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Does Sentinel Lymph Node Biopsy in Cutaneous Head and Neck Melanoma Alter Disease Outcome?

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Background and Objectives: In the head and neck region, value, reliability, and safety of sentinel lymph node biopsy (SLNB) have not yet been determined conclusively. The aim of study was to assess impact of SLNB on disease outcome in cutaneous head and neck melanoma.

Methods: Thirty-six patients with a clinically node-negative head and neck melanoma, $\geq$1.0 mm Breslow thickness, participated in a prospective study from 1995 to 2005. Sentinel lymph node (SLN) tumor-positive patients underwent completion lymphadenectomy. SLN tumor-negative patients underwent clinical monitoring. Median follow-up was 54 (range 10–114) months. Recurrence-free and overall survival curves were constructed by Kaplan–Meier.

Results: SLNs could be identified in 33 patients (92%). In 7 patients (21%) the SLN was tumor-positive. In 1 patient (13%) the SLNB was false-negative. In 17 patients (47%) SLNs could be identified in the parotid region (success rate parotid region 100%). This study showed no significant difference in recurrence-free and overall survival between patients with tumor-positive and tumor-negative SLN.

Conclusions: The safety and accuracy of SLNB in the neck and parotid nodal basins were similar to those in non-head and neck sites. However, the technique is technically demanding in this region. In this small series SLNB did not alter disease outcome.

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KEY WORDS: **melanoma; head; neck; sentinel; in-transit recurrence**

INTRODUCTION

The incidence of cutaneous melanoma in the head and neck region has increased in recent years, along with an overall increase in the incidence of cutaneous melanoma world-wide. The key to survival is early detection of this malignancy and indeed melanoma is currently diagnosed in an earlier stage with thinner melanoma [1]. Early detection and treatment of micrometastatic disease might further improve recurrence-free, and overall survival. Primary cutaneous melanomas in the head and neck region are considered to be more aggressive than melanomas on the arms and legs [2]. Therefore, debate continues about the best management for clinically negative cervical lymph nodes. Prospective studies, performed in the past did not proof any benefit of elective lymphatic dissection for these patients [3–5]. A combination of high relapse rates and the persisting lack of effective treatment for recurrent disease has focused

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attention on optimizing initial management as a means of improving the overall outcome. The value and reliability of SLNB as a staging procedure in melanoma have been well-described in the literature since it was first reported in 1990, but final results of the multicenter selective lymphadenectomy trial (MSLT I) are still pending [6,7]. SLNB can identify indeed patients who may theoretically benefit from complete lymph node dissection. Melanomas located on the head and neck have an extremely unpredictable drainage pattern [8,9]. SLNB in the head and neck region presents unique challenges in terms of anatomy and surgical technique. The value, safety, reliability, recurrence-free and overall survival rates of SLNB in patients with cutaneous melanoma in the head and neck region were evaluated and discussed with respect to the current literature.

MATERIALS AND METHODS

Patients

From May 1995 to 2005, 36 patients (15 females (42%) and 21 males (58%)), median age 58 years (range 25–79 years) with a cutaneous melanoma $\geq$1.0 mm Breslow thickness in the head and neck region were enrolled in a prospective registration study at the Division of Surgical Oncology of the Groningen University Medical Center. Informed consent was obtained from all patients. The primary melanomas were diagnosed by excisional biopsy. None of these patients had undergone excision of the primary tumor with margins of >1.5 cm. Patients with palpable regional lymph nodes and/or clinical evidence of distant metastases, pregnant women and children and adolescents (<18 years) were excluded from this study.

Lymphoscintigraphy

A 2-day protocol on an inpatient basis was used. Lymphoscintigraphy was performed on the day preceding the operation. A single dose of unfiltered 40–60 MBq ^{99m}Tc nanocolloid (Nanocoll®; Amersham Cygne, Eindhoven, the Netherlands) with a particle size of <80 nm in 0.2 ml of saline was injected intradermally around the primary tumor site at two to four locations. Injection sites were covered with lead shielding. Dynamic imaging in the supine position with a low energy high resolution collimator to visualize lymph flow was commenced immediately after tracer administration and continued for 20 min at a frame rate of 30 sec/image. Subsequently, static supine and lateral views were obtained. A radioactive flood source was used to outline the body contour. Another set of static images was taken 2 hr later. All possible lymph drainage regions were imaged. The position of the SLN(s) was marked on the skin with indelible ink. The images were discussed by an interdisciplinary team comprising the nuclear medicine physician and the surgical oncologist prior to the operation.

