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Sentinel Lymph Node Biopsy in Clinically N0 Oral Squamous Cell Carcinoma: A Single-Center Experience with a Focused Review of Current Evidence

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ABSTRACT

Background and Objectives: Accurate assessment of occult cervical metastasis is essential for determining the need for elective neck treatment in oral squamous cell carcinoma (OSCC). This study investigated the safety and clinical relevance of sentinel lymph node biopsy (SLNB) as a strategy to limit the extent of prophylactic neck surgery in patients with clinically N0 OSCC. **Materials and Methods:** Twenty-two patients diagnosed with clinically node-negative OSCC were retrospectively analyzed. Sentinel lymph nodes were localized using preoperative lymphatic mapping with scintigraphic imaging. Intraoperative frozen-section evaluation was performed, and diagnostic performance was determined by comparison with permanent histopathologic examination. **Results:** SLNB showed favorable diagnostic performance in this cohort, with a negative predictive value of 98.8%, although this estimate should be interpreted cautiously because of the small sample size. Management of the neck was guided by the presence or absence of metastatic involvement identified in sentinel lymph nodes among patients with early-stage disease and no clinical evidence of cervical metastasis. **Conclusion:** In this small single-center cohort, SLNB helped identify occult nodal metastasis in clinically N0 OSCC and may support individualized neck management in early-stage oral cancer.

KEY WORDS: Squamous cell carcinoma of head and neck; Sentinel lymph node; Lymphatic metastasis; Neck dissection.

Introduction

Squamous cell carcinoma accounts for the vast majority of malignancies arising in the oral cavity, and the tongue represents the most frequently involved subsite. Among prognostic variables, regional lymph node involvement has consistently been shown to exert the strongest influence on survival in oral tongue carcinoma. Approximately one-third of patients exhibit cervical nodal metastasis at the time of diagnosis, and nodal involvement is associated with a marked decrease in 5-year survival compared with node-negative disease.[1)]

Patients staged as clinically N0 demonstrate no evidence of cervical metastasis on physical examination or imaging studies; however, a proportion of these individuals are subsequently found to harbor occult nodal disease on histopathologic assessment. The incidence of such occult metastasis has been reported to approach 30% in oral and oropharyngeal squamous cell carcinoma. For this reason, elective treatment of the neck—either through radiotherapy or surgical dissection—has traditionally been recommended in many cases. Nevertheless, this strategy inevitably exposes a subset of patients without true nodal involvement to unnecessary intervention.[2)] Furthermore, previous investigations have not demonstrated significant differences in onco-

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logic outcomes between modified radical and selective neck dissection in early-stage disease.[3]

In response to concerns regarding overtreatment, efforts have increasingly focused on tailoring the extent of cervical surgery while preserving oncologic safety. Sentinel lymph node biopsy (SLNB) has emerged as a staging approach aligned with this objective. The technique is grounded in the concept that lymphatic dissemination follows an orderly pattern, whereby the initial draining node reflects the status of the regional basin.[4] Precise localization through preoperative lymphatic mapping and intraoperative gamma probe guidance, combined with histopathologic evaluation using frozen and permanent sections, enables targeted assessment of potential occult metastasis.

SLNB has become an established component of management in breast cancer and melanoma and has been progressively adopted in head and neck oncology. Although multiple studies have supported its role in guiding selective neck dissection, the diagnostic performance and safety profile of SLNB in our institutional setting have not been specifically evaluated. Accordingly, the present study retrospectively examined medical records and imaging data to determine the clinical utility and safety of SLNB in patients with oral squamous cell carcinoma (OSCC) without clinical evidence of cervical lymph node metastasis.

Materials and Methods

Patients

Medical records of patients who underwent surgery for oral cancer at Inje University Busan Paik Hospital between October 2013 and March 2021 were retrospectively reviewed. Patients were eligible for inclusion if they had pathologically confirmed OSCC of the tongue, clinically node-negative disease based on physical examination and preoperative imaging, and underwent SLNB at the time of primary tumor surgery.

