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ORIGINAL ARTICLE

Standard MRI sequence for imaging and methods of calculation of depth of invasion in squamous cell cancers of Tongue

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Abstract

Aim: To establish a standard MRI sequence for imaging of squamous cell cancers (SCC) of tongue and to evaluate various methods of calculation of depth of invasion in SCC of Tongue.

Background: Magnetic resonance imaging (MRI) is the best modality of imaging for tongue cancers. DOI is added to the staging of oral cavity squamous cell cancers by TNM AJCC Cancer Staging.

Materials and Methods: Visual rating: 1 - poor; 2 - acceptable; 3 - good; 4 – excellent, for the assessment of MRI sequences. Four protocols for the measurement of MRI derived DOI : axial reconstructed thickness, axial invasive portion, coronal invasive portion, and optimal method selection. Study design: Prospective study. Sample size: 50n.

Conclusion: This study shows that tongue masses are best evaluated on contrast enhanced scans, but STIR images in non-contrast studies provide near comparable results in delineation of the lesion. Maximum correlation was observed when the DOI was measured when a radiologist, on individual basis, selected the optimal plane among axial, saggital and coronal planes, and chose an optimal method among the invasive portion calculation method or reconstructed thickness calculation method to determine the DOI.

Keywords: DOI, Tongue, Carcinoma, Tumour, MRI, depth

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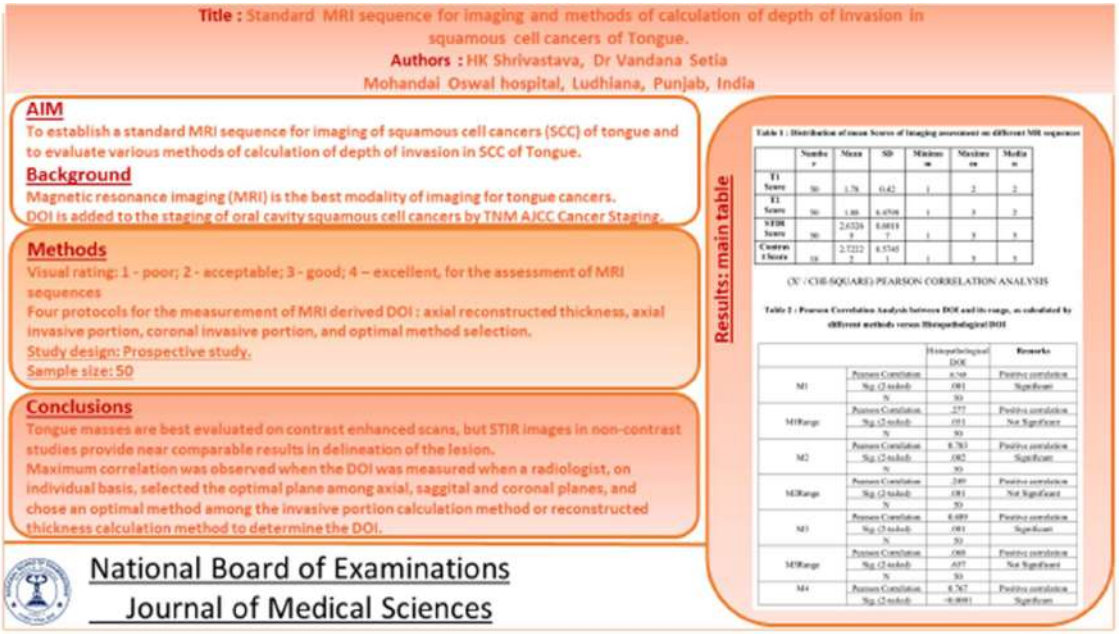
Graphical Abstract



Introduction

In the Indian subcontinent, oral cavity SCC are a major health problem. They are amongst the top three cancers in the country [1]. Risk increases with practices such as tobacco chewing, betel's quid, etc. prevalent in the low-income groups. Delay of detection of oral cancer among these individuals occurs from insufficient exposure to new diagnostic aid [2]. Oral precancerous lesions and pathologies like leukoplakia and submucous fibrosis can also transform to oral cancer [3].

The most common oral cavity site for squamous cell carcinoma (SCC) is tongue. Tongue SCC are one of the most aggressive tumors. Usual subsite of involvement is the lateral border of tongue involving the under surface [4]. Usual location of the tumors situated dorsally in the tongue is near the midline but are uncommon. Invasion of the floor of the mouth is more seen in tumors epi-centered in the anterior third of the oral tongue [5]. The musculature of the tongue as well as the lateral portions of the floor of mouth are usually infiltrated by the carcinomas involving middle-third of tongue. The posterior third lesions also infiltrate the musculature of the tongue and the floor of mouth but they may also involve mandible, base of tongue, anterior tonsillar pillar and glosso-tonsillar sulcus [6].

Surgery is mainstay of treatment of SCC tongue. Adjuvant treatment plan may consist of radiotherapy / concurrent chemo-radiotherapy which depends on various histopathological features like tumour size, lymph node positivity, depth of invasion (DOI) perineural invasion (PNI), resection margin status, etc. Carcinoma tongue patients may suffer from recurrence at primary tumor site or in the neck if not properly evaluated preoperatively [7].

Depth of invasion (DOI) is a characteristic that has been recently added to the staging of oral cavity squamous cell

cancers by the TNM AJCC Cancer Staging, Eighth Edition. DOI of tongue carcinoma is the perpendicular distance of the deepest point of tumor from the level of basement membrane of the nearest intact squamous mucosa.

