Review Article

Accuracy of magnetic resonance imaging in the assessment of depth of invasion in tongue carcinoma: A systematic review and meta-analysis

ABSTRACT

Tongue carcinoma constitutes 10.4–46.9% of all oral squamous cell carcinomas (OSCCs) and is notoriously known for invading tissues deeper than the evident gross margins. The deeper the tumor invades, the higher are its chances of future morbidity and mortality due to extensive neck dissection and risk of recurrence. Magnetic resonance imaging (MRI) is a noninvasive diagnostic aid used for measuring a preoperative tumor's depth of invasion (DOI) as it can efficiently outline soft tissue tumors from adjacent normal tissue. To assess various MRI modalities used in measuring DOI in tongue carcinoma and their reliability compared with other DOI measuring modalities. The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) database (CRD42022330866), and the following Preferred Reporting Items for a Systematic Review and Meta-Analysis (PRISMA) Diagnostic Test Accuracy guidelines were performed. PubMed electronic database was searched using a combination of keywords for relevant articles in the English language since 2016. Critical appraisal was carried out using the Quality Assessment of Diagnostic Accuracy Studies-Comparative (QUADAS-C) risk-of-bias (RoB) assessment tool. A weighted mean difference (WMD) was calculated between MRI and histopathological DOI along with pooled correlation and subgroup analysis, where possible. A total of 795 records were retrieved of which 17 were included in the final review with 13 included for meta-analysis. A high RoB was found for most studies for all parameters except flow and timing. WMD showed a statistically significant MRI overestimation of 1.90 mm compared with histopathology. Subgroup analysis showed the 1.5 Tesla machine to be superior to the 3.0 Tesla machine, while imaging sequence subgroup analysis could not be performed. MRI is a viable preoperative DOI measurement modality that can help in efficient treatment planning to decrease surgical morbidity and mortality.

Keywords: Depth of invasion, diagnostic imaging, magnetic resonance imaging, neoplasm invasiveness, tongue neoplasms

INTRODUCTION

Tongue carcinoma is the most common oral squamous cell carcinoma (OSCC) affecting 10.4% to 46.9% of individuals over varied age groups and having a high chance of locoregional metastasis.[1-4]

Depth of invasion (DOI) was introduced by the American Joint Committee on Cancer (AJCC) and Union for International Committee on Cancer (UICC) in 2017 in the eighth edition of the AJCC Cancer Staging Manual.[5] DOI is measured from a reference plane drawn along the tumor and adjoining unaffected epithelium and does not vary with either the exophytic or endophytic nature of malignant growth in contrast to tumor thickness (TT). A DOI of 5 mm is considered the cutoff value to predict locoregional lymph node

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involvement and metastasis with the prognosis worsening as the depth increases.[5]

Postoperative histopathological evaluation of the excised tissue is the definitive method to know DOI, and it cannot be evaluated using preoperative biopsy samples. Postoperative assessment often requires a second surgical intervention if the preoperative DOI is beyond the cutoff limit and neck dissections have not been performed. Thus, it is important to have preoperative, noninvasive methods to accurately assess DOI to predict the locoregional spread and have a better treatment plan.[6]

Various imaging modalities such as ultrasonography (USG), computed tomography (CT), and magnetic resonance imaging (MRI) have been used among which MRI has been used most frequently. MRI provides sufficient soft tissue resolution and contrast without using ionizing radiations and incorporates less artifacts compared with others.[7,8] Despite the widespread use of MRI in assessing the DOI for OSCC, there is no mutual consensus regarding the imaging method (1.5 Tesla or 3.0 Tesla) and parameter (T1- or T2-weighted) that should be used. Thus, it is important to critically appraise and quantitatively assess the available literature to establish scientific evidence to use MRI for preoperative DOI measurement compared with histopathological DOI.

The following systematic review and meta-analysis were carried out in accordance with the following population, intervention, comparison, and outcome (PICO): P: Patients with tongue carcinoma, I: the use of MRI for measuring DOI, C: any other modality used for measuring DOI such as histopathology and ultrasound or CT, and O: the accuracy of MRI in measuring DOI are considered for comparison. Thus, the final review question was as follows: Can preoperative MRI accurately measures the DOI of the tumor in patients with tongue OSCC when compared to histopathology and/or the use of additional imaging modalities such as ultrasound and CT?

OBJECTIVES

The primary objective of this review was to compare the accuracy of measuring DOI in tongue carcinoma patients using MRI (rDOI) with histopathological DOI (pDOI), while the secondary objective was to identify a suitable MRI machine specification imaging parameter and machine specification to record MRI for DOI assessment in tongue carcinoma.

METHOD

The protocol for this systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (registration number: CRD42022330866) and has been reported following 27-item Preferred Reporting Items for a Systematic Review and Meta-Analysis of Diagnostic Test Accuracy (PRISMA-DTA) Studies Statement Checklist [Supplementary file].[9] A rapid review methodology was used using the search strategy and selection criteria mentioned in Table 1.

Study selection

Duplicate studies were removed using Rayyan (https://www.rayyan.ai/) literature screening software. Two authors (VJ and VKR) individually screened the titles and abstracts to decide their initial inclusion followed by retrieving their full texts, which were individually screened by the same two authors to decide their final inclusion. Any discrepancy was resolved by discussion and mutual consensus.

Critical appraisal

Critical appraisal of included studies was carried out using Quality Assessment of Diagnostic Accuracy Studies-Comparison (QUADAS-C), an extension of the QUADAS-2 scale for RoB assessment. The assessment was conducted individually by two reviewers (VJ and VKR), designating a RoB of either "low," "high," or "unclear," reaching a decision by mutual consensus in case of any discrepancy.

Data extraction

The following data were extracted from each included study: author name, country of article's origin, year of publication, study design, total number of patients subjected to MRI and histopathological evaluation with age range, mean age, standard deviation (SD), and gender distribution, modalities used for DOI assessment, study's research objectives, tumor staging, MRI machine specification and sequencing parameter, time between MRI recording and tumor resection, correlation coefficient between MRI and histopathological finding, and mean difference and SD for MRI and histopathological DOI.

