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ORIGINAL RESEARCH

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Usefulness of post-contrast three-dimensional Fast Field Echo imaging compared with Dixon T2-weighted imaging for the evaluation of radiological depth of invasion in 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 that occurs within the oral cavity, with the tongue being the most frequent site affected. The depth of the carcinoma invasion has been demonstrated to be a predictor of cervical metastasis, recurrence, and disease-specific survival; depth of invasion (DOI) is also clinically used as a criterion for performance of elective neck dissection in early oral SCC. Both post-contrast three-dimensional Fast Field Echo (3D-FFE) imaging and Dixon T2-weighted imaging (T2WI) may be useful to predict pathological DOI and can contribute to a successful treatment plan and patient prognosis. The purpose of this study was to evaluate the usefulness of post-contrast 3D-FFE imaging compared with Dixon T2WI for assessing radiological DOI, compared with pathological DOI, in oral tongue SCC.

Methods: Twenty-two patients who have been diagnosed with tongue SCC were included in this study. The Wilcoxon singed-rank test was used to compare radiological DOI with pathological DOI, using both 3D-FFE imaging and DIXON T2WI.

Results: The correlation coefficient between radiological DOI and pathological DOI using post-contrast 3D-FFE imaging was 0.79 ($p < 0.01$). The correlation coefficient between radiological DOI and pathological DOI using Dixon T2WI was 0.72 ($p < 0.01$).

Conclusion: These data suggest that both post-contrast 3D-FFE imaging and DIXON T2WI may be useful in providing DOI estimations in oral tongue SCC; however, the post-contrast 3D-FFE imaging may be a better imaging technique than Dixon T2WI for cases of oral tongue SCC.

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Depth of invasion (DOI); magnetic resonance imaging (MRI); oral tongue SCC

Introduction

Squamous cell carcinoma (SCC) is the most common malignancy that occurs in the oral cavity, and the tongue is usually the most frequently site affected [1]. The 8th edition of the American Joint Committee on Cancer (AJCC) Staging Manual incorporated depth of invasion (DOI) into the T stage of oral cavity cancer [2]. This measurement method was implemented according to the pathological DOI measurement standards outlined in the AJCC Cancer Staging Manual (8th edition), which includes a statement that "DOI is measured by first finding the 'horizon' of the basement membrane of the adjacent normal squamous mucosa" [2]. DOI has been demonstrated to be an efficient predictor of cervical metastasis, recurrence, and disease-specific survival, and is clinically used as a criterion for the performance of elective neck dissection in early (T1/T2) oral SCC [3–5]. In clinical practice, computed tomography (CT) [6-9], magnetic resonance imaging (MRI) [10–13], and ultrasonography (US) [14] have been used for the measurement of DOI. There was a strong correlation between DOI measurement on MRI (MR-DOI) and pathological DOI ($r = 0.68$) [15], with a difference between pathological

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DOI and MR-DOI of about 2–3 mm [16,17]. There was a strong correlation between CT-DOI and pathological DOI, and the difference between pathological DOI and CT-DOI was about 1.2 mm [15]. Moreover, there was a significant correlation between MR-DOI and pathological DOI [18]. A DOI larger than 5 mm is associated with an increased risk of nodal metastases [19]. Several studies have reported that radiologic tumor thickness measured on contrast-enhanced T1-weighted images had a significant correlation with histologic tumor thickness [20,21]. The post-contrast three-dimensional Fast Field Echo (3D-FFE) imaging is one of the thin slice (acquisition voxel MPS = 0.96/0.95/2.00 mm), contrast-enhanced T1-weighted imaging (T1WI).

Previous studies have suggested that the evaluation of DOI in oral tongue SCC requires fat-suppressed T2-weighted images [17,22]. The Dixon T2-weighted imaging (T2WI) is based on the simultaneous acquisition of in-phase and opposed-phased images, allowing the production of fat-only (water-suppressed) and water-only (fat-suppressed) images through post-processing adjustments [23]. Previous studies have demonstrated that the Dixon T2-weighted images allowed detecting head and neck SCC [23,24]. Both post-contrast 3D-FFE imaging and Dixon T2WI may be useful to predict pathological DOI and can contribute to effective treatment plans and positive patient prognosis. However, there are no reports that described the usefulness of post-contrast 3D-FFE imaging as a radiological DOI measurement method compared with Dixon T2WI in oral tongue SCC.

The purpose of this study was to evaluate usefulness of post-contrast 3D-FFE imaging compared with Dixon T2WI for assessing radiological and pathological DOIs in oral tongue SCC.

