MedCrave
Step into the World of Research

International Clinical Pathology Journal

Mini Review

Open Access

A review of techniques for sentinel lymph node mapping with special reference to the head and neck region

Abstract

Sentinel lymph node biopsy is an extensively explored diagnostic mean for reducing surgical risks while improving staging in different human malignancies. Several different techniques have been introduced to clinical use during last two decades. Methods as ink lymphography and lymphoscintigraphy have already established their position in sentinel nodes mapping. Novel approaches as CT, MRI-lymphography, contrast enhanced ultrasound and near-infrared fluorescence imaging possesses prominent potential advantages and demand further experience gaining. A review of the clinically utilized techniques is presented a special attention is drawn to their usefulness in the head and neck carcinomas work-up.

Keywords: sentinel lymph node, lymphography, lymphoscintigraphy, CT, MRI, ultrasound, near-infrared fluorescence

Volume 2 Issue 2 - 2016

Gvetadze SR,[1,2] Liu M,[3] Xiong P,[4] Li J,[3] Hu J,[3] Ilkaev KD,[5] Yang X,[3] Sun J[3]

[1]Department of Consulting and Diagnostics, Central Research Institute of Dentistry and Maxillofacial Surgery, Russia
[2]Department of oral & maxillofacial surgery, Russian Medical Academy of Postgraduate Education Studies, Russia
[3]Department of Oral Maxillofacial-Head Neck Oncology, Shanghai Jiao Tong University School of Medicine, China
[4]Department of Ultrasound Diagnostics, Shanghai Jiao Tong University School of Medicine, China
[5]Department of Head and Neck Surgery, NN Blokhin Russian Cancer Research Center, Russia

Correspondence: Sun Jian, Department of Oral Maxillofacial-Head Neck Oncology, Shanghai Jiao Tong University School of Medicine, China, Tel +8618201717737, Fax +8614810000468, Email shalvagvetadze@yandex.ru

Received: April 11, 2016 | **Published:** May 06, 2016

Abbreviations: SCC, squamous cell carcinoma; SLN, sentinel lymph node; Tc99m, technetium; CT, computed tomorgarphy; SPECT, single-photon emission computed tomography; MRI, magnetic resonance imaging; US, ultrasound; UPIO, ultrasmall paramagnetic iron oxide; CEUS, contrast enhanced ultrasound; NIF, near-infrared fluorescence

Introduction

To date the mainstay of management of the majority of malignant head and neck tumors is surgical treatment alone or in combination with radio-and/or chemotherapy. The basis of surgery for oral carcinoma consists of two usually significantly invasive procedures which consist of the ablation of the disease at the primary site and regional lymphoadenectomy. Depending on the status of the regional lymph nodes in a given patient the extent and potential morbidity of the neck dissection varies.[1] The possible complications of neck dissection are: wound healing impairment;[2] major vessels damage,[3] internal jugular vein thrombosis;[4] postoperative rupture of the carotid artery or internal jugular vein;[5] damage to the accessory, hypoglossal superior laryngeal and phrenic nerves as well the sympathetic trunk and brachial plexus, and possibility of provoking a vasovagal response;[6–8] chylus fistula and chylothorax;[9] increase of intracranial pressure;[10] visual loss;[11] lymphedema[12] and fracture of the clavicle.[13]

Squamous cell carcinoma (SCC) accounts for more than 90% of the head and neck malignancies and it have a high potency for regional lymphogenic spread. The presence of neck lymph node metastasis is the one most important factor to determine prognosis and treatment strategy. Modern conventional investigation methods commonly used for tumor staging possess low sensitivity for neck metastasis detection, as up to 40% of cN0 necks are left undetected of occult disease, which presents sizes of less than 3mm. Correspondingly the current treatment of regional lymphatic basin in this group of patients depends of a choice between possible under treatment of 30-40% of patients with undetected metastases and overtreatment of the 60-70% of them.[14]

