Original Article

Comparison of SPECT/CT and Planar Lympho-scintigraphy in Sentinel Node Biopsies of Oral Cavity Squamous Cell Carcinomas

Piyush Chandra, Sanket Dhake, Sneha Shah, Archi Agrawal, Nilendu Purandare, Venkatesh Rangarajan

Department of Nuclear Medicine and Molecular Imaging, Tata Memorial Hospital, E. Borges Road, Parel, Mumbai, India

Abstract

Introduction: Evidence supporting the use of Sentinel node biopsy (SNB) for nodal staging of early oral squamous cell carcinomas (OSCC) appears to be very promising. Pre-operative lymphatic mapping using planar lymphoscinitigraphy (PL) with or without SPECT/CT in the SNB procedure is useful in sentinel node localization and for planning appropriate surgery. Recently, a large prospective multi-centric study evaluating SNB in cutaneous melanoma, breast and pelvic malignancies, demonstrated that adding SPECT to PL leads to surgical adjustments in a considerable number of patients. Our aim of this study was to evaluate the incremental value of additional SPECT/CT over PL alone in SNB for OSCC. **Materials and Methods:** This was a retrospective analysis of 44 patients (40- tongue, 4- buccal mucosa) with T1-T2, clinically N0 oral cavity SCC who underwent sentinel node biopsy procedure. PL and SPECT lymphoscinitigraphy images were compared for pre-operative mapping of sentinel nodes. **Results:** Using a handheld gamma probe, a total of 179 sentinel nodes were harvested, with a mean of 4.06 per patient. PL revealed 75 hotspots with a mean of 1.70 per patient, and SPECT/CT revealed 92 hotspots with a mean of 2.09 per patient. Additional hotpots were identified in 14 patients on SPECT/CT, which included 4 patients, where PL did not detect any sentinel nodes. **Conclusion:** Pre-operative SPECT/CT in addition to planar lympho-scinitigraphy in sentinel node biopsies of oral cavity SCC detects more number of sentinel nodes compared to planar imaging alone. The higher sensitivity of SPECT combined with better anatomical localization using diagnostic CT may further improve the precision of SNB procedure.

Key words: *Oral squamous cell carcinoma, OSCC, sentinel node biopsy, SNB, planar, SPECT, CT, SPECT/CT lymphoscinitigraphy,*

Introduction

Oral squamous cell carcinomas (OSCC) are a major health problem in India and account for about 30% of all cancer cases in the country.[1] As with other cancers, prognosis in OSCC depends upon the stage. The 5-year survival decreases from 82% (N0 disease) to 53% as a result of regional nodal involvement, highlighting the importance of early detection and treatment of nodal disease in OSCC. Patients with clinically negative neck (N0) disease after clinical examination/imaging still harbor occult disease within cervical nodes in about 30%. Current gold standard for management of "N0" disease is called selective neck dissection (SND), that is, by dissecting a small group of lymph nodes. The most commonly performed procedure for SND for stage I/II OSCC is the level I-III neck dissection.[2]

Despite the advances in the surgical technique, the routine SND in all N0 neck is still considered invasive and probably an unwanted diagnostic procedure in more than 70% patients. About 22% patients have post-operative shoulder dysfunction, and time and financial constraints are some of other limitations. But a conservative "wait and watch" policy for the No neck may conversely lead to about 1/4th of patients eventually developing nodal metastasis. This would then require a more extensive surgery and adjuvant therapies, or worse, might even present as the non-salvageable

How to cite this article: Chandra P, Dhake S, Shah S, Agrawal A, Purandare N, Rangarajan V. Comparison of SPECT/CT and planar lympho-scintigraphy in sentinel node biopsies of oral cavity squamous cell carcinomas. Indian J Nucl Med 2017;32:98-102.

Address for correspondence:
Dr. Venkatesh Rangarajan, Department of Nuclear Medicine and Molecular Imaging, Tata Memorial Hospital, E. Borges Road, Parel, Mumbai, India. E-mail: drvrangarajan@gmail.com

Access this article online

Website: www.indjsp.org

DOI: 10.4103/0972-3919.202244

Quick Response Code:

disease. Sentinel node biopsy (SNB) appears to be an ideal solution to the above problem, a minimally invasive staging stool, reducing morbidity and overall treatment costs. SNB minimizes the invasiveness of the staging procedure by utilizing lymphatic mapping and selectively targeting small group of lymph nodes, which are likely to harbor disease.[2] However, in contrast to its widespread use in breast cancers and melanoma, SNB for node negative OSCC is evolving and currently considered as investigational.[3] The long-term outcomes of the multi-centric study, the selective European node trial (SENT) in 415 patients was recently published and showed that SNB is a reliable and safe oncological technique for staging clinical node negative T1-T2 oral cancers.[4] Our institutional experience suggests that SNB in "N0" OSCC is an accurate reliable method for nodal staging and has the potential to obviate the need for elective nodal dissection.[5]