Patients were excluded if they had clinically or radiologically evident cervical lymph node metastasis, recurrent disease, previous treatment to the neck, distant metastasis at presentation, non-squamous cell carcinoma histology, insufficient preoperative imaging, or incomplete medical records. Clinical N0 status was assessed using physical examination and preoperative imaging studies, including computed tomography and/or magnetic resonance imaging, with additional imaging performed when clinically indicated.

This retrospective medical record review was approved by the Institutional Review Board of Inje University Busan Paik Hospital (IRB File No. 2023-08-007-003), and the requirement for informed consent was waived because of the retrospective nature of the study.

Sentinel lymph node biopsy

SLNB procedures were coordinated with the Department of Nuclear Medicine and performed either on the day before surgery or on the morning of surgery. After clinical palpation of the primary lesion, technetium-99m phytate (Techne Phytate Kit, FUJIFILM RI Parma, Tokyo, Japan) was administered as the radiotracer by peritumoral injection into four quadrants surrounding the tumor. A 25-gauge needle was used to inject 55.5 MBq of Tc-99m phytate diluted in normal saline, with a total activity ranging from 2 to 6 mCi according to tumor size and location.

Lymphatic mapping was performed 10 minutes after injection using scintigraphic imaging (Symbia Evo Excel, SIEMENS, Berlin, Germany) to determine the number and distribution of sentinel lymph nodes. Intraoperatively, previously identified nodal sites were localized with a handheld gamma probe and marked on the cervical skin surface.

To minimize signal interference from residual radioactivity at the primary tumor site, the primary lesion was excised before neck exploration. After elevation of the cervical flap, lymph nodes with radioactive counts at least threefold higher than background levels were detected using the gamma probe. Suspicious nodes were removed, and sustained radioactivity was verified ex vivo. A reduction in radioactivity in the operative field after node removal was used to confirm sentinel node identification.

Frozen-section examination of the excised sentinel lymph nodes was performed intraoperatively. Subsequent neck management was determined according to the frozen-section findings, either by completing the procedure or by perform-

ing additional selective neck dissection. Diagnostic accuracy was evaluated by comparing intraoperative frozen-section results with final permanent histopathologic findings.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics software (ver 21.0; IBM, Armonk, NY, USA). Descriptive comparisons of disease-free survival according to frozen-section status were performed as exploratory analyses.

Statistical significance was defined as a two-sided p-value < 0.05. Follow-up was calculated up to 2 years and 5 months after treatment of the last enrolled patient. Disease-free survival (DFS) was defined as the time from treatment initiation to the first occurrence of local recurrence, regional lymph node recurrence, distant metastasis, or death.

Results

Patient characteristics

The cohort comprised 12 men and 10 women, with a mean age of 61.3 years. All primary lesions were located on the tongue. Clinical staging showed T1 disease in 13 patients (59.1%) and T2 disease in 9 patients (40.9%), and all cases were classified as clinical N0 (Table 1).

Pathologic findings of sentinel lymph nodes

Preoperative lymphoscintigraphy identified sentinel lymph node locations in 21 of 22 patients (95.5%), and intraoperative gamma-probe detection was successful in all 22 patients (100%). The mean number of sentinel lymph nodes identified per patient was 3.9. Sentinel lymph nodes were most frequently detected in ipsilateral level II (68.2%), followed by ipsilateral level I (40.9%) and ipsilateral level III (36.4%). Sentinel lymph nodes were also identified in contralateral level III in 4.5% of patients.

Table 1. Demographic characteristics of the patients (n=22)

Characteristics	cN0 (n=22)	Nodal metastasis (n=4)	Recurred patients (n=4)
Mean age, year (range)	61.3 (31–85)	59.2 (43–69)	68.3 (51–85)
Sex			
Male	12	1	2
Female	10	3	2
Tumor stage			
T1	13	4	2
T2	9	-	2

Final histopathologic examination identified occult nodal metastasis in 4 of 22 patients (18%). During postoperative follow-up, radiologic evaluation suggested cervical lymph node metastasis in 4 patients (18%), which was subsequently confirmed by surgical biopsy.

