

ORIGINAL ARTICLE

RELIABILITY OF MRI IN MEASURING TONGUE TUMOUR THICKNESS:
A 1.5T STUDY

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Background: Tongue tumour thickness has been shown to have a correlation with neck nodal metastasis and hence patient survival. Current AJCC guidelines recommend inclusion of tongue tumour thickness measurement in routine radiologic staging. Several studies have attempted to define the accuracy of MRI in measuring tongue tumour thickness. The aim of our study was to compare tongue tumour thickness measured at T2-weighted and STIR sequences with histologic tongue tumour thickness. **Methods:** Twenty-eight consecutive patients of tongue cancer who had undergone glossectomy were selected retrospectively. Tumours were measured in both STIR axial and T2-weighted coronal images and compared with histologic tumour thickness on resected specimens. Pearson's analysis was performed to determine the degree of correlation. Paired samples t-test was also used for comparison of mean tumour thicknesses measured on MRI with mean histologic tumour thickness. **Results:** Pearson correlation analysis showed good correlation of tumour thickness measured on MRI with actual histologic tumour thickness ($R=0.876$). **Conclusion:** MRI provides a satisfactory prediction of tongue tumour thickness which in turn can be used to determine the need for elective neck dissection in these patients.

Keywords: Lymphatic Metastasis, Magnetic Resonance Imaging/methods, Tongue Neoplasms

INTRODUCTION

Nodal metastasis from tongue cancer is considered the most important prognostic factor¹⁻⁴ in determining patient survival. Therefore, determining nodal status accurately is an important pre-treatment staging goal. Imaging, however, has not been very reliable in this regard, in particular for early stage T1 and T2 tongue cancers, in which the incidence of occult nodal metastasis has been reported in up to 44% of the cases.^{5,6} Current management strategies advocate elective neck dissection in T2/T3/T4 and clinically No tumours, whereas the issue of elective neck dissection for T1 cN0 is still being investigated.⁷⁻⁹

Owing to superior soft-tissue contrast capability, MRI is the imaging modality of choice in local assessment of head and neck malignancies, including tongue cancer.¹⁰⁻¹² Using depth of tumour invasion measured at MRI, several researchers have attempted to predict the likelihood of nodal metastasis.^{1,13-15} For example, Okura *et al* have proposed a cut-off value of >9.7 mm tumour thickness for a decision to perform elective neck dissection.¹⁴

In our study, we correlated tongue tumour thickness measured at 1.5T MRI, using T2 weighted and STIR sequences with histologic tumour thickness following glossectomy. To the best of our knowledge, no comparison has been made with

histologic tumour thickness utilising STIR sequences in the past.

MATERIAL AND METHODS

We retrospectively reviewed hospital records for patients who had undergone resection of tongue cancer in our institution since 2008. Patients who had received neo adjuvant chemotherapy (T3 disease, tumour crossing midline) were not included in order to avoid overestimation of tumour thickness resulting from treatment-related change. T4-status tumours were excluded as these were inoperable. We also excluded patients in whom the gap between MR imaging and surgery exceeded 6 weeks.

MR imaging was performed with a 1.5T scanner (GE Healthcare, Wisconsin, USA). Sequences obtained were: T2 Coronal (3000/98/1), STIR Axial (5000/60/1). The slice thickness for T2 weighted and STIR sequences was 4 mm and 8 mm respectively. To avoid bias, both the Neuro-radiologist and the histopathologist were blinded from each other's results. We established a uniform protocol for radiological as well as histopathological recording: a horizontal line was drawn joining the tumour-mucosa junction at both ends of the tumour (referred to as 'reference line'), from which a perpendicular was drawn at the point of maximum tumour thickness. This was considered to represent tumour depth. For exophytic masses, an additional line was drawn in the opposite direction from the reference line and both measurements were added

(i.e., tumour depth + exophytic component) to give the total tumour thickness (Figure-1).

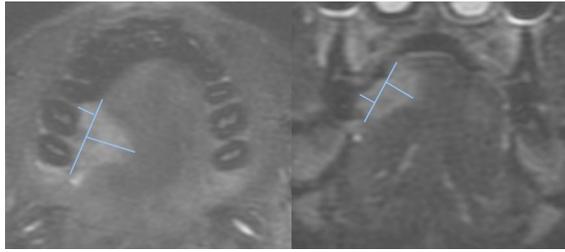


Figure-1: Measurement of an exophytic mass arising from the right lateral border of the tongue.

