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ORIGINAL RESEARCH

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Ultrasound accurately assesses depth of invasion in T1-T2 oral tongue cancer

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Abstract

Background: Depth of invasion (DOI) is important for the T-classification of squamous cell carcinoma of the oral tongue (SCCOT) and incorporated in the TNM 8 classification of oral cavity cancer. To determine DOI clinical palpation is performed, but the preferred radiological modality remains controversial. The aim of this study was to investigate the assessment of DOI using ultrasound (US-DOI).

Methods: The DOI was assessed in 40 patients with T1–T3 SCCOT by ultrasound, palpation, computed tomography and magnetic resonance imaging (MRI). Histopathological DOI (H-DOI) was gold standard. Bland–Altman analysis was used to compare mean difference and 95% limits of agreement (LOA).

Results: The mean difference of US-DOI was −0.5 mm (95% LOA −4.9–4.0) compared to H-DOI and the mean difference for MRI was 3.9 mm (95% LOA −2.3–10.2). In the subgroup analysis of cT1-T2 the US-DOI mean difference was 0.1 mm and the 95% LOA limits −2.5–2.7.

Conclusions: Ultrasound seems to be the most accurate method to assess DOI in T1-T2 SCCOT. MRI overestimates DOI and cannot assess a substantial proportion of the tumors.

Level of Evidence: 2c.

KEYWORDS
depth of invasion, oral cancer, tongue cancer, ultrasonography, ultrasound

1 | INTRODUCTION

Squamous cell carcinoma of the oral tongue (SCCOT) is the most common type and subsite of oral cavity cancer.[1,2] Its incidence is increasing, especially in young adults for unknown reasons.[1,3,4] The correct classification of the primary tumor and nodal status is fundamental before discussing adequate treatment with the patient. Depth of invasion (DOI) was introduced in the TNM8 classification of oral cavity cancer to improve prognostic information from the T-staging.[5–7] There is a strong evidence for the active management of the N0 neck compared to watchful waiting.[8] Sentinel lymph node biopsy is evolving as an option in this situation for T1-T2 tumors.[9–12] In centers

preferring elective neck dissection, DOI is important in deciding whether surgery of the neck should be recommended, and a common cut-off for this is DOI > = 3–4 mm.[8,13,14]

Since DOI is a histopathological measurement of the resected specimen, after the introduction of TNM8, there has been great interest in the preoperative assessment of DOI in SCCOT. Clinical palpation is performed; however, the preferred radiological modality remains controversial. Computed tomography (CT) and magnetic resonance imaging (MRI) are often used, but artifacts from dental restorations and difficulties in visualizing smaller tumors make Ultrasound (US) an interesting alternative.[15–17] US is more accurate than CT and MRI for measuring tumor thickness (TT) in T1–T2 tumors.[15,18,19] There are also some recent US studies assessing DOI reporting promising results.[20–22] Moreover there are several optical methods used in oral cancer to assist in the diagnosis of mucosal lesions, such as optical coherence tomography, even though the depth limit of 1.5–2.0 mm makes it less useful for assessing DOI.[23,24]

The aim of the present study was to determine whether DOI can be accurately assessed preoperatively using US (US-DOI) when histopathology (H-DOI) is the gold standard. The performance of US was compared to that of MRI (MRI-DOI), CT (CT-DOI) and clinical palpation (Palp-DOI). The outcome measures were the mean difference between the assessed DOI and H-DOI analyzed graphically using the Bland–Altman plot and proportion of correct T-classification for the different modalities.

2 | MATERIALS AND METHODS

This study was approved by the Swedish Medical Ethics Committee and registered at ClinicalTrials.gov (ID NCT04059861).

The study population consisted of consecutive patients with biopsy-proven primary SCCOT and floor of the mouth cancer stage T1–T3 according to TNM8[7] who presented to Örebro University Hospital, a tertiary referral hospital, between May 2019 and December 2021. Patients provided written consent after receiving oral and written information about the study. Exclusion criteria were previous surgery and/or radiotherapy in the oral cavity, stage T4 tumors, and patients unsuitable for surgery.

DOI was measured by palpation, and then US was performed preoperatively in an outpatient setting before the multidisciplinary team meeting (MDT). In case of pain or discomfort that could impede the assessment, the patient was offered local anesthesia with either a gauze soaked in Carbocaine® epinephrine 1% + 0.5 ug/ml or lingual nerve block injecting 1–3 ml of the same solution medial to the last molar on the ipsilateral side of the tumor. All but one preoperative examination were performed by the same head and neck surgeon. In one patient another head and neck surgeon at our clinic performed US after which review of recorded pictures was performed. A BK Medical Flex Focus 500 US system with high-frequency linear 8870 probe (Peabody, MA, USA) was used for all patients. US frequency of 18 MHz and a gain between 50% and 65% were used along with water-based Eco gel (Vitric Medical, Stockholm, Sweden) and a transducer cover (Karex Industries Sdn. Bhd, Pontian, Malaysia). The US-DOI was measured in millimeters and rounded to 0.5 mm, Figure 1. Videos and pictures were recorded. The smallest pressure with the probe necessary to achieve an adequate image was applied and the tongue was held gently with a gauze, as different pressures could alter the DOI by several millimeters. An imaginary line from the level of the adjacent hyperechoic basal membrane on either side of the tumor, was used for measurements down to the deepest part of the hypoechoic tumor. In case of an irregular tumor border, the deepest part visualized was used. The examiner was blinded to the CT and MRI findings.