The sentinel lymph node (SLN) apprehension was first addressed by Gould's report on the James Ewing Society in 1960 and later expanded by Cabanas in 1977. Initially investigated in melanoma[15] and breast cancer[16] patients in short time SLN biopsy gained a considerable interest in head and neck research. The concept of SLN may be regarded as a modern approach enrooted and established by continuous anatomic and clinical exploration of the lymphatic systems' anatomy and physiology. The SNL is the first lymph node or nodes in a lymphatic basin which receives lymph flow from a given anatomical site and therefore should be first one to receive metastatic cells from the primary tumor. Analysis of the SLN for the presence of tumor cells has proved itself beneficial for clinically occult regional metastasis exposure and hence careful tumor staging.[17] Microscopic assessment of SLN is the mainstay of this diagnostic measure. For this to be executed the detected SLN must be biopsied. It is accepted that if on pathology the SLN turns out to be free of tumor cells the patient may be spared from the potential morbidity of regional lymphadenectomy. There is growing body of scientific data that proves that the status of the SLN presents an accurate indicant of the condition of the second and subsequent rank regional nodes.[18,19] Disease positive SLN has been correlated with higher loco-regional recurrence rates and poor survival prognosis even in presence of adjuvant therapy.[20,21]

Methods of sentinel lymph node identification

Several techniques are used for lymph node mapping; lymphography (direct, indirect), Radioisotope technique or lymphoscintigraphy, CT-lymphography, MRI lymphography, Conventional ultrasonography, Near-infrared fluorescence. Lymphography visualize lymphatic channels and lymph nodes after contrast injection (usually radiopaque in a lymphatic vessel in a way that chemical and physical features of injected material control transport through lymphatics regarding hydrodynamic diameter of related particles.[22] Particles sized 10 nm and less (macromolecules) will caused high diffusion of the contrast and fast migration through the system, mid-range particles (50 to 200nm; nanoparticles) exhibits slower migration and longer retention in lymphatics, while particles 500nm and larger (micro particles) are slowly retained.[23] SLN imaging depending on time of performance could be preoperative or intraoperative; by means of contrast medium delivery: direct or indirect.[22,24]

Direct lymphography (lymphangiography) was employed by Cabanas (1977) in his SLN pioneer study in penile carcinoma. It requires an iodinated contrast agent injection straight into the lymphatics.[25] This is complimented with X-rays, CT or MRI scans.[26,27] The iodinated contrast agent stays in the vessels for months which allows for long-term follow up but makes repetitive injections impossible. Such features as invasive and technically difficult cannulation of the lymphatic vessel and rare but potentially life threatening complication–contrast induced nephropathy have lead to abandoning lymphangiography in current clinical practice. Similar approaches may be successfully applied on cadaveric studies of lymphatic system anatomy especially in the head and neck region.[28,29]

Indirect lymphography involves several modalities related to SLN mapping. The contrast agent is injected intravenously, intradermally, intramucosally, or interstitially and gets drained to the local lymphatic vasculature with sequential progression to the closest regional (sentinel) lymph node/s. Indirect lymphographic procedures are less invasive, easy to reproduce and cause no direct damage to the lymphatics. Indirect ink lymphography exploits blue dyes (Evans blue, isosulfan blue, methylene blue, patent blue) for visualization of lymphatic drainage after interstitial injection. Influential statements in melanoma and breast cancer introduced intraoperative injections of blue dye which later were adopted in various locations.[15,30] While indirect lymphographyachieves accuracy up to 96% in melanoma of the head and neck its use in solid tumors of oral cavity requiring injections in the mucosa is restricted.[31–34] Generally dyes bear characteristics which dispose their very rapid migration through the lymphatic vessels, low invasive, easy reproducible and cheap but if used alone their productivity in SLN identifying is somehow limited to superficial tissue plains, in particular above the deep fascia on the trunk and the extremities and some allergic reaction on methylene blue, isosulfan blue and patent blue dyes reported in number of papers limited this technique to implement to all patients 3.[35–37] At present dye injections are used in combination with other more up to date methods for better intraoperative orientation.