Comparison between frozen-section and final histopathologic results

Intraoperative frozen-section analysis of sentinel lymph nodes was positive for metastatic disease in 3 patients, involving a total of 5 lymph nodes; all were confirmed as metastatic on final histopathologic examination. One patient had a false-negative frozen-section result, in which one sentinel lymph node was diagnosed as metastatic on final pathology despite a negative frozen-section result (Table 2).

Among the 3 patients with positive frozen-section results, 1 underwent supraomohyoid neck dissection and was diagnosed as pN1 on final pathology. The remaining 2 patients underwent modified radical neck dissection type III; of these, 1 was diagnosed as pN2b and the other as pN1 on final histopathologic examination.

Table 2. Comparison between preoperative SLN results and pathologically proven metastasis site after SCND

Characteristics	SLN site before SCND	Frozen Biopsy	LN metastasis site after SCND (positive LN/ total dissected LN)
Patients with nodal metastasis (n=4)			
	Lt II	Positive	Lt II (1/19)
	Lt II	Positive	Lt II (2/22)
	Lt II	Negative	Lt II (1/5)
	Lt II	Positive	Lt II (2/32)

SLN: sentinel lymph node, LN: lymph node, SCND: sentinel lymph node centered selective neck dissection.

Outcomes

During postoperative follow-up, cervical lymph node metastasis was suspected in 4 patients and confirmed by biopsy. These patients received additional adjuvant therapy, including radiotherapy or chemotherapy.

In 2 of these patients, sentinel lymph nodes had been identified preoperatively at atypical locations, level IV and the right parapharyngeal space, on lymphoscintigraphy. However, intraoperative frozen-section analysis of the sentinel lymph nodes identified using a gamma probe was negative, and neck surgery was concluded. Postoperative nodal recurrence was subsequently confirmed in these patients (Table 3).

Sentinel lymph node localization was successful in all patients except for 1 patient in whom a sentinel lymph node was suspected in the right parapharyngeal space. Sentinel lymph nodes meeting diagnostic criteria were excised intraoperatively using a gamma probe.

The positive predictive value of intraoperative frozen-section analysis of sentinel lymph nodes was 100%, and the negative predictive value was 98.8% (Table 4).

Exploratory comparison of disease-free survival according to frozen-section status showed no statistically significant difference; however, this analysis was limited by the small number of patients with positive frozen-section results.

Table 4. Accuracy of the sentinel lymph node biopsy

Parameter	Result	
SLN detection rate (n=22 patients)		
lymphoscintigraphy	21/22	(95.5%)
Gamma probe	22/22	(100%)
Accuracy of Frozen biopsy (n = 86 SLNs)		
True positive	5	
True negative	80	
False positive	0	
False negative	1	
Sensitivity	5/6	(83%)
Specificity	80/80	(100%)
Positive predictive value	5/5	(100%)
Negative predictive value	80/81	(98.8%)

SLN: sentinel lymph node.

Discussion

In our cohort of 22 patients with clinically node-negative tongue OSCC SLNB was technically feasible and demonstrated high diagnostic accuracy. Preoperative lymphoscintigraphy identified sentinel lymph nodes in 21 of 22 patients, and intraoperative gamma-probe detection was successful in all patients. Occult nodal metastasis was identified in 4 patients, the positive predictive value of intraoperative frozen-section assessment was 100%, and the negative predictive value was 98.8%. These findings are consistent with the diagnostic performance reported in the extracted literature (Table 5): Liu et al.[5] reported a pooled sensitivity of 0.87 and negative predictive value of 0.94 in 3566 patients with early OSCC, Yang et al.[6] reported a pooled sensitivity of 0.92 and negative predictive value of 0.96 in 1084 patients with tongue squamous cell carcinoma, Kim et al.[7] reported sensitivity of 0.827 and specificity of 0.981 in 5917 patients with early OSCC, and Mallo Magarinos et al.[8] reported pooled sensitivity of 88% and specificity of 99% in T1/T2-N0 OSCC. Recent cohort data from Ionna et al. [9] and Kolev et al.[10] also support