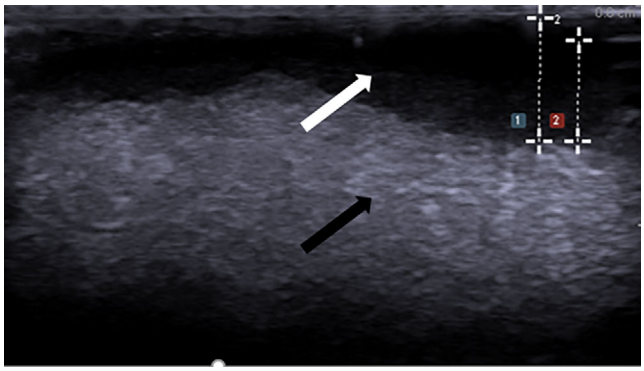

FIGURE 1 Preoperative US measurement of depth of invasion (DOI). The tumor is seen hypoechoic (white arrow) compared to the isoechogenic normal tongue muscle (black arrow). 1 = 5.5 mm represents tumor thickness (TT). 2 = 4.5 mm represents DOI

Surgery was performed 1–3 weeks after the preoperative examination. With the patient under general anesthesia, before the surgical resection, palp-DOI and US-DOI were repeated in the same manner as described above. Thirty-four of the measurements were performed by the same examiners as above, and three by two other head and neck surgeons at our clinic. US was also used to assist tongue resection in another study (ClinicalTrial ID NCT04059861).

The histopathological measurement of DOI was performed from an imaginary line at the level of the basal membrane to the deepest part of the tumor. The MRI-DOI and CT-DOI were assessed by a neuroradiologist when reviewing the images before the MDT. In general the slice thickness was 4 mm for MRI and 1 mm for CT. The sequence plane that best visualized the tumor was chosen and the DOI was measured from an imaginary line drawn at the level of the basal membrane to the deepest point of the tumor.

2.1 | Statistical analyses

A clinically significant difference in the DOI was defined before the study started at 2 mm. A sample size of 19 patients would have a 90% power to detect this difference as statistically significant with a paired *t* test at significance level .05, if the standard deviation for the paired differences was 2.5. Taking into account the subgroup analyses for

T-stage, we aimed to include 42 patients. Alpha was set to .05 and all analyses were performed using IBM SPSS version 25 (Armonk, NY, USA). Bland–Altman plots[25] were used to compare the agreement of the different DOI measurements with histopathology being the gold standard. The difference was plotted on the y-axis and the mean value on the x-axis. The bias between the methods was estimated with mean difference in mm, and 95% limits of agreement (LOA) lines were calculated.

TABLE 1 Patient demographics, examination feasibility with and without anesthesia

n	40	
Age		
Mean (SD)	65 (14)	
Range	34–86	
Gender women	15 (37.5%)	
cT-stage TNM8		
T1	19 (47.5%)	
T2	10 (25.0%)	
T3	11 (27.5%)	
Subsite		
Tongue	40 (100%)	
US examination feasible[a]		
Yes	33 (84.6%)	
No	1 (2.6%)	
Partly	5 (12.8%)	
Local anesthesia		[b]
None	28 (71.8%)	24 (86%)
Lingual nerve block	7 (17.9%)	7 (100%)
Topical anesthesia gauze	4 (10.3%)	2 (50%)

[a]Ultrasound examination preoperatively performed without discomfort or pain influencing the result. $n = 39$, one patient missing data.
[b]*n* (%) of patients with US examination classified as feasible in the different groups of anesthesia.

3 | RESULTS

In the present study 42 patients were included. Since only two had floor of the mouth cancers, these were excluded from the analysis, leaving 40 patients with SCCOT in the final study population. The patient demographics are shown in Table 1. In the outpatient setting 84.6% of the US examinations could be performed without pain or discomfort influencing the results, Table 1. 12.8% percent of the examinations were classified as "partly feasible" because of discomfort, and 2.6% (one patient with T3 tumor, H-DOI 24 mm) as not feasible. Still DOI could be measured in all these cases. The lingual nerve block was successful in all seven cases in which it was used. MRI-DOI could not be assessed in eight of the 38 examinations (21.0%), because smaller tumors were not visible or motion artifacts interfered. CT could assess DOI in two of the 40 examinations. CT-DOI was 5 mm and 9 mm compared to H-DOI, which was 3 mm and 8 mm respectively, therefore in both these cases T-staging according to DOI was correct. Artifacts were the most common reason CT could not determine DOI, but since the radiological review predominantly used MRI for the assessment of DOI there might be an underestimation of the proportion of CT where DOI could be measured.