Radioisotope technique (lymphoscintigraphy) is the most commonly used indirect lymphography modality which involves preoperative radioactive tracer injections (such as Technetium [Tc99m] sulfur colloid) with intraoperative localization of the nodes with external radiation detectors (gamma-probe). The fragments of this tracer or radiocolloids are nanoparticles with respective hydrodynamic behavior.[38,39] Gamma radiation is highly penetrating: tissue depth and density are no obstacles for Tc99m -based lymphoscintigraphy. The patterns of injected tracer distributions are imaged in 2D definition which precludes accurate location of the lymph node. A meta-analysis of SLN biopsy with lymphoscintigraphy for oral and oropharyngeal cancers proved a pooled sensitivity of 93% and negative predictive value rates from 88 to 100%.[40] Recent multicenter trial from Europe revealed sensitivity of 80% and negative predictive value 88%.[41] In general overall accuracy, sensitivity, and negative predictive values for lymphoscintigraphy sentinel lymph node biopsy are above 90%.[14] Surgeon experience in this technique is one important factor influencing results. Combining lymphoscintigraphy with single-photon emission computed tomography (SPECT) allowed for 3D images reconstruction and to improve the accuracy up to 95%. However, poor spatial resolution of the acquired images remained not satisfactory (1-2cm).[42–44] Another moderate limitation of the technique is the so called "shine through" effect, which is encountered in identifying the SLN in level I in cases with primary tumor situated in the mouth floor. The radiation counts of the primary site overshadowing the sentinel node site background counts which bring difficulties for its detection by the gamma-probe. To overcome these conditions several solutions have been proposed: the use of lead shielding; removing the primary tumor prior to SLN; and mandatory level I dissection.[45] A large trial reported that the ability to identify the sentinel node was lower in patients with mouth of the floor SCC compared to other oral cavity sites (88% vs. 96%, p=0.138). The authors recommended the use of SLN biopsy as a single staging procedure in all oral cavity subsites except of mouth floor.[46] Possibly this matter may be at least in part accounted for often overlooked lingual lymph nodes which in a recent anatomical study were reported to be present in 23.8% of individuals and can serve as SLNs for some tongue and mouth floor cancers.[47] Apart from this radioisotope technique craves radiation exposure to both patients and the medical staff and requires special protection and waste disposal policy.[48]

While conventional CT and MRI have limited ability for neck metastasis detection and are used mainly for the primary site lesion extension assessment and staging[49] some researchers investigated their usefulness in SLN detection. CT-lymphography was recently utilized for oral cancer SLN explorations.[50] Saito et al.[51] observed an occult metastasis in a node located in the floor of the mouth, i.e. lingual lymph node with no other regional disease. Honda et at.[52] conducted a study on 31 cNo patients with oral tongue SCC to assess the properties of CT-lymphography for SLN spotting. The authors reported high negative predictive value of 95, 8%, and sensitivity value of 90.3%. Also a simple way for localizing the node has been introduced–a lattice marker was attached to the neck skin during the scan. The SLN location was indicated precisely by the crossing points of the lattice marker and the CT plane light.[52] Overall CT lymphography has the advantage of clear detection of lymph nodes lying in the proximity of the primary tumor, with continuous anatomic visualization.[53,54] Iodine-based contrasts used for CT-lymphography are small sized agents creating very short imaging windows with 1 minute clearance with high reported safety.[55,56]

MRI lymphography has been used for SLN detection mainly in breast,[57] and pelvic tumors.[58] One feature of these techniques is the possibility of differentiating between benign and malignant nodes depending on the node's imaging pattern. Two commonly used agents for enhanced MRI are ultrasmall paramagnetic iron oxide (UPIO) and gadolinium chelates. UPIO is specific for the reticuloendothelial system. Malignant lymph nodes mainly consist of tumor cells these do not take up this contrast because of lacking reticuloendothelial system activity that can be detected by shorter T2 relaxation time.[59] As well as UPIO the gadolinium chelates have a small particle size which leads to poor retention in the lymphatic vessels and diffusion out of the vessels leads to such difficulties in interpretation as the background noise.[60] A meta-analysis of the investigation employed in different body regions has shown the sensitivity and specificity of 90% and 96%, respectively.[61] The method of MRI lymphography is regarded to be an attractive option for SLN investigation as it is non-invasive and provides anatomic and functional information but the presence of an experienced radiologist is essential.

