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ORIGINAL ARTICLE

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The usefulness of intraoral ultrasonography and post-contrast three-dimensional fast field echo imaging in the evaluation of radiological depth of invasion of oral tongue squamous cell carcinoma: Comparison with pathological depth of invasion assessment

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ABSTRACT

Aim: Squamous cell carcinoma (SCC) is the most common malignancy in the oral tongue. Depth of invasion (DOI) of the oral tongue SCC is known as a predictor of recurrence and survival in patients. Both intraoral ultrasonography (ioUS) and post-contrast three-dimensional fast field echo (3D-FFE) imaging are useful for predicting pathological DOI and can contribute to effective treatment plans and a positive prognosis. The purpose of this study was to evaluate the usefulness of ioUS in comparison with post-contrast 3D-FFE imaging for assessing radiological DOI and compare radiological DOI and pathological DOI in patients with oral tongue SCC.

Methods: Fifteen patients were included in this study conducted between August 2018 and March 2020. Spearman's rank correlation coefficient (SRCC) was used to compare radiological DOI with pathological DOI.

Results: Both ioUS-derived DOI (9.96 mm) and 3D-FFE-derived DOI (9.68 mm) were larger than pathological DOI (5.7 mm). The SRCC between ioUS-derived DOI and pathological DOI was 0.63 and between 3D-FFE-derived DOI and pathological DOI was 0.58.

Conclusion: The results suggest that ioUS is as useful as post-contrast 3D-FFE imaging for the assessment of DOI of oral tongue SCC.

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Oral tongue squamous cell carcinoma; depth of invasion; intraoral ultrasonography; post-contrast three-dimensional fast field echo imaging

Introduction

Squamous cell carcinoma (SCC) is the most common malignancy in the oral tongue [1,2]. Alcohol and tobacco are the primary risk factors, while others include wood dust exposure, dietary deficiencies and habits, and poor oral hygiene [3]. Oral tongue SCC is a relatively unfavorable prognosis, possibly due to the absence of a strong barrier to prevent tumor diffusion and the presence of a well-developed lymph-vascular system that increases the risk of metastases [4,5]. The imaging modality is necessary to evaluate the local tumor extension in the tongue and the involvement of lymph nodes [3,6]. Depth of invasion (DOI) of the oral tongue SCC is known as a predictor of recurrence and survival in patients [7] and is recently been included as a criterion for staging oral cancers in the eighth edition of the American Joint Committee on Cancer (AJCC) Staging Manual [8].

In clinical practice, magnetic resonance imaging (MRI) [4,9,10], computed tomography (CT) [11–15], and intraoral ultrasonography (ioUS) [16–18] have been used to measure DOI. MRI and ioUS are not associated with radiation exposure compared with CT. There was a strong correlation between DOI measured using MRI (MR-DOI) and pathological DOI ($r = 0.68$) [19], with a difference of about 2–3 mm between them [17,18]. In the case of oral tongue cancer, tumor thickness (TT) measured using MRI or ioUS correlates well with histopathological DOI measurements [20]. Several studies had reported that radiologic TT measured on post-contrast T1-weighted images was significantly correlated with pathological TT [20,21]. The past reports have

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used T2-weighted images (T2WI), fat-suppressed T2WI, and post-contrast T1-weighted images to measure DOI [4,10,19,22,23]. Kawashima et al. [24] compared the usefulness of post-contrast three-dimensional fast field echo (3D-FFE) imaging and Dixon T2-weighted imaging for evaluating radiological DOI in comparison with pathological DOI in cases of oral tongue SCC. We concluded that post-contrast 3D-FFE imaging might be a better imaging technique than Dixon T2-weighted imaging to estimate the DOI of oral tongue SCC [24]. Both ioUS [16–18] and post-contrast 3D-FFE imaging [24] may be useful for predicting pathological DOI and can contribute to effective treatment plans and a positive prognosis. However, some patients cannot undergo MRI owing to claustrophobia and a history of allergic reactions to gadolinium. In such patients, ioUS is useful to assess the DOI of oral tongue SCC. On the other hand, some patients cannot undergo ioUS because of trismus and difficulty in stretching the tongue because of the SCC. An ioUS is less expensive and less invasive and has less examination time compared with MRI. However, there are no reports describing the usefulness of ioUS as a radiological method of DOI measurement compared with post-contrast 3D-FFE imaging in cases of oral tongue SCC. The purpose of this study was to evaluate the usefulness of ioUS in comparison with post-contrast 3D-FFE imaging for assessing radiological DOI and compare radiological DOI and pathological DOI in patients with oral tongue SCC.