Bland–Altman analysis in Figure 2 and Table 2 demonstrated that the mean difference for US-DOI compared to gold standard H-DOI was −0.5 mm (95% CI −1.2–0.3) with 95% LOA of 4.0 to −4.9. Pearson correlation of mean difference versus mean of US-DOI and H-DOI was −0.6 ($p < .001$), indicating a difference in US-DOI assessment of smaller and larger tumors (US tend to underestimate larger tumors).

MRI-DOI overestimated DOI by 3.9 mm (95% CI 2.7–5.1, $p < .001$) compared to H-DOI, Figure 3, with 95% LOA of −2.3–10.2. These results refer to the 30 patients in whom MRI could assess DOI.

Preoperative Palp-DOI showed a mean difference of −0.9 mm (95% CI −1.8–0.0) compared to H-DOI, Figure 4. The Pearson correlation was −0.4 ($p = .017$), indicating that palpation tend to underestimate larger tumors.

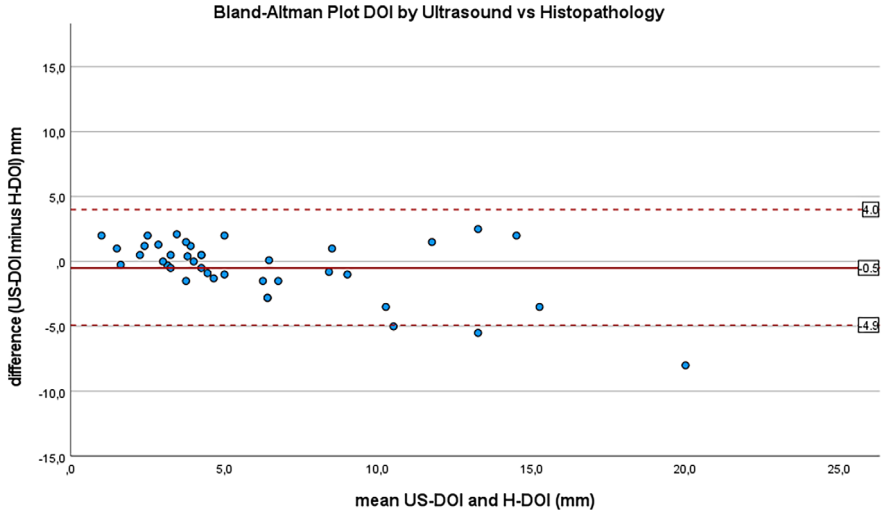

FIGURE 2 Bland–Altman analysis of preoperative US-DOI versus H-DOI. $n = 40$. Solid line represents mean difference and dotted lines 95% limits of agreement (LOA)

TABLE 2 Bland–Altman analysis. Performance of the different modalities in assessing DOI compared to H-DOI (reference method)

		Test modality	H-DOI (gold standard)	Bias[a]	Lower LOA (95% CI)	Upper LOA (95% CI)	Pearson correlation difference vs. mean
	n	Mean (SD)	Mean (SD)	Mean diff (95% CI)			
US-DOI preop	40	6.0 (3.8)	6.4 (5.1)	−0.5 (−1.2–0.3) $p = .21$	−4.9 (−4.2–−5.6)	4.0 (3.3–4.7)	−0.6 $p < .001$
US-DOI preop cT1–T2	29	4.0 (1.4)	3.9 (2.2)	0.1 (−0.4–0.6) $p = .72$	−2.5 (−3.0–−2.0)	2.7 (2.2–3.2)	−0.6 $p = .001$
US-DOI intraop	35	6.3 (5.0)	6.5 (5.4)	−0.2 (−1.4–1.0) $p = .78$	−7.0 (−8.1–−5.8)	6.6 (5.5–7.8)	−0.1 $p = .50$
Palp-DOI preop	40	5.5 (4.1)	6.4 (5.1)	−0.9 (−1.8–0.0) $p = .049$	−6.4 (−7.2–−5.5)	4.6 (3.7–5.4)	−0.4 $p = .017$
Palp-DOI preop cT1–T2	29	3.5 (1.7)	3.9 (2.2)	−0.5 (−1.0–0.1) $p = .089$	−3.3 (−3.9–−2.8)	2.4 (1.9–2.9)	−0.3 $p = .065$
Palp-DOI intraop	35	6.1 (5.7)	6.7 (5.3)	−0.6 (−1.7–0.5) $p = .26$	−6.7 (−7.8–−5.7)	5.5 (4.5–6.6)	0.1 $p = .51$
MRI-DOI	30	10.8 (4.7)	6.8 (5.3)	3.9 (2.7–5.1) $p < .001$	−2.3 (−3.5–−1.2)	10.2 (9.0–11.3)	−0.2 $p = .34$

Abbreviations: CI, confidence intervals; H-DOI, depth of invasion by histopathology of resected specimen; Intraop, examination intraoperatively; LOA, limits of agreement; MRI-DOI, depth of invasion by magnetic resonance imaging; Palp-DOI, depth of invasion by palpation; Preop, examination preoperatively; SD, standard deviation; US-DOI, depth of invasion by ultrasound.
[a]Bias is defined as mean difference in mm between test modality and H-DOI (gold standard) estimated with paired *t* test.

