Female	16 (40)
Smoking status¹	
Smoker	16 (42.1)
Non-smoker	23 (57.9)
Alcohol consumption¹	
Drinker	24 (61.5)
Non-drinker	15 (38.5)
cT	
1	12 (30.0)
2	11 (27.5)
3	2 (5.0)
4	15 (37.5)
cN	
0	32 (80.0)
1	8 (20.0)
2abc	0 (0.0)
cStage	
1	12 (30.0)
2	10 (25.0)
3	3 (7.5)
4	15 (37.5)
pT¹	
1	21 (53.8)
2	11 (28.2)
3	3 (7.7)
4	4 (10.3)
pN¹	
0	23 (59.0)
1	6 (15.4)
2	10 (25.6)
pStage¹	
1	13 (33.3)
2	7 (17.9)
3	5 (12.8)
4	14 (35.9)
Tumour grade²	
Well-defined	6 (15.8)
Moderately defined	26 (68.4)
Poorly defined	6 (15.8)
Neck dissection	
Close follow-up	4 (10.0)
SOHND	8 (20.0)
SOHND+IV	8 (20.0)
MRND	17 (42.5)
Bilateral	3 (7.5)

¹One patient missing. Information not included in pathology report. ²Two patients missing. Information not included in pathology report. MRND, modified radical neck dissection; SOHND, suparomohyoid neck dissection.

Of the 11 patients in whom malignant disease returned (*i.e.* those with DFS events), 5 had a cervical node recurrence, 1 had a tumour site recurrence, 1 had distant metastases and 1 had local, cervical and distant recurrences. Three patients developed second primaries of the upper aerodigestive tract, of which two were in the tongue and one was in the oesophagus. 9 out of the 11 DFS events occurred prior to 24 months after tumour dissection. In the DFS event group, the median T_V was 9.8 cm³ (Q1 1.2 cm³, Q3 29.6 cm³) whereas in the censored group the median T_V was 2.3 cm³ (Q1 0.0 cm³, Q3 6.2 cm³). When grouped using a cut-off

Table 2. Comparison of clinical T (cT) and pathological T (pT) classification parameters for the study population

	pT1	pT2	pT3	pT4	Total
cT1	11	0	0	0	11
cT2	7	3	0	0	10
cT3	1	0	1	1	3
cT4	2	8	2	3	15
Total	21	11	3	4	39 ¹

¹One patient missing. Information not included in pathology report.

value of 8.0 cm³, T_V was found to be a predictor of DFS (χ^2 (1) = 5.6, p = 0.02). DFS was predicted by cN (χ^2 (1) = 11.9, p = 0.001) but not by cT (χ^2 (1) = 4.8, p = 0.19), cStage (χ^2 (1) = 4.8, p = 0.18) or tumour grade (χ^2 (1) = 0.51, p = 0.78). The DFS results are summarised in Tables 3 and 4. A Kaplan–Meier plot is shown in Figure 2b.

Cervical lymph node metastasis

10 of 32 patients classified as cN0 had metastatic SCC on pathological examination. The negative and positive OM groups had median T_V of 1.0 cm³ (Q1 0.0 cm³, Q3 4.7 cm³) and 3.7 cm³ (Q1 1.9 cm³, Q3 5.6 cm³), respectively. When dichotomised using a 3.0 cm³ cut-off, T_V was a significant predictor of OM (p = 0.02, one-sided Fisher's exact test). The median T_T of the negative and positive OM groups were 5.5 mm (Q1 0.0 mm, Q3 12.0 mm) and 13.0 mm (Q1 8.5 mm, Q3 15.0 mm), respectively. T_T did not predict OM at any cut-off value. The relationship between cT and OM was significant (p = 0.05, Fisher's exact test) whereas the relationship between pT and OM was not (p = 0.38, Fisher's exact test). No other significant relationships were found. The OM results are summarised in Tables 4 and 5.