Conventional ultrasonography (US) is an accepted method in clinical work-up of oral cancer patients. It is non-invasive, inexpensive, easy reproducible and offers multilayer and multiplanar imaging.[62] Several methods have been reported regarding the discrimination of malignant lymph nodes with conventional US but the outcome seems not satisfactory enough.[63] Experimental studies demonstrated potential benefits of usage of US related contrasts in SLN detection.[64,65] Contrast enhanced ultrasound (CEUS) agents are composed of a dispersion of microbubbles (each is smaller than a red blood cell) that act as reflectors of the ultrasound beam. In high mechanical index settings the microbubbles are rapidly destroyed by high acoustic pressure known as acoustic emission effect. These contrasts exhibit properties responsible for their fast penetration of the lymphatic vessel wall and drainage to the lymph nodes. Short transit and enhancement times were reported as 15-40 seconds and 1-3 minutes, respectively.[66] Sever et al.[67] applied CEUS for SLN biopsy in breast cancer patients. During imaging the CEUS-identified SLN were localized with a 19.5-gauge hookwire as used for localization of non-palpable screen-detected breast masses. In the operating room the nodes were harvested with dissection along the installed wire. The authors reported overall sensitivity of 89% using lymphoscintigraphy and intraoperative dye injections as control. High level of patient tolerance to the procedure (81%) and low number of patients needing analgesia for contrast injection (23%) are stated.[67] In clinical trials dedicated to contrast' safety profile the most commonly observed adverse reactions were: headache (2.3%), injection site reactions as bruishing, burning and paraesthesia (1.7%), injection site pain (1.4%).[68]

Near-infrared fluorescence [NIF] a novel approach that allows optical imaging during surgery was firstly introduced by Kitai et al.[69] in 2005 for breast cancer. Near-infrared light (700-800nm) is characterized by high tissue penetration rate up to 30mm with decreasing quality of visualization in deeper layers.[70] This technique combines advantage of dye *in vivo* visualization with excellent Intraoperatively the location of peritumorally injected contrast's NIF fluorescence signal is captured and envisioned in real-time with an external fluorescence detector and clear definition of anatomical background.[71] In superficial lesions NIF technique allows transcutaneous illumination of the lymphatic channels and nodes which grants optimal incision design and placement thereby reduces operating time.[72,73] Indocyanine green is used as a contrast a low molecular weight organic molecule, which fluorescence in the near-infrared, it's a negatively charged, amphiphilic, water-soluble tricarbocyanine with very low toxicity, high safety and low number of allergic reactions.[73,74–76] Safety, reliability and high identification rates have been observed in preliminary studies of NIF used for SLN identification in head and neck cancer patients.[77–79] Lately Christensen et al.[80] have described a combined method of NIF and lymphoscintigraphy with preoperative SLN identification in all of 30 patients and intraoperative detection rate of the preoperatively defined nodes was 97% (66/68 nodes).[80] In general this technique has prominent advantages and further clinical research is desired for its practical implementation.

When reviewing the properties of these different procedures one should point out that while ink lymphography, lymphoscintigraphy NIF require in fact only a surgeon trained in sentinel lymph node biopsy the currently evolving CT-, MRI- and US- lymphography requires a close cooperation between the surgeon and the radiologist. Hence the radiologist must also be familiar with lymphography principles and be ready to spot the contrast distribution in a short time after injection. Accuracy of SLN detection relies heavily on the experience of the centre and the clinician with a particular technique. Further clinical research is needed and sufficient learning curve must to be achieved in the newly introduced techniques which in their turn are aimed for achieving less invasiveness, easy reproducibility and better imaging quality.

Acknowledgements

None.

Conflict of interest

The author declares no conflict of interest.

