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RESEARCH PAPER

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Feasibility and diagnostic performance of sentinel node biopsy for staging cN0 oral squamous cell carcinoma in a previously treated neck

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Abstract

Objectives: Staging of the cN0 neck with sentinel node biopsy (SNB) in early-stage oral squamous cell carcinoma (OSCC) is validated in patients with a previously untreated neck. We aimed to investigate the feasibility and diagnostic accuracy of SNB and unexpected drainage patterns in patients with cT1-T2N0 OSCC and a history of previous head and neck cancer comprising treatment of the neck, that is, surgery, radiotherapy, or both.

Methods: Fifty patients with a previously treated neck diagnosed with a new primary or recurrent cN0 OSCC between 2014 and 2021 were included and retrospectively analyzed. Feasibility was assessed by the rate of successfully performed SNB neck staging procedures. Based on follow-up data, the diagnostic performance of SNB was evaluated by calculation of negative predictive value (NPV) and false omission rate (FOR).

Results: A SNB staging procedure was successfully performed in 76% (38/50) of the patients. Technical failures were due to the lack of drainage preoperatively or failure in intraoperative SN detection. In patients successfully staged with SNB, the rate of a positive SN was 13% (5/38). In the SNB-negative group, no patients were diagnosed with a regional node recurrence during follow-up, and the NPV and FOR were 100% and 0%, respectively. Unexpected lymphatic drainage occurred in 32% (12/38) of the patients.

Conclusion: SNB is technically feasible in cT1-2N0 OSCC patients with a previously treated neck with a high diagnostic accuracy. Importantly, SNB enables the detection of individual and unexpected lymphatic drainage patterns.

KEYWORDS
neck metastasis, neck staging, oral squamous cell carcinoma, radiotherapy, sentinel node biopsy

Key points

Significant findings of the study

High diagnostic accuracy using sentinel node biopsy (SNB) to stage a previously treated neck with a negative predictive value of 100%. SNB in a previously treated neck is more technically challenging due to fibrosis and scar tissue.

What this study adds?

This study adds more knowledge of the feasibility and diagnostic accuracy when using SNB to stage patients with oral squamous cell carcinoma and a previously treated neck. It also shows altered lymphatic drainage patterns in these patients.

INTRODUCTION

In 2020, 377,713 new cases of lip and oral cavity cancer were reported worldwide. In northern Europe, the incidence was six per 100,000 for men and 3.1 per 100,000 for women. In the management of oral cancer, nodal disease at the time of diagnosis is one of the most important prognostic factors for outcome and accurate neck staging is of key importance.[1–3]

In the subset of patients with a cN0 neck, based on clinical examination, ultrasonography, and radiological imaging, the risk of regional subclinical metastasis remains 20%–30%.[4,5]

Elective neck dissection (END) of neck levels I–III for cT1-2N0 oral squamous cell carcinoma (OSCC) has traditionally been applied to manage the cN0 neck with the dual purpose of regional staging as well as treatment if occult nodal disease is present. Since the vast majority of patients with no clinical signs of regional spread are pathologically node-negative (pN0), END inherently afflicts unnecessary overtreatment to these patients. Further, patients with an unexpected drainage pattern are at risk of inaccurate neck staging and possible subsequent neck failure as seen in patients with a lateralized tumor site and a contralateral metastasis on the neck.[6] As an alternative to END, sentinel node biopsy (SNB) has been introduced and gradually validated during the last decades in many institutions as a minimally invasive surgical staging method that allows to select those patients that are pathologically node-positive and therefore likely to benefit from a therapeutic END.

Two recent randomized clinical trials have concordantly shown SNB to be noninferior to END in diagnostic staging accuracy, with no statistically significant difference in overall survival (OS) and disease-free survival.[7,8] Also, pooled meta-analytic data deducted from the SNB series show high sensitivity and negative predictive value (NPV).[7–10]

In addition, a significantly lower morbidity of SNB compared to END has been reported in terms of impairment of shoulder function, patient-reported outcome, rebleeding, and nerve damage.[7,11,12] From an economic health care perspective cost–benefit analyses comparing SNB and END, SNB was reported as more cost-effective.[13,14]

Patients treated for a head and neck cancer have a risk of local recurrence of 10%–30%, as well as an annual risk of a new primary head and neck cancer of 3%–4%.[15] In the case of local recurrence or a new primary in the oral cavity and cN0 neck status, accurate staging of the neck remains equally important. However, the vast majority of previous studies that investigated the reliability of SNB have routinely excluded patients with previous neck treatment. A theoretical concern for the oncological safety and reliability of SNB has been stated in this group of patients because drainage in the neck lymphatics could be disturbed.

