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ORIGINAL REPORT

Positron Emission Tomography in Combination With Sentinel Node Biopsy Reduces the Rate of Elective Neck Dissections in the Treatment of Oral and Oropharyngeal Cancer

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ABSTRACT

Purpose
To assess the impact of a diagnostic ladder including [^{18}F]fluorodeoxyglucose positron emission tomography (PET) and lymphoscintigraphy guided sentinel node biopsy (LS/SNB) on neck treatment in patients with oral and oropharyngeal squamous cell carcinoma (OOSCC).

Patients and Methods
Prospectively, 62 patients with resectable T1-3 OOSCC underwent computed tomography (CT) and PET. Patients without neck uptake in PET were defined as cN0 and were accrued for LS/SNB. Results were correlated with histopathology. The traditional guidelines according to CT findings were compared to the actual regimen and the outcome.

Results
Sensitivity, specificity, validity, and positive and negative predictive value of PET versus CT were 72% *v* 89%, 82% *v* 77%, 79% *v* 80.5%, 62% *v* 61.5%, and 88% *v* 94.5% (not significant). Thirty-eight PET negative patients underwent LS/SNB. Sentinel lymph nodes were found in all 38 patients. Five patients had positive nodes (PET false-negatives) and underwent neck dissection (ND). Fifty-one neck sides in 36 patients who were CT-negative would have been treated with selective ND according to the guidelines, and at least 45 neck sides would have had to undergo extensive ND because of positive CT findings (96 of 124 neck sides). In contrast, PET in combination with LS/SNB spared 59 neck sides, and 41 of 124 neck sides actually underwent ND as a result of PET staging, LS/SNB, and intraoperative decision. After a median follow-up of 35 months, two patients (both cN+ve and pN+ve) suffered from neck relapses.

Conclusion
Diagnostics using PET in combination with LS/SNB considerably reduced the number of extensive ND in OOSCC as compared to CT without locoregional hazard.

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INTRODUCTION

Before treatment of patients with oral and oropharyngeal squamous cell carcinoma (OOSCC), the prognosis has to be evaluated and appropriate therapy has to be chosen. Lymph node (LN) involvement is one of the most important prognostic factors that influences the therapy. Therefore, pretreatment staging should be as exact as possible. The assessment of cervical LNs is known to be extremely difficult clinically. In most patients with OOSCC, LNs are dissected despite the fact that less than half of the histologically controlled specimens contain LN metastases.[1] The common diagnostic procedures for cervical LN staging are clinical examination, ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI). In recent years positron

emission tomography (PET) with [^{18}F]fluorodeoxyglucose ([^{18}F]FDG) has become an additional staging tool.[2-4] By having a high specificity, this functional diagnostic technique could be especially useful in reducing false-positive results.

For OOSCC, although all patients are staged clinically with or without imaging, the dilemma is whether all patients should be staged pathologically. Patients staged as clinically N-positive traditionally have been staged pathologically, in the form of a therapeutic neck dissection (ND). For clinically N0 patients, the procedure is not clear because the specificity of the common staging tools is limited, resulting in an uncertainty about the N0 staging. It is generally considered that pathologic staging of the N0 patient is performed when the risk of metastasis is greater than 15% to 20% based on the histopathologic parameters of the primary tumor.[5-6]

Previous incidences of metastasis, however, relied solely on routine hematoxylin and eosin (H&E) staining rather than additional step serial sectioning and immunohistochemistry. For the clinically N0 patient, the novel approach of sentinel node biopsy (SNB) allows the use of these techniques to pathologically stage the neck with minimal node sampling[7-9] and minimal trauma to the neck.

The routine usage of PET as a prerequisite for staging a patient clinically N0 in combination with SNB as sole pathologic staging tool could potentially be an advancement in the treatment of OOSCC. The comparison with staging results based on CT could be extremely useful to demonstrate whether there is a benefit for the patients concerning the surgical treatment of the neck.