Materials and Methods

This retrospective study was approved by the ethics committee of our institution (Approval number: 190321Epi ver.1). This study was conducted according to the Helsinki Declaration.

Patients

Fifteen of the 54 patients who were diagnosed with primary tongue SCC between August 2018 and March 2020 at our hospital were included in this study. The inclusion criteria were as follows: 1) a history of undergoing both post-contrast 3D-FFE imaging and ioUS of the oral tongue and 2) having a pathology report with a recording of pathological DOI. The exclusion criteria were as follows: 1) patients who did not undergo post-contrast 3D-FFE imaging or ioUS of the oral tongue; 2) a pathology report without a recording of pathological DOI; and 3) patients in whom the oral tongue could not be observed by motion artifact on post-contrast 3D-FFE imaging.

Intraoral ultrasonography

In all patients, ioUS was performed using HITACHI Prosound α7 (Hitachi, Japan). A 13-MHz "hockey-stick shaped" transducer (Ultra Sonography Transducer-536,) was placed without exerting pressure on the carcinoma, perpendicularly, with the oral tongue in a non-protruded position to create an axial image in which maximal DOI was measured from the transducer to the end of the hypoechoic border. The tumor was confirmed as a hypoechoic region compared with the normal tongue. The ioUS was performed during the patient's first visit by an oral and maxillofacial radiologist with 20 years of experience in head and neck ultrasonography.

MRI protocol

MRI was performed using a Philips Ingenia 3T CX machine (Amsterdam, Netherlands) with a head/neck 20-channel coil. All patients were examined in the supine position. Post-contrast 3D-FFE imaging was performed using the following parameters: repetition time/echo time, 3.6/1.79 ms; flip angle, 11°; field of view, 230 mm; imaging time, 2 minutes 35 seconds; and acquisition voxel MPS, 0.96/0.95/2.00 mm. Coronal and sagittal reformatted images with a thickness of 2 mm each were obtained from the axial images.

Evaluation of DOI

A picture archiving and communication system (Synapse Viewer; FUJIFILM Medical System, Tokyo, Japan) was used to view and evaluate the images. The DOI on the reformatted coronal, post-contrast 3D-FFE image (MR-DOI) was measured from the horizontal reference line (the line connecting the points where the tumor joined the normal mucosa on both sides) to the deepest aspect of the tumor (Fig. 1a and b). The DOI on ioUS (US-DOI) was measured by drawing a horizontal line corresponding to the basement membrane of the adjacent normal mucosa (Fig. 1c, white line) and a perpendicular line starting from the horizontal line to the deepest point of the tumor (Fig. 1c, double arrow). Both US-DOI and MR-DOI were measured according to the pathological DOI measurement standards outlined in the AJCC Cancer Staging Manual (eighth edition). Three oral and maxillofacial radiologists independently measured MR-DOI and US-DOI in all patients. Average values of these values were obtained as the final MR-DOIs or US-DOIs. After