The drainage to the lymphatics in the neck from different subsites in the oral cavity is, to some extent, predictable in terms of which neck levels to consider at risk of harboring occult metastasis.[16] However, data accumulated in the process of introducing SNB to stage the untreated cN0 in OSCC has shown that one major advantage of using this staging technique is that it allows to detect unusual patterns of drainage, most importantly the detection of contralateral drainage from lateralized tumors and the exact drainage pattern in terms of laterality from tumors evolving the midline.

As the lymphatic drainage in the previously treated neck may be altered due to fibrosis and scarring, the use of SNB in this group of patients may particularly be beneficial because the individual pattern of drainage can be visualized. Also, SNB has the ability to detect occult metastasis in levels that would not be included in an END. In addition, END in a previously treated neck is technically more challenging and carries a higher risk of complications, why performing a less invasive SNB procedure seems more justified.[17]

Two previous retrospective studies, comprising 22 and 53 patients, respectively, investigated SNB neck staging of cN0 OSCC with a previously treated neck, and reported the procedure to be feasible and with an acceptable diagnostic accuracy.[18–20] Based on this data, it was recommended in the Surgical Consensus Guidelines on SNB from 2019 that SNB could be offered to patients with a history of previous treatment to the neck and a new primary OSCC with a clinically negative neck.[21] In our service, we commenced the use of SNB as the standard technique for patients with a previously treated neck in 2019 and before that SNB was offered to selected patients with cN0 neck.

The aim of this study was to investigate the feasibility and diagnostic accuracy of SNB in patients with newly diagnosed cT1-T2N0 OSCC and a history of previous treatment to the neck. Primary endpoints were false-negative rate (FNR), false omission rate (FOR), and NPV based on follow-up as reference. Secondary endpoints were the rate of a successful SNB procedure and the rate of unusual drainage patterns.

MATERIALS AND METHODS

Study design and population

We conducted a retrospective cohort study at Rigshospitalet in Copenhagen, which is a tertiary head and neck cancer center receiving patients from the eastern part of Denmark with a population of approximately 2.8 million people. In Denmark, cancer treatment is only provided at public hospitals and is paid over taxes, hence it is free of charge for all patients. Patients were searched in the Copenhagen Oral Cavity Squamous Cell Carcinoma database that includes patients diagnosed with OSCC and referred to our institution from January 2014 to April 26, 2021.[22] Inclusion criteria were patients with a history of a previous head and neck cancer where the neck was treated with a subsequent new primary or recurrent OSCC cT1-2 with a cN0 neck where SNB was performed. Previous treatment of the neck consisted of either surgery (END/selective neck dissection (SND) or SNB), radiotherapy, or a combination of both. Exclusion criteria were lack of follow-up data and absence of previous neck treatment.

The study was approved by the Ethical Committee of the Capital Region of Denmark (protocol no. H-15016322) and was conducted in accordance with the Declaration of Helsinki from 2002.

Procedure

At Rigshopsitalet, SNB has been the standard treatment for N0 necks for over 20 years. Patients underwent dynamic and static lymphoscintigraphy and single photon emission computed tomography/computed tomography (SPECT/CT) on the day or the day before surgery, according to a previously described protocol.[5] The ^{99m}Tc-Nanocoll tracer was injected by the operating surgeon into four submucosal peritumoral deposits. Imaging was reviewed by a nuclear medicine physician to indicate the presence and location of sentinel nodes (SNs) detected. During surgery, if the SN was located close to the tumor site, the tumor was resected before the SNB procedure in the neck in an attempt to lower the risk of shine through level I. The SNs were detected intraoperatively with a handheld gamma probe. A radioactive count of at least 10% of the count of the hottest node was applied to qualify a detected lymph node as an additional SN. A successful SNB was defined as the retrieval of at least one SN from a neck side where preoperative imaging indicated the presence of an SN.