Materials and Methods

Patients

Of the 54 patients who underwent MRI for the evaluation of the tongue lesions between August 2018 and March 2020 at Kagoshima University Hospital, only 22 patients were included in this study. Inclusion criteria were patients who have been diagnosed with oral tongue SCC, having a pathological DOI recorded in the pathology report, and the application of the conducted post-contrast 3D-FFE imaging.

MRI protocol

MRI was carried out on a Philips Ingenia 3T CX with a head/neck 20 channel coil. All patients were examined in the supine position. Post-contrast 3D-FFE imaging was obtained using the following parameters: Time (TR)/ Echo Time (TE) = 3.6/1.79 ms; flip angle of 11; field of view = 230 mm; imaging time of 2 minutes 35 seconds; and acquisition voxel MPS = 0.96/0.95/2.00 mm. Coronal and sagittal reformatted images with 2 mm thickness were obtained from the axial perspective. The coronal T2-weighted Dixon fat-sat sequence was obtained using the following parameters: TR = 4,000 ms; TE = 80 ms; number of excitations was 1; acquisition voxel MPS = 0.97/1.34/6.00 mm; field of view = 280 mm; and imaging time of 2 minutes 16 seconds.

MRI evaluation

We used a picture archiving and communication system (Synapse viewer Fuji Medical system, Tokyo, Japan) to view and evaluate the images. Radiological DOI was measured from the horizon reference line (the line connecting the junctions of the tumor and the normal mucosa on both sides), to the deepest aspect of the tumor lesion on reformatted coronal post-contrast 3D-FFE image and coronal Dixon T2-weighted image, according to the pathological evaluation. This measurement method was implemented according to the pathological DOI measurement standards outlined in the AJCC Cancer Staging Manual (8th edition) (Fig. 1). Three oral and maxillofacial radiologists measured the radiological DOIs in all patients independently. The average of these values was used for confirmation of final radiological DOI. Intraclass and interclass correlation coefficients were used to determine the validity of measurements taken in this study.

Pathological evaluation

Specimen tissue samples, resected from the coronal plane, were subjected to histopathological analysis. The samples were fixed in 10% neutral buffered formalin, embedded, sectioned, and stained with hematoxylin and eosin. The sliced specimens were evaluated by an oral pathologist. Pathological DOI was measured according to the guidelines of the AJCC Cancer Staging Manual system (8th edition).

Statistical analysis

The agreement of radiological DOI was assessed by using the interclass and intraclass correlation coefficients. The Wilcoxon singed-rank test was used to compare radiological DOI with pathological DOI. Values less than $p = 0.05$ were considered statistically significant. All data were recorded in Microsoft

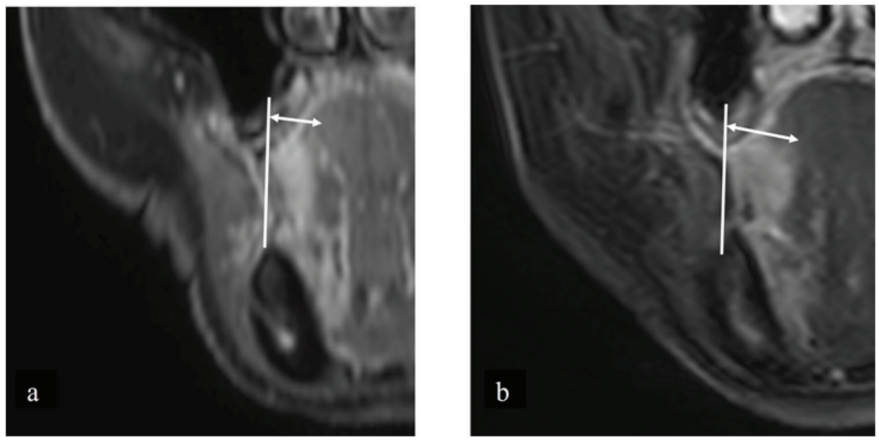


Figure 1. Radiological DOI and pathological DOI measurements taken from the right side of the tongue SCC in an 88-year-old female. Radiological DOI in the post-contrast 3D-FFE image was 9.7 mm (a); the radiological DOI using the Dixon T2WI (b) was 15.5 mm; and the pathological DOI was 9.0 mm.

Excel (Microsoft Corp, Redmond, WA). All statistical analyses were carried out using SPSS version 16.0 (SPSS Inc., Chicago, IL).

Results

Patient characteristics

The study cohort comprised 22 patients [17 male and 5 female; age ranged from 39 to 90 years, with a mean age of 67.3 years; standard deviation (SD) = ±14.7].