Meta-analysis and subgroup analysis

Mean and SD rDOI and pDOI values were grouped for meta-analysis to calculate the weighted mean difference (WMD) at 95% confidence interval (CI). Heterogeneity was checked using the I^2 statistic where $I^2 > 40\%$ was interpreted as heterogeneous data implying the use of random-effects model, if found to be present.[10] In case of high heterogeneity, the probable reason was sought using subgroup analysis based on the availability of required quantitative data. A pooled correlation between rDOI and pDOI was also calculated. RevMan 5.4 and MedCalc software were used for the required analysis.

Table 1: Search strategy and selection criteria

Item	Description
Focus question	Can MRI accurately measure the DOI of the tumor in patients with tongue carcinoma when compared to histopathology and/or the use of additional assessment modalities such as ultrasound and computed tomography?
Search strategy	
Population	#1: ((“Squamous Cell Carcinoma of Head and Neck” [MeSH] OR “Oral cancer” [non-MeSH]) AND (“Tongue Carcinoma” [non-MeSH] OR “Tongue Cancer” [non-MeSH])) AND (“Depth of Invasion” [non-MeSH] NOT “Tumor Thickness” [non-MeSH])
Intervention	#2: “Magnetic Resonance Imaging” [MeSH]
Comparison	Any other modality used for measuring DOI such as histopathology and ultrasound or computed tomography, if used
Outcome	Accuracy of MRI in measuring DOI
Filters	#3: “English” [language] AND “Humans” [MeSH] AND Publication year: 2016 to February 2022
Search combination #1 AND #2 AND #3	
Database search	PubMed (electronic), Cochrane, ClinicalTrials.gov
Selection criteria	
Inclusion criteria	Full-text articles published/available in the English language. Prospective or retrospective studies Articles using pretreatment MRI for measuring tumor DOI in tongue carcinoma patients irrespective of scanning parameters used Comparison of MRI measurements with other modalities used for measuring tumor depth of invasion
Exclusion criteria	Abstracts only, conference proceedings, letters, editorials, animal studies, reviews, case reports, surveys, nonavailability of full text, publications ahead of print Reviews, with or without meta-analysis Use of only single modality for measuring DOI Use of MRI for measuring tumor DOI of anatomical sites other than the tongue Preoperative use of MRI for measuring TT, lymph node metastasis, or bone invasion Postoperative or ex vivo use of MRI for diagnostic or therapeutic purposes Lack of details concerning study design, patient details (when multiple oral carcinomas have been assessed), DOI measurement, and correlation with other modalities

Legend: DOI: depth of invasion; TT: tumor thickness; MRI: magnetic resonance imaging

RESULTS

Search strategy and article selection

A total of 795 records were identified from the PubMed electronic database from which 81 duplicates were removed using Rayyan literature screening software. Cochrane and ClinicalTrials.gov presented no relevant articles. From the 714 records retrieved, 621 records were found to be nonrelevant and excluded after reading the titles and abstract, thus leaving 93 titles for full-text retrieval. Of this, 76 were removed for, using non-MRI modalities for measuring DOI (n = 31),[11-41] using MRI for measuring DOI in non-tongue carcinoma (n = 15),[42-56] lacking statistical details (n = 10),[57-66] using MRI for reasons other than DOI measurement (n = 7)[67-73] or measuring TT (n = 7),[74-80] not comparing MRI measured DOI (n = 5),[81-85] and article ahead of print (n = 1),[86] and are indicated in Table 2. Thus, a total of 17 articles were included in the systematic review [Figure 1]. Further four articles lacking the required quantitative data for meta-analysis were not considered for the same.[1,87-89]

Study and patient characteristics

Of the 17 studies, 12 were retrospective while five were prospective wherein 1,161 tongue carcinoma patients (704 (60.64%) males, 392 (33.76%) females; 18 to 90 years age) were subjected to DOI assessment using MRI and histopathology. Two studies did not comment on the patient’s age.[1,89] The gender distribution for 5.6% of patients could not be determined due to a lack of available information in one study.[89] Six studies originated from Japan,[1,8,88,90-92] four from China,[87,93-95] two from India,[96,97] and one each from the United States of America,[98] Canada,[99] Italy,[6] Finland,[89] and United Kingdom [Table 3].[100]

Modalities used for DOI measurement

All included studies used MRI and histopathology for the measurement of DOI. Additionally, CT and USG were also used individually in two studies.[1,8]

MRI machine characteristics and imaging sequence

The 1.5 Tesla was the most used machine (n = 8),[1,6,8,91-93,97,100] while six studies used the 3 Tesla machine[87,90,94-96,98] and one study used either of the two for MRI recording.[89] One study did not provide details about the MRI machine specification [Figure 2].[88]

All but one study provided details about the image sequence used for MRI recording.[99] T1- and T2-weighted images were captured in all studies except two where only T1 images were utilized.[89,100] Some studies also utilized fat suppression and echo spin imaging with one study using dynamic enhanced T1 high-resolution isotropic volume examination (e-THRIVE).[94]