Positive resection margin has a poor prognosis [8]. According to the NCCN guidelines, the tongue cancer resected margins should be ≥ 5mm [9]. Nearly 35% of patients present with metastatic lymphadenopathy [10]. Among these, submandibular and jugulodigastric nodes are the first echelon involved nodes. Bilateral lymph node involvement is seen in 5% of patients [11]. The overall occult metastatic rate in clinically N0 neck is approximately 30% [12].

Magnetic resonance imaging (MRI) has become the best modality of imaging in detection and evaluation of tongue cancers. The basis of this diagnostic technique relies on variation of hydrogen spin density, longitudinal relaxation time (T1), and transverse relaxation time (T2) of investigated tissues. High sensitivity and specificity can be achieved in lesion detection with contrast enhanced MRI, short tau inversion recovery (STIR) images (fat suppressed). While diagnosing a tongue lesion, T1 weighted (T1W) images provide fine anatomical details and fat suppressed enhanced scans provide good contrast between the normal portion of the tongue and the tumor [13].

MRI can accurately measure DOI and size of tumor, and can detect perineural invasion (PNI) and neck lymph nodes [14]. Some clinical studies that correlate the likelihood of cervical nodal metastasis with DOI have been performed. According to these studies, DOI is the single most important factor predicting the lymph node metastasis. While there have been various studies where MRI has been used to predict DOI in tongue SCC, most had some limitations like retrospective study design, small sample size, and exclusion of superficial lesions [15]. The rationale behind conducting the study is to compare and co-relate the accuracy of DOI in tongue squamous cell cancers on MRI and histopathology.

The current study was conducted in Radiology Department of a tertiary care hospital in northern part of India over a span of 1.5-year period between December 2020 and May 2022. Protocol of the study was pre-approved by the institutional ethics committee (IEC) before subjects were recruited; this is done in line with Second Declaration of Helsinki wherein the ethical principles for human investigation are laid. Before their enrollment in this study, from all patients, a written informed consent was obtained (IEC – IEC, Mohandai Oswal Hospital; IEC Approval Reference Number- IEC/MOH/2020-03; IEC Approval Date: 10/12/2020) (Figures 1 to 6).

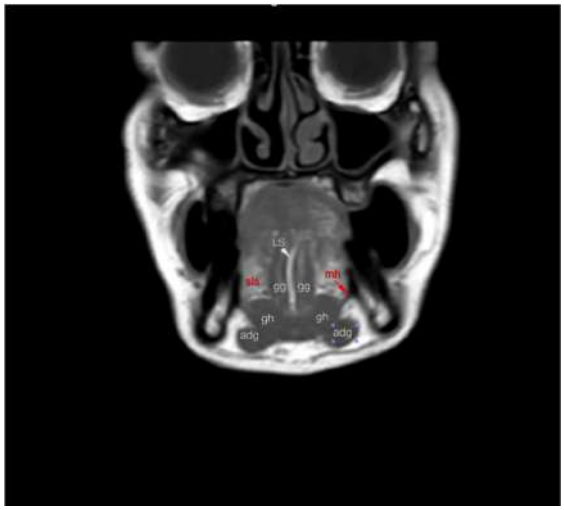


Figure 1. Anatomy: Coronal T1W MRI shows genioglossus (gg) muscles delineated as vertical pillar-like para-midline structures. The geniohyoid (gh) muscles appear subtly wider than and below the genioglossus muscles. The sublingual spaces (sls) and lingual septum (LS) show high signal intensity on T1W images. Mylohyoid (mh) separates oral cavity from the floor of mouth which contains the anterior belly of Digastric (Adg) muscles.

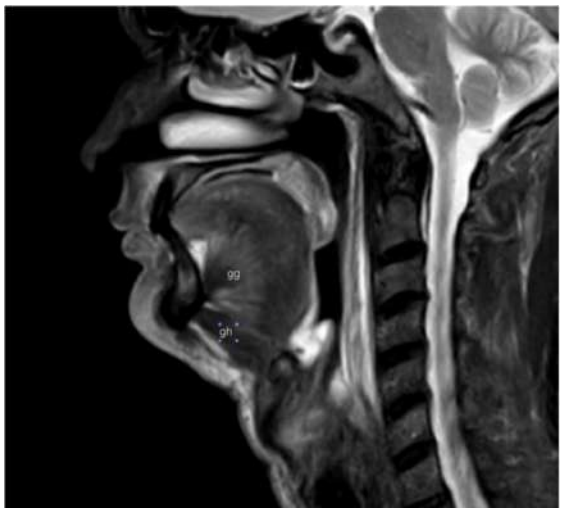


Figure 2 Anatomy: Sagittal T2-weighted MR image demonstrates dark-hypointense geniohyoid muscles (gh) from genial tubercle to hyoid and the fan-shaped genioglossus muscles (gg).