While most studies to date tried to assess the validity of SNB by comparing its results with the histologic results of the complete ND specimen, the present study consequently uses SNB as only pathologic staging tool. Therefore, observation time had to serve as control of results.

PATIENTS AND METHODS

In the 4-year period from January 2000 to December 2003, 62 consecutive patients with previously untreated resectable T1-3 OOSCC were examined with PET in the Department of Nuclear Medicine and CT in the Department of Neuroradiology (Johann Wolfgang Goethe University Medical School, Frankfurt am Main, Germany). Data from patients can be seen in Table 1. Patients with synchronous second malignancies and who were older than 80 years were excluded.

In order to evaluate the role of PET with [^{18}F]FDG for the treatment of the neck, and especially in SNB, it was decided that participants in the sentinel program would only have resectable primaries and be clinically N0, and that N0 would be defined as showing no neck uptake in PET.

PET-studies were acquired on an ECAT Exact 47 whole body tomograph (Siemens-CTI, Knoxville, TN) with a transaxial field of view of 16.2 cm (slice thickness, 3.4 mm; spatial resolution, 4 mm). Before the PET, patients had been fasting for at least 12 hours. Forty-five to 60 minutes after intravenous (IV) administration of 370 MBq [^{18}F]FDG, PET transmission and emission studies were performed using a whole body technique. Image reconstruction was done using an iterative algorithm. Regional [^{18}F]FDG uptake was expressed as the standardized uptake value and calculated for all primary tumors and nodal lesions. Only patients without hypermetabolic lesions in the neck were included into the sentinel program.

Table 1. Demographic Data and Tumor Characteristics

Characteristic		No. of Patients
Total		62
Sex		
Male		36
Female		26
Age, years		
Mean	61.5	
Range	44-77	
Primary tumor site		
Floor of the mouth		28
Tongue		19
Mandibular alveolar process		2
Buccal mucosa		4
Retromolar trigone		1
Oropharynx		8
UICC clinical T classification		
T1		15
T2		35
T3		12
UICC clinical staging		
I		15
II		21
III		21
IV		5

Abbreviation: UICC, International Union Against Cancer.

All patients were routinely examined with CT. Axial CT scans of the primary lesion and the cervical region were performed with a conventional CT scanner (Somatom Plus; Siemens, Erlangen, Germany). Slice thickness was 4 to 5 mm in continuous slices. For the facial skull, angulation was parallel to the palate; for the neck, angulation was parallel to the vocal chord or to the intervertebral space between the fifth and the sixth vertebral body. Contrast media enhancement was achieved by IV administration of 100 to 150 mL of nonionic contrast material (Ultravist 300; Schering, Berlin, Germany) having an iodine concentration of 300 mg/mL. The common criteria for suspect neck lymph nodes have been used as a diameter $>$ 1 cm, marginal enhancement following IV administration of a contrast medium, central necrosis, spherical form, unsharp or not definable contour, and unusual number.[10] Patients with suspect neck lymph nodes in CT have been documented in the neuroradiologic reports, but have been accrued for SNB because of the above mentioned definition (Fig 1).

Following staging examinations, one cycle of preoperative transfemoral superselective intra-arterial high-dose chemotherapy of the primary cancer region was performed with 150 mg/m^2 cisplatin and systemic neutralization with sodium thiosulfate.[11-12] Patients with dacron prostheses of the carotid