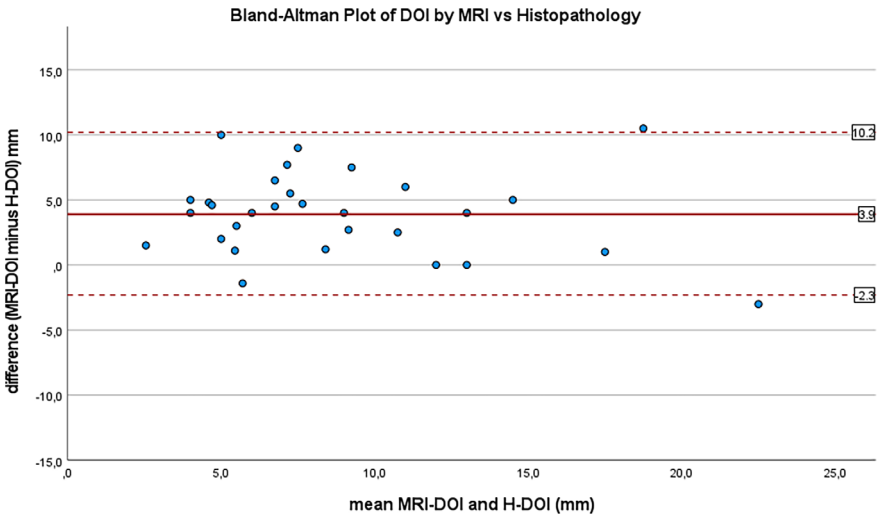

FIGURE 3 Bland–Altman analysis of MRI-DOI versus H-DOI. $n = 30$. Solid line represents mean difference and dotted lines 95% limits of agreement (LOA)

In the subgroup analysis of cT1–T2 tumors, the Bland–Altman plot for preoperative US-DOI showed a mean difference of 0.1 mm (95% CI −0.4–0.6) and the 95% LOA limits −2.5–2.7 were narrower, Figure 5. Palp-DOI for cT1-T2 showed a mean difference of −0.5 mm (95% CI −1.0–0.1) and the 95% LOA limits −3.3–2.4 were narrower, Figure 6.

No obvious improvement was seen in the intraoperative US-DOI and Palp-DOI mean difference and 95% LOA limits in comparison to the preoperative examinations, Table 2.

In Table 3 the ability of the different modalities to classify DOI into correct intervals according to TNM8 (T1 < = 5 mm, T2 > 5 mm, < = 10 mm, T3 > 10 mm) is demonstrated in proportions with 95% CI. For T1 tumors, US-DOI and Palp-DOI were correct in 95% (95% CI 77%–100%) of the patients and significantly better than 5% (95% CI 0%–25%) for MRI-DOI. For T2 and T3 tumors, no significant differences in classification ability were seen but the sample sizes were low. For the entire study population, MRI-DOI was correct in only 29% (95% CI 14%–46%) and significantly lower than the other modalities. No improvement was seen in the intraoperative US-DOI or Palp-DOI compared to preoperative examination in this classification.

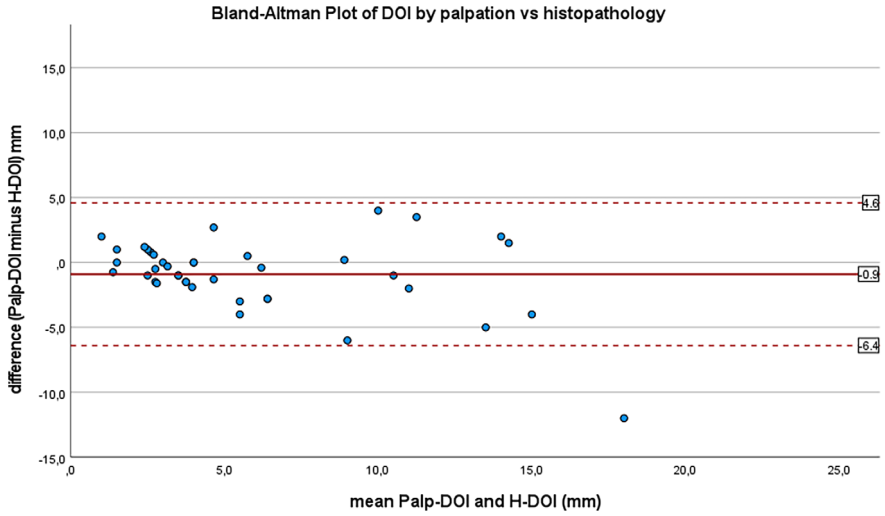

FIGURE 4 Bland–Altman analysis of preoperative Palp-DOI versus H-DOI. $n = 40$. Solid line represents mean difference and dotted lines 95% limits of agreement (LOA)