Table 3. Four cases of recurrence

Recurred patients	Case A	Case B	Case C	Case D
Sex/Age	Female/69	Male/51	Male/68	Female/85
Tumor side and pathologic stage	Lt, pT1N1	Lt, pT2N0	Rt, pT2N0	Lt, pT1N0
Disease free survival (month)	7.5	6.0	7.0	6.0
SLN site	Lt. II	Lt. IV	Rt. Parapharynx	Lt. II, III
SCND	Lt. mRND	Lt. IV	Rt. IB, II	Lt. II, III
Recurred LN	Lt. IB	Lt. I, II	Rt. II	Lt. I
Adjuvant therapy	PORT	PORT	Chemotherapy	-

LN: lymph node, SCND: sentinel lymph node centered selective neck dissection, mRND: modified radical neck dissection, PORT: postoperative radiation therapy.
Pathologic stage refers to the initial surgical pathology before recurrence.

Table 5. Summary of representative studies on sentinel lymph node biopsy in early OSCC

Author/year	Study design	Number of patients	Sensitivity	Negative predictive value	Key clinical finding
Yamauchi, 2015[11]	Meta-analysis	987	0.86	0.94	High sensitivity and NPV in early HNSCC
Liu, 2017[5]	Meta-analysis	3,566	0.87	0.94	High sensitivity and NPV in OSCC
Yang, 2017[6]	Meta-analysis	1,084	0.92	0.96	High sensitivity and NPV in early tongue SCC
Molstrom, 2019[13]	Prospective cohort	220	0.83	0.93	Identified atypical lymphatic drainage
den Toom, 2019[14]	Retrospective multicenter cohort	53	0.75	0.98	SLNB feasible after previous neck treatment
Kim, 2021[7]	Systematic review/ meta-analysis	5,917	0.83	NR	High specificity supports SLNB as staging tool
Garrel, 2020[12]	Phase III randomized equivalence trial	279 analyzed	NR	NR	Oncologic equivalence to END with lower morbidity
Hasegawa, 2021[15]	Randomized multicenter noninferiority trial	271	NR	NR	Noninferior to END with reduced neck disability
Mallo Magarinos, 2021[8]	Systematic review/ meta-analysis	457	0.88	0.88	High sensitivity and specificity in T1/T2-N0 OSCC
Ionna, 2024[9]	Retrospective cohort	122	NR	NR	High detection rate supports SLNB staging
Kolev, 2026[10]	Consecutive cohort	40	0.92	0.96	High sensitivity and NPV in OTSCC
Seferin, 2025[16]	Prospective non-randomized comparative study	70	0.78	1.00	No significant survival difference vs SND

NPV: negative predictive value, HNSCC: squamous cell carcinoma of head and neck, SCC: squamous cell carcinoma, OTSCC: oral tongue squamous cell carcinoma.

the diagnostic value of SLNB in oral tongue cancer; Kolev et al.[10] reported a sensitivity of 92.3% and negative predictive value of 96.4%. Although our sample size was smaller, our findings support the diagnostic utility of SLNB in the specific institutional setting of clinically N0 tongue cancer. Given the small cohort size, these diagnostic-performance estimates should be interpreted as descriptive institutional findings rather than definitive population-level estimates.

In our study, one patient had a false-negative intraoperative frozen-section result, in which metastatic involvement was identified on final permanent histopathologic examination despite a negative frozen-section diagnosis. This finding highlights an important limitation of intraoperative pathology rather than the mapping procedure alone. Yamauchi et al.[11] reported a pooled false-negative rate of 13.7% and a negative predictive value of 94.2% in early head and neck squamous cell carcinoma, while Liu et al.[5] reported that the false-negative rate was 13% in early OSCC. Garrel et al.[12] also reported that false-negative intraoperative histologic analysis led to a second intervention in 8.6% of patients in the sentinel-node arm, with intraoperative histology sensitivity of 63.6%. Taken together, these data suggest that negative frozen-section findings should be interpreted cautiously, particularly when micrometastatic disease or anatomically atypical drainage is suspected.