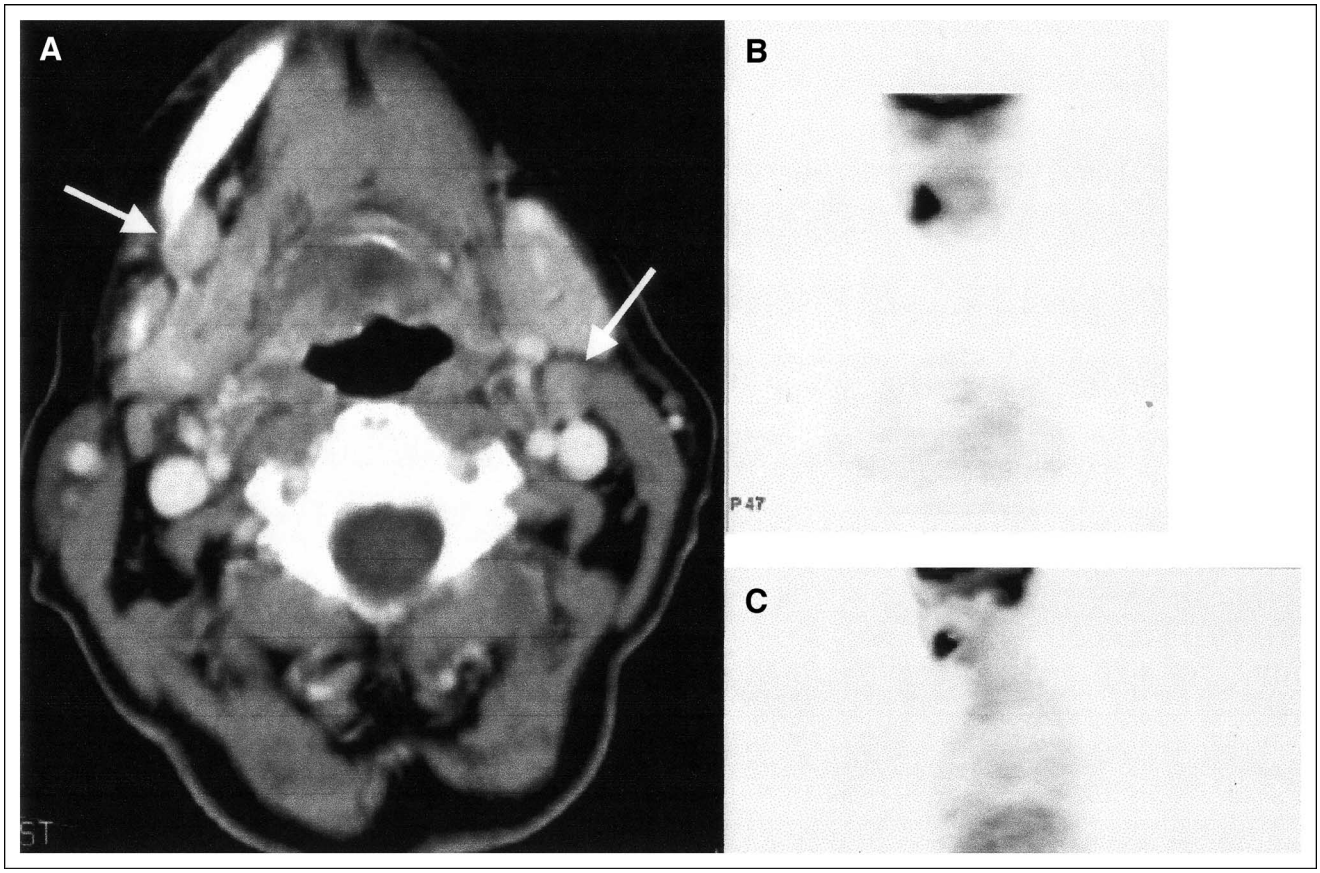

Fig 1. Bilateral suspect nodes in (A) computed tomography (arrows) in neck level 1 and (B and C) negative positron emission tomography scan (cancer of the right floor of the mouth).

arteries, severe occlusions of the carotid arteries, or renal dialysis have been excluded.

After recovery (3 to 4 weeks), sentinel lymph node (SLN) scintigraphy was performed before surgery at the day of operation. Informed consent was obtained from each patient. In case of stage 1 and 2 disease, the Ethics Committee of the Medical Faculty of the University of Frankfurt, in accordance with the declaration of Helsinki, approved SLN biopsy without mandatory ND in case of tumor negativity.