The reference line has been drawn along the projected mucosal-line, from which two perpendiculars in opposite directions give invasive and exophytic tumour components, adding up to give the total tumour thickness

For histologic measurement, the reference line was established using the epithelial basement membrane, from which perpendicular measurements were performed to the deepest point of invasion as with MR imaging. In heavily keratinized lesions, we measured from the surface of tumour exclusive of the keratin layer. In case of ulcerated lesion, we took the reference line as the arbitrary measure of tumour surface.

Data was analysed using SPSS-17 and correlation between tongue tumour thickness on histology and MRI was performed using Pearson's correlation. A one-tailed *p*-value of <0.05 was considered the reference standard for statistical significance.

RESULTS

Out of 33 initial patients, 4 were excluded because of unavailability of histology slides. One more patient was excluded because the tumour was not visible on any imaging sequence in that case. Of the final 28 patients, T2 weighted imaging failed to demonstrate tumour in 18 in whom measurement was done solely on STIR imaging.

The mean age was 50 years (19–79), with male-to-female ratio of 18:10. All patients were either T1 or T2 stage disease. Histologic tumour thickness ranged from 4mm to 16mm (mean 8.54mm). Results for neck dissection were available for 20 cases, and showed nodal metastasis in 9 patients. Scatterplots (Figure-2) show the degree of concordance between radiologic and histologic tumour thickness.

Pearson correlation analysis demonstrated a positive correlation between histologic tumour thickness and MR-measured tumour thickness (Table-1)

Mean MRI thicknesses were greater than histologic thickness for T2 weighted images and were less for STIR sequences with a difference of mean of 0.36 and -1.2 respectively. However, the results did not reach statistical significance for T2 weighted sequence.

Table-1: Results from Pearson correlation analysis between MRI measured and actual histologic tumour thickness

	STIR (Axial)	T2 (Coronal)
R-value (Pearson)	0.710	0.876
<i>p</i> -value (2-tailed)	<0.001	0.001

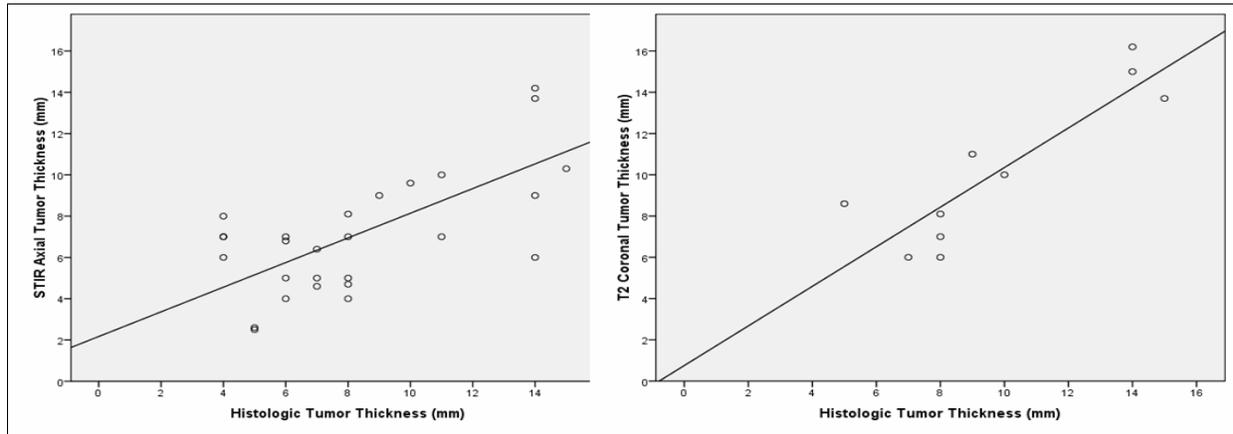


Figure-2: Graphical representation of degree of concordance between histologic tumour thickness and STIR axial (left) and T2 weighted coronal (right) sequences. The best-fit line shows better concordance for T2 weighted coronal sequence, as compared with STIR axial. R=0.71 (STIR axial) and 0.876 (T2 coronal)