Due to complexity in lymphatic drainage in head/neck, pre-operative lymphatic mapping under gamma camera is important and correlates well with the precision of the surgical procedure.[6,7] Mapping lymphatics using single photon emission computed tomography/computed tomography (SPECT/CT) in addition to planar lymphoscinitigraphy (PL) has been shown to be of additional clinical relevance in breast, melanoma of head/neck and trunk, and pelvic malignancies, leading to surgical adjustments in a considerable number of patients.[8] This additional value of SPECT/CT in OSCC has been demonstrated in a few studies.[9-13] The aim of this study was to assess whether the addition of SPECT/CT offers any incremental benefit over PL alone for pre-operative lymphatic mapping in SNB for OSCC.

Materials and Methods

This was a retrospective analysis of 44 patients with clinically node negative oral cavity SCC who underwent sentinel node biopsy and subsequent selective neck dissection (levels I–IV). On the morning of surgery, with patient in supine position, using a tuberculin syringe, about 0.5mCi/15MBq 99mTc-labelled Human Serum Albumin Nanocolloid was injected at 2-4 sites on the edge of the tumor (i.e., peritumoral). No local anesthetic was used during injection. Mild bleeding was noticed at the injection site, which was controlled by local gauze pressing for few seconds and mouth rinse was given to minimize pooling of radiotracer in oral cavity. Using a dual head gamma camera, LEHR collimator, 10-20% energy window centered on 140 keV, dynamic imaging in the supine position was done immediately (20s/frame in 128 × 128 matrix) after injection was done in anterior–posterior projection for 20 minutes or till any draining node was visualized. After visualization of the lymph nodes on dynamic images, static lymphoscintigraphy in two planes (anterior and lateral) was done (for approximately 300 seconds with a 256 × 256 matrix) followed by SPECT/CT acquisition. To facilitate topographical localization, a 57Co flood source was used for transmission imaging in each static projection. In the event no drainage was identified at 20 minutes of dynamic imaging, static views in antero-posterior projection were taken at 1 hour followed by SPECT/CT acquisition. SPECT was acquired in a 128 × 128 matrix, in 3 degree steps with

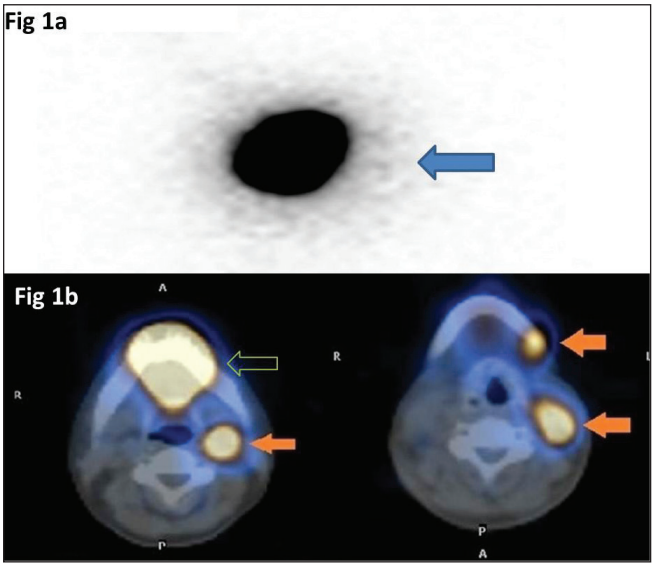

Figure 1: Detection of more sentinel nodes on SPECT as compared to planar imaging. (a) shows planarlymphoscintigraphy with injection site (blue arrow); no hotspots are seen. SPECT/CT scan done in the same patient is shown in (b) showing the injection site (hollow arrow) and three hotspots at left cervical levels IB, II, and III (red arrows)