Between 15 and 55 MBq of Tc-99m labeled albumin-microcolloids (in < 0.1 mL; Nanocoll; Amersham Sorin, Saluggia, Italy) with a mean size of 30 nm were injected intramucodermally in two to eight depots circumferentially around the primary tumor with a fine needle. The lymphatic drainage was monitored at the gamma camera visually, and static scans (in anterior and lateral view plus additional anterior view with the head tilted back) were obtained every 15 minutes up to 1 hour after injection (10 to 20 kcts/image, analogous imaging; Searle Pho/Gamma, LFOV Basic; Scintillation Camera Systems, Des Plaines, IL).

SLN were marked on the skin surface under scintigraphic guidance of a 57-colabeled pen and controlled with the gamma probe. Operation was performed about 2 to 3 hours after tracer administration. Intraoperatively, the SLNs were reached using one or two minimally invasive neck approaches and removed from level 1 to 4 according to the Robbins classification.[13] Magnifying glasses were mandatory. A sterile latex-covered hand-held gamma probe (SI Gamma Finder; Silicon Instruments, Berlin, Germany) with a diameter of 10 mm was used to detect radioactivity. After removal, radioactivity was determined ex vivo. Inactive LN found in the immediate vicinity were also removed. Following lymphadenectomy, the primary tumor was resected in the same session. In case of a positive histology of an SLN or an inactive node, modified radical ND (MRND) was added 1 week later.

Definitive pathologic assessment of SLN involved fixing the nodes in 10% neutral buffered formalin, initial routine histologic examination, and additional step-serial sections at approximately 150 μm intervals through the block with H&E staining and immunocytochemistry using the multicytokeratin antibody AE1/3. All immunocytochemistry positivity has been compared with the H&E serial section.

All patients with positive PET scans underwent MRND (levels 1 to 5) of the afflicted neck side. In case of midline involvement by the primary, a contralateral selective neck dissection of the neck levels 1 and 2b (suprahyoid ND [SHND]) was performed. In case of dorsally located tumors with known risk for contralateral metastases (base of tongue, retromolar trigone and soft palate, oropharynx), a contralateral SHND was also performed. Pathohistologic examination of the neck specimens was used as "gold standard" for the evaluation of true and false positivity or negativity of the diagnostic procedures.

The traditional regimen of neck treatment according to the CT findings and the guidelines would have been SHND in case of

clinical N0; in case of midline involvement of the primary and dorsally located tumors, this procedure would have been performed bilaterally.[14] To enable correct comparison with the regimen according to PET findings, however, it was assumed that in case of clinical N0 there would have been performance of SNB. All patients with positive CT scans would have had the same surgical neck treatment as outlined above.

Evaluation methods follow Fadem.[15] For comparison of the different procedures, sensitivity, specificity, accuracy, and positive and negative predictive value were calculated for presence or absence of nodal metastases and their detection per patient. It was counted as a correct positive finding when at least one pathologic lymph node was found in the preoperative examination as well as histologically. Statistical analysis for comparison of the imaging results was conducted using Fisher's exact test. However, PET results have to be seen together with LS/SNB results that complement each other.

For the comparison of the incidence of ND, the number of neck sides was considered, which was spared by each diagnostic method.

Postoperative radiation therapy depended on pathologic results. All patients with pathologic stages 2 to 4 were admitted to postoperative radiation therapy. Therefore, the possible incidence of neck relapses did not depend on pretherapeutic imaging diagnosis and clinical staging, and did not affect the comparison of PET and CT. Patients were followed up in the out-patient clinic of the Department of Maxillofacial Surgery every month in the first year post-treatment, and on alternate months in the second year and so on.

RESULTS

The results of the comparison between clinical findings of PET and CT in the examined patients and the pathohistologic reports are demonstrated in Table 2. The highest difference in percentage between PET and CT concerned sensitivity where CT had a clear advantage (89% *v* 72%), while PET had a clear advantage concerning specificity (82% *v* 77%). The differences were not significant. Utilized CT criteria for possible infiltration had been the diameter of the nodes (between 10 and 17 mm), a spherical form of enlarged nodes, and a suspect high number of nodes in the lymphatic basin. In contrast, PET has been more practical in interpretation—a spot has been interpreted as a positive node, irrespective of the standard uptake value.

