Indian J Surg (September–October 2013) 75(5):377–382
DOI 10.1007/s12262-012-0497-5

ORIGINAL ARTICLE

The First and Second Echelon Sentinel Lymph Node Evaluation in Oral Cancer

Kuldeep Kumar Bassi · Anurag Srivastava · Vuthaluru Seenu · Rakesh Kumar · Rajinder Parshad · Sunil Chumber · Siddarth Datta Gupta · Sudhir Bahadur

Received: 16 February 2011 / Accepted: 5 April 2012 / Published online: 2 June 2012
© Association of Surgeons of India 2012

Abstract Sentinel lymph node biopsy shows promise as a minimally invasive technique that samples the first echelon (station) of nodes to predict the need for more extensive neck dissection. This paper discusses the accuracy and feasibility of sentinel node and "station II node" biopsy for predicting the status of neck in 20 patients of oral cancer. We identified sentinel node in these patients. The next higher-order nodes, that is, second echelon of nodes known as "station II nodes" were delineated by further injecting 0.1 ml of isosulfan blue dye in sentinel lymph node. Identification rate for station I nodes was 95 %. Station II nodes were identified in 84 % of patients. One patient had false negative station I node. Station II node status was false negative in two patients. "Station I and station II concept" is feasible in early-stage tumors of oral cavity.

Keywords Sentinel node (station I node) · Oral cancer · Second echelon (station) node · Neck dissection

Presentation at a meeting Organisation: 21st Annual Conference, Delhi State Chapter ASI, Place: Maurya Sheraton, New Delhi, INDIA. Date: Nov 2-2003.

K. K. Bassi (✉) · A. Srivastava · V. Seenu · R. Parshad · S. Chumber
Department of Surgical disciplines,
All India Institute of Medical Sciences (AIIMS),
New Delhi 29, India
e-mail: bassi_kuldeep@rediffmail.com

R. Kumar
Department of Nuclear Medicine,
All India Institute of Medical Sciences (AIIMS),
New Delhi 29, India

S. D. Gupta
Department of Pathology,
All India Institute of Medical Sciences (AIIMS),
New Delhi 29, India

S. Bahadur
Department of ENT,
All India Institute of Medical Sciences (AIIMS),
New Delhi 29, India

A. Srivastava (✉)
Department of Surgery,
All India Institute of Medical Sciences (AIIMS),
New Delhi 29, India
e-mail: dranuragsrivastava@gmail.com

Introduction

The presence of lymph nodal metastasis is an important indicator of long-term outcome for patients with squamous cell carcinoma of oral cavity [1]. The treatment of these cancers always includes treatment of the regional lymph nodes. Even in patients without any clinical or radiological evidence for cervical lymph node metastasis, a prophylactic treatment by radiotherapy or elective neck dissection is recommended because of high incidence (over 30 %) of occult metastasis. This implicates that probably 70 % of patients with N0 neck are overtreated [2].

Supraomohyoid neck dissection (SOND) provides same information as radical neck dissection in patients with clinically N0 (node negative) neck disease. Extensive lymph node dissection appears to offer no diagnostic or therapeutic advantage over limited neck dissection in the evaluation of occult cervical metastasis [3, 4].

Sentinel lymph node (SLN) is the first draining lymph node for a tumor of a particular site. All other nodes are presumed to be afflicted subsequently. This concept has already been proven in malignant melanoma and breast cancer [5, 6]. SLN identification has been attempted in oral cancer and shows promise as a minimally invasive staging procedure for neck metastases [7]. Possibly in future, SLN

biopsy may be used to find patients who may not benefit from elective neck dissection.

Deo et al. have conducted one such study in the Department of Surgical Oncology at our institute in 30 patients of oral cancer with SLN identification rate of 94 % [8]. Going a step further, we have done the histologic analysis of sentinel lymph node and next higher nodes. Peritumoral injection of dye and submucosal injection of isotope demonstrated sentinel lymph nodes, which we labeled as station I nodes. Injection of dye into these lymph nodes delineated lymph nodes, which we labeled station II nodes or second echelon nodes (Fig. 1).