Table 2: Reason for exclusion of articles

Study	Reason for exclusion
Satgunaseelan *et al*. (2016)[11]	Only histopathological assessment of DOI was performed
Brockhoff *et al*. (2017)[12]	Only histopathological assessment of DOI was performed
Almangush *et al*. (2018)[13]	Only histopathological assessment of DOI was performed
Mascitti *et al*. (2018)[15]	Only histopathological assessment of DOI was performed
Masood *et al*. (2018)[16]	Only histopathological assessment of DOI was performed
Amit *et al*. (2019)[17]	Only histopathological assessment of DOI was performed
Berdugo *et al*. (2019)[18]	Only histopathological assessment of DOI was performed
Chatterjee *et al*. (2019)[19]	Only histopathological assessment of DOI was performed
Ebrahimi *et al*. (2019)[21]	Only histopathological assessment of DOI was performed
Hasmat *et al*. (2019)[22]	Only histopathological assessment of DOI was performed
Kozak *et al*. (2019)[23]	Only histopathological assessment of DOI was performed
Tam *et al*. (2019)[24]	Only histopathological assessment of DOI was performed
Toom *et al*. (2019)[25]	Only histopathological assessment of DOI was performed
Zenga *et al*. (2019)[26]	Only histopathological assessment of DOI was performed
Bjerkli *et al*. (2020)[27]	Only histopathological assessment of DOI was performed
Larson *et al*. (2020)[28]	Only histopathological assessment of DOI was performed
Sahoo *et al* (2020)[30]	Only histopathological assessment of DOI was performed
Shin *et al*. (2020)[31]	Only histopathological assessment of DOI was performed
Aaboubout *et al*. (2021)[33]	Only histopathological assessment of DOI was performed
D'Cruz *et al*. (2021)[34]	Only histopathological assessment of DOI was performed
Lau *et al*. (2021)[36]	Only histopathological assessment of DOI was performed
Muhammad *et al*. (2021)[37]	Only histopathological assessment of DOI was performed
Salama *et al*. (2021)[39]	Only histopathological assessment of DOI was performed
Tandon *et al*. (2022)[41]	Only histopathological assessment of DOI was performed
Cho *et al*. (2019)[20]	MRI not used for DOI assessment
Locatello *et al*. (2020)[29]	Computed tomography used for DOI assessment
Chin *et al*. (2021)[35]	Computed tomography used for DOI assessment
Yoon *et al*. (2020) [32]	Compared sonography to histopathological DOI
Iida *et al*. (2018)[14]	Ultrasonography was used for DOI assessment
Rocchetti *et al*. (2021)[38]	Ultrasonography was used for DOI assessment
Hiyama *et al*. (2022) [40]	Used CT for DOI assessment
Ng *et al*. (2016)[42]	Oropharyngeal or hypopharyngeal carcinoma
Padma *et al*. (2017)[43]	Buccal mucosa carcinoma
Gencturk *et al*. (2019)[44]	Sinonasal carcinoma
Pillai *et al*. (2019)[45]	Buccal mucosa carcinoma
Soni *et al*. (2019)[46]	Carcinoma of gingiva–buccal complex
Kim *et al*. (2020)[47]	Tonsillar cancer
Marinelli *et al*. (2020)[48]	Buccal mucosa carcinoma
Joo *et al*. (2020)[49]	Carcinoma of tonsil
Baba *et al*. (2021)[51]	Carcinoma of floor of the mouth
Baba *et al*. (2021)[50]	Buccal mucosa carcinoma
Jain *et al*. (2021)[52]	Laryngeal carcinoma
Kosugi *et al*. (2021)[53]	Maxillary sinus cancer
Tokat *et al*. (2021)[54]	Larynx cancer
Chen *et al*. (2022)[55]	Hypopharyngeal squamous cell carcinoma
Wang *et al*. (2022)[56]	Buccal mucosa carcinoma
Ren *et al*. (2018)[58]	Lacking statistical details
Dang *et al*. (2019)[57]	Lacking statistical details
de Koning *et al*. (2019)[59]	Lacking statistical details
Morand *et al*. (2019)[60]	Lacking statistical details
Jani *et al*. (2020)[61]	Lacking statistical details
Jović *et al*. (2020)[62]	Lacking statistical details
Kanno *et al*. (2020)[63]	Lack of statistical details
Filauro *et al*. (2021)[64]	Lacking statistical details
Harada *et al*. (2021)[65]	Lacking statistical details
Waech *et al*. (2021)[66]	Lacking statistical details
Kouketsu *et al*. (2016)[67]	MRI used for non-DOI purpose
Howe *et al*. (2017)[68]	MRI used for non-DOI purpose
Faraji *et al*. (2018)[69]	MRI used for non-DOI purpose
Han *et al*. (2018)[70]	MRI used for non-DOI purpose
Martens *et al*. (2019)[71]	MRI used for non-DOI purpose
Meyer *et al*. (2021)[72]	MRI used for non-DOI purpose
Shah *et al*. (2021)[73]	MRI used for non-DOI purpose
Kwon *et al*. (2016)[80]	MRI used for tumor thickness
Tsushima *et al*. (2016)[79]	MRI used for tumor thickness
Imai *et al*. (2017)[77]	MRI used for tumor thickness
Smiley *et al*. (2019)[78]	MRI used for tumor thickness
Noorlag *et al*. (2020)[76]	MRI used for tumor thickness
Park *et al*. (2021)[74]	MRI used for tumor thickness
Saenthasuk *et al*. (2021)[75]	MRI used for tumor thickness
Sahin *et al*. (2016)[81]	Not comparing MRI-measured DOI
Faisal *et al*. (2018)[82]	Not comparing MRI-measured DOI
Baik *et al*. (2019)[83]	Not comparing MRI-measured DOI
Minamitake *et al*. (2021)[84]	Not comparing MRI-measured DOI
Papoutsaki *et al*. (2021)[85]	Not comparing MRI-measured DOI
Zhang *et al*. (2022)[86]	Article ahead of print

Legend: DOI: depth of invasion; MRI: magnetic resonance imaging; CT: computed tomography

Tumor staging

All studies performed clinical, radiological, and histological staging and grading of tongue carcinoma. One study each enrolled patients with only T1 and T2 cancer stages, respectively,[87,90] while six each enrolled patients