References

1. Patel KN, Shah JP. Neck dissection: past, present, future. *Surg Oncol Clin N Am*. 2005;14(3):461–77.
2. Maran AGD, Amin M, Wilson JA. Radical neck dissection: a 19-year experience. *J Laryngol Otol*. 1989;103(8):760–764.
3. Gavilán J, Ferlito A, Silver CE, et al. Status of carotid resection in head and neck cancer. *Acta Otolaryngol*. 2002;122(4):453–455.
4. Cappiello J, Piazza C, Berlucchi M, et al. Internal jugular vein patency after lateral neck dissection: a prospective study. *Eur Arch Ororhinolaryngol*. 2002;259(8):409–412.
5. Cleland-Zamudio SS, Wax MK, Smith JD, et al. Ruptured internal jugular vein: a postoperative complication of modified /selected neck dissection. *Head Neck*. 2003;25(5):357–360.
6. Shone GR, Yardley MPJ. An audit into the incidence of handicaps after unilateral radical neck dissection. *J Laryngol Otol*. 1991;105(9):760–762.
7. de Jong AA, Mann JJ. Phrenic nerve paralysis following neck dissection. *Eur Arch Otorhinolaryngol*. 1991;248(3):132–134.
8. Babin RW, Panje WR. The incidence of vasovagal reflex activity during radical neck dissection. *Laryngoscope*. 1980;90:1321–1323.
9. Prabhu V, Passant C. Left-sided neck dissection and chylothorax: a rare complication and its management. *J Laryngol Otol*. 2012;126(6):648–50.
10. Karaman E, Saritzali G, Cansiz H. A case of increased intracranial pressure after unilateral modified radical neck dissection. *Am J Otolaryngol*. 2009;30(4):261–263.
11. Raj P, Moore PL, Henderson J, et al. Bilateral cortical blindness: an unusual complication following unilateral neck dissection. *J Laryngol Otol*. 2002;116(3):227–229.
12. Ahlberg A, Nikolaidis P, Engstrom T, et al. Morbidity of supraomohyoidal and modified radical neck dissection combined with radiotherapy for head and neck cancer: a prospective longitudinal study. *Head Neck*. 2012;34(1):66–72.

13. Kanda T, Kitajima K, Saito M, et al. Insufficiency fracture of the clavicle after neck dissection: imaging features. *Jpn J Radiol*. 2014;32(3):172–178.

14. Leusink FK, van Es RJ, de Bree R, et al. Novel diagnostic modalities for assessment of the clinically node-negative neck in oral squamous-cell carcinoma. *Lancet Oncol*. 2012;13(12):e554–561.

15. Morton DL, Wen DR, Wong JH, et al. Technical details of intraoperative lymphatic mapping for early stage melanoma. *Arch Surg*. 1992;127(4):392–399.

16. Borgstein PJ, Meijer S, Pijpers R. Intradermal blue dye to identify sentinel lymph-node in breast cancer. *Lancet*. 1997;349(9066):1668–1669.

17. Sleeman JP. The lymph node as a bridgehead in the metastatic dissemination of tumors. *Recent Results Cancer Res*. 2000;157:55–81.

18. Ball CG, Sutherland F, Kirkpatrick AW, et al. Dramatic innovations in modern surgical subspecialties. *Can J Surg*. 2010;53(5):335–341.

19. Coughlin A, Resto VA. Oral cavity squamous cell carcinoma and the clinically n0 neck: the past, present, and future of sentinel lymph node biopsy. *Curr Oncol Rep*. 2010;12(2):129–135.

20. Sebbesen L, Bilde A, Therkildsen M, et al. Three-year follow-up of sentinel node-negative patients with early oral cavity squamous cell carcinoma. *Head Neck*. 2014;36(8):1109–1112.

21. Monroe MM, Pattisapu P, Myers JN, e al. Sentinel lymph node biopsy provides prognostic value in thick head and neck melanoma. *Otolaryngol Head Neck Surg*. 2015;153(3):372–378.

22. Bechyne M, Zyb AF, Nestajko OV. *Atlas of lymphography*. Prague: Avicenum, Russian; 1983.

23. Cousins A, Thompson SK, Wedding AB, et al. Clinical relevance of novel imaging technologies for sentinel lymph node identification and staging. *Biotechnol Adv*. 2014;32(2):269–279.