We propose that if station II nodes are negative, it is reasonable to assume that no distal lymph nodes are involved. If station II nodes are also positive, then complete dissection of regional lymphatic basin is suggested, as probability of distal lymphatic spread is expected to be high. After delineation of two "echelon" of nodes, comprehensive neck dissection was carried out and specimen was sent for H&E (hematoxylin and eosin) staining.

Patients and Methods

We enrolled 20 patients of biopsy-proven operable oral cavity tumors (T1-T4) with N0/N1 nodal disease. We excluded patients who had previously undergone neck surgery or radiation therapy of the head and neck or who had a history of any noncutaneous malignancy or tubercular lymphadenitis of neck. The sentinel node mapping was carried by a combination of isosulfan blue dye and Tc-99 sulphur colloid (combined technique) in 10 patients and isosulfan blue in 10 patients. In combination technique, the day before the operation, tumor was injected with 0.40 mCi (0.1 ml) of unfiltered Tc-99 m sulfur colloid radiotracer by 26 G needle, submucosally and in case of ulcerative tumors, tracer injection was given around the tumors. The time elapsed between tumor injection and surgery was approximately 17 h.

On the day of operation, after cleaning and draping of operation site, 4 ml of 1 % isosulfan blue dye was injected peritumorally at 3–4 sites. The procedure began with an attempt to transcutaneously identify the sentinel node in the neck with a 'gamma probe' [Navigator, USA]. Skin flap was raised after the blue dye injection in the peritumoral region and the sentinel node(s) was identified along with draining lymphatics from the tumor region (Fig. 2). Radioactive count was noted with gamma probe. Sentinel node was labeled "hot" if the uptake was10 times higher than the background count. Blue dye 0.1 ml was injected into the sentinel node(s) and lymphatics were traced to station II nodes (Fig. 3).

The higher radioactivity from the injection site, termed the "shine through artifact", obscured the localization of the sentinel nodes at the first echelon in tumors, which were near the mandible. In some patients, we experienced difficulty in visualizing lymphatics below the skin flap, because of rapid washout of the dye. Later on, we tried to solve this problem by raising the flap first, and then injecting the isosulfan blue dye pritumorally, so that we could visualize the flow of dye in the lymphatics directly.

After the removal of the sentinel nodes (hot and blue/hot/blue nodes), the tissue bed was reevaluated to confirm the removal of all the sentinel nodes. Subsequently, therapeutic neck dissection was performed and nodes at various levels were dissected out separately.

After removal of the station I and II nodes and completion of the neck dissection procedure, surgical specimens were sent to the Department of Pathology. The specimens were properly labeled and preserved in 10 % formal saline. The lymph nodes were identified by palpation and visual inspection. An attending pathologist, experiencing in

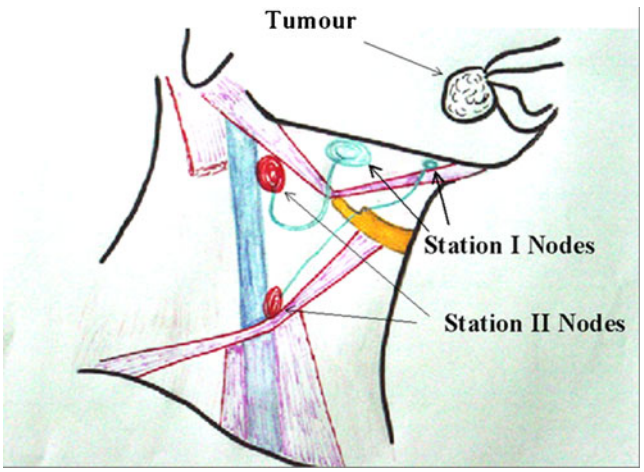

Fig. 1 Line diagram to show the concept of "Station I and II Nodes" in oral cancer