Table 3 shows the results of the examination with respect to the laterality and site of the primaries and the neck sides. Pathohistology of the lymph nodes and neck dissection specimens resulted 44 patients staged pN0, and 18 pN-positive. PET predicted negative neck sides more often and, consequently, more accurately than CT, and served as prerequisite for the execution of LS/SNB. Fifty-nine neck sides, therefore, did not receive extensive ND, whereas 51 neck sides would have traditionally been treated with selective ND in the 36 patients diagnosed as cN0 by CT. CT more frequently falsely demonstrated bilaterally-affected necks (cN2c) as compared with PET. In sum, 35 neck sides had to be operated on due to PET findings and PET false-negative results, while 45 necks would have been operated on due to CT findings and CT false-negative results.

In practice, however, there have been some changes in surgical procedure. One patient staged cN0 by PET had the oropharyngeal primary resected, but SNB could not be carried out because of poor general state. The patient had no neck relapse in the observation time of 52 months. Two patients having voluminous T3 tumors of the lateral tongue were staged cN0 by PET, but had a high probability of occult metastases (Table 4). The PET result was deemed to be unreliable because the large spot would not allow any differentiation between primary and positive nodes. In both these patients, CT had suspicious results. Comprehensive and selective NDs were executed according to the tumor extension. These NDs revealed positive nodes (false-negative PET results). The patients received adjuvant radiation (51.3 Gy) and are disease free to date, with an observation time of 17 and 22 months after the end of treatment. In five patients with positive PET scans and clinically unilateral tumors of the anterior floor of the

Table 2. Comparative Results of PET and CT Concerning Patients With Statistical Analysis

	PET			CT			
	%	No. of Patients	95% CI	%	No. of Patients	95% CI	*P* (Fishers' exact test)
False negative		5			2		
True negative		36			34		
False positive		8			10		
True positive		13			16		
Sensitivity	72		47 to 90	89		65 to 99	.40
Specificity	82		72 to 92	77		66 to 89	.79
Accuracy	79		70 to 88	80.5		72 to 90	.66
PPV	62		38 to 82	61.5		45 to 78	.99
NPV	88		74 to 96	94.5		81 to 99	.44

NOTE. CIs calculated exactly using the binomial distribution.
Abbreviations: PET, positron emission tomography; CT, computed tomography; PPV, positive predictive value; NPV, negative predictive value.

Table 3. Comparative Results of PET and CT Concerning Neck Sides

	No. of Patients	
	PET	CT
Imaging negative	41	36
Primary with midline involvement	13	12
Primary of dorsal site	5	3
Neck sides spared by respective technique in case of combination with SNB	59	51
Imaging positive	21	26
cN1	17	8
cN2b	3	10
cN2c	1	8
Primaries with midline involvement	+6	+7
Primaries with midline involvement and cN2c	−1	−3
Primaries without midline involvement and cN2c	0	+5
Primaries of dorsal site and unilateral nodes	+4	+5
Primaries of dorsal site and cN2c	0	−1
Primaries without dorsal site or midline involvement and cN2c	0	+4
Neck sides to be operated on with ND according to respective findings	30	43
Neck sides to be operated on with ND according to false-negative results	+5	+2
Sum of neck sides to be operated on	35	45
Pathohistologically negative	44	
Pathohistologically positive	18	
pN1	10	
pN2b	6	
pN2c	2	

Abbreviations: PET, positron emission tomography; CT, computed tomography; SNB, sentinel node biopsy; ND, neck dissection.

Table 4. Actual Surgical Neck Treatment According to PET Findings and Pathohistologic Results

Surgical Neck Treatment	No. of Patients
PET-negative patients	41
SNB	21
SNB, SNB	17
No neck surgery (poor general state)	1
ND against study protocol	
MRND	1*
MRND, SHND	1*
MRND due to positive SNB	3
PET-positive patients	21
MRND	6
MRND, MRND	3†
MRND, SHND	9†
SHND	1
SHND, SHND	2†
Actual sum of neck sides operated on with ND	41

Abbreviations: PET, positron emission tomography; SNB, sentinel node biopsy; ND, neck dissection; MRND, modified radical ND; SHND, suprahyoid ND.