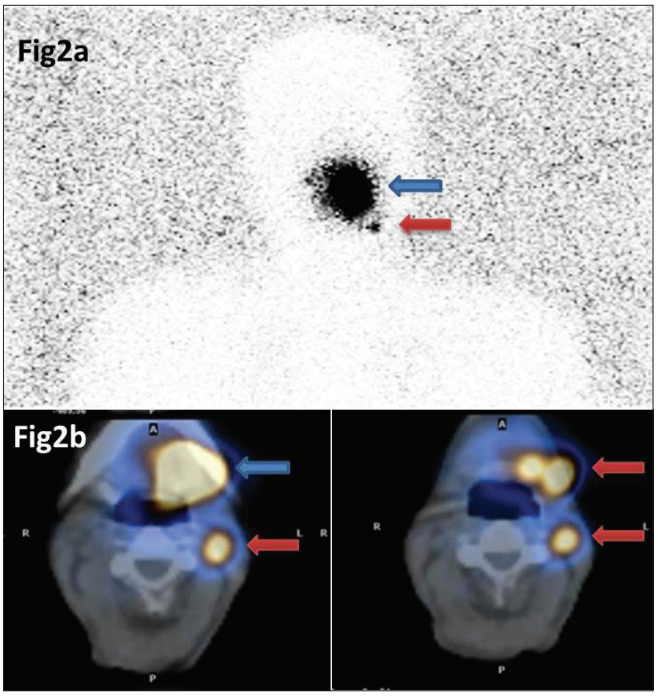

Figure 2: (a) shows a static flood source (using the Co57 transmission source) image in the anterior projection showing injection site (blue arrow) and the single hotspot (red arrow). SPECT/CT of the same patient is shown in (b) showing the injection site (blue arrow) and three sentinel nodes (red arrows) at left cervical levels IB and II

25 seconds per step with low-dose CT (fixed tube current of 2.5mA) used for attenuation correction and anatomical correlation. After the SPECT/CT acquisition, patients were shifted to the operation theatre and sentinel nodes were harvested using a handheld gamma probe. The probe used was Neo2000-Model 1017 (Neoprobe Corporation, OH, USA), a collimated 14 mm reusable probe using the Cadmium Zinc Telluride (CdZnTe) detector, having energy range 27–364 keV and detector efficiency for 99mTc detection > 75%. Anatomical location and radioactivity of all excised sentinel nodes were recorded. Criteria normally used for the sentinel node was counts more than 8–10 times the background activity. Histo-pathology findings served as the standard of reference.

Results

The cohort consisted of 44 patients, 37 males and 7 females, with a mean age of 46. Site of primary disease was tongue in 91% (n = 40) and buccal mucosa in 9% (n = 4) [Table 1]. Final histopathology revealed occult nodal disease in 29.5% (n = 13) patients. Sensitivity, specificity, NPV, and PPV of SNB procedure was 76%, 100%, 91%, and 100%, respectively. No unsuccessful procedures were recorded. A total of 179 sentinel nodes were harvested, with a mean of 4.06 per patient. PL and SPECT/CT revealed hotspots in the ipsilateral neck in 95% (n= 42) and in contra lateral neck additionally in 9% (n=4). PL revealed 75 hotspots with a mean of 1.70 per patient, and SPECT/CT revealed 92 hotspots with a mean of 2.09 per patient. Additional hotpots were identified in 14 patients on SPECT/CT, which included 4 patients, where PL did not detect any sentinel nodes. SPECT/CT identified 23 hotspots in ipsilateral IB, 24 in level II, 25 in level III, and 16 in level IV (all ipsilateral) [Table 2]. Contra-lateral hotspots were identified on planar and SPECT/CT, two in level IB and two in level IV. In two patients, where both PL and SPECT were negative, the sentinel node was identified in one patient only by the gamma probe, and in the other patient, no sentinel node could be identified intra-operatively. Based on the final histo-pathological results, the detection rate by PL, SPECT/CT, and gamma probe guidance was 93%, 95%, and 97%, respectively.

Table 1: Patient characteristics.

	(N=44)
Male	37 (84%)
Female	07 (16%)
Mean Age	46.3 Years
Age Range	
Primary Site	
Tongue	40 (91%)
Buccal Mucosa	07 (09%)
Clinical Stage	
T1	25 (57%)
T2	19 (43%)

Table 2: Comparison of Planar and SPECT/CT lymphoscintigraphy

	Planar	SPECT/CT
Sentinel nodes / hot spots	75	92
Mean sentinel nodes / hot spots per patient	1.70	2.09
Detection Rate	93%	95%

Discussion

The purpose of an additional SPECT/CT over PL in SNB is to (1) identify nodes closer to the injection site, (2) identify nodes that are small or below the spatial resolution of the PL, (3) identify any contra-lateral drainage that are not identified on PL, and (4) to precisely identify the anatomical level of sentinel nodes, which might aid the surgical procedure. The value of SPECT/CT over PL was assessed in a large prospective multicentre study in carcinoma breast, pelvic malignancies, and melanoma. The results of this study showed that SPECT/CT detected more sentinel nodes and lead to surgical adjustments in a considerable number of patients.[8]