Surgery

After the induction of general anesthesia, but 15–20 min before surgery, an injection of 0.3–1.0 ml Patent Blue V (Bleu Patenté V®, Laboratoire Guerbet, Aulnay-sous-Bois, France) was administered intradermally around the melanoma scar. All nodal basins identified by lymphoscintigraphy were explored surgically through limited incisions. Surgical dissection was guided by a hand-held γ-detection probe (Neoprobe®1000 and 1500, Johnson & Johnson Medical BV) and by looking for blue-stained afferent lymphatic vessels that led to blue-stained SLNs. Once the SLNs had been excised the probe was used to search the resection bed to ensure that there were no residual areas of high radioactivity. If necessary, additional hot nodes were removed until the ratio of the hottest ex vivo SLN to the residual basin was >10:1 [10].

After SLNB, wide local excision of the primary melanoma scar was performed with 1 or 2 cm margin depending on the tumor thickness (Breslow) and the anatomical location of the melanoma. If pathological examination was positive for tumor cells on hematoxylin-eosin (HE) or immunohistochemical (IHC) staining, cervical or posterior lymph node dissection was performed with the standard surgical procedure. If SLNs were negative for tumor cells on pathological examination, the lymph node basins were monitored clinically during follow-up.

Pathology

After marking the hottest part of the SLN with a stitch, each harvested SLN was sent for pathological examination. Owing to low sensitivity (38%) of frozen section analysis with HE in the first 11 patients, we subsequently delayed SLN evaluation in order to perform permanent sectioning.

The SLNs were fixed in 10% neutral buffered formalin and blocked in paraffin. Serial 4 μm thick sections of all paraffin-embedded material were evaluated with routine HE and IHC staining for S100 protein and melanoma-associated antigen HMB45. This procedure was repeated at levels of 500 μm until all the tissue was sectioned (average: 9 levels). Two paraffin-embedded cross-sections of each lymph node were stained with HE without any additional IHC.

Follow-Up

Patients were seen for physical examination every 3, 4, 6, and 12 months in the 1st, 2nd, 3rd–5th and

5th–10th years, respectively. A chest X-ray was taken once a year. In patients who developed tumor recurrence in the same nodal basin, recurrence patterns were analyzed. All previously identified tumor-negative SLNs were re-evaluated on original slides and IHC-stained additional deeper sections of the SLNs. Duration of follow-up was calculated in months from the date of SLNB to the date of last follow-up or death. None of the patients were lost to follow-up. Median follow-up was 54 (range 10–114) months.

Statistical Analysis

Recurrence-free and overall survival curves were constructed for SLN-positive and SLN-negative patients using the Kaplan–Meier method and compared using the log-rank procedure. Significance was defined as $P < 0.05$. Results are presented as median (range) and as percentages when appropriate.

RESULTS

Fifteen females (42%) and 21 males (58%) with a median age of 58 (range 25–79) years with a cutaneous melanoma, ≥1.0 mm Breslow thickness (median 2.5 mm, range 1.0–8.1) were included (Table I). At least one SLN was identified in 33 (92%) out of the 36 patients. Wide local resection with 1–2 cm margin had to be performed before SLNB in 10 patients (28%), to reduce the high background counts that interfered with SLN localization by the γ-detection probe.

TABLE I. Clinical and Pathological Characteristics of 36 Patients With a Cutaneous Melanoma in the Head and Neck Region

	Number of patients	%
Sex		
Male	21	58
Female	15	42
Age (years)		
Median	58 (25–79)	
Lesion location		
Face	14	39
Neck	5	14
Ear	4	11
Scalp	13	36
Lesion depth (mm)		
≤1.0	1	3
1.01–2.0	12	33
2.01–4.0	16	44
>4.0	7	20
Ulceration	8	22
Histological subtype		
Superficial spreading	11	30
Nodular	17	47
Lentigo maligna	2	6
Unclassified	1	3
Other	5	14

A total of 97 SLNs were excised (median 2.9 nodes per patient; range 1–7). These 97 SLNs were removed from a total of 48 nodal basins (median 1.5 basin per patient; range 1–3). In 23 patients (70%) the blue tracer was seen together with the radioactive tracer intraoperatively. In 10 patients (30%) the SLNs were identified by the radioactive tracer alone.