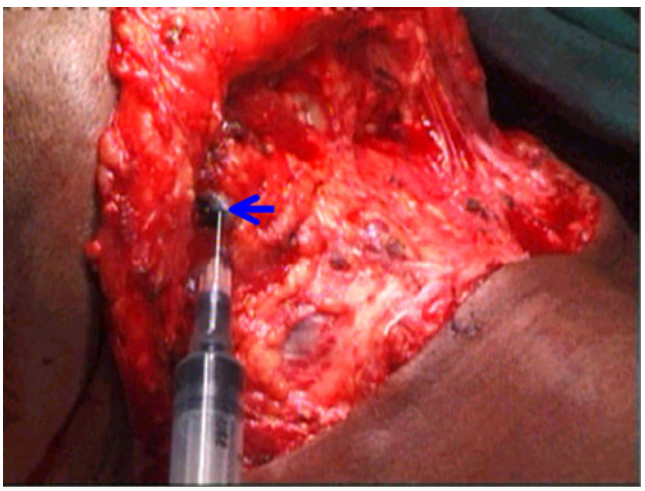

Fig. 2 Injection of isosulphan blue dye into "Station I Node"

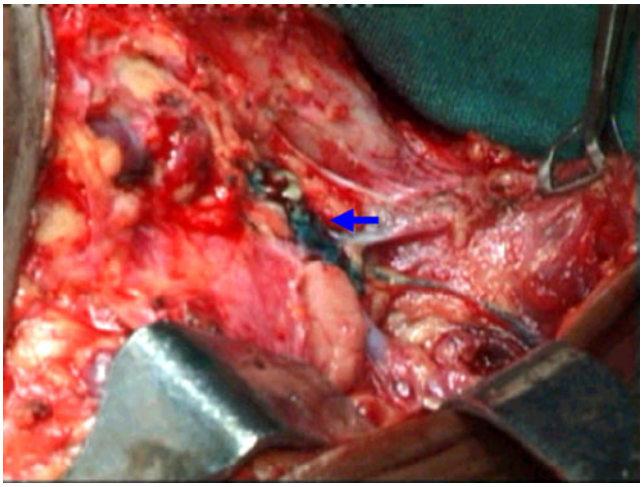

Fig. 3 "Station II Node"

sentinel node reporting histologically examined minimum of 3 (range 3–5) cross sections of each lymph node, stained with H&E. The nodes from the neck dissection specimens were processed and examined in an identical fashion to the sentinel nodes. Afterward, the histopathologic status of the station I and II nodes was compared with that of the remainder of the neck dissection specimens.

Results

We studied 20 (age 34–75 years) patients of squamous cell carcinoma of oral cavity. We included tumors with N0/N1 disease (soft to firm small palpable nodes) based on clinical examination. We took N1 nodal disease because in our population, large hyperplastic nodes are common due to poor dental hygiene.

Combined technique was used in 10 patients and only isosulfan blue was used in the rest of 10 patients to find station I nodes (Table 1). We took 10 times the background count significant to label a node "hot station I node" by the gamma probe. Identification rate of SLN with combined method was 100 % (10/10). Identification rate with blue dye was 90 % (9/10).

Station I nodes were found in 19 of the 20 patients (95 %) (Table 2). Nine of the 19 patients had no metastases to station I nodes and no disease in rest of the neck. One patient had false negative station I nodes.

We found station II nodes in 84 % (16/19) patients. In 87 % (14/16) patients, station II nodes accurately predicted the status of neck. Station II status was false negative in two patients.

Nine patients had metastases to station I nodes. Of these, station II was identified in 7 patients and predictability of station II was 71 % (5/7).

Another observation was that clinically palpable nodes were sentinel nodes in 50 % (3/6) of the patients (Table 1).

Discussion

In neck dissection, the surgeon removes the whole cervical lymphatic basin of the neck along with the nodes, fibrofatty tissues and cutaneous nerves, hence the resultant morbidity of the neck dissection. Ideally, we should develop a method to delineate the lymphatic pathway from tumor to the draining nodes. Studies have shown that rich lymphatic network of upper aerodigestive tract has a constant distribution characterized by predictive patterns of lymph drainage into the regional lymph nodes. Floor of the mouth drains into submandibular and upper jugular nodes. Buccal mucosal lymph mainly drains into facial (submandibular) nodes and the lymph fluid of the anterior oral cavity is directed primarily to the lymph nodes of level I. However, drainage from the lateral oral tongue and the posterior floor of the mouth is directed to the lymph nodes in level II [9]. The theory behind SLN biopsy approach is that lymph flows from a tumor sequentially to the "first echelon node" (SLN) then to the remaining nodal basin, that is, to next higher group of nodes, labeled in our study as station II nodes, from where lymph goes to next higher station nodes in an orderly way.