Discussion

The prognostic value of TNM staging of oral malignancy has been called into question by numerous authors [4–7]. In our study, the cT predicted pT in only

46.2% of cases. Despite this, cT was found to predict OM and DRS, but not DFS. The fact that pT, the gold standard, did not predict OM or survival shows that the problem goes beyond clinical accuracy. The fundamental flaw in the use of pT as a predictor of prognosis is not our inability to make accurate clinical and pathological measurements but rather the fact that visible diameter is a poor indicator of tumour growth patterns. Tumours of the oral cavity are 3D lesions. Lesions covering large surface areas of the oral cavity may be superficial or, conversely, lesions of limited surface diameter may penetrate deeply into the oral tissue. These differences in dimensions are of vital importance to surgical management and call for a more representative system of T classification.

There is a growing body of evidence to show that T_D and T_T are more robust indicators of OM and survival [8]. T_D and T_T are thought to reflect tumour aggression and increased lymphatic invasion, as well as the ease of surgical resection and attainment of clear margins. Unfortunately, disagreement amongst investigators as to the cut-off value has prevented the development of a thickness-based staging system. Some studies suggest single values ranging from 2–10 mm [8], whereas others have suggested a dual cut-off approach, for example at 3 mm and 9 mm [13]. T_D and T_T remain one dimensional measurements, and are subject criticisms similar to those aimed at surface diameter. In addition, several studies have concluded that T_D and T_T are of no value for predicting OM [14–16] or survival [16–19]. Further, the majority of studies have relied on the use of post-operative resected specimens. Thus, T_D and T_T are of questionable value in a staging system that must be valid during the pre-treatment phase of management.

MRI is a valuable adjunct to the pre-operative staging of oral cancers. Iwai et al [20] have shown that MRI-measured T_T is a valid proxy for histopathological measurement. However, limited spatial resolution makes the measurement of distances of less than 3–4 mm impractical. Lesions with dimensions of less than 3–4 mm were subsequently given a T_T value of 0.0 mm and a T_V value of 0.0 cm³ by Iwai et al [20]. This led to a bimodal distribution of volume and thickness values that was not amenable to statistical transformation. Classification

Table 3. Summary of the results of 2 year DFS and DRS studies using the 8.0 cm³ and 6.0 mm cut-offs

	Events	Censored	Mean survival (95 % CI) (in months)	HR (95% CI)	p-value
2 year DRS					
Volume					
<8.0 cm ³	2	28	22.7 (21.0–24.0)	7.3 (1.4–37.6)	0.01
≥8.0 cm ³	5	5	17.7 (13.8–21.7)		
Thickness					
<6.0 mm	1	13	22.6 (19.8–25.3)	2.9 (0.3–23.9)	0.31
≥6.0 mm	6	20	20.7 (18.3–23.0)		
2 year DFS					
Volume					
<8.0 cm ³	4	26	21.6 (19.4–23.8)	4.3 (1.2–16.1)	0.02
≥8.0 cm ³	5	5	15.7 (10.4–21.0)		
Thickness					
<6.0 mm	3	11	20.2 (16.3–24.0)	1.0 (0.3–4.2)	0.95
≥6.0 mm	6	20	20.0 (17.1–22.8)		

HR, hazard ratio.

Table 4. Tested cut-off values for tumour volume and tumour thickness with associated *p*-values and effect sizes. *p*-values of less than 0.05 were considered significant (*)

Cut-off	OM		DRS		DFS	
	P	OR	p	HR	P	HR
Volume						
2.0 cm ³	0.04*	5.3	0.10	5.0	0.38	1.8
3.0 cm ³	0.02*	6.7	0.07	5.6	0.29	2.1
4.0 cm ³	0.20	2.7	0.11	3.5	0.31	1.9
5.0 cm ³	0.20	2.7	0.11	3.5	0.31	1.9
6.0 cm ³	0.54	0.7	0.07	4.1	0.18	2.4
7.0 cm ³	0.36	0.9	0.04*	4.7	0.12	2.7
8.0 cm ³	0.43	2.1	0.01*	7.3	0.02*	4.3
Thickness						
2.0 mm	0.23	2.8	0.14	30.8	0.29	2.9
3.0 mm	0.16	3.8	0.12	32.4	0.22	3.4
4.0 mm	0.10	4.1	0.09	34.7	0.56	1.6
5.0 mm	0.07	5.0	0.07	37.3	0.45	1.8
6.0 mm	0.07	5.0	0.31	2.9	0.95	1.0
7.0 mm	0.07	5.0	0.31	2.9	0.95	1.0
8.0 mm	0.07	5.0	0.31	2.9	0.95	1.0