The interclass and intraclass correlation coefficients of measurement of radiological DOI were 0.88 and 0.94, respectively. The radiological DOIs on both post-contrast 3D-FFE images (mean = 12.21 mm; range = 2.0–45.25 mm; SD = ±10.62) and the Dixon T2-weighted images (mean = 14.74 mm; range = 3.73–43.5 mm; SD = ±9.34) were larger than the pathological DOI (mean = 9.68 mm; range = 1.0–45.0 mm; SD = ±11.18). The mean discrepancy between the radiological DOI and the pathological DOI on post-contrast 3D-FFE imaging was 2.5 mm (range = −4.95 to 13.3 mm) (Table 1). The mean discrepancy between the radiological DOI and the pathological DOI on Dixon T2WI was 5.1 mm (range = −2.51 to 15.8 mm) (Table 1). The correlation coefficient between the post-contrast 3D-FFE image-assessed radiological DOI and pathological DOI was 0.79 ($p < 0.01$) (Fig. 2). The correlation coefficient between the Dixon T2-weighted image-assessed radiological DOI and pathological DOI was 0.72 ($p < 0.01$) (Fig. 3). The correlation coefficient between the radiological DOIs on the post-contrast 3D-FFE imaging and Dixon T2WI was 0.88 ($p < 0.01$) (Fig. 4).

Discussion

The 8th edition of the AJCC Cancer Staging Manual incorporated DOI as an assessment during the T stage of oral cavity cancer [2]. As such, the criteria of assessing radiological DOI have been established. Numerous studies have reported that US is a non-invasive diagnostic imaging technique and is useful for measuring DOI. However, when performing the intraoral US examination, the tongue is fixed in a stable position by pulling it forward, which can deform the shape of the tumor. Furthermore, depending on the patient's intraoral condition, such as painful or hemorrhagic, intraoral US may not be a feasible option. In such cases, DOI could be measured using CT or MR images. Some published studies have reported that there is excellent correlation and accurate measurement using contrast-enhanced CT [6,7], but a common limitation of CT when evaluating DOI of oral tongue cancer is dental metal artifact [6–8]. Recently, there have been some commercial techniques made available for metal artifact reduction in CT, but are not sufficient to reduce the dental metal artifacts [8,9].

On the other hand, since MRI has a high resolution for soft tissue and less dental metal artifact compared with CT image, MRI is useful to evaluate the extension of the tumor and DOI. Regarding MRI as a radiological DOI measurement method, it is reported that T2WI and contrast enhanced (CE)-T1WI with fat suppression a provide higher mean score among the visual assessments of DOIs, between the four differential MRI sequences, such as T1WI, T2WI, Short Tau Inversion Recovery, and CE-T1WI methods [23]. There are advanced MRI

Table 1. Comparison of the different measured values between radiological DOI and pathological DOI.

	mesured value (mm)				difference of mesured values (mm)	
	3D FFE DOI	Dixon T2 DOI	*p*DOI*		3D FFE DOI - *p*DOI	D ixon T2 DOI-*p*DOI
case 1	2.00	3.73	1.00		1	2.73
case 2	6.47	7.49	1.00		5.47	6.49
case 3	8.80	13.90	1.00		7.8	12.9
case 4	7.20	8.20	2.00		5.2	6.2
case 5	6.45	11.60	3.00		3.45	8.6
case 6	6.00	7.16	4.00		2	3.16
case 7	2.74	7.90	4.00		1.26	3.9
case 8	4.74	15.01	4.00		0.74	11.01
case 9	6.92	9.71	4.00		2.92	5.71
case 10	9.20	15.50	4.00		5.2	11.5
case 11	3.14	4.32	4.00		0.86	0.32
case 12	18.30	20.80	5.00		13.3	15.8
case 13	7.80	7.87	5.00		2.8	2.87
case 14	7.62	7.85	6.00		1.62	1.85
case 15	8.50	11.00	6.00		2.5	5
case 16	9.70	15.50	9.00		0.7	6.5
case 17	9.20	15.40	11.00		1.8	4.4
case 18	25.65	26.90	20.00		5.65	6.9
case 19	23.91	22.34	24.00		0.09	1.66
case 20	20.05	22.49	25.00		4.95	2.51
case 21	29.00	26.00	25.00		4	1
case 22	45.25	43.50	45.00		0.25	1.5
*pDOI: pathological DOI				mean	3.343636364	5.568636364
				SD	3.06296	4.17114
						Paierd T-test, *P*< 0.002