In two patients, SLNs were identified in an unexpected node field, that is, the supraclavicular basin. In one of them with a primary lesion on the earlobe, dynamic lymphoscintigraphy showed direct drainage to both the parotid region and the supraclavicular region. In the other patient, direct drainage was seen from the pre-auricular melanoma scar site to the subdigastric and supraclavicular regions. In both patients, histopathology of the SLNs in the unexpected and expected basins was tumor-negative.

In 17 patients (47%), lymphoscintigraphy showed a SLN in the parotid region. All SLNs could be identified in this region (success rate 100%). In 12 patients (71%), the parotid SLNs were tumor-free. In five patients (29%) the parotid SLNs were tumor-positive. These patients underwent subtotal parotidectomy with modified neck dissection. No additional tumor-positive lymph nodes were found on histopathological examination. After exploration of the parotid gland or after re-operation that comprised subtotal parotidectomy no complications occurred.

In total, a tumor-positive SLN was diagnosed in seven patients (tumor-positive SLN-rate 21%).

So far, 12 patients (33%) have developed recurrence of the disease. The distribution of the first site of the metastases was as follows: 4 (11%) with in-transit recurrence; 2 (6%) with recurrence in the regional lymph node basin; and 6 (17%) with a distant recurrence. The distribution of the first site of the metastases according to tumor status of the SLN is shown in Table II. The SLNB result was false-negative in one of seven positive SLNB results (false-negative rate 13%).

Recurrence-free and overall survival were not significantly associated with the results of the SLNB. The 5-year recurrence-free survival in SLN-tumor-negative patients and SLN-tumor-positive patients was 65% and 50% respectively ($P < 0.6133$). The overall survival at 5 years was 55% and 66% respectively ($P < 0.5951$) (Figs. 1 and 2).

The overall morbidity related to this procedure was minimal. No anaphylactic reactions occurred following the injection of radioactive tracer or Patent Blue V. All the patients had normal postoperative cranial nerve function, including the facial nerve.

DISCUSSION

Sentinel lymph node biopsy in head and neck melanoma is a challenge for the surgeon. In this series

TABLE II. Recurrence Characteristics According to SLN Status

Characteristic	All patients (N = 36)	SLN− (N = 26)	SLN+ (N = 7)
Median follow-up, months	54 (range, 10–114)	49 (range, 10–99)	54 (range, 13–88)
Recurrence, No (%)	12 (33)	8 (31)	3 (43)
Median time to recurrence, months	43 (range, 3–110)	40 (range, 3–87)	38 (range, 6–85)
Site of first recurrence, No (%)			
In-transit	4 (11)	2 (8)	2 (29)
Nodal	2 (6)	1 (4)	0
Systemic	6 (17)	5 (19)	1 (14)

SLN−, sentinel lymph node tumor-negative; SLN+, sentinel lymph node tumor-positive.

SLNB succeeded in 33 of the 36 patients (success rate 92%). This is in contrast to our series of 266 non-head and neck melanoma patients in which we could identify all SLNs (success rate 100%) [11].

Various features may have contributed to the failures: (1) primary tumor site overlying the draining basin(s), (2) learning curve of the surgeon, (3) high radioactivity level (40–60 MBq), (4) lymphoscintigraphy collimator problems, artefacts, (5) volume of tracer too large, (6) spillover into second echelon nodes, and (7) incorrect injection technique, that is, if injection is not intradermal, the lymphatic drainage may not be adequately demonstrated.