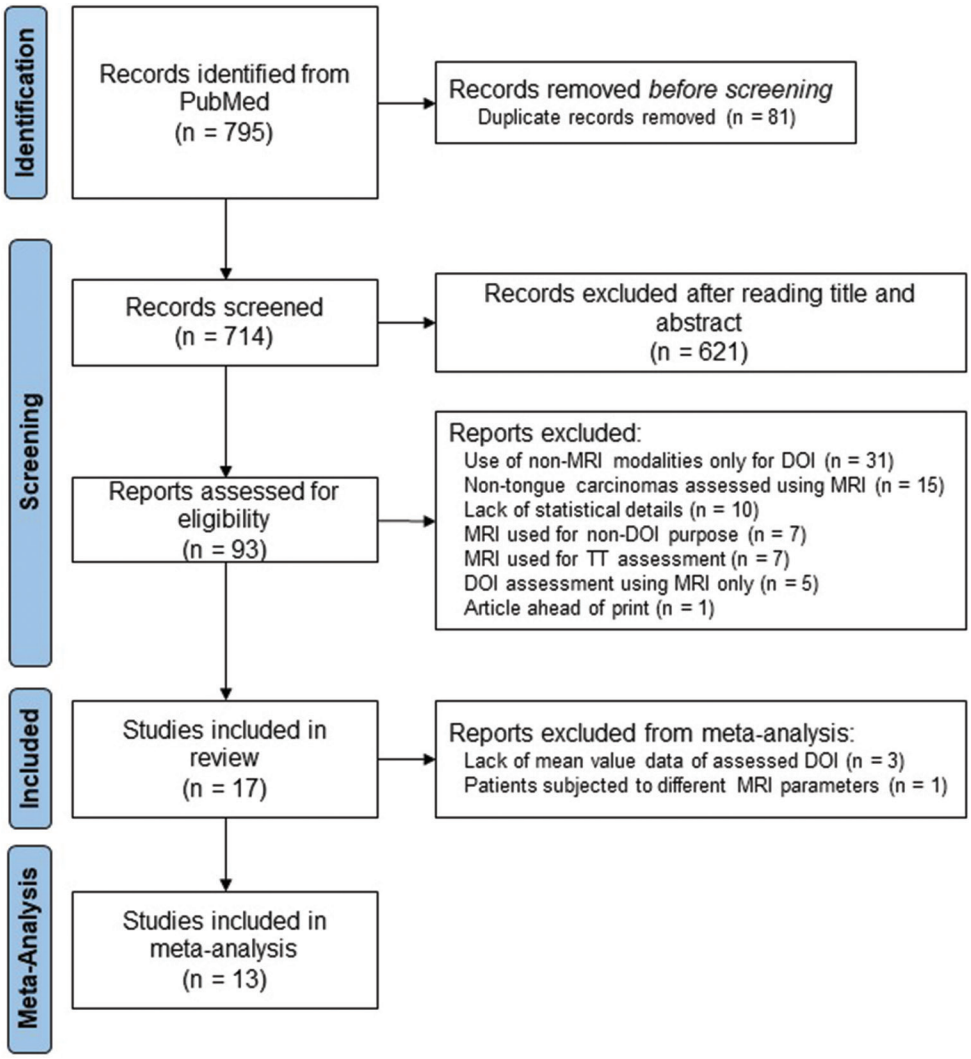

Figure 1: PRISMA flowchart for included studies

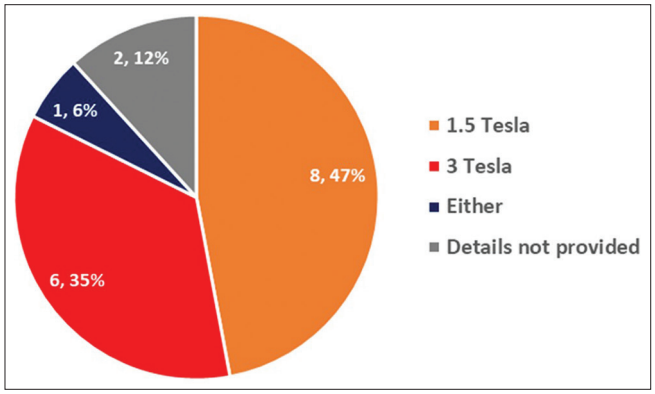

Figure 2: MRI machine specification used in different studies

with T1 to T3 and T1 to T4 tumor stages. Three studies included patients of either the T1 or T2 clinical tumor stage [Figure 3].[8,91,92]

Time between imaging and tumor resection

Eight studies did not disclose the time between imaging and tumor resection.[1,88,89,91,92,95,97,99] In other studies, this difference ranged from 1 day to 40 days.

Additionally assessed parameters

Cervical lymph node metastasis,[87,88,92,97,98] locoregional control rate,[91,92] involvement of sublingual space, extrinsic muscles, and mylohyoid muscles,[96] disease-free survival rate,[87,91-93] overall survival rate,[91-93] and recurrence pattern[90] were other parameters assessed in the reviewed literature.

RoB assessment

Based on the QUADAS-2 assessment for histopathology and MRI, the QUADAS-C RoB was found to be high for eight studies, while it was unclear for one. Comparing the index text and reference standard, a high RoB was seen for eight and seven studies, respectively, while seven and five had low risk with the remaining presenting an unclear risk. Flow and timing showed high risk for four studies with 13 having low risk and no study presenting an unclear bias [Figure 4].