Harvested SNs were formalin-fixated, paraffin-embedded, and submitted for step-serial sectioning with staining of sections for hematoxylin–eosin and for pancytokeratin. According to guidelines, if an SN was positive, a completion SND was performed in a second surgery. Metastases were divided into isolated tumor cells (<0.2 mm), micrometastases (≥0.2 and ≤2 mm), and macrometastases (>2 mm).[23] The 8th edition of the tumor node metastasis (TNM) staging manual was applied.[24] Following primary treatment, patients entered a surveillance program and were seen for regular control visits for a total of 5 years according to national guidelines.[25] Control visits included physical examination and ultrasonography of the neck.

To evaluate the diagnostic performance of SNB, a false-negative (FN) event was defined as an isolated regional recurrence in a prior SNB-negative neck. FNR was calculated from the FN and the true positive (TP) using the equation (FN/FN + TP). FOR was calculated from FN and the true negative (TN) using the equation (FN/FN + TN). NPV was calculated as 1 − FOR. Unexpected lymphatic drainage was defined as drainage only on the outside levels I–III ipsilaterally, and drainage to a lymph node located on the contralateral side of the neck from a well-lateralized tumor side (1 cm from the midline).[16] OS was defined from the time of diagnosis to death of all causes. Recurrence-free survival (RFS) was defined from the time of diagnosis until recurrence, whereas regional recurrence-free survival (RRFS) was defined from the time of diagnosis until the diagnosis of a neck nodal recurrence.

Data collection

Data parameters collected from patient medical records included demographic data, tumor characteristics, current treatment, previous head and neck cancer, type of previous neck treatment, neck-side laterality of treatment, number of SNs harvested, pathological SN status, and follow-up status. Previous radiated neck data concerning the side of the neck was unavailable. Follow-up was noticed in January 2022.

Statistical methods

Statistical analyses were performed in SAS Enterprise Version 9.4. Survival curves were analyzed by the Kaplan–Meier method, and we used log rank for comparisons. Endpoints in the survival analysis were OS, RFS, and RRFS. The descriptive statistics as frequencies, mean, median, and range was calculated in Microsoft Excel Version 16.64.

RESULTS

Characteristic

A total of 50 patients were included in the study (Table 1). All patients were previously treated for head and neck cancer (OSCC, pharyngeal, or laryngeal cancer). Table 2 shows an overview of the previous treatment and cancer history of the cohort.

Five patients had a positive SNB, hence the rate of SNB positivity in the cohort was 13% (5/38). An average of two (range: 0–6) SNs per patient were identified and removed during the procedure. The median follow-up time was 25 months (range: 1–77 months).

In 12 patients, the current SNB procedure was performed on the side of the neck without a history of previous treatment. Hence, they were excluded from the analysis of lymphatic

TABLE 1 Patient and tumor characteristics ($n = 50$).

Characteristics	N (%)
Number of patients	
Female	17 (34)
Male	33 (66)
Mean age (years, range)	67 (36–90)
Injection day before	7 (14)
Injection same day	43 (86)
pT status	
T1	37 (74)
T2	11 (22)
T3	2 (4)
Tumor subsite	
Tongue	26 (52)
Floor of mouth	14 (28)
Retromolar	4 (8)
Buccal mucosa	3 (6)
Lower gingiva	2 (4)
Soft palate	1 (2)
Depth of invasion (mm, range)	3.1 (0.3–11.0)
Midline involvement	12 (24)
Sentinel node biopsy ($n = 38$)	
Negative	33 (87)
Positive	5 (13)
Previous neck treatment	
Surgery alone ipsilaterally	8 (16)
Surgery alone contralaterally	11 (22)
Surgery alone bilaterally	2 (4)
Radiotherapy alone bilaterally	16 (32)
Radiotherapy alone contralaterally	1 (2)
Surgery and radiotherapy bilaterally	12 (24)

drainage patterns since the current SNB was performed on the nontreated side of the neck.

Preoperative imaging and intraoperative SN detection rates

A successful SNB procedure was performed in 76% (38/50) of the cases. Hence, in 12 patients, the SNB procedure was not technically possible due to a lack of drainage preoperatively (six patients) or failure to detect the SNs intraoperatively (six patients), and they were excluded from the analysis of diagnostic accuracy. The patients where SNB staging failed had either an END performed or watchful waiting of the neck.

SNs were identified preoperatively on the SPECT/CT in 44/50 patients, hence the preoperative SN imaging rate was 88%. In one patient, SNs were only visualized bilaterally in the axillary regions and not in the neck. All six patients with nondetectable SNs preoperatively had previously received radiotherapy bilaterally either alone or with surgery.