The success rate of SLNB in the parotid region was 100%. After SLNB in the parotid region, no complications were observed. Our experience supports the findings of others that SLNB of intraparotid nodes can be performed safely by experienced surgical oncologists specialized in surgical oncology procedures in the head and neck area without formal parotidectomy [12,13]. The procedure was performed with equivalent safety in the neck and parotid nodal basins. In our opinion, when it has been decided to do a SLNB, surgical oncologists should not be reluctant to perform subtotal parotidectomy and/or posterolateral neck dissection if the SLNB result is tumor-positive.

Is our false-negative rate of 13% high? Table III illustrates the great variation in the false-negative rates for SLNBs in head and neck melanoma as published in the literature [14–31]. In determining the rate of false-negative results, a mistake that is sometimes made is to calculate the rate over the entire group of patients, both those who are tumor-positive and those who are tumor-negative. The outcome is too flattering with this

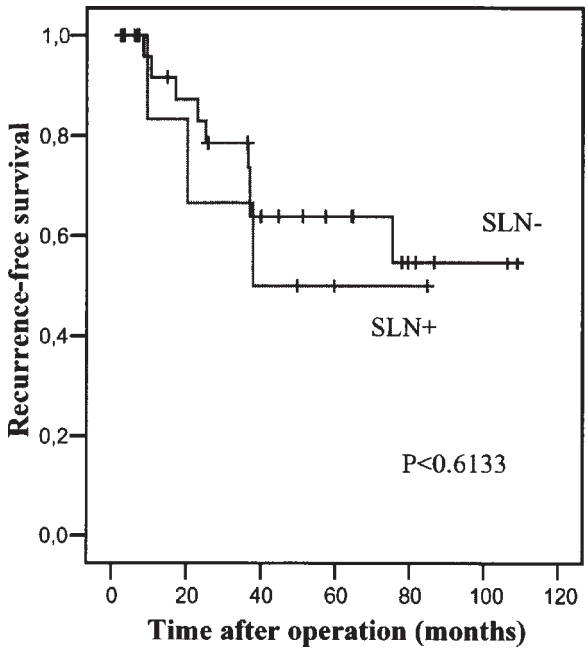

Fig. 1. Recurrence-free survival plot according to Kaplan–Meier. SLN−, sentinel lymph node tumor-negative; SLN+, sentinel lymph node tumor-positive.

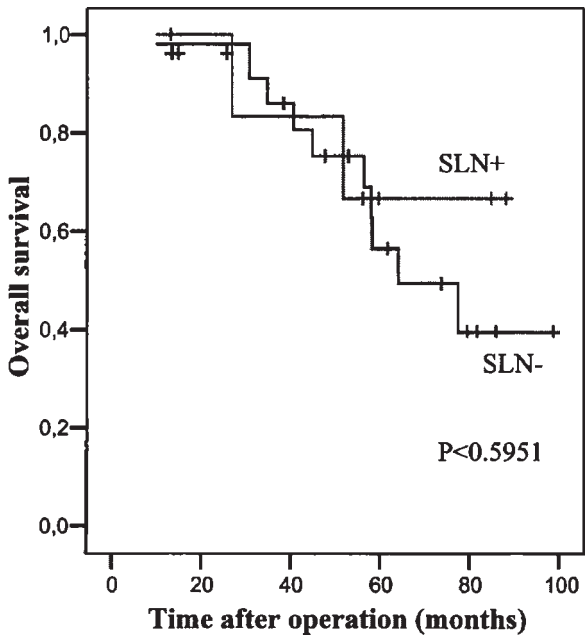

Fig. 2. Overall survival plot according to Kaplan–Meier. SLN−, sentinel lymph node tumor-negative; SLN+, sentinel lymph node tumor-positive.

TABLE III. Results of SLNB in Head and Neck Melanomas Obtained by Various Investigators

Author	Year of publication	Number of patients	SLN identified (%)	False-negative (%)[b]
Morton [14]	1993	72[a]	90	0
O'Brien [15]	1995	20	75	50
Wells [16]	1997	58	95	0
Bostick [17]	1997	117[a]	93	0
Alex [18]	1998	23	96	0
Wagner [19]	2000	70[a]	99	12
Jansen [20]	2000	30	90	20
Carlson [21]	2000	57	96	0
Medina-Franco [22]	2001	38	92	20
Eicher [23]	2002	43	98	0
Patel [24]	2002	56	96	20
Schmalbach [25]	2003	80	96	18
Chao [26]	2003	321	97	12
De Wilt [27]	2004	362	99	44
Fincher [28]	2004	51	100	0
Shpitzer [29]	2004	30	93	20
Lin [30]	2005	80	99	24
Carlson [31]	2005	132	95	29
Current study	2005	36	92	13

SLN, sentinel lymph node.
[a]Including trunk.
[b]The percentage of false-negative procedures is calculated over the patients with tumor-positive SLNs.