Multiple studies have been done to explore this clinical utility of pre-operative SPECT/CT lymphoscintigraphy in sentinel node biopsies for oral cancers. In 2006, Khafif *et al.* evaluated the additional benefit of SPECT over PL in 20 patients with T1-T4 oral cavity SCC. The sensitivity of SNB for detection of nodal metastases was 87.5%. SPECT improved SN identification/localization in about 30% of the patients.[10] In the same year, Bilde *et al.* compared SPECT with PL in 33 patients who underwent SNB and showed that SPECT/CT identified extra sentinel nodes compared to the PL in about 47% of patients.[11] In 2009, a larger study was done by Haerle *et al.* in 58 patients with T1-T2 OSCC with a mean follow-up of 21 months. Although both SPECT/CT and PL identified the same median number of hotspots (two hotspots per patient), additional sentinel nodes were identified in about 18% of patients and in one patient, SPECT/CT identified sentinel nodes that were missed by PL. The authors acknowledged that both SPECT and PL had lower sensitivity in detection of level I nodes that were closed to injection sites. The authors concluded that adding SPECT/CT to PL alone should be routinely recommended as it detects more number of SLN, improves topographical orientation with surrounding structures, and reduces surgical time.[12] Recently, sub-analysis of the SENT study done to assess the impact of image acquisition techniques for pre-operative lymphoscinitigraphy revealed that best results were obtained with a combination of dynamic scans and SPECT/CT.[13]

In our study, occult nodal metastases were seen in 29.5% of patients (n = 13). A total of 179 sentinel nodes were harvested, with a mean of 4.06 per patient. This high number of nodes per patients may be attributed to the long time interval between the injection of tracer and probing

and probably contributed by a long SPECT acquisition time. SPECT/CT identified 92 sentinel nodes with a mean of 2.09 per patient (range 0-14). Compared to PL, SPECT identified additional sentinel nodes in 31% of patients (14/44) [Figure 1 and 2]. Among this, SPECT/CT identified sentinel nodes in four patients, where planar imaging was negative. Out of these four patients, in three patients, SPECT identified sentinel nodes in ipsilateral level IB, and in one patient, sentinel nodes were identified in ipsilateral level III. The increased detection of ipsilateral level IB nodes shows the incremental benefit of SPECT over PL in identifying nodes adjacent to the injection site [Figure 1]. In one patient, where both SPECT and PL did not show any drainage, the sentinel node was identified intra-operatively, showing the added value of gamma probe exploration even in patients where no sentinel nodes are identified on pre-operative lymphatic mapping. The long-term follow-up of low-risk T1–T2 oral cancers have shown that contra-lateral neck recurrence accounts for about 40% of the treatment failures.[14] In 9% (4/44) of patients, contra-lateral drainage was seen on both planar and SPECT, demonstrating the incremental value of pre-operative mapping. SPECT identified more number of contra-lateral nodes than PL. In our study, however, contra-lateral neck dissection was obviated as these tumors were small (T1) and unilateral. These patients had no evidence of any contra-lateral nodes on follow-up. Contra-lateral drainage would be of clinical significance especially for midline tumors or large unilateral tumors that might obstruct the ipsilateral lymphatic drainage.[2]

The routine use of SPECT/CT lymphoscintigraphy in sentinel node biopsies does have its limitations. These include longer acquisition times, low spatial resolution with conventional SPECT/CT systems, and susceptibility for imaging artifacts. Recent technological advances in SPECT instrumentation highlight the constant efforts toward overcoming these limitations. These include availability of newer semiconductors technology, replacing photon multiplier tubes with position sensitive PMTs and avalanche photodiodes, better collimator design, development of diagnostic quality hybrid SPECT/CT systems, and sophisticated software for scatter corrections with noise compensations.[15]

There are a few limitations in our study. First, the study is a retrospective cohort. Second, all the tumors were T1-T2 and predominantly involving the unilateral tongue. As discussed earlier, lack of large tumors or midline tumors in our study could possibly attribute to the less incidence of contra-lateral drainage seen in our study. Also, our study lacked more heterogeneous tumor locations (such as those from the palate/floor of mouth), which would be a better representative sample for the study than tumors that were located only in tongue. Lastly, we used a low mA CT that was of non-diagnostic quality. This could decrease the spatial resolution and can alter the overall diagnostic accuracy of SPECT/CT lymphoscinitigraphy. In perspective, state-of-the-art SPECT/CT imaging with newer systems will truly reflect its additional clinical benefit over the combined use of PL and intra-operative gamma.