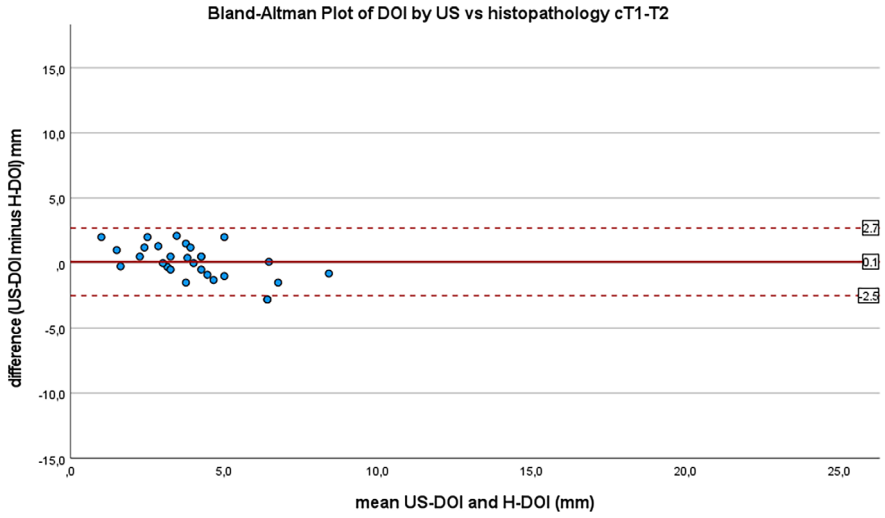

FIGURE 5 Bland–Altman analysis of preoperative US-DOI versus H-DOI in cT1-T2. $n = 29$. Solid line represents mean difference and dotted lines 95% limits of agreement (LOA)

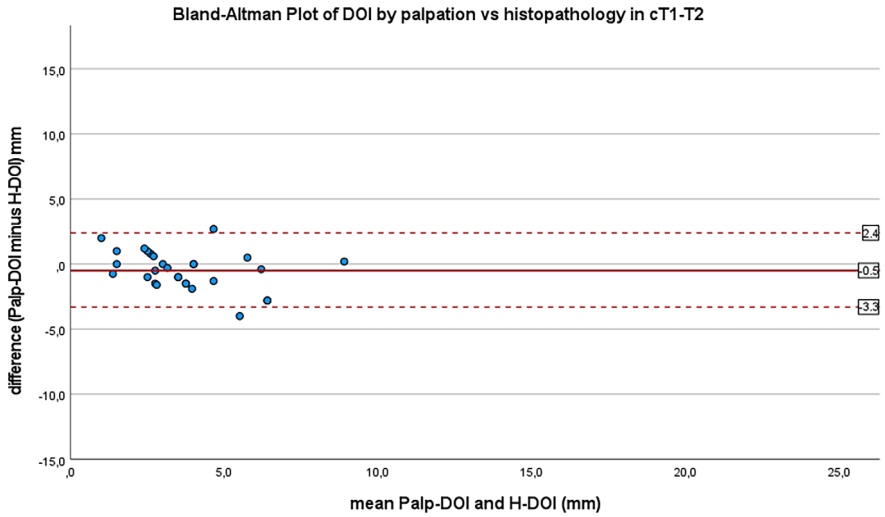

FIGURE 6 Bland–Altman analysis of preoperative Palp-DOI versus H-DOI in cT1-T2. $n = 29$. Solid line represents mean difference and dotted lines 95% limits of agreement (LOA)

4 | DISCUSSION

In the present study, the US-DOI and the Palp-DOI were significantly better than MRI-DOI. MRI could not assess DOI in eight of 38 (21.0%) of the patients and overestimated DOI by 3.9 mm in those that were assessable. The wider 95% LOA limits in MRI-DOI indicate higher random variability for this modality. US and palpation could be performed preoperatively in an

outpatient setting, and no clear advantage of intraoperative examination was observed.