TABLE IV. In-Transit as First Site of Recurrence According to SLN Status (Update of the European Journal of Surgical Oncology 2004 [33])

					In-transit recurrence				
					SLN−		SLN+		
Author	Year of publication	Primary site	Breslow (mm)	Number of patients	N	%	N	%	FU (months)
Gershenwald [35]	1998	Trunk and extremities	1.60	243[b]	12[a]	5	—	—	35
Gadd [36]	1999	Extremities and axial	1.8	89[b]	2[a]	2.2	—	—	23
Essner [37]	1999	All	1.9	267	6[a]	2.7	4[a]	9.5	45
Clary [38]	2001	All	2.1	303	14[a]	5.6	9[a]	16.1	23
Statius Muller [39]	2002	All	1.4	248	10[a]	5	13[a]	27	38
Estourgie [40]	2003	All	2.7	250	24[a]	12.6	17[a]	28.3	72
Vuylsteke [41]	2003	All	1.41	209	11	6.5	13	32.5	23
Wagner [42]	2003	All	2.27	408	13[a]	4.0	5[a]	5.9	31.4
Tiffet [43]	2004	All	3	132	3	2.7	2	9	27.1
Ariyan [44]	2004	All	1.7	263	2	1	3	11	32
Macripo [45]	2004	All	1.5 and 2.6[c]	274	8	3.5	2	4.3	34.8
Borgognoni [46]	2004	All	?	385	6	2.0	1	1.3	35
Gipponi [47]	2004	All	?	180	1	1.1	2	5.5	16.5
Yee [48]	2005	All	1.7	836[b]	10	1.2	—	—	42.1
Van Poll [49]	2005	All	1.85	754	11	1.7	7	6.9	42
Pawlik [50]	2005	All	1.5	1,395	40	3.5	28	12.0	46.8
Current study	This study	Head and neck	2.5	36	2	8	2	29	54

—, not mentioned.
FU, follow-up.
[a]Local and in-transit recurrence.
[b]SLN-negative patients only.
[c]Breslow thickness in SLN- en SLN+ patients, respectively.

approach. It is not possible to miss metastasis in a patient who has no metastasis. The false-negative rate should be calculated over the entire group of tumor-positive patients, as follows:

$$\text{False-negative rate} = \frac{\text{no. of false-negative procedures}}{\text{no. of false-negative} + \text{true-positive procedures}} \times 100\%$$

The false-negative rates in Table III are adjusted accordingly [32].

The number of patients with a positive SLN in our study was small, which might have led to a high false-negative rate on the basis of one false-negative result. Reporting the false-negative rate for this procedure is problematic, because it is difficult to make a reliable assessment of the status of the remainder of the nodal basin by using non-surgical means. The most accurate approach would be to perform lymph node dissection immediately after SLNB, so that the status of the entire ''at risk'' nodal basin can be compared to that of the SLN(s). An ideal solution would be to examine SLNs and non-SLNs using immunohistochemical methods and serial sectioning in equal detail to enable a truly valid evaluation of the technique, but this is obviously impractical. We used the current, generally more acceptable method to determine false-negative rates: documentation of the rate of nodal failure over time within SLN-negative basins.

The performance of SLNB may in itself alter the pattern of subsequent recurrence of melanoma, thus increasing the incidence of in-transit recurrence [33,34]. In-transit recurrence is defined as that occurring between the primary excision site and the regional node basin, but excluding local recurrences within 3 cm of the primary tumor site. In this small series we found two cases in SLN-positive ($2/7 = 29\%$) and two cases in SLN-negative ($2/26 = 8\%$) patients. Also other series are now publishing high incidence rates in SLN-tumor-positive patients (Table IV). However, our concern is not shared by others like Coit [51], who stated that the overall incidence of in-transit recurrence after SLNB is low and is most likely influenced much more by patient, tumor, and lymph node variables than by any treatment variable.