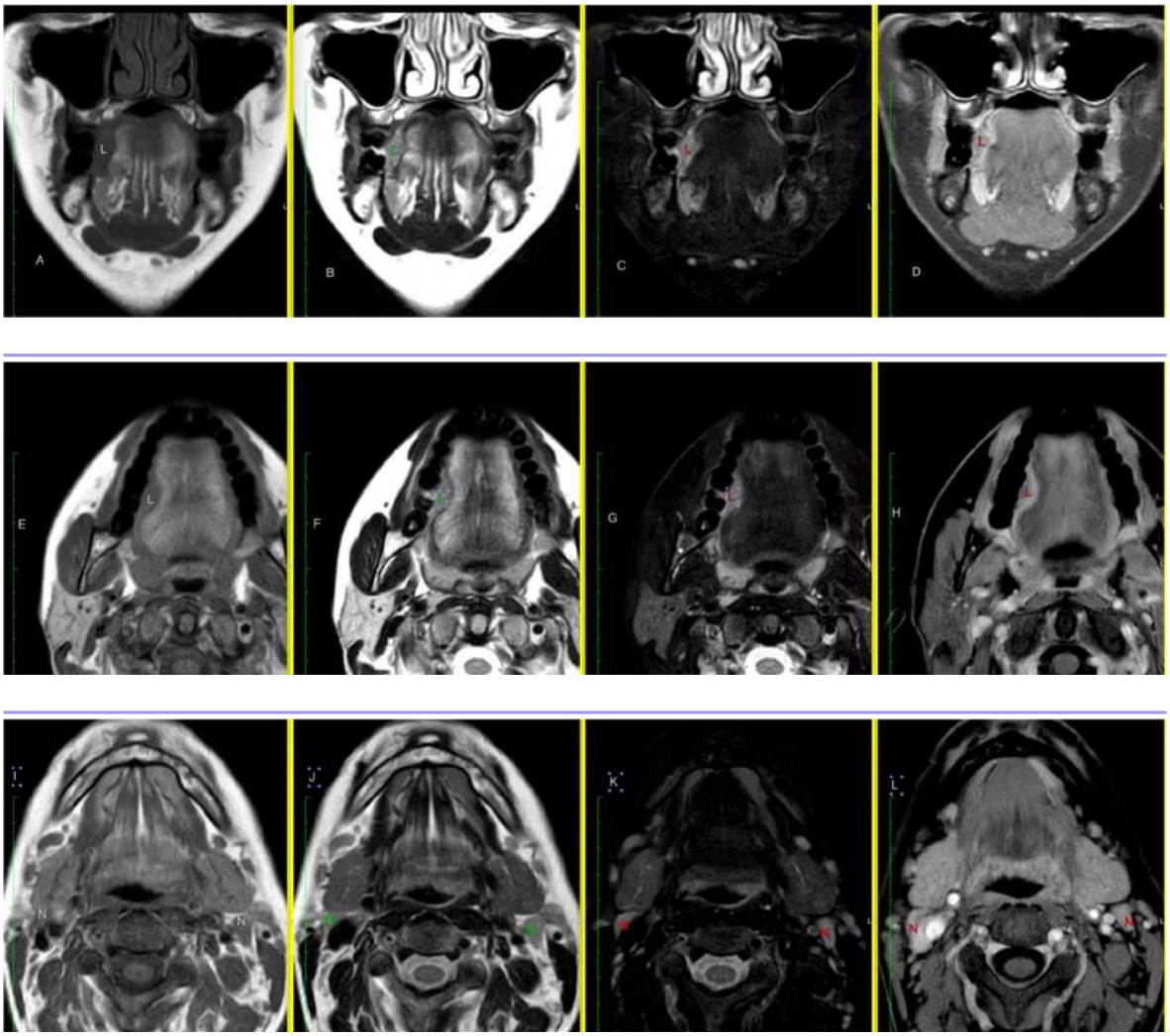


Figure 3. Pathology: **A** T1W Coronal **B** T2W Coronal **C** STIR Coronal **D**- Contrast T1W Coronal **E** T1W Axial **F** T2W Axial **G** STIR Axial **H** Contrast T1W Axial **I** T1W Axial **J** T2W Axial **K** STIR Axial **L** Contrast T1W Axial

A uniformly enhancing mass lesion (marked L in subsets A-H of figure 3), hyperintense on T2W sequence, is seen in the right anterolateral portion of tongue, beginning 2 cm posterior to the tip & extending over an AP span of 2 cm. Craniocaudally it measures 2 cm.
A mildly enlarged node(N) (10 mm in short axis) in the ipsilateral level II location & a mildly enlarged node(N) (12 mm in short axis) are seen in the contralateral (left) level II location.
The depth of invasion measured by MRI was 6.3mm by method 1, 6.2mm by method 2 and 4.8 mm by method 3. On histopathology it has a depth of invasion of 5 mm. 30 lymph nodes were evaluated, none was metastatic (0/30).

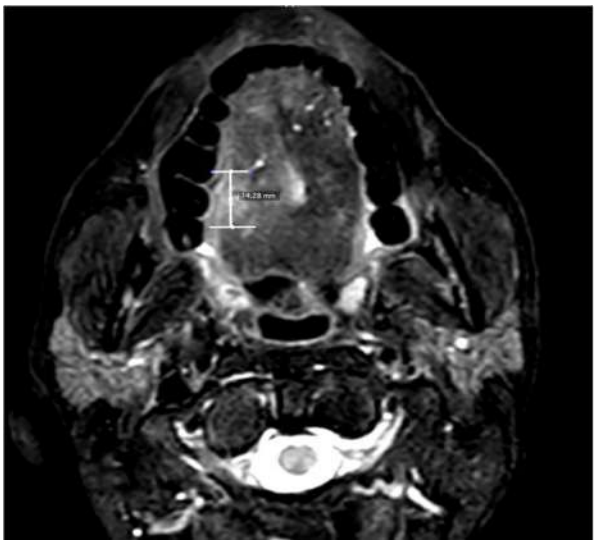


Figure 4. STIR Axial: Size in anteroposterior (AP) dimension: The length of a lengthiest vertical line separating two parallel horizontal lines drawn anteriorly and posteriorly along the tumor-mucosal junction.