*In these patients classified cN0 by PET, NDs were nevertheless executed instead of SNB, and revealed positive nodes (false-negative results of PET). Three other false-negative PET results were exactly diagnosed by SNB.

†Contralateral ND has been executed in five patients (one with MRND, MRND; three with MRND, SHND; and one with SHND, SHND) with unilateral SCC according to intra-operative decision.

mouth and the lateral tongue, intraoperative inspection revealed midline involvement and, therefore, led to the decision to carry out contralateral selective ND (Table 4). Three ipsilateral neck specimens had metastases, and the contralateral neck specimens were free of tumor. Radiation was executed according to the guidelines.

Thirty-eight patients classified as cN0 underwent SNB (Table 4). In all patients, sentinels could be visualized. According to the results of LS, SNB was carried out in 55 neck sides. In 17 patients, there had been bilateral drainage. A total of 111 hot sentinel nodes (range, 1 to 12 nodes) could be harvested over minimally invasive surgical approaches to the neck (Fig 2). Seventy-three adjacent nodes (range, 1 to 9 nodes) were additionally excised in 21 patients. There have been no complications of this surgical procedure, which lasted between 15 and 90 minutes. There has been no morbidity, and scars are scarcely visible (Fig 2).

In three patients, there were positive sentinel nodes following extensive histopathologic examination (false-negative PET results). The metastases have been 2, 4, and, reticulated, 7.3 mm in diameter. The sentinel nodes had a mean diameter of 13 mm. The patients with the 4 and 7.3 mm metastases were classified as node-positive on CT.

All three positive patients underwent MRND of the afflicted neck side. No further positive node was found in the neck dissection specimens. These additions led to a total of 41 neck sides operated on with ND. The remaining 35 patients did not undergo further surgical neck treatment. Twenty patients were followed up according to "wait-and-see"; 15 had postoperative radiation (51.3 Gy) according to the guidelines. Two patients who had been cured of cancers of the floor of the mouth and the anterior tongue, respectively, developed second primaries, all in the oropharynx, after 10 and 12 months, respectively. One patient could be operated on successfully, but the other died after treatment with induction chemotherapy and concurrent chemoradiotherapy 1 year later. Four other patients developed local recurrences between 5 and 21 months after initial treatment. All could be operated on. Two of them suffered from immediate local relapses that were treated by salvage surgery and brachytherapy, respectively, but one patient died as a result of distant metastases.

After a median observation time of 33 months (range, 10 to 52 months), none of the 41 patients diagnosed cN0 by PET had a neck relapse.

In the group of patients classified cN-positive who consequently were treated with MRND, one developed a second primary of the tongue base, two patients had local relapses, two had neck metastases, and one suffered from distant metastases. Both patients with neck relapses had pathohistologically positive necks after primary treatment.