Unfortunately, initial attempts at using isosulfan blue dye for visual identification of SLN in head and neck squamous cell carcinoma (HNSCC) by Pitman et al. [10] proved discouraging, probably due to the early washout of the dye from the rich lymphatic network or cutting of the lymphatics while raising the flap for neck dissection.

Zitsch et al. [11] in a study of 8 patients found SLN at levels (I–IV) for tumors of oral cavity (carcinoma floor of mouth, carcinoma oropharynx, carcinoma of retromolar trigone, carcinoma of oral tongue) using intraoperative lymphoscintigraphy [11].

Altinyollar et al. [12] showed localized SLN in 18 patients of 20 with carcinoma of the lower lip and found SLN at submandibular region in 12 and submental region in 6 patients with patent blue dye. No false negative or false positive results were seen in this study. SLN identification rate was 90 % [12]. Ross et al. [13] and Taylor et al. [14] found most of SLN at level II (level I–level III). In another study by Shoaib et al. [15], in studying 40 patients with blue dye and lymphoscintigraphy (intraoperative and preoperative with Tc-99 sulfur colloid) found SLN with 94 % sensitivity. Hart et al. [16] in a prospective study of 20 patients of N0 HNSCC who underwent lymphoscintigraphy and SLN biopsy (intraoperative gamma probe localization) found that SLN had negative predictive value of 100 % and accurately predict the presence of occult metastatic disease [16].

We consistently found "station I" at submandibular region (near facial vessels) in most of our patients. Station II nodes were located at level II (jugulodigastric node) or/and level III (jugulo-omohyoid nodes) (Table 1).

Table 1 Results of station I & II study in oral cancers

	Tumor Site	TN Stage	Method	Site of station I	Blue/Hot Nodes	Station I	Station II	Rest of neck	Metastases at other nodal levels	Clinically Palpable Node
1	Lower (Lo) Lip	T1N0	Dye	(f) Sub-mand Sub-mental	3	0\3	0\1-Level 2	0\21		
2	Lower Lip	T2N0	Dye	Sub-mand	1	0\1	0\1-Level 2	0\15		
3	Lower Lip	T2N0	Com	Sub-mand	1\1	0\1	0\1-Level 2	0\12		
4	Lower Lip	T3N0	Com	(f) Sub-mand	2\2	0\2	0\2-Level 2	0\10		
5	Rt Angle Lip	T2N0	Com	(f) Sub-mand	2\2	0\2	0\2-Level 1&2	0\9		
6	Lt Lo Alveolus	T4N1	Com	(f) Sub-mand	1\1	0\1	0\2-Level 2	0\26		Sub-mand
7	Lt Lo Alveolus	T4N0	Com	(a.b.d.) Sub-mand	0\2	2\2	0\2-Level 2	0\10		
8	Lt Lo Alveolus	T2N0	Dye	(f) Sub-mand	1	1\1	0\2-Level 2	0\8		
9	Lt B Mucosa	T4N0	Dye	(f) Sub-mand	2	2\2	0\2-Level 2	0\5		
10	Rt B Mucosa	T2N1	Com	Sub-mand	2\2	1\2	0\2-Level 2	0\11		Sub-mand
11	Rt B Mucosa	T3N1	Dye	(f) Sub-mand	2	1\2	1\4-Level 2&3	0\5		Sub-mand
12	Floor of mouth	T2N0	Com	(f) &(a.b.d.) Sub-mand	4\4	0\4	0\2-Level 2	0\6		
13	Rt Oral Tongue	T3N1	Dye	Sub-mand	2	0\2	0\1-Level 3	0\4		Sub-mand
14	Lt Oral Tongue	T2N0	Dye	(f) Sub-mand	2	0\2	0\1-Level 3	0\3		
15	Rt Lo Alveolus	T4N0	Com	(f) Sub-mand	1\1	1\1	0\4-Level 2[b]	2\11	Anterior Sub-mand	
16	Lt Lo Alveolus	T4N0	Com	(f) Sub-mand	3\2	1\3	0\1-Level 2&3[b]	1\10	Sub mental	
17	Rt Lo Lip	TxN1	Com	(f) Sub-mand Sub-mental	4\4	1\4	NOT FOUND	0\9	Sub-mand	Sub-mand
18	Rt Oral Tongue	T3N1	Dye	(f) Sub-mand	2	0\2[a]	Lymphatic cut	4\18	Up jugular & jugulo- omohyoid	Jugular chain
19	Lt B Mucosa	T4N0	Dye	(f) Sub-mand	3	1\3	NOT FOUND	3\22	Up jugular and Sub-mand	
20	Rt Oral Tongue	T2N1	Dye	NOT FOUND	0		–	2\12		Jugulo- omohyoid