CONCLUSIONS

In the head and neck region, the multiplicity of lymph nodes, their widespread distribution, small size, and their proximity to vulnerable structures make the SLNB procedure technically challenging. This study addressed the value, safety, and reliability of SLNB to accurately detect occult regional metastases in patients with cutaneous melanoma in the head and neck region. During a median follow-up of 4½ years, one patient developed an isolated regional recurrence following a tumor-negative SLNB. A sensitivity rate of 87% with minimal morbidity indicates that SLNB is a reliable procedure for regional staging of patients with cutaneous melanoma in the head and neck region.

Recurrence-free and overall survival were not significantly associated with the results of SLNB, but the number of patients in this study was too small to draw any definitive conclusions. The main question which is still unanswered is whether SLNB will improve disease-free and overall survival. Results of MSLT I are pending [7].

Although no consensus has been reached among investigators as to whether SLNB followed by early regional node dissection improves regional tumor control (and patient survival), lymphatic mapping definitely provides prognostic information [52]. If this is also true for head and neck melanoma is questionable and is not supported by this small study.

REFERENCES

1. Vries de E, Coebergh JW: Cutaneous malignant melanoma in Europe. Eur J Cancer 2004;40:2355–2566.
2. Daryanani D, Plukker JTh, Jong de MA, et al.: Increased incidence of brain metastases in cutaneous head and neck melanoma. Melanoma Res 2005;15:119–124.
3. Veronesi U, Adamus J, Bandiera DC, et al.: Inefficacy of immediate node dissection in stage 1 melanoma of the limbs. N Engl J Med 1977;297:627–630.
4. Veronesi U, Adamus J, Bandiera DC, et al.: Delayed regional lymph node dissection in stage I melanoma of the skin of the lower extremities. Cancer 1982;49:2420–2430.
5. Sim FH, Taylor WF, Ivins JC, et al.: A prospective randomized study of the efficacy of routine elective lymphadenectomy in management of malignant melanoma. Preliminary results. Cancer 1978;41:948–956.
6. Morton DL, Wen DR, Wong JH, et al.: Technical details of intraoperative lymphatic mapping for early stage melanoma. Arch Surg 1992;127:392–399.
7. Reintgen D, Pendas S, Jakub J, et al.: National trials involving lymphatic mapping for melanoma: The multicenter selective lymphadenectomy trial, the sunbelt melanoma trial, and the Florida melanoma trial. Semin Oncol 2004;31:363–373.
8. Statius Muller MG, Hennipman FA, Leeuwen van PAM, et al.: Unpredictability of lymphatic drainage patterns in melanoma patients. Eur J Nucl Med Mol Imaging 2002;29:255–261.
9. Uren RF, Howman-Giles R, Thompson JF: Patterns of lymphatic drainage from the skin in patients with melanoma. J Nucl Med 2003;44:570–582.
10. Albertini JJ, Cruse CW, Rapaport D, et al.: Intraoperative radio-lymphoscintigraphy improves sentinel lymph node identification for patients with melanoma. Ann Surg 1996;223:217–224.
11. Vries de M, Jager PL, Suurmeijer AJH, et al.: Sentinel lymph node biopsy for melanoma: Prognostic value and disadvantages in 300 patients. Ned Tijdschr Geneeskd 2005;149:1845–1851.
12. Schmalbach CE, Nussenbaum B, Rees RS, et al. Reliability of sentinel lymph node mapping with biopsy for head and neck cutaneous melanoma. Arch Otolaryngol Head Neck Surg 2003; 129:61–65.
13. Ollila DW, Foshag LJ, Essner R, et al.: Parotid region lymphatic mapping and se ntinel lymphadenectomy for cutaneous melanoma. Ann Surg Oncol 1999;6:150–154.
14. Morton DL, Wen DR, Foshag LJ, et al.: Intraoperative lymphatic mapping and selective cervical lymphadenectomy for early-stage

