INTRODUCTION

Nodal metastasis from tongue cancer is considered the most important prognostic factor 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. 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.

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. Using depth of tumour invasion measured at MRI, several researchers have attempted to predict the likelihood of nodal metastasis. 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.

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 perpendicualrs 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

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<tr>
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<th>STIR (Axial)</th>
<th>T2 (Coronal)</th>
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<tbody>
<tr>
<td>R-value (Pearson)</td>
<td>0.710</td>
<td>0.876</td>
</tr>
<tr>
<td>p-value (2-tailed)</td>
<td>&lt;0.001</td>
<td>0.001</td>
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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. In contrast, it has been shown repeatedly that tumour thickness has a closer correlation with lymph node metastases in such patients. 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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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\textsuperscript{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 (7\textsuperscript{th} edition) recommendation of reporting tumour thickness during oral cancer staging.\textsuperscript{7}

In our study, we investigated the reliability of 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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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 signal 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.\textsuperscript{13,15} Counter intuitively however, mean tumour thickness measured on STIR sequences was less than histologic thickness.

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 measure able tumour thickness in our study was 4mm (n=4), which is already at the cut-off point proposed in literature for elective cervical.\textsuperscript{28} Secondly, it has been suggested that assignment of cut-off values to continuous variables in such studies should have larger sample sizes.\textsuperscript{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


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).

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