Table 3: Characteristics of the included studies

Author (Year)	Origin country	Study type	Total patients#		Age (in years) Mean±SD (range)	Modalities used	Research object	Tumor staging	MRI machine	MRI sequence	Time between MRI recording and tumor resection
			M	F							
Alsaffar *et al.* (2016)[99]	Canada	Prospective	34	19	64	Clinical, MRI, histopathological	DOI	T1–T4	NP	NP	NP
Jayasankaran *et al.* (2017)[96]	India	Prospective	42	17	51.81 (18–74)	Clinical, MRI, histopathological	DOI Infiltration of sublingual space Infiltration of extrinsic muscles Involvement of mylohyoid muscle	T1–T4	3.0 Tesla	T1WI spin echo T2WI T2WI with FS T1WI with FS	Less than 1 week
Moreno *et al.** (2017)[98]	USA	Prospective	14	6	58 (29–80)	Clinical, MRI, histopathology	DOI Cervical LN metastasis	T1–T4	3.0 Tesla	T1WI T2WI	1–40 days
Baba *et al.* (2019)[91]	Japan	Retrospective	18	10	66.2±15.2 (31–86)	Clinical, MRI, histopathological	DOI Locoregional control rate Disease-free SR Overall SR	T1–T2	1.5 Tesla	T1WI T2WI T1WI with FS	NP
Mao *et al.* (2019)[93]	China	Prospective	80	70	58.01±12.10	Clinical, MRI, histopathological	DOI Disease-specific SR Overall SR	T1–T3	1.5 Tesla	T1WI T2WI T2WI with FS	1 week
Murakami *et al.* (2019)[90]	Japan	Retrospective	15	14	(46–87)	Clinical, MRI, histopathological	DOI Recurrence pattern	T2	3.0 Tesla	T1WI T2WI CE T1WI STIR	1 month
Baba *et al.* (2019)[92]	Japan	Retrospective	31	14	63.4±16.1 (31–86)	Clinical, MRI, histopathological	DOI Cervical LN metastasis Locoregional control rate Disease-free SR Overall SR	T1–T2	1.5 Tesla	T1WI T2WI T1WI with FS	NP
Vidiri *et al.*≤ (2020)[6]	Italy	Retrospective	18	25	(31–82)	Clinical, MRI, histopathological	DOI	T1–T3	1.5 Tesla	T1WI T2WI	3–4 weeks
Ravikanth (2020)[97]	India	Prospective	27	3	(41–70)	Clinical, MRI, Histopathological	DOI Cervical LN metastasis	T1–T4	1.5 Tesla	T1WI T2WI	NP
Xu *et al.* (2020)[87]	China	Retrospective	111	40	57.1 (30–78)	Clinical, MRI, histopathological	DOI Cervical LN metastasis Disease-specific SR	T1	3.0 Tesla	T1WI T2WI T2WI with FS	1 week
Fu *et al.* (2020)[95]	China	Retrospective	95	61	58.7±9.2 (27–92)	Clinical, MRI, histopathological	DOI	T1–T3	3.0 Tesla	T1WI spin echo T2WI turbo spin echo T1WI with FS	NP
Haraguchi *et al.* (2021)[88]	Japan	Retrospective	57	44	63.9 (22–88)	Clinical, MRI, histopathological	DOI Cervical LN metastasis	T1–T4	NP	T1WI T2WI	NP
Baba *et al.* (2021)[1]	Japan	Retrospective	16	5	NP	Clinical, MRI, CT, histopathological	DOI	T1–T3	1.5 Tesla	T2WI T1WI with FS	NP

Contd...

Table 3: Contd...

Author (Year)	Origin country	Study type	Total patients#		Age (in years) Mean±SD (range)	Modalities used	Research object	Tumor staging	MRI machine	MRI sequence	Time between MRI recording and tumor resection
			M	F							
Huopainen *et al.* (2021)[89]	Finland	Retrospective	45 NP		NP	Clinical, MRI, histopathological	DOI	T1–T3	1.5 Tesla or 3.0 Tesla	T1WI with FS	NP
Mair *et al.* (2021)[100]	UK	Retrospective	60	20	56.7	Clinical, MRI, histopathological	DOI	T1–T4	1.5 Tesla	Post-contrast, FS T1WI	2 weeks
Takamura *et al.* (2022)[8]	Japan	Retrospective	48	20	65.7 (23–90)	Clinical, MRI, US, histopathological	DOI	T1–T2	1.5 Tesla	T1WI with FS T2WI with FS	8–34 days
Tang *et al.* (2022)[94]	China	Retrospective	122	44	(28–76)	Clinical, MRI, histopathological	DOI	T1–T3	3.0 Tesla	T1WI T2WI with FS DWI e-THRIVE	2 weeks

#Patients with tongue carcinoma included in the analysis; *: the author used the term tumor thickness, which was confirmed to be DOI measurement after reading the full text

M: male; F: female; SD: standard deviation; MRI: magnetic resonance imaging; DOI: depth of invasion; NP: not provided; T1WI: T1-weighted image; T2WI: T2-weighted image; T: tumor; FS: fat suppression; CE: contrast-enhanced; STIR: short tau inversion recovery; SR: survival rate; CT: computed tomography; ≤: only mean difference was provided; LN: lymph node; US: ultrasound; DWI: diffusion-weighted image; e-THRIVE: dynamic enhanced T1 high-resolution isotropic volume examination

Figure 3: Distribution of tumor stage enrollment

Meta-analysis

Thirteen of 17 studies either directly provided mean and SD DOI values or provided derivation data, thus being included for meta-analysis. An I^2 value of 85% (p-value < 0.00001) indicated high heterogeneity, and thus, a random-effects model was used. The funnel plot showed unequal distribution with more studies toward one side of the overall effect line [Figure 5]. Meta-analysis of these 13 studies found a WMD of 1.90 mm (95% CI: 0.84 to 2.95, *P* value = 0.0004) between MRI and histopathological DOI [Figure 6].

Subgroup analysis

Subgroup meta-analysis based on the type of MRI machine, that is, 1.5 Tesla and 3.0 Tesla, included seven and five studies, respectively. High heterogeneity with I^2 values of 86% (p-value < 0.00001) and 81% (p-value = 0.0003), respectively, indicated the use of random-effects model. For the 1.5 Tesla machine, a statistically nonsignificant WMD of 1.37 mm (95% CI: 0.02–2.73, *P* value = 0.05) was seen, while the 3.0 Tesla machine had a statistically significant WMD of 3.10 mm (95% CI: 1.19–5.01, *P* value = 0.001) [Figure 7a and 7b].

The correlation coefficient between MRI assessed and histopathological DOI was given in 13 studies, which when pooled gave a cumulative correlation coefficient of 0.837 (p-value < 0.001) [Figure 8].