In our cohort, atypical lymphatic drainage was clinically

relevant because sentinel lymph nodes were not confined to conventional ipsilateral levels I–III. Sentinel nodes were most frequently identified in ipsilateral level II, followed by ipsilateral levels I and III, but contralateral level III drainage was also observed, and two patients with postoperative nodal recurrence had preoperative sentinel-node localization at atypical sites, including level IV and the right parapharyngeal space. These observations align with Mølstrom et al.,[13] which reported unexpected bilateral or contralateral drainage patterns in 22.6% of patients with lateralized OSCC and showed that SLNB was helpful in clarifying unexpected drainage patterns. den Toom et al.[14] similarly reported unexpected drainage patterns in 30% of cT1-2N0 OSCC patients after previous neck treatment. Therefore, our findings reinforce that individualized lymphatic mapping may provide clinically important information that may not be fully captured by a uniform elective neck dissection template.

In our study, SLNB was used to guide the need for additional neck treatment rather than to perform prophylactic neck dissection uniformly in all clinically N0 patients. This approach is supported by randomized evidence from the extracted literature. Garrel et al.[12] reported oncologic equivalence between sentinel-node biopsy and neck dissection in operable T1-T2N0 oral and oropharyngeal cancer, with lower morbidity in the sentinel-node arm during the first 6 months after surgery. Hasegawa et al.[15] reported that SLNB-navigated neck dissection was noninferior to elective neck dissection for survival and reduced postoperative neck disability in early-stage oral cavity squamous cell carcinoma. Recent comparative data from Seferin et al.[16] also showed no significant difference between SLNB and selective neck dissection in overall survival or disease-free survival, although the study was non-randomized. Our study was not designed to prove equivalence or noninferiority, and the absence of a direct END control group precludes any conclusion regarding oncologic equivalence between SLNB and END. Nevertheless, our institutional data support the role of SLNB as a staging tool that may help identify patients who require additional neck treatment.

In our study population, the main clinical implication is that SLNB may support individualized management of the clinically N0 neck in early tongue cancer. The high intraoperative detection rate, identification of occult metastasis, and favorable predictive values suggest that SLNB can provide actionable staging information at the time of primary tumor surgery. At the same time, the false-negative frozen-section case and the recurrence cases associated with atypical drainage indicate that SLNB should not be interpreted as a standalone guarantee of regional control. The results support a practical strategy in which SLNB findings are integrated with permanent pathology, nodal location, drainage pattern, and close postoperative surveillance.

Our study has several limitations that should be considered when interpreting these findings. The analysis was retrospective and conducted at a single institution, and the cohort included only 22 patients, all of whom had tongue cancer. Depth of invasion, an important predictor of occult cervical metastasis in oral cavity cancer, was not consistently available in the retrospective pathology records. Therefore, DOI-based subgroup or comparative analysis could not be performed, and this limitation should be considered when interpreting the diagnostic utility of SLNB in this cohort. The small sample size and limited number of nodal events restricted the precision of diagnostic-performance estimates, including sensitivity and negative predictive value, and precluded reliable estimation of confidence intervals. The study also lacked a direct elective neck dissection control group, so it cannot establish oncologic equivalence between SLNB and elective neck dissection. In addition, intraoperative frozen-section assessment may underestimate micrometastatic disease compared with permanent histopathology or additional ultrastaging techniques. These limitations should be considered when applying the findings beyond the present institutional cohort.

Conclusion

SLNB enables identification of occult cervical metastasis that may not be detected through conventional radiologic or clinical evaluation in patients with OSCC, particularly those with clinically N0 tongue cancer. In this small single-center cohort, SLNB provided useful staging information and may

help guide individualized neck management in early-stage oral cancer.

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Conflicts of Interest
No potential conflict of interest relevant to this article was reported.

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Ethics Approval
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