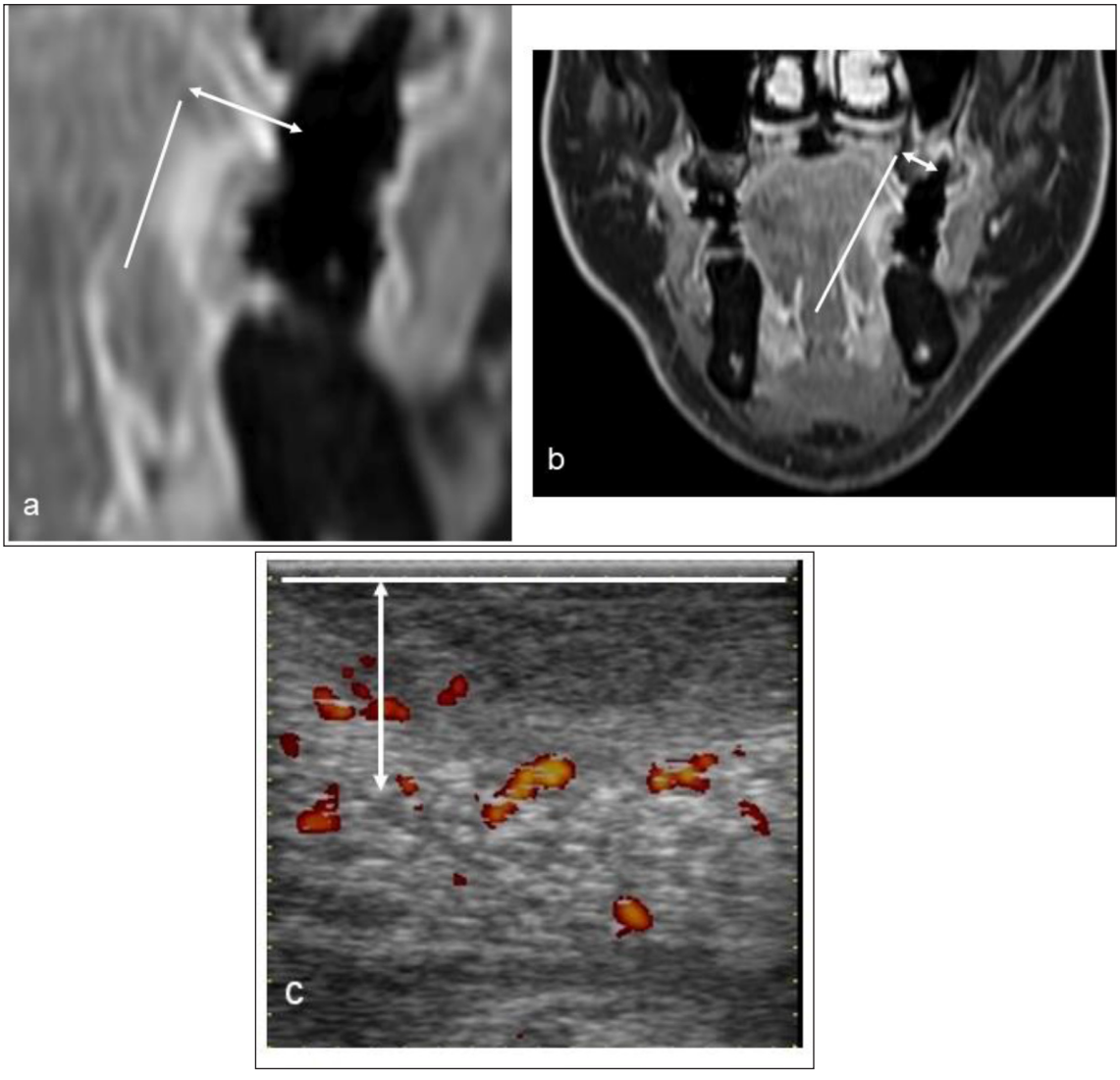


Figure 1. MR-DOI and US-DOI measurements at the left side of the oral tongue SCC in a 63-year-old male patient. (a and b) MR-DOI was 7.2 mm, (c) US-DOI was 7.3 mm, and (d) pathological DOI was 4.0 mm.

an interval of 1 week, the same evaluation was repeated in both MR-DOI and US-DOI to evaluate the intra-observer agreement. Inter-observer agreements and intra-observer agreements were evaluated by the intraclass correlation coefficient (ICC).

Histopathological evaluation

Specimen tissue samples, resected with the coronal plane, were subjected to pathological diagnosis. The samples were fixed in 10% neutral buffered formalin, segmented, and stained with hematoxylin and eosin. The sliced samples were evaluated by two oral pathologists. Pathological DOI was measured according to a past study [24]. We have collected pathological DOIs written on the histopathological reports.

Statistical analysis

The agreement between the MR-DOI and US-DOI was assessed using ICCs. Spearman's rank correlation coefficient (SRCC) was used to compare radiological DOI with pathological DOI. A *p*-value less than 0.05 was considered statistically significant. All data were recorded in Microsoft Excel (Microsoft Corp., Redmond, WA). All statistical analyses were performed using SPSS (version 16.0; SPSS Inc., Chicago, IL).