melanomas of the head and neck. J Clin Oncol 1993;11:1751–1756.
15. O'Brien CJ, Uren RF, Thompson JF, et al.: Prediction of potential metastatic sites in cutaneous head and neck melanoma using lymphoscintigraphy. Am J Surg 1995;170:461–466.
16. Wells KE, Rapaport DP, Cruse CW, et al.: Sentinel lymph node biopsy in melanoma of the head and neck. Plast Reconstr Surg 1997;100:591–594.
17. Bostick P, Essner R, Sarantou T, et al.: Intraoperative lymphatic mapping for early-stage melanoma of the head and neck. Am J Surg 1997;174:536–539.
18. Alex JC, Krag DN, Harlow SP, et al.: Localization of regional lymph nodes in melanomas of the head and neck. Arch Otolaryngol Head Neck Surg 1998;124:135–140.
19. Wagner JD, Park HM, Coleman JJ 3rd, et al.: Cervical sentinel lymph node biopsy for melanomas of the head and neck and upper thorax. Arch Otolaryngol Head Neck Surg 2000;126:313–321.
20. Jansen L, Schraffordt Koops H, Nieweg OE, et al.: Sentinel node biopsy for melanoma in the head and neck region. Head Neck 2000;22:27–33.
21. Carlson GW, Murray DR, Greenlee R, et al.: Management of malignant melanoma of the head and neck using dynamic lymphoscintigraphy and gamma probe-guided sentinel lymph node biopsy. Arch Otolaryngol Head Neck Surg 2000;126:433–437.
22. Medina-Franco H, Beenken SW, Heslin MJ: Sentinel node biopsy for cutaneous melanoma in the head and neck. Ann Surg Oncol 2001;8:716–719.
23. Eicher SA, Clayman GL, Myers JN, et al.: A prospective study of intraoperative lymphatic mapping for head and neck cutaneous melanoma. Arch Otolaryngol Head Neck Surg 2002;128:241–246.
24. Patel SG, Coit DG, Shaha AR, et al.: Sentinel lymph node biopsy for cutaneous head and neck melanomas. Arch Otolaryngol Head Neck Surg 2002;128:285–291.
25. Schmalbach CE, Nussenbaum B, Rees RS, et al.: Reliability of sentinel lymph node mapping with biopsy for head and neck cutaneous melanoma. Arch otolaryngol head neck 2003;129:61–65.
26. Chao C, Wong SL, Edwards MJ, et al.: Sunbelt Melanoma Trial Group. Sentinel lymph node biopsy for head and neck melanomas. Ann Surg Oncol 2003;10:21–26.
27. De Wilt JH, Thompson JF, Uren RF, et al.: Correlation between preoperative lymphoscintigraphy and metastatic nodal disease sites in 362 patients with cutaneous melanomas of the head and neck. Ann Surg 2004;239:544–552.
28. Fincher TR, O'Brien JC, McCarty TM, et al.: Patterns of drainage and recurrence following sentinel lymph node biopsy for cutaneous melanoma of the head and neck. Arch Otolaryngol Head Neck Surg 2004;130:844–848.
29. Shpitzer T, Segal K, Schachter J, et al.: Sentinel node guided surgery for melanoma in the head and neck region. Melanoma Res 2004;14:283–287.
30. Lin D, Kashani-Sabet M, Singer MI: Role of the head and neck surgeon in sentinel lymph node biopsy for cutaneous head and neck melanoma. Laryngoscope 2005;115:213–217.
31. Carlson GW, Murray DR, Lyles RH, et al.: Sentinel lymph node biopsy in the management of cutaneous head and neck melanoma. Plast Reconstr Surg 2005;115:721–728.
32. Nieweg OE, Estourgie SH: What is a sentinel node and what is a false-negative sentinel node? Ann Surg Oncol 2004;11:169S–173S.
33. Thomas JM, Clark MA: Selective lymphadenectomy in sentinel node-positive patients may increase the risk of local/in-transit recurrence in malignant melanoma. Eur J Surg Oncol 2004; 30:686–689.
34. Estourgie SH, Nieweg OE, Kroon BB: High incidence of in-transit metastases after sentinel node biopsy in patients with melanoma. Br J Surg 2004;91:1370–1371.