Since DOI is part of T-staging in TNM8 and is important in the decision to treat the N0 neck, accurate preoperative assessment is needed. CT is often used for nodal classification and can be helpful to correctly delineate the extent of the primary tumor including DOI, when the tumor is visible.[26,27] Unfortunately in a large majority artifacts have been reported to make visualization impossible,[22,26] in line with the results of this study. Instead, MRI is often used to better assess the primary tumor, including DOI. In the literature, the results of MRI-DOI in SCCOT vary, with most studies reporting an overestimation of 2–3.5 mm.[18,22,28–30] In agreement with those results, the present study showed an overestimation as well, even though the mean difference of 3.9 mm by MRI was slightly larger. On the contrary a subgroup analysis in a systematic review found T1-weighted MRI images to perform substantially better with a mean difference of 0.77 mm (95% LOA −4.5–6.8) compared to T2-weighted images with a mean difference of 2.1 mm (95% LOA −5.2–9.5).[31] However, another important issue is that there is a considerable proportion of patients in whom MRI cannot assess the tumor or DOI at all, especially in T1 tumors.[15,16,28–30] These circumstances and the fact that US is a well-established method to measure tumor thickness have led to expectations in US to assess DOI in early SCCOT defined as T1–T2 according to TNM8.

In this prospective study, US could preoperatively assess the DOI in all patients, with local anesthesia used when indicated. In the Bland–Altman analysis, US-DOI had a smaller mean difference and width of the 95% LOA limits compared to MRI-DOI, suggesting US to be a better method. This result was reinforced by the subgroup analysis of cT1–T2. In a retrospective study of US-DOI in T1–T2 tumors, Takamura[22] demonstrated a mean difference of 0.2 mm (95% LOA −2.6–2.9), very similar to the mean difference of 0.1 mm (95% LOA −2.5–2.7) in our study, and they conclude that US is the most accurate method. Filauro prospectively studied 40 patients and reported a mean difference of 0.3 mm for US-DOI.[20] Moreover they had even better results for MRI-DOI with a mean difference of 0.2 mm, in contrast to the overestimation of DOI by MRI seen in most studies, including the present one. Lida retrospectively found US to correctly classify DOI < = 5 mm,[21] in line with our study, where US correctly classified 95% of the DOIs < = 5 mm. In the present study, Palp-DOI was very accurate in T1 tumors, but not as good as US-DOI in T2 tumors. Intraoperative palpation did not improve these results, Table 3.

Intraoperative frozen section analysis of DOI is another method to decide the DOI and if an elective neck dissection is indicated, and seems accurate in comparison to histopathological analysis.[32,33] The technique assumes availability of intraoperative pathology analysis and greater operative resources since the preoperative planning is more difficult.

Limitations of the present study include a small sample size, especially when considering the subgroup analyses. Moreover there was a lack of details of the MRI examinations. The study focused on US-DOI, and the performance of MRI-DOI could possibly differ depending on how the MRI examinations were performed, including the slice thickness and image sequences used. The present results of the MRI-DOI were the actual assessments before MDT and, in that sense, generalizable. Palp-DOI and US-DOI were measured simultaneously and palpation could have influenced the US assessment since it was performed first. However, the two methods can be viewed as complementary and thereby improving the preoperative assessment

TABLE 3 Proportion of correct classification of DOI by the different modalities according to the TNM8 T-stage interval (T1 < = 5 mm, T2 > 5 mm and < = 10 mm, T3 > 10 mm). DOI by histopathology is reference

	T1 ($n = 22$)		T2 ($n = 10$)		T3 ($n = 8$)		All ($n = 40$)	
T-stage based on DOI by histopathology report.	***n***	**Percentage (95% CI)**	***n***	**Percentage (95% CI)**	***n***	**Percentage (95% CI)**	***n***	**Percentage (95% CI)**
Correct US preop	21	95% (77–100)	6	60% (26–88)	6	75% (35–97)	33	83% (67–93)
Correct Palp preop	21	95% (77–100)	3	30% (7–65)	5	63% (24–91)	29	73% (56–85)
Correct MRI	1	5%[a] (0–25)	3	30% (7–65)	7	88% (47–100)	11	29%[b] (15-46)
Correct US intraop	19	95%[a] (75–100)	4	57%[c] (18-90)	6	75% (35–97)	29	83%[d] (66-93)
Correct Palp intraop	18	95%[e] (74–100)	3	38%[f] (9-76)	5	63% (24–91)	26	74%[d] (57-88)

[a] $n = 20$ patients included.
[b] $n = 38$ patients included (in eight patients MRI could not produce DOI and therefor classified as incorrect T-staging).
[c] $n = 7$ patients included.
[d] $n = 35$ patients included.
[e] $n = 19$ patients included.
[f] $n = 8$ patients included. Patients not included is because of missing data.

of DOI. As DOI is a histopathological measurement of the resected specimen, all preoperative assessments have several possible biases.[18] Shrinkage of the specimen after resection and fixation in formalin[34,35] decreases the H-DOI and potentially leads to preoperative measurements falsely overestimating the DOI. Inflammation from biopsy or the tumor itself could also be mistaken for tumor tissue and result in overestimation of DOI, especially by MRI. Pressure from the US probe or stretching of the tongue could lead to the underestimation by the US-DOI. Tumor growth from the preoperative measurements until surgical resection could result in a false underestimation of DOI. All of these biases could theoretically influence the results, but in the end, the agreement is what matters. The present study benefits from data on both preoperative and intraoperative measurements of DOI, and since these were quite similar, substantial tumor growth seems unlikely.