24. Xiong L, Engel H, Gazyakan E, et al. Current techniques for lymphatic imaging: state of the art and future perspectives. *Eur J Surg Oncol*. 2014;40(3):270–276.

25. Cabanas RM. An approach for treatment of penile carcinoma. *Cancer*. 1977;39(2):456–566.

26. Vogl TJ, Bartjes M, Marzec K. Cotrast-enhanced lymphography. CT or MR imaging? *Acta Radiol Suppl*. 1997;412:47–50.

27. Cabanas RM. The concept of the sentinel lymph node. *Recent Results Cancer Res*. 2000;157:109–120.

28. Suami H, Taylor GI, Pan WR. A new radiographic cadaver injection technique for investigating the lymphatic system. *Plast Reconstr Surg*. 2005;115(7):2007–2013.

29. Pan WR, Suami H, Taylor I. Lymphatic drainage of the superficial tissues of the head and neck: anatomic study and clinical implications. *Plast Reconstr Surg*. 2008;121(5):1614–1624.

30. Giuliano AE. Intradermal blue dye to identify sentinel lymph node in breast cancer. *Lancet*. 1997;350(9082):958.

31. Ross MI, Reintgen D, Balch CM. Selective lymphadenectomy: emerging role for lymphatic mapping and sentinel node biopsy in the management of early stage melanoma. *Semin Surg Oncol*. 1993;9(3):219–223.

32. Morton DL, Wen DR, Foshang LJ, et al. Intraoperative lymphatic mapping and selective cervical lymphadenectomy for early stage melanomas of the head and neck. *J Clin Oncol*. 1993;11(9):1751–1756.

33. 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(5):536–539.

34. Pitman KT, Johnson JT, Edington H, et al. Lymphatic mapping with isosulfan blue dye in squamous cell carcinoma of the head and neck. *Arch Otolaryngol Head Neck Surg*. 1998;124(7):790–793.

35. Bustos ME, Camargo JJ, Resin Geyer G, et al. Intraoperative detection of sentinel lymph nodes using Patent Blue V in non-small cell lung cancer. *Minerva Chir*. 2008;63(1):29–36.

36. Cimmino VM, Brown AC, Szocik JF, et al. Allergic reactions to isosulfan blue during sentinel node biopsy- a common event. *Surgery*. 2001;130(3):439–442.

37. Brockow K, Sanchez-Borges M. Hypersensitivity to contrast media and dyes. *Immunol Allergy Clin North Am*. 2014;34(3):547–564.

38. Alex JC, Sasaki CT, Krag DN, et al. Sentinel lymph node radiolocalization in head and neck squamous cell carcinoma. *Laryngoscope*. 2000;110:198–203.

39. Von Buchwald C, Bilde A, Shoaib T, et al. Sentinel node biopsy: the technique and feasibility in head and neck cancer. *ORL*. 2002;64(4):268–274.

40. Govers TM, Hannink G, Merkx MA, et al. Sentinel node biopsy for squamous cell carcinoma of the oral cavity and oropharynx: a diagnostic meta-analysis. *Oral Oncol*. 2013;49(8):726–732.

41. Flach GB, Bloemena E, Klop WM, et al. Sentinel lymph node biopsy in clinically N0 T1- T2 staged oral cancer: the Dutch multicenter trial. *Oral Oncol*. 2014;50:1020–1024.

42. Ever-Sapir E, Lerman H, Lievshitz G, et al. Lymphoscintigraphy for sentinel node mapping using a hybrid SPECT/CT system. *J Nucl Med*. 2003;44(9):1413–1420.

43. Khafif A, Schneebaum S, Fliss DM, 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(10):874–879.

44. Hauveling DA, van Weert S, Karagozoglu KH, et al. Evaluation of the use of freehand SPECT for sentinel node biopsy in early stage oral carcinoma. *Oral Oncol*. 2015;51(3):287–290.

45. Pitman KT, Ferlito A, Devaney KO, et al. Sentinel lymph node biopsy in head and neck cancer. *Oral Oncol*. 2003;39:343–349.