DISCUSSION

Several studies in the past have highlighted the unreliability of T-staging of head and neck malignancies to predict lymph node metastases or survival.¹⁶⁻²² In contrast, it has been shown repeatedly that tumour thickness has a closer correlation with lymph node

metastases in such patients.¹⁶⁻²⁶ This is based on the premise that with deeper local invasion, tumour proliferation may come close to deep blood vessels and lymphatics which would then carry tumour emboli to the local lymph nodes. Moreover, it has been observed that it is more difficult for tumour emboli to form in the

small-calibre lymphatics of superficial areas than in the wider lymphatics of deeper tissue.^{1,27}

Numerous investigators have attempted to define a relationship, and in particular, a cut-off point for oral cavity cancer thickness that correlates well with nodal spread. For example, Yuen *et al* have demonstrated a 44% incidence of nodal metastases for tumours having a thickness between 3mm and 9mm.⁴ In a relatively recent meta-analysis by Huang *et al.*, the authors conducted a literature review of all studies measuring the relationship of tumour thickness of oral cavity malignancies with lymph node metastases.²⁸ Their sample included 16 studies and a total of 1136 patients. In an attempt to resolve the discrepancy involving the differences in opinion about the degree of local disease at which elective neck dissection should be carried out, the authors proposed a unified cut-off of 4mm as a strong predictor of lymph node metastases based upon their pooled results. In general, a risk of >20% for nodal metastasis is considered a fair justification for elective cervical lymph node dissection^{7,29} and most of the studies have reported a significantly high risk of sub-clinical nodal metastases above the cut-off of 4 mm. These and similar studies have led to AJCC (7th edition) recommendation of reporting tumour thickness during oral cancer staging.⁷

In our study, we investigated the reliability MRI in assessing tongue tumour thickness as an in-vivo preoperative measure of tumour depth of invasion. We included STIR sequences in the measurement protocol as it has been shown to be a reasonable alternative to T1-weighted fat-suppressed contrast-enhanced sequences.³¹ We found a high degree of concordance for both studied sequences with histologic tumour thickness (R value of 0.87 and 0.71 for T2 coronal and STIR axial sequences respectively). This is in agreement with data in published literature where R values of 0.609–0.94 have been reported.^{13,15,32} It can be assumed that exam settings utilizing higher resolution, thinner slices on modern scanners could reach greater sensitivity and degree of concordance.³²

We found a greater degree of correlation between T2 sequences and histology than there was for STIR sequences, accountable for the thinner slices in T2 weighted sequences (4 mm), compared with STIR axial (8 mm). On the other contrary, tumour was undetectable on T2 imaging in a significant number of cases (n=18) (Figure-3) This was due to the fact that STIR, with its fat suppression allows visualisation of subtle signal intensity differences not otherwise appreciable.

When we look at the difference of means, we find that the T2 weighted sequences tended to overestimate actual tumour thickness. This overestimation has been reported previously.^{13,15} Counter intuitively however, mean tumour thickness measured on STIR sequences was less than histologic thickness.

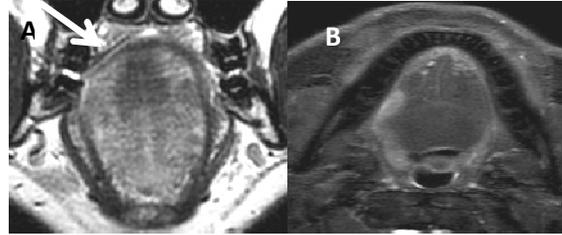


Figure-3: Tumour was not visible on T2 coronal images (A). The only clue to the presence of tumour is the disruption of black mucosal line on right lateral surface (arrow in A), with no clear demarcation from native tissue at a deeper level. The tumour is easily appreciable on STIR axial images (B).

The main drawback of our study was the relatively small sample size of 28 patients who met the inclusion criteria. Although, we reached statistical significance for comparison of MR-measured tumour thickness with histologic tumour thickness, we did not have enough cases to conclusively determine its relationship with nodal status.

We did not attempt to define a cut-off value the measured tumour thickness for two reasons. Firstly, the minimum measureable tumour thickness in our study was 4mm (n=4), which is already at the cut-off point proposed in literature for elective cervical.²⁸ Secondly, it has been suggested that assignment of cut-off values to continuous variables in such studies should have larger sample sizes.³⁶

CONCLUSION

Tongue tumour thickness can be measured reliably on MRI, and has a significant bearing on patient prognosis. Although relatively less precise, STIR sequences are more sensitive than T2-weighted sequences in detection of small tongue tumours. Future research should be directed at establishing cut-off values for MRI tumour thickness correlating with positive nodal disease, possibly with the inclusion of DWI/ADC values to differentiate between true tumour margin and oedema in a prospective study design.