The US-DOI measurements in our study were performed by a head and neck surgeon, in contrast to most other studies where a radiologist performed the US.[20,22] The ability of US to detect the deep tumor margin support the possibility of US-assisted tongue resection,[36–40] which is facilitated by the fact that a trained head and neck surgeon can perform the US.

Based on these results we conclude that palpation together with US better determines DOI in cT1–T2 tumors compared to MRI. MRI seems to be more indicated for T3 tumors. This approach has the potential to improve the accuracy of preoperative DOI and save resources.

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FUNDING INFORMATION

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CONFLICT OF INTEREST

All authors declare that they have no conflicts of interest.

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REFERENCES

1. Ng JH, Iyer NG, Tan MH, Edgren G. Changing epidemiology of oral squamous cell carcinoma of the tongue: a global study. *Head Neck*. 2017;39(2):297-304.
2. Regionalt cancercentrum. Nationellt vårdprogram Huvud- och Halscancer 2019 Available from: https://kunskapsbanken.cancercentrum.se/diagnoser/huvud-och-halscancer/.
3. Annertz K, Anderson H, Palmér K, Wennerberg J. The increase in incidence of cancer of the tongue in the Nordic countries continues into the twenty-first century. *Acta Otolaryngol*. 2012;132(5):552-557.
4. Sturgis EM, Cinciripini PM. Trends in head and neck cancer incidence in relation to smoking prevalence: an emerging epidemic of human papillomavirus-associated cancers? *Cancer*. 2007;110(7):1429-1435.
5. Ebrahimi A, Gil Z, Amit M, et al. Primary tumor staging for oral cancer and a proposed modification incorporating depth of invasion: an international multicenter retrospective study. *JAMA Otolaryngol Head Neck Surg*. 2014;140(12):1138-1148.
6. Lydiatt WM, Patel SG, O'Sullivan B, et al. Head and neck cancers-major changes in the American joint committee on cancer eighth edition cancer staging manual. *CA Cancer J Clin*. 2017;67(2):122-137.
7. Brierley J, Gospodarowicz MK, Wittekind C. *TNM Classification of Malignant Tumours. Chichester*. John Wiley & Sons, Inc; 2017.
8. D'Cruz AK, Vaish R, Kapre N, et al. Elective versus therapeutic neck dissection in node-negative Oral cancer. *N Engl J Med*. 2015;373(6):521-529.
9. Pedersen NJ, Jensen DH, Hedbäck N, et al. Staging of early lymph node metastases with the sentinel lymph node technique and predictive factors in T1/T2 oral cavity cancer: a retrospective single-center study. *Head Neck*. 2016;38(Suppl 1):E1033-E1040.
10. Schilling C, Stoeckli SJ, Haerle SK, et al. Sentinel European node trial (SENT): 3-year results of sentinel node biopsy in oral cancer. *Eur J Cancer*. 2015;51(18):2777-2784.
11. Hasegawa Y, Tsukahara K, Yoshimoto S, et al. Neck dissections based on sentinel lymph node navigation versus elective neck dissections in early Oral cancers: a randomized, multicenter, and noninferiority trial. *J Clin Oncol*. 2021;39(18):2025-2036.
12. Garrel R, Poissonnet G, Moyà Plana A, et al. Equivalence randomized trial to compare treatment on the basis of sentinel node biopsy versus neck node dissection in operable T1-T2N0 Oral and oropharyngeal cancer. *J Clin Oncol*. 2020;38(34):4010-4018.
13. NCCN Guidelines Head and Neck Cancers 2022 https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf.
14. UpToDate treatment of stage I and II head and neck cancer: the oral cavity https://www.uptodate.com/contents/treatment-of-stage-i-and-ii-early-head-and-neck-cancer-the-oral-cavity?search=gingival%20cancer&topicRef=3389&source=see_link.
15. Shintani S, Yoshihama Y, Ueyama Y, et al. The usefulness of intraoral ultrasonography in the evaluation of oral cancer. *Int J Oral Maxillofac Surg*. 2001;30(2):139-143.
16. Yesuratnam A, Wiesenfeld D, Tsui A, et al. Preoperative evaluation of oral tongue squamous cell carcinoma with intraoral ultrasound and magnetic resonance imaging-comparison with histopathological tumour thickness and accuracy in guiding patient management. *Int J Oral Maxillofac Surg*. 2014;43(7):787-794.
17. Tarabichi O, Bulbul MG, Kanumuri VV, et al. Utility of intraoral ultrasound in managing oral tongue squamous cell carcinoma: systematic review. *Laryngoscope*. 2018;129:662-670.
18. Noorlag R, Klein Nulent TJW, Delwel VEJ, et al. Assessment of tumour depth in early tongue cancer: accuracy of MRI and intraoral ultrasound. *Oral Oncol*. 2020;110:104895.
19. Klein Nulent TJW, Noorlag R, van Cann EM, et al. Intraoral ultrasonography to measure tumor thickness of oral cancer: a systematic review and meta-analysis. *Oral Oncol*. 2018;77:29-36.
20. Filauro M, Missale F, Marchi F, et al. Intraoral ultrasonography in the assessment of DOI in oral cavity squamous cell carcinoma: a comparison with magnetic resonance and histopathology. *Eur Arch Otorhinolaryngol*. 2021;278(8):2943-2952.
21. Iida Y, Kamijo T, Kusafuka K, et al. Depth of invasion in superficial oral tongue carcinoma quantified using intraoral ultrasonography. *Laryngoscope*. 2018;128(12):2778-2782.
22. Takamura M, Kobayashi T, Nikkuni Y, et al. A comparative study between CT, MRI, and intraoral US for the evaluation of the depth of invasion in early stage (T1/T2) tongue squamous cell carcinoma. *Oral Radiol*. 2022;38(1):114-125.
23. Romano A, di Stasio D, Petruzzi M, et al. Noninvasive imaging methods to improve the diagnosis of Oral carcinoma and its precursors: state of the art and proposal of a three-step diagnostic process. *Cancers (Basel)*. 2021;13(12):2864.