46. Alkureishi LW, Ross GL, Shoaib T, et al. Sentinel node biopsy in head and neck squamous cell cancer: 5-year follow-up of a European multicenter trial. *Ann Surg Oncol*. 2010;17(9):2459–2464.

47. Ananian SG, Gvetadze SR, Ilkaev KD, et al. Anatomic-histologic study of the floor of the mouth: the lingual lymph nodes. *Jpn J Clin Oncol*. 2015;45(6):547–554.

48. Miner TJ, Shriver CD, Flicek PR, et al. Guidelines of the safe use of the radioactive materials during localization and resection of the sentinel lymph node. *Ann Surg Oncol*. 1999;6(1):75–82.

49. Arya S, Rane P, Deshmukh A. Oral cavity squamous cell carcinoma: role of pretreatment imaging and its influence on management. *Clin Radiol*. 2014;69(9):916–930.

50. Motomura K, Sumino H, Noguchi A, et al. Sentinel nodes identified by computed tomography-lymphography accurately stage the axilla in patients with breast cancer. *BMC Med Imaging*. 2013;13:42.

51. Saito M, Nishiyama H, Oda Y, et al. The lingual lymph node identified as a sentinel node on CT lymphography in a patient with cN0 squamous cell carcinoma of the tongue. *Dentomaxillofac Radiol*. 2012;41(3):254–258.

52. Honda K, Ishiyama K, Suzuki S, et al. Sentinel lymph node biopsy using computed tomographic lymphography in patients with early tongue cancer. *Acta Otolaryngol*. 2015;135(5):507–512.

53. Suga K, Ogasawara N, Okada M, et al. Interstitial CT lymphography-guided localization of breast sentinel lymph node: preliminary result. *Surgery*. 2003;133(2):170–179.

54. Sato M, Fukuda F, Okafuji M, et al. Computed tomographic (CT) lymphography for sentinel lymph node localization in oral cancer. *Jpn J Head Neck Cancer*. 2006;32:24–28.

55. Hayashi H, Tangoku A, Suga K, et al. CT lymphography-navigated sentinel lymph node biopsy in patients with superficial esophageal cancer. *Surgery*. 2006;139(2):224–235.

56. Hyung WJ, Kim YS, Lim JS, et al. Preoperative imaging of sentinel lymph nodes in gastric cancer using CT lymphography. *Yonsei Med J*. 2010;51(3):407–413.

57. Lu Q, Hua J, Kassir MM, et al. Imaging lymphatic system in breast cancer patients with magnetic resonance lymphangiography. *PLoS One*. 2013;8(7):e69701.

58. Heesakkers RA, Hövels AM, Jager GJ, et al. MRI with a lymph-node-specific contrast agent as an alternative to CT scan and lymph-node dissection in patients with prostate cancer: a prospective multicohort study. *Lancet Oncol*. 2008;9(9):850–856.

59. Curvo-Semedo L, Diniz M, Miguéis J, et al. USPIO-enhanced magnetic resonance imaging for nodal staging in patients with head and neck cancer. *J Magn Reson Imaging*. 2006;24(1):123–131.

60. Kobayashi H, Kawamoto S, Bernardo M, et al. Delivery of gadolinium-labeled nanoparticles to the sentinel lymph node: comparison of the sentinel node visualization and estimations of intra-nodal gadolinium concentration by the magnetic resonance imaging. *J Control Release*. 2006;111(3):343–351.

61. Wu L, Cao Y, Liao C, et al. Diagnostic performance of USPIO-enhanced MRI for lymph-node metastases in different body regions: a meta-analysis. *Eur J Radiol*. 2011;80(2):582–589.

62. Joshi PS, Pol J, Sudesh AS. Ultrasonography - A diagnostic modality for oral and maxillofacial diseases. *Contemp Clin Dent*. 2014;5(3):345–351.

63. Tregnaghi A, De Candia A, Calderone M, et al. Ultrasonographic evaluation of superficial lymph node metastases in melanoma. *Eur J Radiol*. 1997;24(3):216–221.