Results

The study cohort comprised 15 patients [10 men and 5 women; age range: 39–90 years; mean age ± standard deviation (SD), 66.3 ± 16.0 years]. The inter-observer reliability on US-DOI was 0.88, 0.82,

and 0.80, respectively. The inter-observer reliability on MR-DOI was 0.76, 0.85, and 0.81, respectively. inter-observer reliability on US-DOI was 0.88, 0.82 and 0.80, respectively. The intra-observer reliability on US-DOI was 0.81, 0.83 and 0.78, respectively. The intra-observer reliability on MR-DOI was 0.89, 0.85 and 0.88, respectively. Both US-DOI (mean ± SD: 9.96 ± 6.3 mm; range: 2.0–23.6 mm) and MR-DOI (mean ± SD: 9.68 ± 5.7 mm; range: 3.95–25.6 mm) were larger than the pathological DOI (mean ± SD: 5.7 ± 4.4 mm; range: 1.0–20.0 mm). The results of US-DOI, MR-DOI, and pathological DOI are shown in Table 1. The SRCC between US-DOI and pathological DOI was 0.63 ($p < 0.05$) (Fig. 2). The SRCC between MRI-DOI and pathological DOI was 0.58 ($p < 0.05$) (Fig. 3).

Discussion

Results of this study revealed that US-DOI and MR-DOI showed the same positive strength of correlation compared with pathological DOI.

DOI of oral tongue SCC should be assessed preoperatively. Several studies have described that imaging modalities such as CT, MRI, and ioUS are useful for the measurement of DOI [4,9–18]. However, each imaging modality has limitations when evaluating the DOI of oral tongue SCC. MRI may be limited by ferromagnetic dental materials or motion artifacts [25]. CT may be limited by metal artifacts from dental materials, X-ray beam hardening, and motion artifacts [25]. In this study, in 7 out of 15 patients, DOI could not be assessed on CT images because of streak artifacts from dental materials. Assessing DOI using ioUS may be limited by forward pulling of the oral tongue, which can deform the shape of the tumor, and patients' intraoral conditions such as hemorrhage from the oral tongue or trismus [24].

Takamura et al. [26] showed that ultrasonography is useful to evaluate oral tongue SCC compared with MRI, CT, or histopathological evaluation. Shintani et al. [27] showed a strong correlation between ultrasonographic and histopathological measurements ($r = 0.988$), revealing the superiority of ultrasound over MRI and CT in the assessment of oral cancer. Baek et al. [25] showed the usefulness of ultrasonography in prognosticating TT in pathologic sections of oral cavity SCC. Furthermore, even if both CT and MRI have some limitations, MRI provides more detailed soft tissue invasion by tongue cancer compared with CT. Songra et al. [28] showed a significant correlation ($r = 0.948$) of ultrasound in measuring primary TT compared with histopathological evaluation. Natori et al. [29] investigated 110 patients with tongue SCC and showed a strong correlation ($r = 0.74$; $p < 0.001$) between the assessment of TT using ultrasound and histopathological assessment. Yesuratnam et al. [18] observed that TT obtained using preoperative ioUS showed a higher correlation with histopathological TT ($r = 0.80$) than TT obtained using MRI ($r = 0.69$). Rocchetti et al. [30] observed a very strong correlation between

Table 1 The results of DOI assessment on MR (MR-DOI), US (US-DOI), and histopatho-logical reports (pDOI) in 15 cases.

Case	Sex	Age	US-DOI (mm)	MR-DOI (mm)	pDOI (mm)
1	Female	61	4.8	9	4
2	Female	90	10	9.7	9
3	Female	43	2	3.95	1
4	Male	71	23.6	17.7	5
5	Male	86	10	6.75	2
6	Male	43	4.5	4.98	4
7	Male	66	22.6	25.65	20
8	Male	75	6.04	7	6
9	Female	39	5.6	5.25	5
10	Male	64	7.6	7.2	4
11	Male	72	10.8	10.5	6
12	Male	63	7.2	8.1	3
13	Male	59	13.6	4.5	5
14	Female	88	14.4	13	7
15	Male	76	7	12	4