24. Reddy RS, Sai Praveen KN. Optical coherence tomography in oral cancer: a transpiring domain. *J Cancer Res Ther*. 2017;13(6):883-888.
25. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*. 1986;1(8476):307-310.
26. Baba A, Ojiri H, Ogane S, et al. Usefulness of contrast-enhanced CT in the evaluation of depth of invasion in oral tongue squamous cell carcinoma: comparison with MRI. *Oral Radiol*. 2021;37(1):86-94.
27. Chin SY, Kadir K, Ibrahim N, Rahmat K. Correlation and accuracy of contrast-enhanced computed tomography in assessing depth of invasion of oral tongue carcinoma. *Int J Oral Maxillofac Surg*. 2021;50(6):718-724.
28. Fu JY, Zhu L, Li J, et al. Assessing the magnetic resonance imaging in determining the depth of invasion of tongue cancer. *Oral Dis*. 2021;27(3):457-463.
29. Mao MH, Wang S, Feng ZE, et al. Accuracy of magnetic resonance imaging in evaluating the depth of invasion of tongue cancer. *A Prospective Cohort Study Oral Oncol*. 2019;91:79-84.
30. Murakami R, Shiraishi S, Yoshida R, et al. Reliability of MRI-derived depth of invasion of Oral tongue cancer. *Acad Radiol*. 2019;26(7):e180-e186.
31. Li M, Yuan Z, Tang Z. The accuracy of magnetic resonance imaging to measure the depth of invasion in oral tongue cancer: a systematic review and meta-analysis. *Int J Oral Maxillofac Surg*. 2022;51(4):431-440.
32. Moe J, McHugh JB, Udager AM, Braun TM, Helman JI, Ward BB. Intraoperative depth of invasion is accurate in early-stage Oral cavity squamous cell carcinoma. *J Oral Maxillofac Surg*. 2019;77(8):1704-1712.
33. Kumar SS, George NA, Anila KR, Sebastian P. Can frozen section be used to assess depth of invasion of early carcinoma of tongue? *Oral Oncol*. 2015;51(11):e87-e88.
34. Johnson RE, Sigman JD, Funk GF, Robinson RA, Hoffman HT. Quantification of surgical margin shrinkage in the oral cavity. *Head Neck*. 1997;19(4):281-286.
35. Umstattd LA, Mills JC, Critchlow WA, Renner GJ, Zitsch RP 3rd. Shrinkage in oral squamous cell carcinoma: an analysis of tumor and margin measurements in vivo, post-resection, and post-formalin fixation. *Am J Otolaryngol*. 2017;38(6):660-662.
36. Baek CH, Son YI, Jeong HS, et al. Intraoral sonography-assisted resection of T1-2 tongue cancer for adequate deep resection. *Otolaryngol Head Neck Surg*. 2008;139(6):805-810.
37. Bulbul MG, Tarabichi O, Parikh AS, et al. The utility of intra-oral ultrasound in improving deep margin clearance of oral tongue cancer resections. *Oral Oncol*. 2021;122:105512.
38. Helbig M, Flechtenmacher C, Hansmann J, Dietz A, Tasman AJ. Intraoperative B-mode endosonography of tongue carcinoma. *Head Neck*. 2001;23(3):233-237.
39. Kodama M, Khanal A, Habu M, et al. Ultrasonography for intraoperative determination of tumor thickness and resection margin in tongue carcinomas. *J Oral Maxillofac Surg*. 2010;68(8):1746-1752.
40. Tarabichi O, Kanumuri V, Juliano AF, Faquin WC, Cunnane ME, Varvares MA. Intraoperative ultrasound in Oral tongue cancer resection: feasibility study and early outcomes. *Otolaryngol Head Neck Surg*. 2017;194599817742856:645-648.

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