[a] False negative station I

[b] False negative station II. Abbreviations: (f), facial group of nodes; Com, combined (isotope+blue dye); (a.b.d.), anterior belly of digastric; sub-mand, sub-mandibular node; B Mucosa, Buccal Mucosa

Table 2 Histopathological status of lymph nodes in 20 patients of oral cancer

No of patients	Status of Station I Nodes	Status of Station II Nodes	Status of rest of neck
9	(−)	(−)	(−)
4	(+)	(−)	(−)
1	(+)	(+)	(−)
2	(+)	(−)	(+)
1	(+)	Not Found	(+)
1	(+)	Not Found	(−)
1	(−)	Not Found	(+)
1	Not Found	–	(+)

We could not find station II nodes in 3 of the 19 patients. In one patient with T3N1 tumor, lymphatics were cut while raising the flap. In the second patient with tumor staged TxN1, a large sentinel node that was also clinically palpable probably led to blockage of lymph flow to next higher nodes. Histopathologically it was a positive node. In the third patient, T4N0 was found to have multiple enlarged positive nodes at various levels, which might have caused impedance to lymph flow.

There were 3 patients, who were staged false negative, one at station I and others at station II. In one patient with T3N1 tumor, we found station I node at facial group of submandibular nodes. There were multiple enlarged nodes at level II and III. It was the advanced nodal disease that might have lead to untrue mapping of SLN, and hence false negative SLN (station I node). In second patient, (T4) positive station I nodes (facial group) and closely associated positive nonsentinel submandibular nodes were found. We attribute our failure to choking of sentinel nodes due to tumor emboli and rerouting of lymph to alternate station II echelon nodes. In the third patient with T4 tumor, metastases were found in nonsentinel submental nodes. Tumor was large and was involving the mandible close to submental region. We found difficulty in identifying the node with gamma probe due to "shine-through effect" and also could not see any blue nodes in this region. Tumor was very aggressive in this patient and recurred at primary site within 2 months and second primary was detected in opposite alveolar region within 4 months. It can be discerned from the above study that false negative SLN is more with the larger tumor size and with palpable nodal neck disease.

The sentinel node concept in HNSCC is in developmental phase and is undergoing refinement. We hope that after sufficient experience is attained in sentinel lymph node biopsy in oral cancer, the following approach can be recommended: after localization of SLN by gamma probe and blue dyes, skin incision should be given and deepened till subplatysmal plane and SLN removed and examined histopathologically to look for metastatic cancer cells. If SLN does not harbor any metastasis, then one might plan to abandon further neck dissection assuming that rest of neck is negative for cancer cells. In our study, there were 9 patients with negative SLN and had no disease in the rest of the neck, and they were the potential candidates for abandoning therapeutic neck dissection.

However, it is likely that metastases outside the first echelon nodes (SLN) can occur with sufficient frequency that a sole biopsy of these nodes may fail to stage the neck in all patients, especially patients with SLN positive ones, where we need to know the status of higher order nodes. To know the status of higher order nodes we suggest mapping of station II nodes.