The intraoperative SN detection rate was 86% (38/44). At least one SN was removed in 40 patients—two patients had bilateral drainage preoperatively but only SNs on one side of the neck were possible to be removed during surgery.

Of the six patients with failure to detect SNs intraoperatively, two patient courses were as described above. In two patients, during surgery it was doubted whether the T-site was sufficiently injected, and preoperative visualized drainage was considered unreliable. In the last two patients, diffuse γ-radiation was found but without a nodal hotspot. For three of the patients with nondetectable SNs intraoperatively, the SNB was converted to END. In the other three patients, observation of the nonstaged neck was decided.

Positive SN

At least one positive SN was detected in five (13%) patients. In four of the latter patients, ipsilateral drainage from the current tumor site was visualized at the same side of the neck as the previous treatment. Two patients were previously treated with ipsilateral surgery alone, one with bilateral radiotherapy alone, and two with bilateral radiotherapy and surgery.

Lymphatic drainage analysis

Previous treatment on the same side of the neck as the current harvested SNs was seen in 38 of the 50 patients. The previous treatment was as follows: In one patient (3%), the surgical treatment had previously only been applied on one side of the neck and was now staged bilaterally, seven patients (18%) were previously treated with surgery ipsilaterally to the current staging procedure, two patients (5%) were staged bilaterally as they were previously treated with bilateral surgery, 12 (32%) were previously treated with bilateral radiotherapy and surgery, and the remaining 16 patients (42%) had been treated with radiotherapy bilaterally.

In six of the patients with SNB performed on a previously treated side of the neck, no drainage occurred, hence the preoperative SN detection was 84% (32/38). The intraoperative detection rate was 81% (26/32) since the previously described patients with intraoperative detection failure were included in this group.

Unexpected lymphatic drainage occurred in 32% (12/38) of the patients and details about SN distribution are shown in Figure 1. Three of the patients had a history of radiotherapy bilaterally, five patients with bilateral radiotherapy and surgery, three patients with ipsilateral surgery, and one patient with a bilateral surgery. Overall, the unexpected drainage occurred as follows: in seven patients with a well-lateralized tumor without midline involvement, bilateral SNs were found, of which

TABLE 2 Previous TNM classification and treatment modality history.

Pt	Tumor type	Stage	Side	Head and neck history	Neck history	Side
1	Tongue	T1N0M0	R	T1N0M0 Tongue	Surgery	B
2	Soft palate	T1N0M0	L	T1N0M0 Floor of mouth	Surgery	I
3	Tongue	T1N0M0	L	T1N0M0 Tongue	Surgery	B
4	Tongue	T2N0M0	L	T1N0M0 Floor of mouth	Surgery	C
5	Tongue	T1N0M0	L	unknown Tonsil	Surgery and radiotherapy	B
6	Retromolar	T1N0M0	L	T1N0M0 Tonsil	Surgery	C
7	Tongue	T2N1M0	R	T1N0M0 Tongue	Surgery	I
8	Floor of mouth	T1N0M0	M	T2N2bM0 Hypopharynx	Surgery and radiotherapy	B
9	Tongue	T3N1M0	R	T1N0M0 Tongue and retro maxillary sarcoma	Surgery and radiotherapy	B
10	Tongue	T1N0M0	L	T2N2bM0 Hypopharynx	Radiotherapy	B
11	Tongue	T1N0M0	R	T3N2bM0 Tonsil	Radiotherapy	B
12	Tongue	T1N0M0	R	T1N0M0 Tongue	Surgery	C
13	Tongue	T1N0M0	L	T1N0M0 Tongue	Surgery	C
14	Floor of mouth	T2N0M0	M	T2N0M0 Oral cavity	Radiotherapy	B
15	Floor of mouth	T3N0M0	L	T2N0M0 Floor of mouth	Surgery	C
16	Buccal mucosa	T1N0M0	L	T4N0M0 Gingiva	Surgery and radiotherapy	B
17	Floor of mouth	T1N0M0	L	T2N2bM0 Retromolar	Surgery and radiotherapy	B
18	Buccal mucosa	T2N1M0	R	T1N0M0 Buccal mucosa	Surgery	I
19	Floor of mouth	T1N0M0	L	T3N0M0 Larynx and T4bN0 esophageal	Radiotherapy	B
20	Floor of mouth	T1N4M0	R	T2N0M0 Sinus piriformis	Surgery and radiotherapy	B
21	Retromolar	T1N0M0	L	T2N0M0 Hypopharynx	Radiotherapy	B
22	Tongue	T1N0M0	R	T1N0M0 Floor of mouth	Surgery	C
23	Tongue	T1N0M0	R	T3N0M0 Oropharynx	Radiotherapy	B
24	Tongue	T1N0M0	R	T0N1M0 Unkown	Surgery and radiotherapy	B
25	Floor of mouth	T1N0M0	L	T1N0M0 Floor of mouth	Surgery	B
26	Floor of mouth	T1N0M0	M	T2N2aM0 Oropharynx	Radiotherapy	B
27	Floor of mouth	T1N0M0	L	T2N0M0 Buccal mucosa	Surgery	C
28	Tongue	T1N0M0	L	T4N2bM0 Gingiva	Surgery and radiotherapy	B
29	Floor of mouth	T2N0M0	R + L	T2N1M0 Glottis	Radiotherapy	B
30	Tongue	T2N0M0	R	T4N2cM0 Floor of moth	Surgery and radiotherapy	B
31	Retromolar	T1N0M0	L	T2N0M0 Retromolar	Surgery	I
32	Tongue	T2N0M0	R	T1N2M0 Tonsil	Radiotherapy	C
33	Tongue	T1N0M0	R	T1N0M0 Tongue	Surgery	I
34	Retromolar	T2N0M0	L	T0N2aM0 Unknown	Surgery	C
35	Buccal mucosa	T2N0M0	R	T1aN0M0 Glottis	Radiotherapy	B
36	Tongue	T1N0M0	L	T1N0M0 Floor of mouth	Surgery	C
37	Floor of mouth	T1N0M0	R	T3N1M0 Oropharynx	Radiotherapy	B
38	Lower gingiva	T1N0M0	R	T2N2bM0 Tongue	Radiotherapy	B