DISCUSSION

The tongue is a mobile muscular organ commonly affected by squamous cell carcinoma. It has an increased risk of locoregional metastasis and recurrence following excision due to its rich blood supply and abundant lymphatic vessels[4,101] responsible for distant metastasis, disease recurrence, and associated morbidity and mortality.[4,101] DOI helps in determining tumor prognosis by predicting this

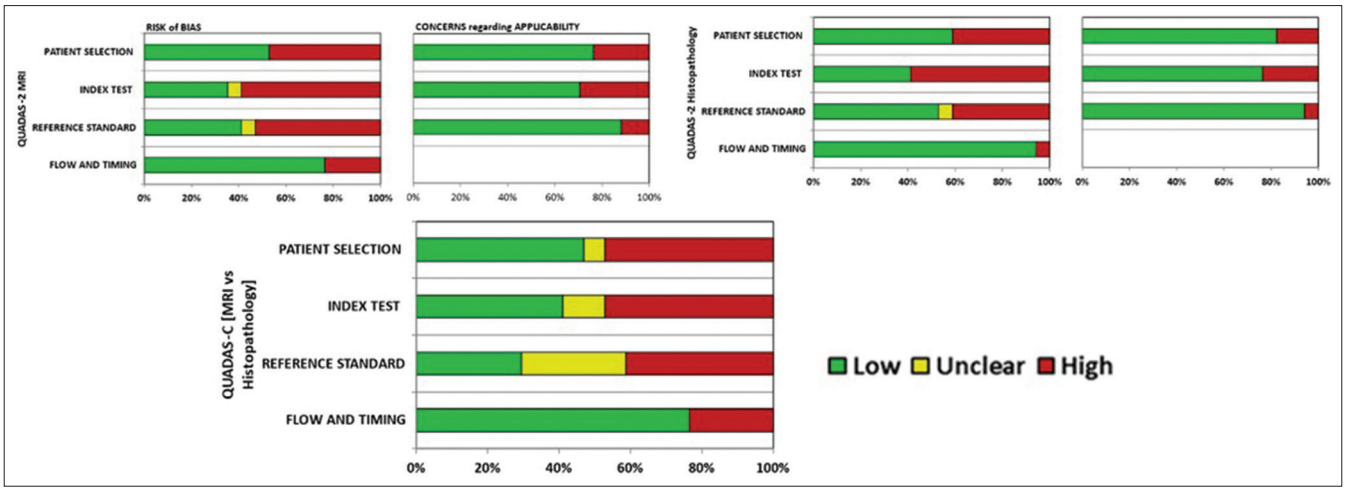

Figure 4: QUADAS-2 risk-of-bias assessment for A. MRI, B. histopathology, and C. QUADAS-C risk-of-bias assessment

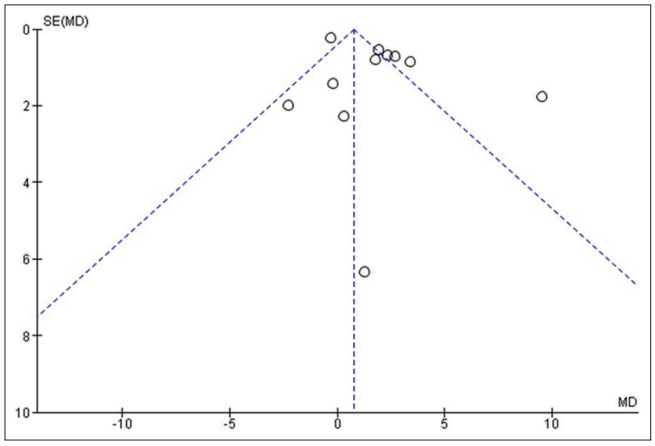

Figure 5: Funnel plot

metastasis, helping in better treatment planning. Previously, terms such as DOI and TT were used interchangeably; however, the eighth AJCC edition removed this ambiguity. DOI assessment has been performed for various head and neck OSCC sites such as buccal mucosa,[56,64,102,103] gingiva,[46,103] floor of the mouth,[64] and hypopharynx;[55] however, the notorious nature of tongue carcinoma has made them the most frequent study subject.

This review retrieved 17 studies to be included for review since 2016, which were more than the studies considered in the systematic review published in 2022.[101] Many studies had a high RoB, which can be due to greater retrospective studies, which are more vulnerable to missed data due to the lack of focused data collection pro formas, high chances of having confounding factors, and presence of recall bias with selective data reporting.[104] Similar observations were noted in the previously performed work.[101] Also, most studies focused either on lower tumor stages or on unequal distribution over different tumor stages, which also discouraged the authors to perform subgroup meta-analysis and verify whether MRI is equally acceptable for all stages. Nondisclosure of time between imaging and histopathology or wide variation between the two formed another reason for the high RoB, which was another similar observation.[101] This review is also the first one to use QUADAS-C for RoB assessment, which is an extension of the QUADAS-2 and allows comparison of diagnostic modalities at the same time compared with its counterpart.

Meta-analysis

This meta-analysis showed a statistically significant overestimation of 1.90 mm (95% CI: 0.84–2.95, *P* value = 0.0004) in WMD of DOI measured using MRI and histopathology. This was quantitatively more than the statistically significant MRI overestimation of 1.64 mm (95% CI: 0.87–2.40 mm, *P* value < 0.001) reported by Li *et al*.[101] This can be due to shrinkage of the excised specimen when fixed in formalin, which has a reported range of 4.10%–30% for head and neck specimens.[5,105,106] Thus, it is critical to spend the minimum time between formalin immersion of the sample and histopathological examination. Overestimation can also be due to difficulty in differentiating edema and inflammation from soft tissue tumor boundary, as previously mentioned. Inflammation is inherently present in a carcinomatous lesion due to physiologic and pathologic factors, which becomes more pronounced when scanning is performed after an incisional biopsy.[107,108] Most studies presented MRI overestimation of less than 2 mm but whether this was recorded after biopsy is not clear.[90,94,97,98,100] Thus, whenever possible, MRI should be recorded before incisional biopsy sample collection.