DFS, disease-free survival; DRS, disease-related survival; HR, hazard ratio; OM, occult metastasis; OR, odds ratio.

into low-risk and high-risk groups was necessary to overcome this limitation in the gathered data. Intraoral ultrasound by skilled operators is capable of measuring the dimensions of superficial lesions and may be useful in discriminating lesions that are invisible on MRI.

Only one study has examined the predictive value of MRI T_T, finding a significant cut-off at 6.0 mm for OM when T4 tumours were excluded [20]. The present study included T4 tumours and was limited to the oral and oropharyngeal tongue, making a direct comparison of the two studies difficult. It may be that our failure to find a significant T_T cut-off reflects this difference. As noted by Pentenero et al [8], sample heterogeneity is widespread in published studies concerning tumour thickness and tumour depth, and is a contributing factor to disagreement about suitable cut-off values.

T_V has been shown to be of prognostic value in head and neck malignancies [10, 11, 21–26]. Chong et al [27] recently validated a semi-automated method for measuring the T_V of lingual carcinomas on T₂ weighted MRI images. The same research group, in a retrospective study of 17 patients undergoing surgical resection with curative intent, used this technique to show that T_V is predictive of DFS and overall survival using a cut-off of 13.0 cm³ [28]. Yuen et al [13] evaluated T_V using postoperative histopathology specimens. Preda et al [12] measured T_V on MRI by measuring the maximum tumour extent in three orthogonal planes and calculating the volume assuming an elliptical shape. Neither group found T_V to be of significant predictive value.

We have shown that the MRI measured T_V is a significant predictor of 2 year DRS and DFS using a cut-off of 8.0 cm³. Our findings are consistent with those of Chew et al [28], although our cut-off value is smaller than theirs (8.0 cm³ vs 13.0 cm³). This may reflect our larger sample size (*n* = 40 vs *n* = 17), differing patient populations or the increased accuracy of manual T_V measurement over semi-automated segmentation.

Our study is the first of its kind to show a relationship between the MRI measured T_V of lingual SCC and OM, finding a significant cut-off of 3.0 cm³. We were not able to demonstrate a similar relationship between the T_T and OM, despite exploring a range of cut-off values. Our data disagree with that of Iwai et al [20] study in that they were able to find a significant cut-off value for T_T, however differences in the study populations make detailed comparison difficult. In the oral cancer pathology literature, it is generally agreed that T_D and, to a lesser extent, T_T are useful predictors of OM and survival. The present study indicates that this may not be the case for MRI measured T_T, although it must be emphasised that direct comparison of MRI-based and pathology-based tumour measurements is impossible because of fundamental differences in methodology.

30% of cN0 patients had nodal metastases on histopathology of neck dissection specimens. This is

Figure 2. Kaplan–Meier curves of 2 year (a) disease-related and (b) disease-free survival using the 8.0 cm³ cut-off. Statistical

Table 5. Results demonstrating the relationship between tumour volume or depth and occult metastasis

	N+	N–	Sensitivity (95% CI)	Specificity (95% CI)	OR (95% CI)	p-value
Volume						
<3.0 cm ³	3	15	0.72 (0.39–0.93)	0.71 (0.48–0.88)	6.7 (1.3–34.0)	0.02
≥3.0 cm ³	8	6				
Depth						
<6.0 mm	3	11	0.82 (0.48–0.97)	0.52 (0.30–0.74)	2.9 (0.6–14.2)	0.07
≥6.0 mm	8	10				

OR, odds ratio.