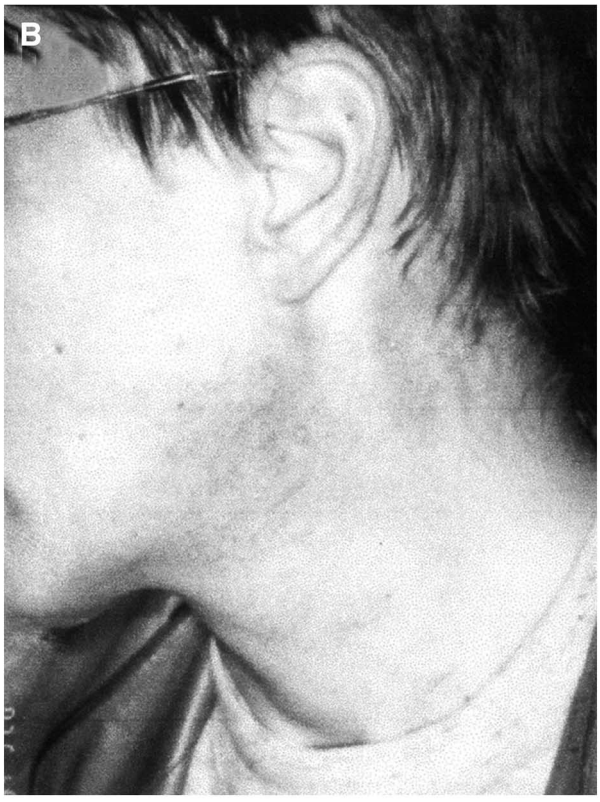

Fig 2. Neck morbidity following (A) suprahyoid neck dissection compared with (B) minimally invasive sentinel node biopsy. Both patients suffered from T2 squamous cell carcinoma of the anterior floor of the mouth.

The patient with the second primary, one patient with local relapse, and one patient with neck metastases could be treated surgically. One patient with a neck metastasis is living with disease after 1 year due to repeated systemic docetaxel and cisplatin. The other two patients with relapses died due to rapidly progressive disease.

The median overall observation time for the 62 patients was 35 months (range, 10 to 52 months). Six patients died (10%); in four of them, death was disease-specific.

DISCUSSION

According to the interdisciplinary guidelines of the German Societies for Otorhinolaryngology and Maxillofacial Surgery,[14] 51 neck sides in 36 patients without suspect nodes in CT examination would have been treated with at least a prophylactic selective ND of the levels 1 and 2a, in 15 patients bilaterally (Table 3). Forty-five neck sides in 26 patients with suspect nodes in the CT examination should have had an extensive therapeutic neck dissection. This means that 96 (77.5%) of a possible 124 neck sides in 62 patients of the study population would have undergone extensive ND due to presurgical imaging. This number would have increased to approximately 100 neck sides due to intraoperative evaluation of tumor extention.

In contrast to this traditional regimen, only 41 (33%) of a possible 124 neck sides had the necessity of extensive ND after PET staging or having positive sentinel nodes in SNB. The radiotherapeutic regimen depended on histopathologic staging and did not interfere with the pretherapeutic diagnostic techniques. After a median observation time of nearly 3 years, there have been two neck metastases. This result has a safety of more than 80% according to the natural history of oral cancer[16] because 80% of occult metastases become evident after 24 months of follow-up. It seemed that the new diagnostic procedure reduced the rate of extensive ND without locoregional hazard, and promises to be the result of the diagnostic combination of PET and LS/SNB.

Even in the case of a combination of CT and LS/SNB, which has been assumed in the calculations, the neck sides spared would have been 51, in comparison to 59 neck sides spared by PET plus LS/SNB. When adding the difference between the actual number of operated neck sides due to PET- and SNB-based staging (41 neck sides), and the neck sides which would have at least been operated on due to CT based staging (45 neck sides), there would have been a total of at least 12 neck sides spared by the newly presented diagnostic ladder.

In head and neck melanoma, recent reports did not prove an advantage of the combination of PET and SNB. PET detected only between 17% and 20% of positive SLNs.[17-18] The conclusions drawn from these results were not consistent—they ranged from judging the methods to be complementary to estimating PET as being insufficiently sensitive. SNB was estimated the procedure of choice.

On the other hand, presurgical staging of the neck has very different consequences for patients with oral and oropharyngeal cancer. Positive nodes lead to extensive neck dissection with the known chronic sequelae. Therefore, the combination of PET and SNB might have another impact. Studies on this topic included patients without palpable or radiologic evidence of neck metastasis.[19-21] PET results were compared with SNB results: PET was regarded as

Table 5. Approximate Cost Comparison Between the Two Paradigms in Germany in 2004