Subgroup analysis

Subgroup analysis concerning the MRI machine's magnetic field specification, that is, 3.0 Tesla versus 1.5 Tesla, has been carried out for the first time in the current review. It showed a statistically nonsignificant overestimation of 1.37 mm in

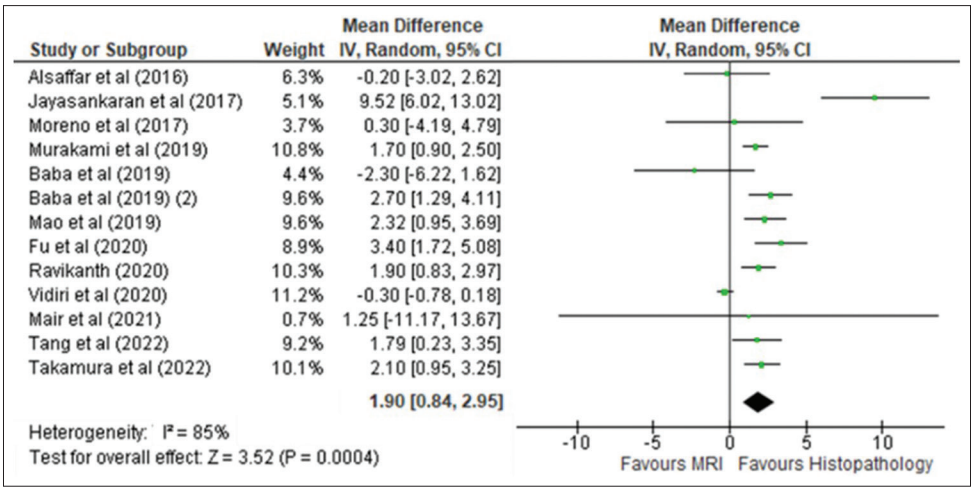

Figure 6: Forest plot of cumulative analysis

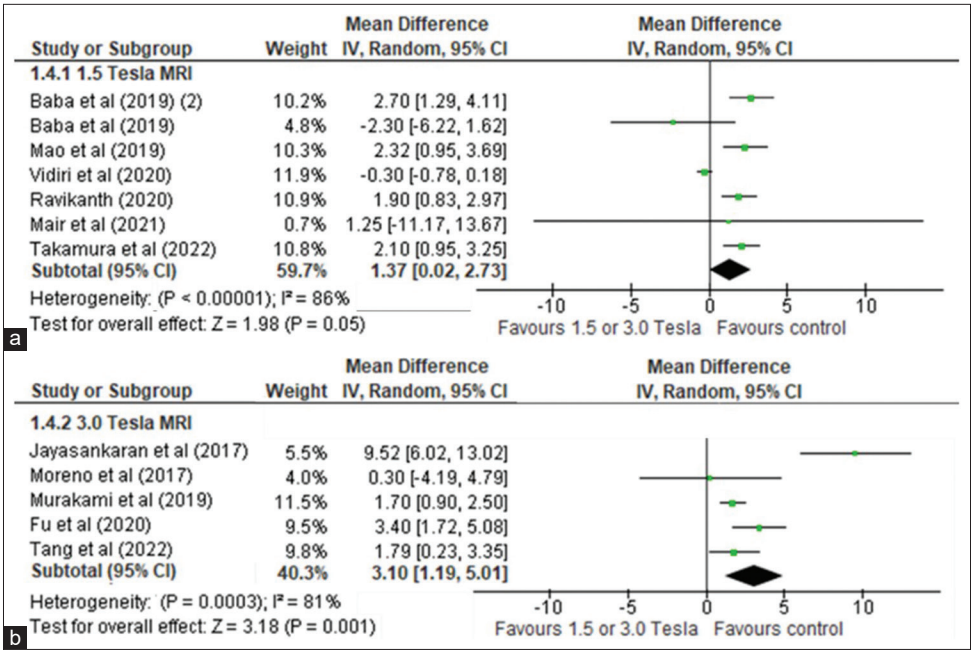

Figure 7: (a) Forest plot of subgroup meta-analysis of the 1.5 Tesla MRI machine. (b) Forest plot of subgroup meta-analysis of the 3.0 Tesla MRI machine

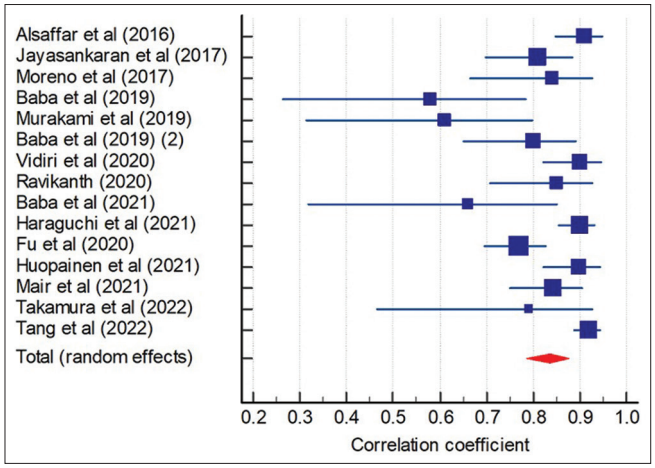

Figure 8: Pooled correlation of 13 studies

DOI assessment with the 1.5 Tesla machine compared with statistically significant overestimation of 3.10 mm with the 3.0 Tesla machine. This contrasted with literature evidence, which shows the 3.0 Tesla machine superior to the 1.5 Tesla machine due to higher signal-to-noise and contrast-to-noise ratios in the former, which helps in reducing either acquisition time or increasing spatial resolution or both, helping in the detection of small focal lesions.[109,110] Variation in the results can be due to a small number of studies using the 3.0 Tesla machine. Although recent times have seen a higher number of upcoming imaging centers installing the 3.0 Tesla machine, the debate about the choice of the machine's magnetic field continues. A higher magnetic field makes the recording more susceptible to the development of artifacts and the

presence of a lack of homogeneity.[111] Also, increased patient discomfort in terms of nausea, weakness, metallic taste in the mouth, peripheral nerve stimulation, dizziness, and noise associated with sequencing (acoustic noise) has been reported with the 3.0 Tesla machine than with the 1.5 Tesla machine.[111] These observations in addition to our results indicate the superiority of the 1.5 Tesla MRI machine in DOI recording for tongue carcinomas. Thus, the authors wish to provide a direction toward the possible differences and need for more studies focusing on this comparative aspect so that conclusive scientific evidence can be generated, and MRI can be recorded in the future with higher clinical relevance.