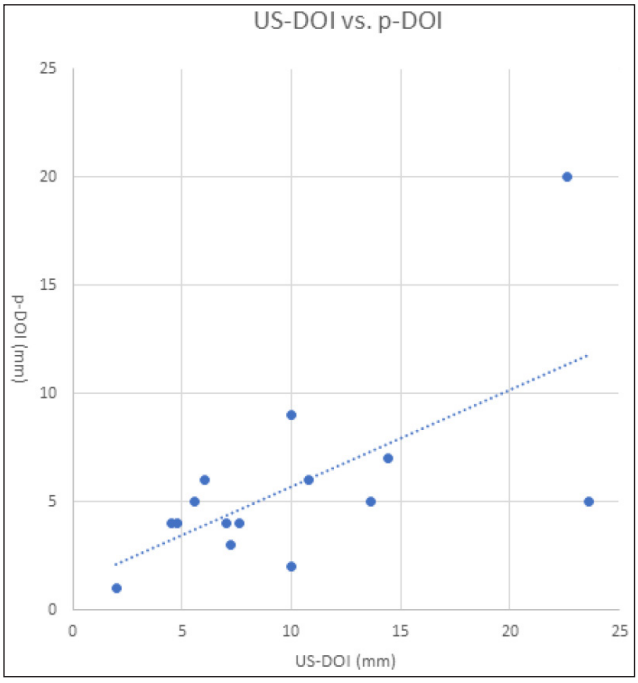


Figure 2. Correlation between US-DOI and pathological DOI. The correlation coefficient between US-DOI and pathological DOI was 0.63 ($p < 0.05$).

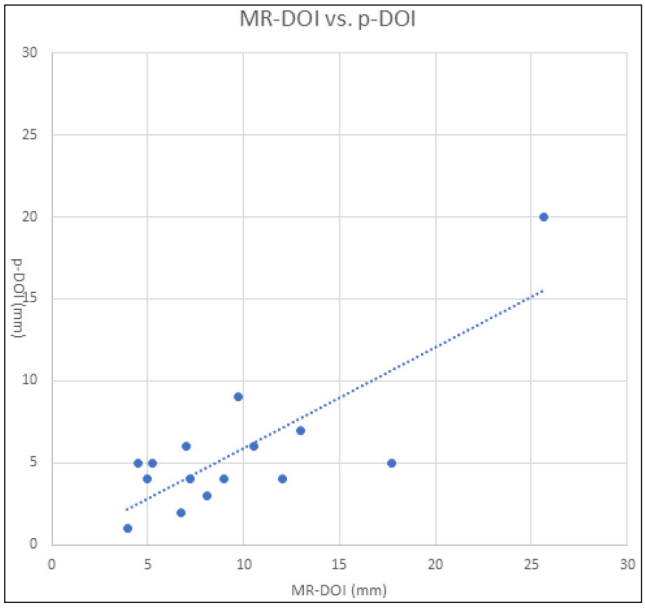


Figure 3. Correlation between MR-DOI and pathological DOI. The correlation coefficient between MR-DOI and pathological DOI was 0.58 ($p < 0.05$).

DOI measurements using ultrasound and histopathological examination ($r = 0.907$; $p < 0.001$). Filauro et al. [31] reported that SRCC between MR-DOI and histopathological DOI was 0.83 and between ioUS-DOI and histopathological DOI was 0.76. However, they evaluated the tongue, floor of mouth, and buccal mucosa. Therefore, the correlation coefficient for assessing DOI of tongue SCC is uncertain.

Results of this study showed a moderate correlation between US-DOI and pathological DOI ($r = 0.63$, $p < 0.05$) and MR-DOI and pathological DOI ($r = 0.58$, $p < 0.05$). These results showed less correlation compared with that observed by Rocchetti et al. [30]. This difference may be due to the difference in the number of patients included in both studies. There was a discrepancy between MR-DOI and pathological DOI, and US-DOI and pathological DOI. These discrepancies may be caused by distortion and shrinkage of specimens during the formalin fixation process in histopathological processing [32]. The strength of this study was that we have revealed that ioUS may be as useful as MRI for the evaluation of DOI of oral tongue SCC. The weakness of this study was patients who have difficulties in conducting ioUS and MRI cannot gain the benefits from this study.

This study has a few limitations. This was a retrospective study with a relatively small number of patients. Therefore, further prospective research using a large sample on this topic is necessary to validate the results. When conducting ioUS of the oral tongue, we stretched the patients' tongue as much as they can. Stretching of the oral tongue may have shortened US-DOI measurement. A standard method for ioUS of the oral tongue needs to be established in future studies.

Conclusion

This was the first study to demonstrate the usefulness of ioUS compared with post-contrast 3D-FFE imaging for assessing radiological DOI in patients with oral tongue SCC and comparing radiological DOI with pathological DOI. The results suggest that ioUS is as useful as post-contrast 3D-FFE imaging for the assessment of DOI of oral tongue SCC; ioUS can be used when MRI is contraindicated or unavailable and vice versa.

Conflict of interest

There is no potential conflict of interest.

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