Conclusion

Pre-operative SPECT/CT in addition to planar lymphoscinitigraphy in sentinel node biopsies of oral cavity SCC detects more number of sentinel nodes and detects sentinel nodes that are likely to be missed on planar imaging alone. Along with better anatomical localization, this higher sensitivity of SPECT/CT will probably further improve the precision of the surgical procedure. Routine recommendation of SPECT in SNB for oral cavity SCC, however, awaits larger, prospective, controlled studies with newer SPECT/CT systems that would be better to demonstrate its true clinical value.

Financial support and sponsorship

Nil

Conflicts of interest

There are no conflicts of interest

References

1. Coelho KR. Challenges of the oral cancer burden in India. J Cancer Epidemiol 2012 2012;701932.
2. Myers J. Oral cancer metastasis. New York: Springer; 2009. Print
3. Kuriakose MA, Trivedi NP. Sentinel node biopsy in head and neck squamous cell carcinoma. Curr Opin Otolaryngol Head Neck Surg 2009;17:100-10.
4. Schilling C, Stoeckli SJ, Haerle SK, Broglie MA. Sentinel European Node Trial (SENT): 3-year results of sentinel node biopsy in oral cancer. Eur J Cancer 2015;51:2777-84.
5. Chaturvedi P, Datta S, Arya S, Rangarajan V. Prospective study of ultrasound-guided fine-needle aspiration cytology and sentinel node biopsy in the staging of clinically negative T1 and T2 oral cancer. Head Neck 2015;37:1504-8.
6. Ross GL, Soutar DS, Shoaib T, Camilleri IG, MacDonald DG, Robertson AG, *et al.* The ability of lymphoscintigraphy to direct sentinel node biopsy in the clinically N0 neck for patients with head and neck squamous cell carcinoma. Br J Radiol 2002;75:950-8.
7. Alkureishi LW, Burak Z, Alvarez JA, Ballinger J, Bilde A. European Association of Nuclear Medicine Oncology Committee; European Sentinel Node Biopsy Trial Committee. Joint practice guidelines for radionuclide lymphoscintigraphy for sentinel node localization in oral/oropharyngeal squamous cell carcinoma. Ann Surg Oncol 2009;16:3190-210.
8. Jimenez-Heffernan A, Ellmann A, Sado H, Huić D. Results of a prospective multicenter international atomic energy agency sentinel node trial on the value of SPECT/CT over planar imaging in various malignancies. J Nucl Med 2015;56:1338-44.
9. Wagner A, Schicho K, Glaser C, Zettinig G, Yerit K, Lang S, *et al.* SPECT-CT for topographic mapping of sentinel lymph nodes prior to gamma probe-guided biopsy in head and neck squamous cell carcinoma. J Craniomaxillofac Surg 2004;32:343-9.
10. Khafif A, Schneebaum S, Fliss DM, Lerman H, Metser U, Ben-Yosef R, *et al.* Lymphoscintigraphy for sentinel node

mapping using a hybrid single photon emission CT (SPECT)/CT system in oral cavity squamous cell carcinoma. Head Neck 2006;28:874-9.

11. Bilde A, Von Buchwald C, Mortensen J, Marving J, Hamilton Therkildsen M, Kirkegaard J, *et al.* The role of SPECT-CT in the lymphoscintigraphic identification of sentinel nodes in patients with oralcancer. Acta Otolaryngol 2006;126:1096-103.
12. Haerle SK, Hany TF, Strobel K, Sidler D, Stoeckli SJ. Is there an additional value of SPECT/CT over planar lymphoscintigraphy for sentinel node mapping in oral/oropharyngeal squamous cell carcinoma?. Ann Surg Oncol 2009;16:3118-24.
13. Tartaglione G, Stoeckli SJ, de Bree R, Schilling C. Sentinel node in oral cancer: The nuclear medicine aspects. A survey from the Sentinel European Node Trial. Clin Nucl Med 2016;41:534-42.
14. Ganly I, Goldstein D, Carlson DL, Patel SG, O'Sullivan B, Lee N, *et al.* Long-term regional control and survival in patients with "low-risk," early stage oral tongue cancer managed by partial glossectomy and neck dissection without postoperative radiation: the importance of tumor thickness. Cancer 2013;119:1168-76.
15. Madsen MT. Recent advances in SPECT imaging. J Nucl Med 2007;48:661-73.