REFERENCES

1. Pentenero M, Gandolfo S, Carrozzo M. Importance of tumor thickness and depth of invasion in nodal involvement and prognosis of oral squamous cell carcinoma: a review of the literature. *Head Neck* 2005;27:1080–91.
2. Yuen AP, Lam KY, Wei WI, Lam KY, Ho CM, Chow TL, *et al*. A comparison of the prognostic significance of tumor diameter, length, width, thickness, area, volume, and clinicopathological features of oral tongue carcinoma. *Am J Surg* 2000;180(2):139–43.
3. Bonnardot L, Bardet E, Steichen O, Cassagnau E, Piot B, Salam AP, *et al*. Prognostic factors for T1-T2 squamous cell carcinomas of the mobile tongue: A retrospective cohort study. *Head Neck* 2011;33:928–34.
4. Po Wing Yuen A, Lam KY, Lam LK, Ho CM, Wong A, Chow TL, *et al*. Prognostic factors of clinically stage I and II oral tongue carcinoma-A comparative study of stage, thickness, shape, growth

- pattern, invasive front malignancy grading, Martinez-Gimeno score, and pathologic features. *Head Neck* 2002;24:513–20.
5. Anzai Y, Brunberg JA, Lufkin RB. Imaging of nodal metastases in the head and neck. *J Magn Reson Imaging* 1997;7:774–83.
 6. Akoğlu E, Dutipek M, Bekiş R, Değirmenci B, Ada E, Güneri A. Assessment of cervical lymph node metastasis with different imaging methods in patients with head and neck squamous cell carcinoma. *J Otolaryngol* 2005;34:384–94.
 7. Brandwein-Gensler M, Smith RV. Prognostic indicators in head and neck oncology including the new 7th edition of the AJCC staging system. *Head Neck Pathol* 2010;4(1):53–61.
 8. Yuen AP-W, Ho CM, Chow TL, Tang LC, Cheung WY, Ng RW-M, *et al*. Prospective randomized study of selective neck dissection versus observation for N0 neck of early tongue carcinoma. *Head Neck* 2009;31:765–72.
 9. Edge S, American Joint Committee on Cancer. *AJCC cancer staging manual*. 7th ed. New York: Springer; 2010.
 10. Ross MR, Schomer DF, Chappell P, Enzmann DR. MR imaging of head and neck tumors: comparison of T1-weighted contrast-enhanced fat-suppressed images with conventional T2-weighted and fast spin-echo T2-weighted images. *Am J Roentgenol* 1994;163(1):173–78.
 11. Lufkin RB, Wortham DG, Dietrich RB, Hoover LA, Larsson SG, Kangaroo H, *et al*. Tongue and oropharynx: findings on MR imaging. *Radiology* 1986;161(1):69–75.
 12. Unger JM. The oral cavity and tongue: magnetic resonance imaging. *Radiology* 1985;155:151–53.
 13. Lam P, Au-Yeung KM, Cheng PW, Wei WI, Yuen AP-W, Trendell-Smith N, *et al*. Correlating MRI and histologic tumor thickness in the assessment of oral tongue cancer. *Am J Roentgenol* 2004;182(3):803–8.
 14. Okura M, Iida S, Aikawa T, Adachi T, Yoshimura N, Yamada T, *et al*. Tumor thickness and paralingual distance of coronal MR imaging predicts cervical node metastases in oral tongue carcinoma. *Am J Neuroradiol* 2008;29(1):45–50.
 15. Preda L, Chiesa F, Calabrese L, Latronico A, Bruschini R, Leon ME, *et al*. Relationship between histologic thickness of tongue carcinoma and thickness estimated from preoperative MRI. *Eur Radiol* 2006;16:2242–8.
 16. Byers RM, El-Naggar AK, Lee YY, Rao B, Fornage B, Terry NH, *et al*. Can we detect or predict the presence of occult nodal metastases in patients with squamous carcinoma of the oral tongue? *Head Neck* 1998;20(2):138–44.
 17. Brown B, Barnes L, Mazariegos J, Taylor F, Johnson J, Wagner RL. Prognostic factors in mobile tongue and floor of mouth carcinoma. *Cancer* 1989;64:1195–202.