consistent with published rates of OM, which range from 20%–40% [29]. T_V is able to stratify patients into groups at low- and high-risk of OM using the 3.0 cm³ cut-off (OR 6.7 [95% C.I. 1.3–34.0]). In the low-risk group, 15 patients (83%) would have correctly been spared neck dissection whereas 3 (17%) would have gone on to have a neck recurrence. In the head and neck literature, many authors report that elective neck dissection is appropriate if the risk of metastases is greater than 20% [30]. Although 17% may be a higher recurrence rate than many surgeons and patients are comfortable with, the risk can be further mitigated in this group with techniques for early detection of metastases, such as close follow-up with clinical exam and ultrasound or other surveillance imaging techniques.

6 patients (43%) in the high-risk group would have received unnecessary neck dissections, but the cut-off value of 3.0 cm³ was chosen to minimise false-negative classifications to the detriment of false-positive results. A multiple cut-off classification system would improve this situation; however the sample size available for this study was insufficient for exploration of this option.

Further, we have demonstrated that T_V is a predictor of DRS and DFS whereas T_T is not. The risks of disease-related death and recurrence were 7.3 and 4.3 times greater, respectively, when the T_V was greater than 8.0 cm³. Thus, T_V measurement has the potential to yield more information to guide surgical management.

This study has several shortcomings. First, when T_2 weighted images are used tumours appear as high signal intensity relative to the surrounding muscle. This area of high signal intensity on the MRI is, however, a composite of the tumour and peritumoural oedema of identical signal intensity. In a study comparing T_2 weighted MRI and histology, T_T measurements were consistently found to be larger on MRI than on histology [12]. Second, the MRI study parameters were inconsistent, reflecting the retrospective nature of the study. However, this inconsistency reflects normal patient-to-patient and institution-to-institution variability and lends validity to our results. Nonetheless, there is a need for standardisation in future studies. Finally, MRI T_V measurement is a time-intensive activity although the throughput can be enhanced by the use of semi-automation, as demonstrated by Chong et al [27].

The 2-year follow-up period used in this study was relatively short. The majority of disease progression events and disease-related deaths are, however, expected early in oral cavity SCC. Stell et al [31] found that the median time to recurrence was 24 weeks (95% CI 19–28 weeks) for oral cancer and 32 weeks (95% CI 23–41 weeks) for oropharyngeal cancer.

One case was designated an outlier and excluded from our analysis. It was agreed that this case represented an unusually advanced case of oral cavity SCC, perhaps beyond the limits of resection. In this case, the patient was young and a decision was made to adopt an aggressive approach for surgical cure. The implication of the exclusion of this outlier is that we cannot draw any conclusions about the prognostic value of tumour volume for cases of extensive local disease. Failure to exclude such an unusual case would, however, have affected our ability to draw conclusions from the remaining sample.

The sample size of this study was small, only 40 cases. As a result, its statistical power was small and the possibility remains that we were unable to detect clinically significant differences in OM and survival as a result. For the same reason, a multifactor analysis was not feasible. Multifactor analysis is important for evaluating the usefulness of T_V compared with other important prognostic factors. Tumour measurements were carried out by a single observer only, making assessment of interobserver variability impossible. If interobserver variability is substantial, this could impact generalisability and limit the usefulness of T_V as a prognostic factor.

Conclusion

Our work has demonstrated that statistically significant relationships exist between MRI measured T_V and OM and survival, using cut-off values of 3.0 cm³ and 8.0 cm³, respectively. T_T is not a significant predictor of OM or survival.

T_V shows promise as a novel staging parameter. As T_V can be measured on MRI prior to surgical intervention, it is suitable for incorporation into a decision algorithm concerning the management of the clinically lymph-node-negative neck. Similarly, T_V can provide prognostic information, allowing the surgeon and the patient to make an informed clinical decision.

This pilot study demonstrates the need for a multi-institutional, prospective evaluation of T_V and its usefulness as a prognostic factor in the surgical management of lingual SCC. The impact of interobserver variability must also be addressed.

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