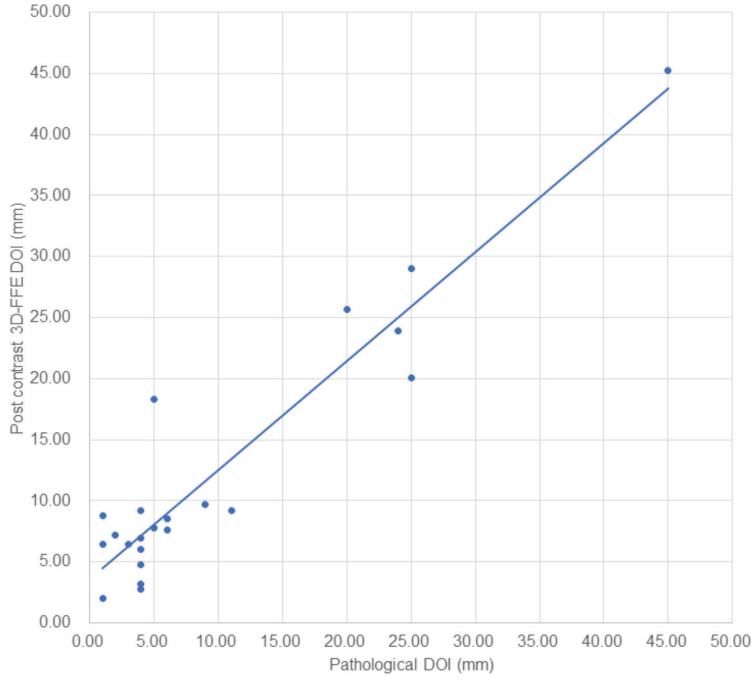


Figure 2. The correlation between radiological DOI and pathological DOI using post-contrast 3D-FFE imaging. The correlation coefficient between radiological DOI and pathological DOI was 0.79 ($p < 0.01$).

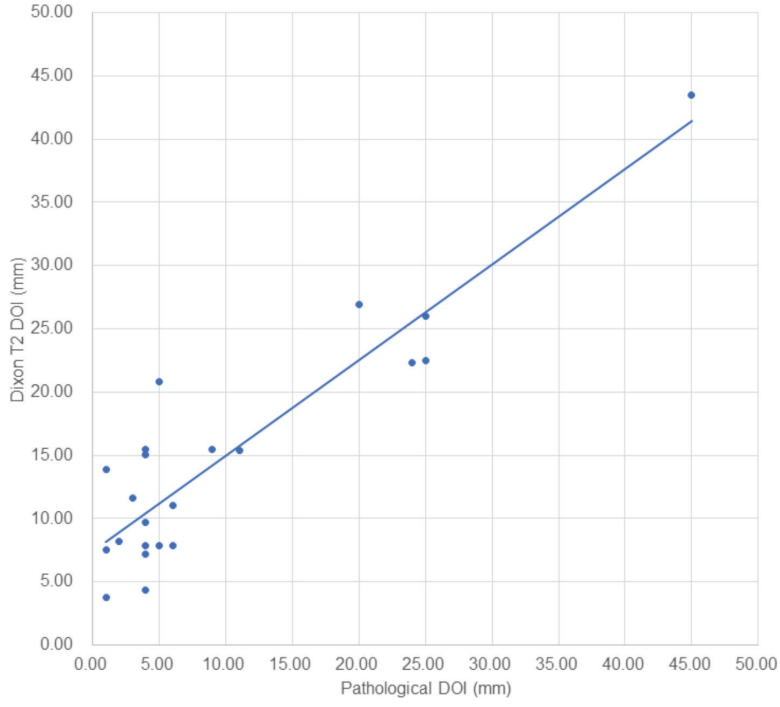


Figure 3. The correlation between radiological DOI and pathological DOI using Dixon T2WI. The correlation coefficient between radiological DOI and pathological DOI was 0.72 ($p < 0.01$).