 18. Asakage T, Yokose T, Mukai K, Tsugane S, Tsubono Y, Asai M, *et al*. Tumor thickness predicts cervical metastasis in patients with stage I/II carcinoma of the tongue. *Cancer* 1998;82:1443–8.
 19. O-charoenrat P, Pillai G, Patel S, Fisher C, Archer D, Eccles S, *et al*. Tumour thickness predicts cervical nodal metastases and survival in early oral tongue cancer. *Oral Oncol* 2003;39:386–90.
 20. Yamazaki H, Inoue T, Teshima T, Tanaka E, Koizumi M, Kagawa K, *et al*. Tongue cancer treated with brachytherapy: is thickness of tongue cancer a prognostic factor for regional control? *Anticancer Res* 1998;18:1261–5.
 21. Matsuura K, Hirokawa Y, Fujita M, Akagi Y, Ito K. Treatment results of stage I and II oral tongue cancer with interstitial brachytherapy: maximum tumor thickness is prognostic of nodal metastasis. *Int J Radiat Oncol Biol Phys* 1998;40:535–9.
 22. Fukano H, Matsuura H, Hasegawa Y, Nakamura S. Depth of invasion as a predictive factor for cervical lymph node metastasis in tongue carcinoma. *Head Neck* 1997;19:205–10.
 23. Spiro RH, Huvos AG, Wong GY, Spiro JD, Gnecco CA, Strong EW. Predictive value of tumor thickness in squamous carcinoma confined to the tongue and floor of the mouth. *Am J Surg* 1986;152:345–50.
 24. Moore C, Kuhns JG, Greenberg RA. Thickness as Prognostic Aid in Upper Aerodigestive Tract Cancer. *Arch Surg* 1986;121:1410–14.
 25. Woolgar JA, Scott J. Prediction of cervical lymph node metastasis in squamous cell carcinoma of the tongue/floor of mouth. *Head Neck* 1995;17:463–72.
 26. O'Brien CJ, Lauer CS, Fredricks S, Clifford AR, McNeil EB, Bagia JS, *et al*. Tumor thickness influences prognosis of T1 and T2 oral cavity cancer—but what thickness? *Head Neck* 2003;25:937–45.
 27. DiTroia JF. Nodal metastases and prognosis in carcinoma of the oral cavity. *Otolaryngol Clin North Am* 1972;5:333–42.
 28. Huang SH, Hwang D, Lockwood G, Goldstein DP, O'Sullivan B. Predictive value of tumor thickness for cervical lymph-node involvement in squamous cell carcinoma of the oral cavity: a meta-analysis of reported studies. *Cancer* 2009;115:1489–97.
 29. Weiss MH, Harrison LB, Isaacs RS. Use of decision analysis in planning a management strategy for the stage N0 neck. *Arch Otolaryngol Head Neck Surg* 1994;120:699–702.
 30. Morton RP, Ferguson CM, Lambie NK, Whitlock RM. Tumor thickness in early tongue cancer. *Arch Otolaryngol Head Neck Surg* 1994;120:717–20.
 31. Tokuda O, Harada Y, Matsunaga N. MRI of Soft-Tissue Tumors: Fast STIR Sequence as Substitute for T1-Weighted Fat-Suppressed Contrast-Enhanced Spin-Echo Sequence. *Am J Roentgenol* 2009;193:1607–14.
 32. Iwai H, Kyomoto R, Ha-Kawa SK, Lee S, Yamashita T. Magnetic resonance determination of tumor thickness as predictive factor of cervical metastasis in oral tongue carcinoma. *Laryngoscope* 2002;112:457–61.
 33. Wallwork BD, Anderson SR, Coman WB. Squamous cell carcinoma of the floor of the mouth: tumour thickness and the rate of cervical metastasis. *ANZ J Surg* 2007;77:761–4.
 34. Tetsumura A, Yoshino N, Amagasa T, Nagumo K, Okada N, Sasaki T. High-resolution magnetic resonance imaging of squamous cell carcinoma of the tongue: an in vitro study. *Dentomaxillofac Radiol* 2001;30(1):14–21.
 35. Ong CK, Chong VFH. Imaging of tongue carcinoma. *Cancer Imaging* 2006;6:186–93.
 36. Buettner P, Garbe C, Guggenmoos-Holzmann I. Problems in defining cutoff points of continuous prognostic factors: Example of tumor thickness in primary cutaneous melanoma. *J Clin Epidemiol* 1997;50:1201–10.

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