(Continues)

TABLE 2 (Continued)

Pt	Tumor type	Stage	Side	Head and neck history	Neck history	Side
39	Tongue	T1N0M0	L	T2N2aM0 Tongue	Surgery and radiotherapy	B
40	Tongue	T1N0M0	L	T1N0M0 Floor of mouth	Surgery	C
41	Tongue	T1N0M0	R	T1N0M0 Tongue	Surgery	I
42	Tongue	T1N0M0	R	T1N0M0 Tongue	Surgery	I
43	Floor of moth	T1N0M0	M	T2N0M0 Epiglottis	Radiotherapy	B
44	Lower gingiva	T1N0M0	L	T2N0M0 Oropharynx	Radiotherapy	B
45	Floor of mouth	T1N0M0	L	T4aN0M0 Oropharynx	Surgery and radiotherapy	B
46	Floor of mouth	T1N0M0	R	T2N2M0 Hypopharynx	Surgery and radiotherapy	B
47	Tongue	T1N0M0	L	T1N0M0 Tongue	Surgery	C
48	Tongue	T2N0M0	L	T3N2cM0 Oropharynx	Radiotherapy	B
49	Tongue	T2N3M0	R	T2N2bM0 Oropharynx	Radiotherapy	B
50	Tongue	T1N0M0	R	T3N2bM0 Tongue	Surgery and radiotherapy	B

Abbreviations: B, bilateral; C, contralateral; I, ipsilateral; L, left; M, midline; Pt, patient; R, right; TNM, tumor node metastasis.