In our study, we found 5 patients with sole metastases to station I nodes (SLN) of the total 11 pathologically positive necks. Rest of the neck was negative for metastases in these patients. On "station II" mapping, we found these patients with sole metastasis to SLN. Ross et al. [13] studied 48 patients, clinically staged T1 in 22, T2 in 14, T3 in 1, T4 in 11 and found 15 patients with positive sentinel node, of which 7 patients had SLN as the only positive node . Taylor et al. [14] found 4 patients with only positive SLN node of oral and oropharyngeal squamous cell cancer, of the 9 patients studied with preoperative lymphoscintigraphy and intraoperative gamma probe. Shoaib et al. [15] examined 40 necks with clinically N0 neck disease and being tumor staged T1 in 14, T2 in 14, T3 in 3, and T4 in 9 necks. Twenty necks were classified N0 and 20 as pathologically node positive (pN+). In pN+ group, sentinel nodes were found in 17. In the 16 necks from which sentinel lymph nodes containing tumor were harvested, the sentinel nodes were the only lymph nodes containing tumor in 12. Thus, in only four cases, nonsentinel lymph nodes contained tumor in the presence of pathologically positive sentinel lymph nodes [15]. Can such patients be spared of neck dissection? It is too early to say but we are of the opinion that procedure of neck dissection can be abandoned here if "station II nodes" are negative. "Second station approach" is advancement over SLN biopsy concept, which proposes that in early-stage cancers of oral cavity, there is no need for the removal of whole of the lymph node basin where SLN comes out to be the 'only positive node'. This concept of sequential spread of cancer cells through lymphatics proposes that next higher station could be detected by injecting 0.1 ml of dye in the SLN. If it comes out to be negative for cancer

cells then procedure of neck dissection should be abandoned there, in early-stage tumors of oral cavity (T1-2/N0).

Recent studies have shown that SLN biopsy offers patients' decreased morbidity compared with selective neck dissection, and have also shown reproducibly low false negative rates, high-negative predictive values, and high sensitivities [17–19]. The main clinical aim of sentinel node biopsy is to achieve better staging and there is now evidence that the procedure reduces morbidity [20]. Intraoperative identification of sentinel nodes in the head and neck region with a portable gamma-camera is feasible [21]. It is also proven by our study.

We submit humbly that we have yet not perfected this technique. Concerns of "skip metastases" may be raised by many clinicians. However, studying the lymphatic mapping by dye and isotope, and hence the delineating the sequential path of spread of tumor cells, should theoretically eliminate the possibility of skip metastases in early-stage tumors. Larger tumor burden in large sized tumors will choke the usual draining lymphatic pathways and alternate channels will open up. Mapping nodes one station further (station II) may help in resolving the issue, but answer will come from study of larger number of patients. As far as false negative cases are concerned, we recommend SLN biopsy and station II node biopsy in early stage tumors to decrease false negative rate of sentinel nodes, once the learning curve is over.

We are still in the process of learning in our endeavor to unravel the intricacies of distal spread of cancer cells. In the present group of patients, we have studied the feasibility of doing station I and II nodal biopsy. We would need to establish the practical way of doing the SLN biopsy and station II biopsy in future studies and compare with the standard neck dissection (SOND/MRND).

Although further study is warranted, SLN biopsy could potentially guide head and neck oncosurgeons to treat the patients with T 1-2/N0 disease who would otherwise benefit most from MRND/selective neck dissection and prevent the morbidity of unnecessary neck dissection. Station II concept is further extrapolation of SLN lymphatic mapping with possible role in identifying SLN only positive patients.