35. Gershenwald JE, Colome MI, Lee JE, et al.: Patterns of recurrence following a negative sentinel lymph node biopsy in 243 patients with stage I or II melanoma. J Clin Oncol 1998;16:2253–2260.
36. Gadd MA, Cosimi AB, Yu J, et al.: Outcome of patients with melanoma and histologically negative sentinel lymph nodes. Arch Surg 1999;134:381–387.
37. Essner R, Conforti A, Kelley MC, et al.: Efficacy of lymphatic mapping, sentinel lymphadenectomy, and selective complete lymph node dissection as a therapeutic procedure for early-stage melanoma. Ann Surg Oncol 1999;6:442–449.
38. Clary BM, Brady MS, Lewis JJ, et al.: Sentinel lymph node biopsy in the management of patients with primary cutaneous melanoma: Review of a large single-institutional experience with an emphasis on recurrence. Ann Surg 2001; 233:250–258.
39. Statius Muller MG, van Leeuwen PA, van Diest PJ, et al.: Pattern and incidence of first site recurrences following sentinel node procedure in melanoma patients. World J Surg 2002;26:1405–1411.
40. Estourgie SH, Nieweg OE, Valdes Olmos RA, et al.: Review and evaluation of sentinel node procedures in 250 melanoma patients with a median follow-up of 6 years. Ann Surg Oncol 2003;10:681–688.
41. Vuylsteke RJ, van Leeuwen PA, Statius Muller MG, et al.: Clinical outcome of stage I/II melanoma patients after selective sentinel lymph node dissection: Long-term follow-up results. J Clin Oncol 2003;21:1057–1065.
42. Wagner JD, Ranieri J, Evdokimow DZ, et al.: Patterns of initial recurrence and prognosis after sentinel lymph node biopsy and selective lymphadenectomy for melanoma. Plast Reconstr Surg 2003;112:486–497.
43. Tiffet O, Perrot JL, Gentil-Perret A, et al.: Sentinel lymph node detection in primary melanoma with preoperative dynamic lymphoscintigraphy and intraoperative gamma probe guidance. Br J Sur 2004;91:886–892.
44. Ariyan S, Ariyan C, Farber LR, et al.: Reliability of identification of 655 sentinel lymph nodes in 263 consecutive patients with malignant melanoma. J Am Coll Surg 2004;198:924–932.
45. Macripo G, Quaglino P, Caliendo V, et al.: Sentinel lymph node dissection in stage I/II melanoma patients: Surgical management and clinical follow-up study. Melanoma Res 2004;14:S9–S12.
46. Borgognoni L, Urso C, Vaggelli L, et al.: Sentinel node biopsy procedures with an analysis of recurrence patterns and prognosis in melanoma patients: Technical advantages using computer-assisted gamma probe with adjustable collimation. Melanoma Res 2004;14:311–319.
47. Gipponi M, Solari N, Di Somma FC, et al.: New fields of application of the sentinel lymph node biopsy in the pathologic staging of solid neoplasms: Review of literature and surgical perspectives. J Surg Oncol 2004;85:171–179.
48. Yee VS, Thompson JF, McKinnon JG, et al.: Outcome in 846 cutaneous melanoma patients from a single center after a negative sentinel node biopsy. Ann Surg Oncol 2005;12:429–439.
49. van Poll D, Thompson JF, Colman MH, et al.: A sentinel node biopsy does not increase the incidence of in-transit metastasis in patients with primary cutaneous melanoma. Ann Surg Oncol 2005;12:597–608.
50. Pawlik TM, Ross MI, Johnson MM, et al.: Predictors and natural history of in-transit melanoma after sentinel lymphadenectomy. Ann Surg Oncol 2005;12:587–596.
51. Coit DG: In-transit recurrence after sentinel lymph node biopsy in melanoma: Primum non nocere. Surg Oncol 2005;12:575–578.
52. Gershenwald JE, Thompson W, Mansfield PF, et al.: Multi-institutional melanoma lymphatic mapping experience: The prognostic value of sentinel lymph node status in 612 stage I or II melanoma patients. J Clin Oncol 1999;17:976–983.