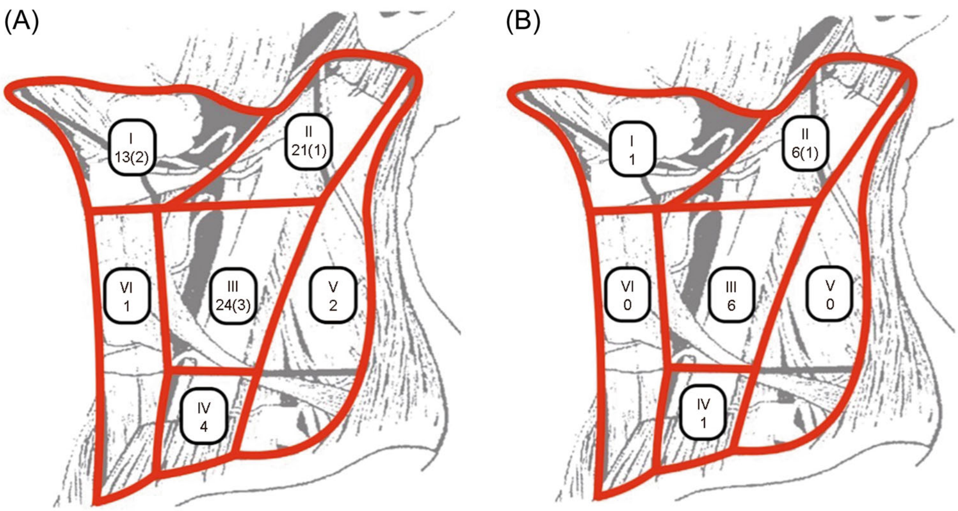

FIGURE 1 Sentinel nodes identified and removed. (A) Ipsilateral sentinel nodes and (B) contralateral sentinel nodes. Metastasis is specified within parenthesis.

three of these patients had SNs in levels IV and V. Further, three patients showed ipsilateral drainage in levels IV and VI and in two patients drainage appeared contralateral from the tumor side.

In total, 18 of the 38 patients (47%) included in the drainage pattern analysis had either no lymphatic drainage or an unexpected drainage pattern.

Survival and diagnostic performance of SNB

All 50 patients were included in the survival analysis. During the follow-up, in total 28% (14 patients) were diagnosed with a recurrence or new primary; the distribution was as follows: 12% (six patients) were diagnosed with a T-site recurrence, 12% (six patients) with a new primary tumor, and 6% (three patients) with a lymph node recurrence. One patient was diagnosed with a combined T- and N-site recurrence.

In one patient, a single metastasis in an SN was detected in the contralateral side on the neck (level II) from a lateralized tumor on the tongue. The patient had previously been treated with radiotherapy bilaterally and was following the current performed SNB treated with SND. Six months later, the patient was diagnosed simultaneously with a T- and N-side recurrence and died after 10 months.

At follow-up, 16 patients (32%) had died from all causes, of which five patients (10%) died of OSCC. The 2-year OS for all 51 patients was 75%, the 2-year RFS was 90%, and the 2-year RRFS was 94%. In patients with a positive SN, the 2-year OS was 25%.

At follow-up, no patients with a successfully performed SNB procedure and a negative SN were diagnosed with a regional lymph node recurrence. Hence, as no FN events occurred, the accuracy, sensitivity, and NPV were 100% (Table 3) as was the FNR and FOR of 0%.

DISCUSSION

We found a sensitivity of 100% and an NPV of 100% when the SNB technique was performed successfully, which was the case in 76% of the patients. Two recent meta-analyses including between 457 and 3566 patients with an untreated neck reported sensitivity rates between 83% and 88%, specificity 98% and 99%, and NPV 94%.[10,26,27] Only three other studies have investigated SNB in cohorts of patients with OSCC and previously treated necks; the studies are summarized in Table 4. The sensitivity rate was reported between 50% and 75% in the study of den Toom and NPVs of 91% and 100%.[19,20,28] The somewhat low sensitivity of 50% found in the study of den Toom et al. has a wide 95% confidence interval of 22%–98%, which the authors suggest may be due to a low number of SN-positive patients (7%) in the cohort. This is also an important factor in our study, with a positive rate of 13% compared to a rate of 23%–34% in patients with untreated necks.[3,7,29] It may reflect a generally lower propensity of metastatic spread to the neck due to a damaged lymphatic drainage system. Also, the cohort in our study was enrolled in a systematic clinical follow-up program after the first diagnosed cancer, which may have led to early detection of a new oral malignancy. A low mean depth of invasion of 3.1 mm (range: 0.3–11.0 mm) in this study may reflect early detection of cancerous lesions. However, with no FN cases, the data from our study show a high accuracy of SNB to stage a previously treated neck, which is in line with the previously published comparable studies.