Acknowledgement: nil

Source(s) of support: nil

References

1. Shah J (1990) Patterns of cervical lymph node metastasis from squamous cell carcinomas of the upper aero digestive tract. Am J Surg 160:405–409
2. Shah JP, Andersen PE (1995) Evolving role of modifications in neck dissection for oral squamous carcinoma. Br J Oral Maxilla Fac Surg 33:3–8
3. Medina JE, Byers RM (1989) Supraomohyoid neck dissection: rationale, indications and technique. Head Neck 11:111–122
4. Byers RM, Weber RS, Andrews T, McGill D, Kare R, Wolf P (1997) Frequency and therapeutic implications of "Skip Metastases" in the neck from squamous cell carcinoma of the oral tongue. Head Neck 1:14–19
5. Giuliano AE, Kirgan DM, Guenther JM, Morton DL (1994) Lymphatic mapping and sentinel lymphadenectomy for breast cancer. Ann Surg 220:391–401
6. Veronesi U, Paganelli G, Galimberti V, Viale G, Bedoni M (1997) Sentinel lymph node biopsy to avoid axillary dissection in breast cancer with clinically negative nodes. Lancet 349:1864–1867
7. Civantos FJ, Gomez C, Duque C, Pedroso F, Goodwon WJ, Weed DT, Arnold D (2003) Sentinel lymph biopsy in oral cancer: correlation with PET scan and immunohistochemistery. Head Neck 25:1–9
8. Asthana S, Deo SVS, Shukla NK, Jain P, Anand M, Kumar R (2003) Intraoperative neck staging using sentinel node biopsy and imprint cytology in oral cancer. Head Neck 25:368–372
9. Werner JA, Dunne AA, Myers JN (2003) Functional anatomy of the lymphatic drainage of the upper aero digestive tract and its role in metastasis of squamaous cell carcinoma. Head Neck 25:322–332
10. Pitman KT, Johnson JT, Edington H, Barnes EL, Wagner (1998) Lymphatic mapping with isosulfan blue dye in squamous cell carcinoma of head and neck. Arch Otolaryngol Head Neck Surg 124:790–793
11. Zitsch RP, Todd DW, Renner GJ, Singh A (2000) Intraoperative radiolymphoscintigraphy for detection of occult metastasis in patients with head and neck squamous cell carcinoma. Otolaryngol Head Neck Surg 122:662–666
12. Altinyollar H, Berberoglu U, Celen O (2002) Lymphatic mapping and sentinel lymph node biopsy in squamous cell carcinoma of the lower lip. Eur J Surg Oncol 28:72–74
13. Ross G, Shoaib T, Soutar DS, Robertson AG, MacDonald DG (2002) The use of sentinel lymph node biopsy to upstage the clinically N0 neck in head and neck cancer. Arch Otolaryngol Head Neck Surg 128:1281–1291
14. Taylor RJ, Wahl RL, Sharma PK, Bradford CR, Terrell JE, Heard EM, Chepeha DB (2001) Sentinel node localization on oral cavity and oropharynx squamous cell cancer. Arch Otolarngyol Head Neck Surg 127:970–974
15. Shoaib T, Soutar DS, MacDonald DG, Camilleri IG, Dunaway DJ, Gray HW, McCurrach GM, Bessent RG, MacLeod TIF, Robertson AG (2001) The accuracy of head and neck carcinoma sentinel lymph node biopsy in the clinically N0 neck. Cancer 91:2077–2083
16. Hart RD, Henry E, Nasser JG, Trites RJ, Taylor SM, Bullock M, Barnes D (2005) Sentinel lymph node biopsy in N0 squamous cell carcinoma of the oral cavity and oropharynx. Arch Otolaryngol Head Neck Surg 131:34–38
17. Civantos FJ, Zitsch RP, Schuller DE, Agrawal A, Smith RB, Nason R, Petruzelli G, Gourin CG et al (2010) Sentinel lymph node biopsy accurately stages the regional lymph nodes for T1-T2 oral squamous cell carcinomas: results of a prospective multi-institutional trial. J Clin Oncol 28(8):1395–1400
18. Burcia V, Costes V, Faillie JL, Gardiner Q, de Verbizier D, Cartier C, Jouzdani E, Crampette L, Guerrier B, Garrel R (2010) Neck restaging with sentinel node biopsy in T1-T2N0 oral and oropharyngeal cancer: Why and how? Otolaryngol Head Neck Surg 142(4):592–597
19. Coughlin A, Resto VA (2010) Oral cavity squamous cell carcinoma and the clinically n0 neck: the past, present, and future of sentinel lymph node biopsy. Curr Oncol Rep 12(2):129–135. Review
20. Sloan P (2009) Head and neck sentinel lymph node biopsy: current state of the art. Head Neck Pathol 3(3):231–237
21. Vermeeren L, Valdés Olmos RA, Klop WM, Balm AJ, van den Brekel MW (2010) A portable gamma-camera for intraoperative detection of sentinel nodes in the head and neck region. J Nucl Med 51(5):700–703