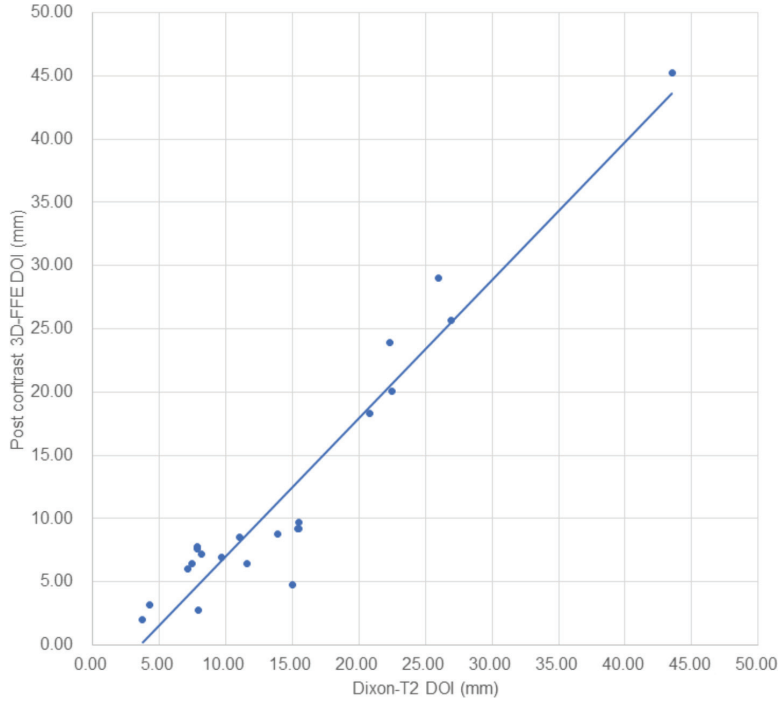


Figure 4. The correlation between radiological DOIs using post-contrast 3D-FFE imaging and Dixon T2WI. The correlation coefficient between radiological DOIs on post-contrast 3D-FFE imaging and Dixon T2WI was 0.88 ($p < 0.01$).

with regard to the evaluation of head and neck SCC [25–27]. Razek et al. [25] conclude that the Ch/Cr levels, determined using proton magnetic resonance spectroscopy (^{1}H-MRS) and apparent diffusion coefficient (ADC) values, are well correlated with several prognostic parameters of head and neck SCC. Razek et al. [26] concluded that tumor blood flow is a non-invasive imaging parameter that correlates well with the pathological degree of tumor differentiation, clinical stage, and nodal metastasis

of head and neck SCC. Razek [27] concluded that mean diffusivity and fractional anisotropy parameters of diffusion tensor imaging are non-invasively reliable and reproducible parameters that can help in differentiating residual head and neck SCC from post-radiation changes. Recently, post-contrast 3D-FFE imaging has been used for the diagnosis of various diseases [28–30]. Since post-contrast 3D-FFE imaging facilitates more efficient scans of thin slices compared with 2D imaging, it may allow for more accurate evaluations of lesions. Therefore, we evaluated the usefulness of post-contrast 3D-FFE imaging and compared it with Dixon T2WI, as a method for measuring radiological DOI and pathological DOI in oral tongue SCC. Previous studies have reported that there was a significant correlation between MR-DOI and pathological DOI. Preda et al. [15] showed MR-DOI and pathological DOI have a strong correlation (r = 0.68). Murakami et al. [16] indicated that the agreement between MRI and pathological measurements of oral tongue cancer had a good correlation (Intraclass correlation coefficients (ICC) = 0.611). The result of this study showed that the correlation coefficient in radiological DOI in post-contrast 3D-FFE image and pathological DOI was greater than the radiological DOI measured in Dixon T2-weighted images. This suggests that post-contrast 3D-FFE imaging has better visualization of the tongue SCC when compared with T2WI.

There is a discrepancy between radiological DOI and pathological DOI. This is potentially explained by tumor shrinkage after radical resection, which has been reported to be about 87% [31], and during the preparation of the pathological specimen, the shrinkage was reported to be about 20% [31]. Additionally, factors that affect radiological DOI may include inflammatory changes around the tumor, the limitation of the spatial resolution of post-contrast 3D-FFE imaging, and the discrepancies in the radiological DOI measurements between the three oral and maxillofacial radiologists. However, we used post-contrast 3D-FFE imaging to evaluate radiological DOI. The combination of advanced MRI and radiological DOI measurement on post-contrast 3D-FFE imaging may add more value to the evaluation of head and neck SCC.

There are some limitations in this study. This study was retrospective study with a limited number of patients. Therefore, further research on this topic is necessary to validate the result. The limitation of the post-contrast 3D-FFE imaging is that it is feasible to the artifact caused by a patient's body motion.

Conclusion

This is the first study to describe the usefulness of post-contrast 3D-FFE imaging compared with Dixon T2WI for assessing radiological DOI in oral tongue SCC, compared with pathological DOI. The data suggest that both post-contrast 3D-FFE imaging and Dixon T2WI may useful in providing assessments of DOI in oral tongue SCC; however, post-contrast 3D-FFE imaging may be a better imaging technique than Dixon T2WI in this context.

Ethical approval

This retrospective study was approved by the Ethics Committee on Epidemiological Studies, Kagoshima University (Approval number: 200016Epi ver.1, apporoval date: October, 10th, 2020.).

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