	Imaging Costs	Pathology Costs	Gainings (case-based lump sum)	Duration of Surgery	Drainage and Dressing	Hospitalization
PET/SNB	PET 1,100 Euros LS/SNB 400 Euros	250 Euros	10,000-12,000 Euros	15-90 minutes	No	n days
CT/ND	500 Euros	260-430 Euros	10,000-12,000 Euros	45-180 minutes	Yes	n + 3 days

NOTE. Some of the mentioned parameters and the avoided morbidity of ND cannot be expressed in absolute figures.
Abbreviations: PET, positron emission tomography; SNB, sentinel node biopsy; LS/SNB, lymphoscintigraphy-guided sentinel node biopsy; CT, computed tomography; ND, neck dissection.

being less useful in evaluation of otherwise clinically N0 necks. Only 0% to 20% of positive SLNs have been diagnosed by PET. This result was clearly due to the technical limitations of resolution (4 to 5 mm) and was comparable to the results presented in this study. Micrometastases found in the sentinel nodes were generally smaller. However, all investigators regarded SNB as highly useful. Results have been controlled by pathologic examination of the specimen of an elective ND as gold standard. Twenty-one percent to 55% of patients have been node-positive in SNB and have undergone therapeutic ND. This is in contrast to the results reported here: only five (12%) of 41 patients underwent therapeutic neck dissection in the cN0 group. After a median observation time of 33 months, there is no hint for a change of this percentage, because no occult metastasis became clinically evident.

SNB was used as single pathologic staging method following PET examination. Elective NDs have been avoided. The reason for this difference between the mentioned studies and the present one is not clear. It might be that micrometastases have been overseen. But this is unlikely considering the natural history of the disease and the long observation time. It is possible that there is a correlation with intra-arterial chemotherapy, but this is speculative to date and justifies further investigation. Another possible reason might be the mode of selection for the study, which was done before any treatment. By defining cN0 as absent neck uptake in [^{18}F]FDG PET, the known high specificity of PET allowed the exclusion of highly probable N-positive patients. In the remaining patients, LS/SNB was used as the next step in the staging procedure. It is likely that in this context, few positive SLNs could be found. The sensitivity of LS/SNB was high, and the ND specimens did not reveal additional afflicted nodes. The detected metastases had diameters beyond the capacity of PET, which is around 5 mm. The addition of LS/SNB seemed to be reasonable under this condition.

The incidence of two neck metastases (3%) in a population of 62 patients with oral and oropharyngeal cancer treated with curative aim after a median observation time of nearly 3 years is comparable to the literature, where rates of between 0% and 15% regional failures following MRND are reported in N0-2 patients.[22] LS/SNB is not feasible in patients who were previously surgically treated in the mouth or neck.[23]

The proposed staging ladder has the advantage of avoiding unnecessary extensive NDs. Evidence of neck metastasis is insecure in patients staged N0 functionally. Accuracy of PET is around 80%. PET should not be used as concurrence for LS/SNB because micrometastases are beyond the limits of PET resolution. PET results should, therefore, not be compared with LS/SNB results. Rather, PET should be used as a prerequisite for LS/SNB. The combination of the high specificity of PET and the high sensitivity of LS/SNB has the potential to be a staging ladder of high validity, and the ability to spare a large number of patients from unnecessary extensive NDs. This would also be true for a supraomohyoidal ND undertaken in the case of a clinically N0 neck, which has similarly moderate morbidity and equally acceptable cosmetic results as a suprahyoid ND, but surely takes longer as a surgical procedure, needs more drainage and dressing material, and a longer hospitalization as compared to SNB. The cost benefit ratios for the compared diagnostic and therapeutic procedures are shown in Table 5. The extensive pathologic examination of sentinel nodes seemed to be justified because the biopsy has been executed as single surgical staging procedure in an attempt to maintain a maximum of safety. It may be that in the future, step-serial sections and immunohistochemistry will be omitted. Several authors claimed that micrometastases could be diagnosed correctly by routine H&E examination.[24,25] To date, the proposed new paradigm is more expensive, but the benefit for the patients is evident if the results were lasting and could be affirmed by other working groups.

Authors' Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.

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