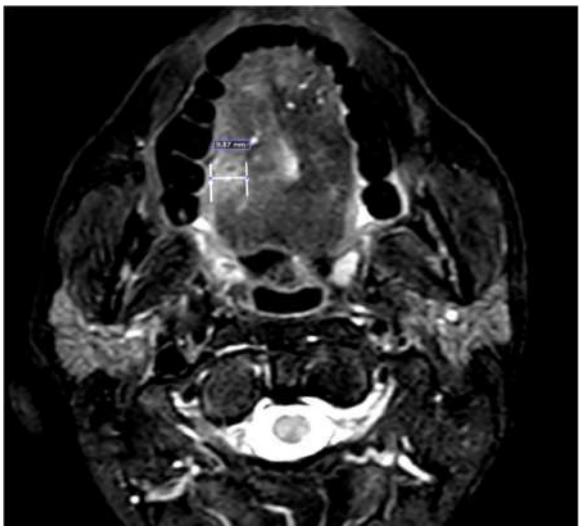


Figure 5. STIR Axial: Size in transverse (Tr) dimension. The length of a lengthiest horizontal line separating two parallel vertical lines drawn laterally from the lateral aspect of the tumor, and medially along the tumor-mucosal junction.

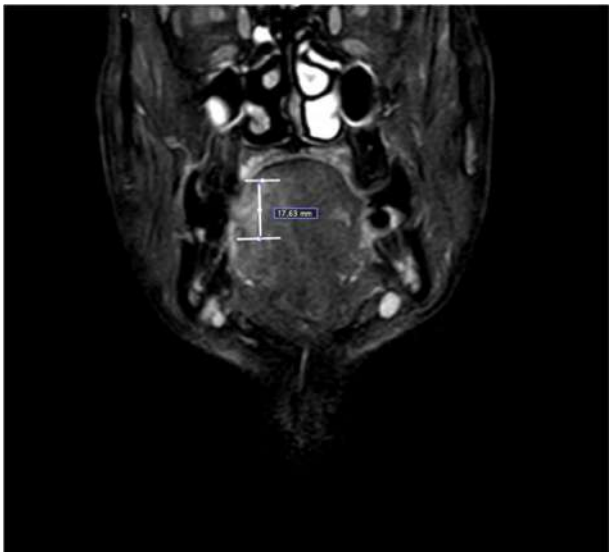


Figure 6. Contrast T1W Coronal: Size of the craniocaudal (CC) dimension: The length of a lengthiest horizontal line separating two parallel horizontal lines drawn superiorly from the superior aspect of the tumor, and inferiorly along the tumor-mucosal junction.

Aim

To establish a standard MRI sequence for imaging of squamous cell cancers (SCC) of tongue and to evaluate various methods of calculation of depth of invasion in SCC of Tongue.

Materials and Methods

Hypothesis: There is no difference between DOI calculated by MRI & histopathological report in SCC of tongue.

Study area: The study shall be conducted in the Department of Radio-diagnosis, Mohandai Oswal hospital, Ludhiana

Study design: It was a Prospective study.

Study duration: 1.5 year time period

Study population: This study was conducted on the patients of either sex eligible for the study during the study duration on the basis of clinical suspicion.

Sample size determination: Assumption of 90% power and 1% significance level (significant at 99% confidence level) was considered for calculating the sample size. In the reference study *(Correlation between clinical and MRI assessment of depth of invasion in oral tongue squamous cell carcinoma),* the correlation between measurements of DOI was 0.64 with a 95 % C.I. between 0.43 - 0.84 ($p < 0.001$). If we consider 99% accuracy and true relative error for experimental subjects is 10% along with 0.8 effect size, it was estimated that at least 30 experimental subjects needed for the study. Sample Size Formula = $N = [(Z\alpha+Z\beta)/C]2 + 3$ Where $C = 0.5 * \ln[(1+r)/(1-r)] = 0.758$ at $r=0.64$. The standard normal deviate for $\alpha = Z\alpha = 2.58$ The standard normal deviate for $\beta = Z\beta = 1.28$ $\alpha = 0.05$ (i.e. Confidence level = 95%) By 18 months, 50 patients were included in the study.

Inclusion criteria:

- History of no previous malignancies.

- A measurable tumor must be present on pretreatment MRI done within 1 month before surgery.
- Histo-pathological data on the surgical specimens should be available.
- No previous pre-operative chemo-therapy or radio-therapy.

Exclusion criteria:

- Allergic reaction to contrast agent
- Pre-existing nephrogenic systemic fibrosis
- Estimated Glomerular filtration rate less than 30 mL/min/1.73m^2
- Referral-in with a MRI scan that was already reviewed by the surgeon prior to the clinical exam and enrolment in the study
- Only CT imaging.
- Carcinoma in situ or a previous incisional or excisional biopsy
- Previous head and neck radiation or chemoradiation

Data collection methods:

Patients who had to undergo MRI for tongue cancer were included in this study. A 1.5-T imaging MRI (Phillips achieva or Phillips ambition) was used to undertake the MRI examinations. The imaging parameters were as follows: 4.6/2.2; flip angle - 10°; Field of view (FOV) - 34 × 34 cm; matrix - 320 × 320; section thickness - 2 mm; and acquisition time - 180 seconds. T1W, T2W, STIR and Contrast T1W sequences and some additional MRI sequences were obtained as per requirement. Gadotrast (gadoteric acid 279.32mg meglumine 97.60mg) (amount - 0.01 mmol/kg, rate -2 ml/s) was used for contrast imaging followed by saline flush (20ml, 2 ml/s). Dynamic contrast enhanced images were obtained at minutes one, two, and six after contrast material injection.