MRI uses a range of imaging protocols, which are optimally selected based on the requirement, of which T1- and T2-weighted (T1W and T2W) remain the most frequently used. T1W sequences assist in anatomical assessments, delineating the fat planes along with visualization of bone marrow and lymph node capsules and thus considered optimal for various head and neck anatomic locations. In contrast, T2W is primarily used for pathological assessments, helping in knowing the lymph node involvement and extracapsular disease spread.[112] In the current review, subgroup analysis based on imaging was not carried out due to a lack of adequate number of studies to conduct the same. Thus, it is recommended to undertake studies with imaging protocol as a study objective.

Subgroup analysis for individual tumor stage and imaging parameters could not be performed due to last of concerned data. For the same reason, sensitivity and specificity analysis too could not be performed. Thus, it cannot be said confidently whether MRI can be used to assess DOI with equal confidence for all tumor stages when compared to histopathological DOI. The current review searched only a single database, failing to cover other possibly published literature.

Future recommendations

This systematic review and meta-analysis highlight the need for more studies using preoperative MRI for measuring DOI in cases of tongue carcinoma with details about MRI magnetic field, imaging parameters, and individual data with respect to tumor stage for better scientific evidence.

CONCLUSION

MRI is a feasible preoperative imaging modality for knowing the DOI in tongue carcinoma that can help in knowing the locoregional spread of the tumor and appropriately planning surgical intervention to decrease patient morbidity and mortality.

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Conflicts of interest

There are no conflicts of interest.

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PRISMA-DTA Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
TITLE / ABSTRACT			
Title	1	Identify the report as a systematic review (+/- meta-analysis) of diagnostic test accuracy (DTA) studies.	1
Abstract	2	Abstract: See PRISMA-DTA for abstracts.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3 and 4
Clinical role of index test	D1	State the scientific and clinical background, including the intended use and clinical role of the index test, and if applicable, the rationale for minimally acceptable test accuracy (or minimum difference in accuracy for comparative design).	4 and 4
Objectives	4	Provide an explicit statement of question(s) being addressed in terms of participants, index test(s), and target condition(s).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (participants, setting, index test(s), reference standard(s), target condition(s), and study design) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Table 1
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Table 1
Search	8	Present full search strategies for all electronic databases and other sources searched, including any limits used, such that they could be repeated.	Table 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Definitions for data extraction	11	Provide definitions used in data extraction and classifications of target condition(s), index test(s), reference standard(s) and other characteristics (e.g. study design, clinical setting).	5
Risk of bias and applicability	12	Describe methods used for assessing risk of bias in individual studies and concerns regarding the applicability to the review question.	5
Diagnostic accuracy measures	13	State the principal diagnostic accuracy measure(s) reported (e.g. sensitivity, specificity) and state the unit of assessment (e.g. per-patient, per-lesion).	5 and 6
Synthesis of results	14	Describe methods of handling data, combining results of studies and describing variability between studies. This could include, but is not limited to: a) handling of multiple definitions of target condition. b) handling of multiple thresholds of test positivity, c) handling multiple index test readers, d) handling of indeterminate test results, e) grouping and comparing tests, f) handling of different reference standards	5 and 6

PRISMA-DTA Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
Meta-analysis	D2	Report the statistical methods used for meta-analyses, if performed.	5 and 6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	5 and 6
RESULTS			
Study selection	17	Provide numbers of studies screened, assessed for eligibility, included in the review (and included in meta-analysis, if applicable) with reasons for exclusions at each stage, ideally with a flow diagram.	6
Study characteristics	18	For each included study provide citations and present key characteristics including: a) participant characteristics (presentation, prior testing), b) clinical setting, c) study design, d) target condition definition, e) index test, f) reference standard, g) sample size, h) funding sources	6
Risk of bias and applicability	19	Present evaluation of risk of bias and concerns regarding applicability for each study.	8
Results of individual studies	20	For each analysis in each study (e.g. unique combination of index test, reference standard, and positivity threshold) report 2x2 data (TP, FP, FN, TN) with estimates of diagnostic accuracy and confidence intervals, ideally with a forest or receiver operator characteristic (ROC) plot.	6, 7, and 8
Synthesis of results	21	Describe test accuracy, including variability; if meta-analysis was done, include results and confidence intervals.	8 and 9
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression; analysis of index test: failure rates, proportion of inconclusive results, adverse events).	6, 7, and 8
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence.	9, 10, and 11
Limitations	25	Discuss limitations from included studies (e.g. risk of bias and concerns regarding applicability) and from the review process (e.g. incomplete retrieval of identified research).	11
Conclusions	26	Provide a general interpretation of the results in the context of other evidence. Discuss implications for future research and clinical practice (e.g. the intended use and clinical role of the index test).	11
FUNDING			
Funding	27	For the systematic review, describe the sources of funding and other support and the role of the funders.	12

Adapted From: McInnes MDF, Moher D, Thombs BD, McGrath TA, Bossuyt PM, The PRISMA-DTA Group (2018). Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement. JAMA. 2018 Jan 23;319(4):388-396. doi: 10.1001/jama.2017.19163.

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