64. Goldberg BB, Merton DA, Liu JB, et al. Contrast-enhanced sonographic imaging of lymphatic channels and sentinel lymph nodes. *J Ultrasound Med*. 2005;24(7):953–965.

65. Nielsen KR, Grossjohann HS, Hansen CP, et al. Use of contrast-enhanced ultrasound imaging to detect the first draining lymph node (FDLN) in a swine model: correlation of imaging findings with the distance from the injection site to the FDLN. *J Ultrasound* Med. 2008;27(8):1203–1209.

66. Goldberg BB, Merton DA, Liu JB, et al. Sentinel lymph nodes in a swine model with melanoma: contrast-enhanced lymphatic US. *Radiology*. 2004;230(3):727–734.

67. Sever AR, Mills P, Jones SE, et al. Preoperative sentinel node identification with ultrasound using microbubbles in patients with breast cancer. *AJR Am J Roentgenol*. 2011;196(2):251–256.

68. Piscaglia F, Bolondi L. Italian Society for Ultrasound in Medicine and Biology (SIUMB) Study Group on Ultrasound Contrast Agents. The safety of Sonovue in abdominal applications: retrospective analysis of 23188 investigations. *Ultrasound Med Biol*. 2006;32(9):1369–1375.

69. Kitai T, Inomoto T, Miwa M, et al. Fluorescence navigation with indocyanine green for detecting sentinel lymph nodes in breast cancer. *Breast Cancer*. 2005;12(3):211–215.

70. Frangioni JV. New technologies for human cancer imaging. *J Clin Oncol*. 2008;26(24):4012–4021.

71. Troyan SL, Kianzad V, Gibbs-Strauss SL, et al. The FLARE intraoperative near-infrared fluorescence imaging system: A first-in-human clinical trial in breast cancer sentinel lymph node mapping. *Ann Surg Oncol*. 2009;16(10):2943–2952.

72. Goetz M, Deris I, Vieth M, et al. Near-infrared conofocal imaging during mini-laparoscopy: a novel rigid endomicroscope with increased imaging plane depth. *J Hepat*. 2010;53(1):84–90.

73. Schaafsma BE, Mieog JSD, Hutteman M, et al. The clinical use of indocyanine green as a near-infrared fluorescent contrast agent for image-guided oncologic surgery. *J Surg Oncol*. 2011;104(3):323–332.

74. Ogawa M, Kosaka N, Choyke PL. In vivo molecular imaging of cancer with a quenching near-infrared fluorescent probe using conjugates of monoclonal antibodies and indocyanine green. *Cancer Res*. 2009;69(4):1268–1272.

75. Alford R, Simpson HM, Duberman J, et al. Toxicity of organic fluorophores used in molecular imaging: Literature review. *Mol Imaging*. 2009;8(6):341–354.

76. Speich R, Saesseli B, Hoffmann U, et al. Anaphylactoid reactions after indocyanine-green administration. *Ann Intern Med*. 1998;109(4):345–346.

77. Van der Vorst JR, Schaafsma BE, Verbeek FP, et al. Near-infrared fluorescence sentinel lymph node mapping of the oral cavity in head and neck cancer patients. *Oral Oncol*. 2013;49(1):15–19.

78. Iwai T, Maegawa J, Hirota M, et al. Sentinel lymph node biopsy using a new indocyanine green fluorescence imaging system with a color charged couple device camera for oral cancer. *Br J Oral Maxillofac Surg*. 2013;51:e26–28.

79. Peng H, Wang SJ, Niu X, et al. Sentinel node biopsy using indocyanine green in oral/oropharyngeal cancer. *World J Surg Oncol*. 2015;13:278.

80. Christensen A, Juhl K, Charabi B, et al. Feasibility of real-time near-infrared fluorescence tracer imaging in sentinel node biopsy for oral cavity cancer patients. *Ann Surg Oncol*. 2015;23:65–72.

Citation: Gvetadze SR, Liu M, Xiong P, et al. A review of techniques for sentinel lymph node mapping with special reference to the head and neck region. *Int Clin Pathol J*. 2016;2(2):43–47. DOI: 10.15406/icpjl.2016.02.00037