Image Interpretation:

Radiologist was blinded from the pathological information. He used a visual rating: 1 - poor; 2 - acceptable; 3 - good; 4 – excellent, for the assessment of MRI sequences in delineation of tumor. Adjustment of the grayscale, window width, and zoom factor were allowed for optimized interpretation of images.

Four protocols were utilized for the measurement of MRI derived DOI -

In method 1, the axial reconstructed thickness, the difference between (A) the distance between the lingual septum and the surface on the unaffected side and (B) the distance between the septum and the point of deepest invasion on a horizontal line is measured on axial images.

In method 2, the axial invasive portion, junctions of the tumor and the normal mucosa on both sides were connected by a reference line. The length of the line perpendicular to reference line connecting reference line with the deepest point of tumor invasion is measured on axial MRI while ignoring the protruding portion.

In method 3, the coronal invasive portion, the invasive portion was measured on coronal MRI just as method 2 while ignoring the protruding portion.

In method 4, optimal method selection, when a radiologist, on individual basis, selected the optimal plane among axial, saggital and coronal planes, and chose an optimal method among the invasive portion calculation method or reconstructed thickness calculation method to determine the DOI, for example, coronal for dorsum of the tongue or axial plane for lateral edge (Figures 7 and 8).

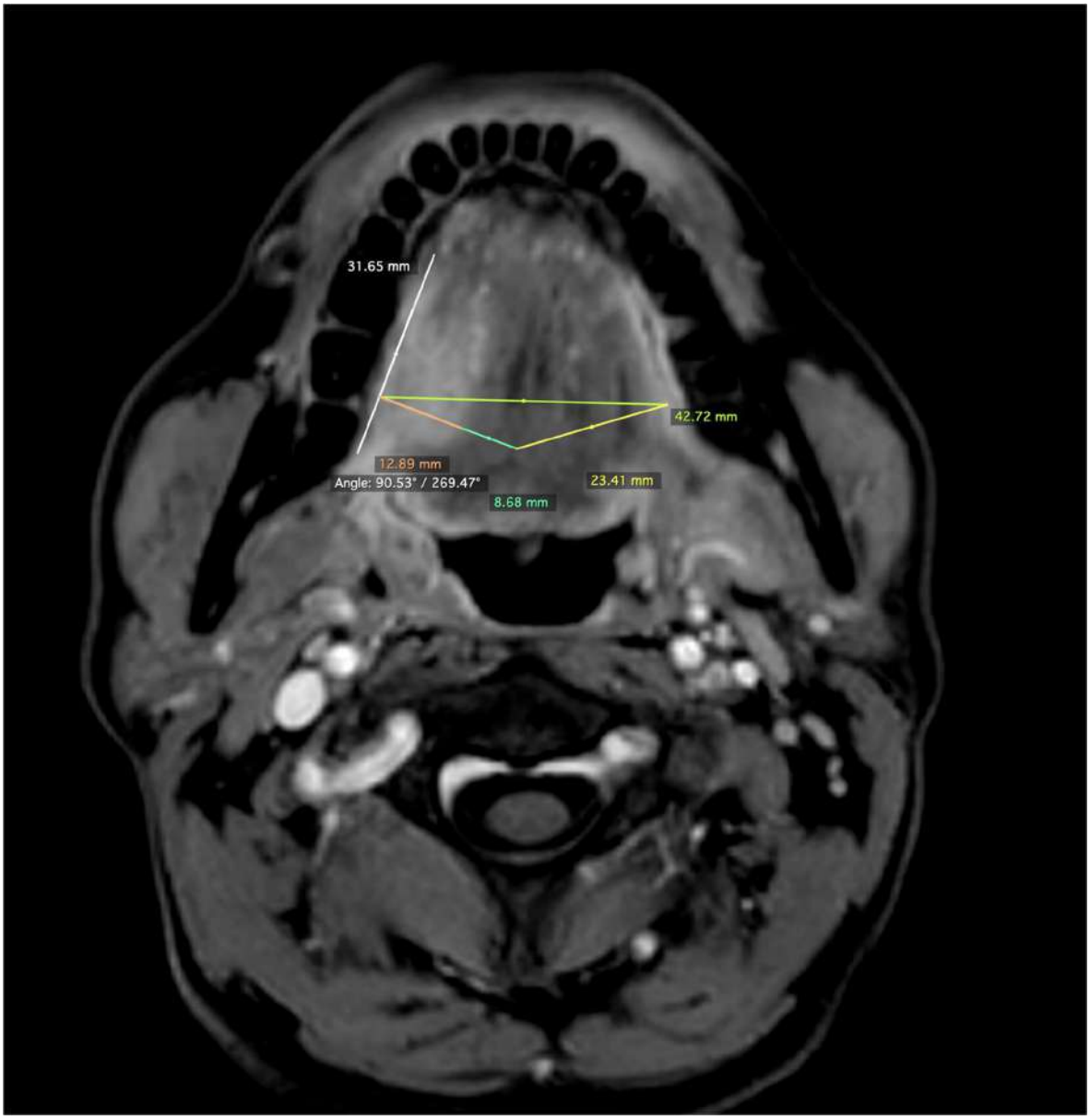


Figure 7. Depth of Invasion : Method-1 and Method-2: Axial T1 weighted with contrast enhancement image shows a tongue cancer radiological DOI measured 12.9 mm by method 1, 14.7 mm by method 2 (23.4-8.7).