We found a preoperative imaging detection rate of 88% and an intraoperative identification rate of 86%. This is lower compared to rates between 95% and 100% reported from a series of SNB staging of patients with untreated necks.[18,29,30] Considering the detection rates in the patients with currently harvested SNs on the same side as previous treatment, they are even lower (preoperative detection rate was 84% and intraoperative rate was 81%). In other types of cancer where SNB staging is applied, the same pattern following previous treatment has been reported. In recurrent breast cancer, a meta-analysis found an intraoperative detection rate of 59.6%.[31] den Toom et al.[20] reported an SN identification rate of 85% and Flach et al.[19] found an SN detection rate of 83%. All the patients in both studies with nondetectable SNs had received radiotherapy. This is in line with our results where all the patients with an unsuccessful SNB procedure were previously treated with radiotherapy. It was clear that previous treatment of the neck, specifically radiotherapy, exerts a more pronounced influence on the SN identification rate compared to surgery alone. Besides the varied impact of the different techniques, it is likely that END has a greater impact on the alteration of the lymphatic drainage pattern than removing a single SNB since it is a greater surgical procedure. This presumption is predicated on the premise that END presents more extensive surgical interventions than the SNB procedure. Development of unexpected drainage pathways may appear, as illustrated in the patient with drainage to the axillary regions, which are highly unusual. SNB has been suggested to be operator-sensitive, which should be considered when the procedure is applied to a treated neck. Thus, it appears feasible to perform the SNB procedure in a previously treated neck, but it is technically more challenging, and a lower SN detection rate is to be anticipated.

TABLE 3 Diagnostic performance of SNB in a treated neck nodal recurrence at follow-up.

Characteristics	Nodal recurrence	No nodal recurrence	Total
SNB+	5 (TP)	0 (FP)	5
SNB−	0 (FN)	33 (TN)	33
Total	5	33	38

Abbreviations: FN, false negative; FP, false positive; SNB, sentinel node biopsy; TN, true negative; TP, true positive.

TABLE 4 Previous studies investigating the accuracy of SNB in a previously treated neck.

Study	Hart et al.[28]	Flach et al.[19]	den Toom et al.[20]
Design	Prospective case series	Prospective observational study	Retrospective analysis
Number of patients included	11	22	53
Positive rate	9%	7%	7%
SN detection rate	100%	83%	85%
Sensitivity	-	-	50% and 75%
NPV	91%	100%	98%
Unexpected lymphatic drainage	0	67%	30%

Abbreviations: NPV, negative predictive value; SN, sentinel node; SNB, sentinel node biopsy; -, no data.

We found a 2-year OS rate of 75%, RFS of 90%, and lymph node RFS of 94%. In a long-term follow-up study evaluating the reliability of SNB compared to END including 229 untreated patients, a 5-year rate of recurrence-free patients of 80% was reported.[11] Other studies in untreated patients reported a 3-year OS from 82% to 89%.[7,32] A lower survival rate in this present study may be related to a higher morbidity and frailty in patients previously treated for head and neck cancer compared to patients with only one primary cancer. The OS of patients diagnosed with a positive SN was 25%. This emphasizes the importance of accurate neck staging to estimate prognosis and confirms the powerful negative impact of nodal metastasis at the time of diagnosis, which many studies have reported.

Bilateral and contralateral drainage from lateralized tumors in untreated patients has been reported to be 10% and 2.4%, respectively.[29] We found the rate of unexpected drainage to be 32% in previously treated patients. Flach et al.[19] and den Toom et al.[20] reported 67% and 30%, respectively. It appears that unexcepted drainage occurs more frequently in patients who have undergone previous treatment. Also, in our cohort a metastasis was found on the contralateral side of the neck, which would not have been detected if the patients had received END. These findings demonstrate a major advantage of SNB over END in previously treated necks: The unusual drainage patterns, which frequently occur, can be detected to more accurately guide the indication and the extent of a neck dissection. SNB depicts the drainage specifically for each patient. In addition, the risk of complications and related morbidity from an END in previously treated necks is higher compared to untreated necks,[33] and SNB can accurately guide to select the patients who should have a major surgical neck procedure performed from those who can be managed with a more limited procedure.

Based on these results, we still recommend SNB as a staging procedure in a previously treated neck in our institution.

This study was limited by the retrospective study design, a notable range in the follow-up time, and a small study population. Also, the previous treatment, TNM stage, and comorbidity had a broad variety among the patients, which makes this a very heterogenic cohort of patients.

CONCLUSION

This study supports the feasibility and high diagnostic accuracy of SNB to stage the cN0 neck in patients with OSCC and a history of previous neck treatment. Importantly, SNB has the ability to detect unexpected drainage patterns in these types of patients, where an altered lymphatic system in the neck is frequent.

AUTHOR CONTRIBUTIONS

Not applicable.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data are not available for sharing due to national legislation.

ETHICS STATEMENT

Not applicable.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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