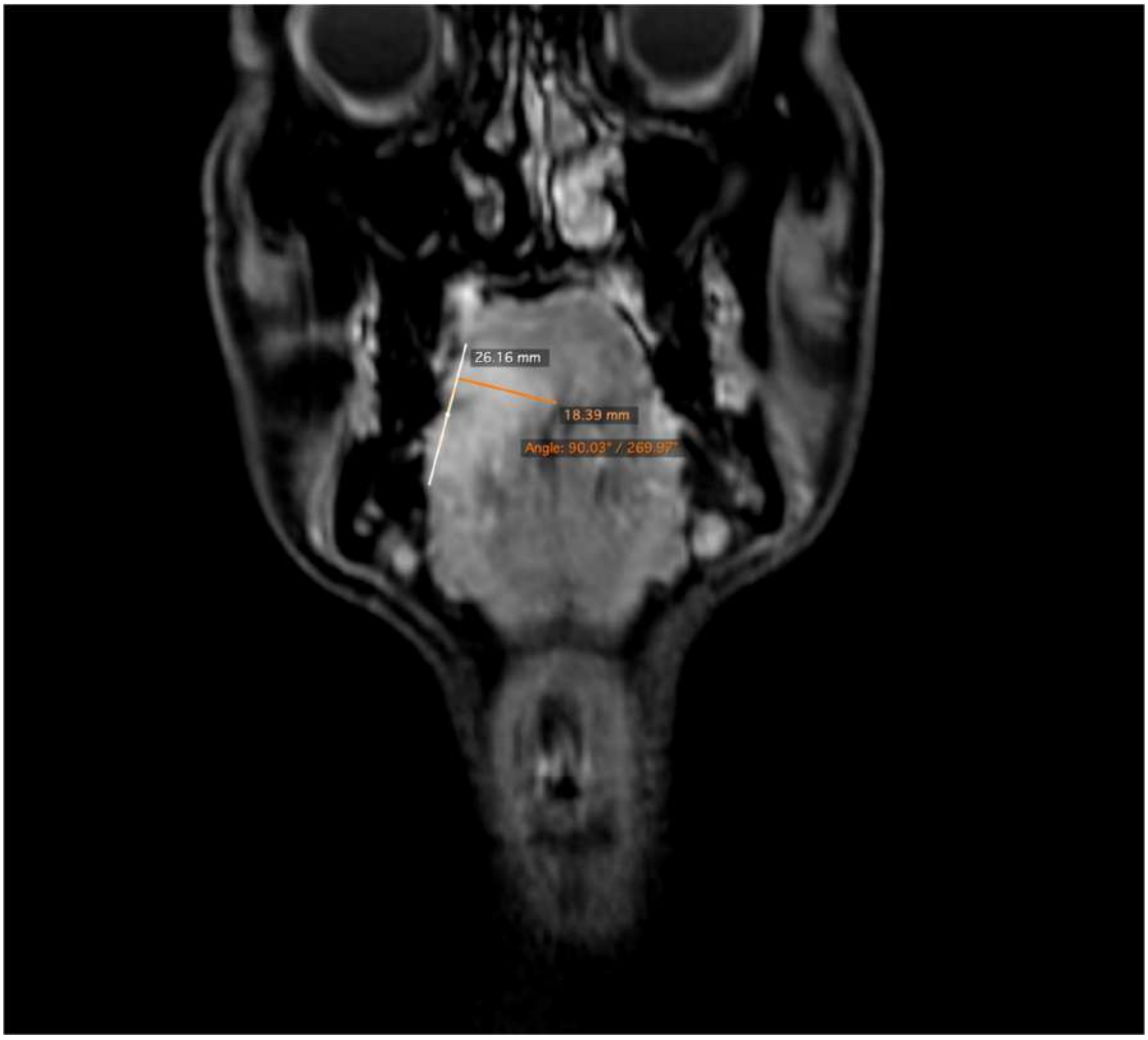


Figure 8. Depth of Invasion Method-3: Coronal T1 weighted with contrast enhancement image shows radiological DOI measured 18.3 mm by method 3.

Surgical Procedure and Histopathological Analyses

All patients had to undergo trans-oral surgical resection of tongue and selective lymph node dissection in the neck as primary treatment. The specimen were sent for histopathological analysis. Fixation was done in neutral buffered 10% formalin. Staining was done with hematoxylin and eosin. Slides were evaluated by an experienced pathologist blinded to the DOI evaluated on MRI. If the surgical margin were found to be negative on all slides, DOI was measured. It corresponded to the maximum distance between the basement membrane of the adjacent normal mucosa to the deepest point of invasion while ignoring the presence or absence of ulceration or protrusion.

Statistical assessment of output

The visual assessment of different MRI sequences was evaluated. Comparison between MRI derived DOI and histo-pathological DOI was done using Chi square tests and using Pearson correlation. Results were considered as significant only if the p-value was found to be less than or equal to 0.05.

Result & Analysis (Tables 1 and 2)

Table 1: Distribution of mean Scores of Imaging assessment on different MR sequences

	Number	Mean	SD	Minimum	Maximum	Median
T1 Score	50	1.78	0.42	1	2	2
T2 Score	50	1.88	0.4798	1	3	2
STIR Score	50	2.63265	0.60187	1	3	3
Contrast Score	18	2.72222	0.57451	1	3	3

(X^2 / chi-square) pearson correlation analysis

Table 2. Pearson Correlation Analysis between DOI and its range, as calculated by different methods versus Histopathological DOI

		Histopathological DOI	**Remarks**
M1	Pearson Correlation	0.749	Positive correlation
	Sig. (2-tailed)	.001	Significant
	N	50	
M1Range	Pearson Correlation	.277	Positive correlation
	Sig. (2-tailed)	.051	Not Significant
	N	50	
M2	Pearson Correlation	0.783	Positive correlation
	Sig. (2-tailed)	.002	Significant
	N	50	
M2Range	Pearson Correlation	.249	Positive correlation
	Sig. (2-tailed)	.081	Not Significant
	N	50	
M3	Pearson Correlation	0.689	Positive correlation
	Sig. (2-tailed)	.001	Significant
	N	50	
M3Range	Pearson Correlation	.068	Positive correlation
	Sig. (2-tailed)	.637	Not Significant
	N	50	
M4	Pearson Correlation	0.767	Positive correlation
	Sig. (2-tailed)	<0.0001	Significant
	N	50	
M4Range	Pearson Correlation	.304*	Positive correlation
	Sig. (2-tailed)	.032	Significant
	N	50	

M1

The value of Pearson Correlation Coefficient (r) was 0.749. The positive correlation was found between Histopathological DOI versus M1. The P-Value was .001. The result was statistically significant.

M2

The Pearson Correlation Coefficient value (r) was 0.783*. The positive correlation was found between Histopathological DOI versus M2. The P-Value was .002. The result was statistically significant.

M3

The Pearson Correlation Coefficient value (r) was 0.689. The positive correlation was found between Histopathological DOI versus M3. The P-Value was .001. The result was statistically significant.

M4

The Pearson Correlation Coefficient value (r) was 0.766. The positive correlation was found between Histopathological DOI versus MIV. The P-Value was <0.0001. The result was statistically significant (Figures 9 to 12).

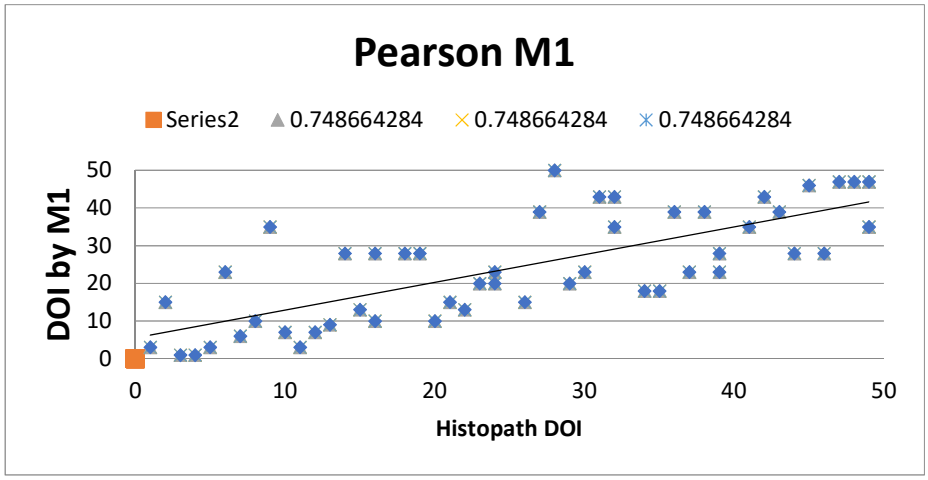


Figure 9. Intraclass correlation coefficient for DOI measured by M1 with histopathological DOI = 0.860887.

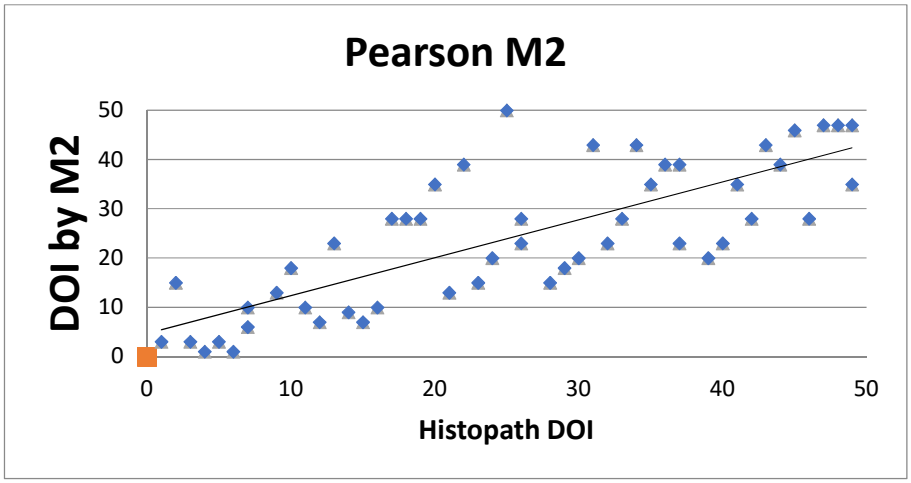


Figure 10. Intraclass correlation coefficient for DOI measured by M2 with histopathological DOI = 0.855315

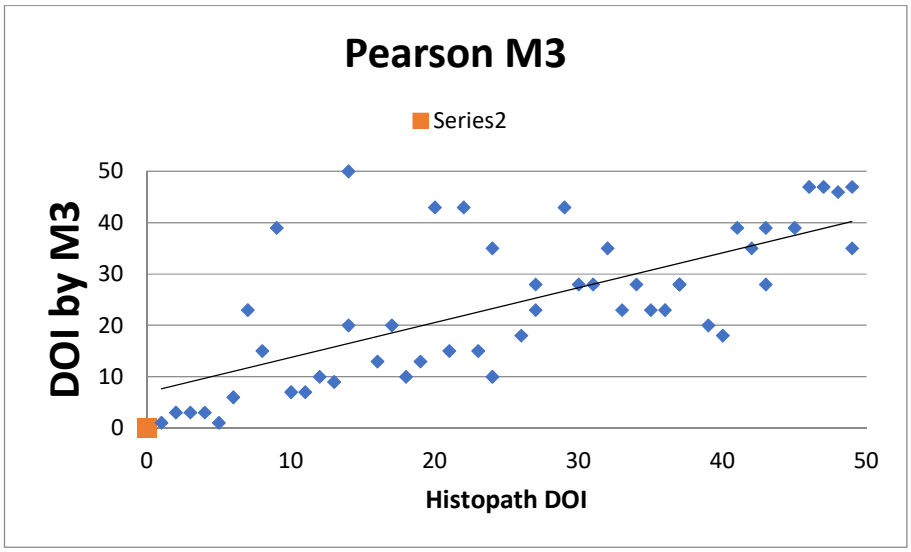


Figure 11. Intraclass correlation coefficient for DOI measured by M3 with histopathological DOI = 0.870972

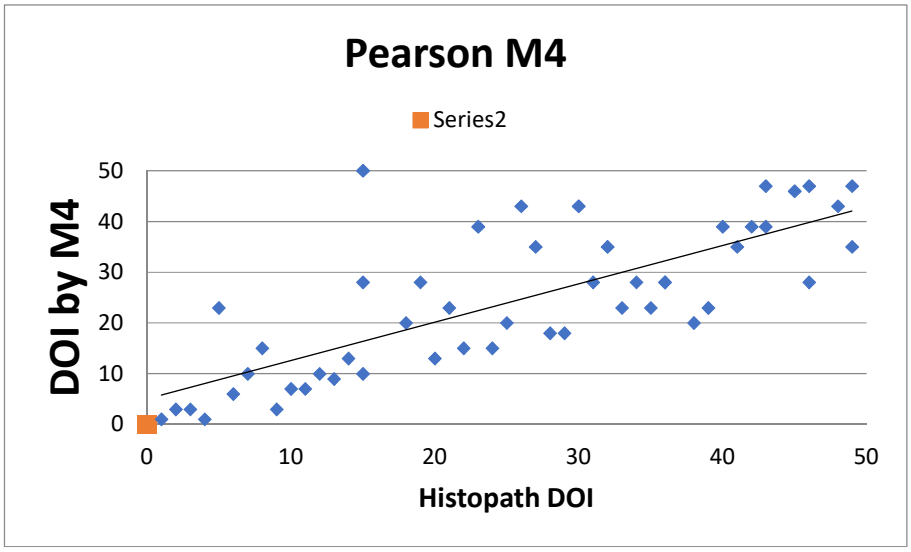


Figure 12. Intraclass correlation coefficient for DOI measured by M4 with histopathological DOI = 0.879721

Discussion

This study was a Prospective study which included a total of 50 patients and was conducted at Department of Radio-diagnosis, Mohandai Oswal hospital, Ludhiana.

To Establish a Standard MRI Sequence for Imaging of SCC of Tongue

In our study, for analysis of adequateness of MR sequence for optimal image visualization, the four-point visual scale detailed in the methodology of this thesis was used to delineate the tumour; the mean T1 Score was [1.7800± 0.42], the mean T2 Score was [1.8800± .4798], the mean STIR Score was [2.63265± 0.60187] and the mean Contrast enhanced Score was [2.72222 ± 0.57451]. Murakami et al. [16]

(2019) found that T2WI and fat suppressed CE-T1WI provided high mean scores, however, the MRI sequence for optimal evaluation of SCC of tongue had to be selected individually each patient. In our study, STIR images in non-contrast studies provide near comparable results to the contrast enhanced sequence in delineation of the lesion.

Determination of Best Method for Evaluation of DOI On MRI

In Bland Altman analysis in our study, Intraclass correlation coefficient (ICC) for histopathological DOI with DOI measured by M1 was 0.860887, by M2 was 0.855315, by M3 was 0.870972 and by M4 was 0.879721.

Our results are in concurrence with the study done by Murakami et al. [16] (2019) in which the correlation between MRI derived DOI and histo-pathological DOI were found to be good by when the radiologist selected the optimal method (ICC of 0.611). Method of determination of DOI on MRI cannot be standardized because the anatomical orientation of the tongue in 3-dimension is in a curvilinear fashion, so most lesions cannot be captured in the entirety in one plane; secondly there is extreme variability in the location of the lesion with respect to tongue margin in different planes; hence, the decision on the method to be used has to be taken on case to case basis by the radiologist.

Conclusion

MRI is now considered an essential component in the pre-treatment evaluation of SCC tongue. It provides precise information regarding the size and DOI to optimize treatment strategy.

This study shows that tongue masses are best evaluated on contrast enhanced scans, but STIR images in non-contrast studies provide near comparable results in delineation of the lesion, rendering contrast enhanced evaluation a modality reserved for problem solving circumstances due to its additional cost, invasive nature and the possibility of contrast reaction.

According to the study, maximum correlation was observed when a radiologist, on individual basis, selected the optimal plane among axial, saggital and coronal planes, and chose an optimal method among the invasive portion calculation method or reconstructed thickness calculation method to determine the DOI, for example, coronal for dorsum of the tongue or axial plane for lateral edge.

Limitations of the Study

Lacunae are present in my study in spite of my sincere efforts. The short falls include:

1. The study has been done in a single tertiary care hospital.
2. Hospital bias cannot be ruled out.

Ethics declarations

Funding This study did not receive any funding.

Conflict of interest

The authors declare that they have no competing interests.

Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability

Not applicable.

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