Case Report

Sentinel node mapping in vulvar cancers: report of two cases and literature review

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ABSTRACT

Vulvar cancer is a rare gynecological malignancy with mainly lymphatic spread. Sentinel node mapping plays an important role in the management of this gynecological malignancy. In the current study, we reported our experience in sentinel node mapping of vulvar cancer and review the literature accordingly. Since the introduction of sentinel node mapping to the surgical oncology community of our university in 2004, we had two operable vulvar cancer patients who were candidate for sentinel node mapping for inguinal lymph node staging. In the current study, we reported these two cases in details and a brief review of literature on sentinel node mapping in vulvar cancer was done. We specifically discussed the overall accuracy, importance of blue dye injection, learning curve effect, frozen section, excisional biopsy and location of the tumors. Overall sentinel node mapping is a safe and effective method for inguinal lymph node staging in vulvar cancers. In order to perform sentinel node mapping efficiently, paying attention to the details is of utmost importance.

Key words: Sentinel node; Lymphoscintigraphy; Vulva; Radiotracer; Blue dye

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INTRODUCTION

Vulvar cancer is a rare gynecological malignancy with very low incidence in Iran. Many of these patients present in very late stage of their disease due to cultural issues [1, 2]. The standard treatment for early stage vulvar malignancies is complete surgical removal and inguinal lymph node dissection [3]. However, inguinal lymph node dissection is associated with considerable morbidity and can decrease the quality of life in the affected patients [4]. In addition, inguinal lymph node involvement occurs in a low ratio of patients in early stage of the disease, so most of the patients would not benefit from inguinal lymphadenectomy [5].

Sentinel node mapping is an effective method of regional lymph node staging in various solid tumors including urological and gynecological tumors [6, 7]. Sentinel node mapping has been used for lymphatic staging of vulvar cancer [8-12]. The bulk of literature shows its high accuracy and safety. GROINSS-V study has been specially a powerful impetus for the high interest in sentinel node mapping in vulvar cancer [13, 14].

Since the introduction of sentinel node mapping in the surgical oncology community of Mashhad University of Medical Sciences in 2004, we have had an extensive experience in several cancers including gynecological tumors [15, 16]. Since 2004, we had two cases of vulvar cancer treated with sentinel node mapping. In the current study, we reported the details of these two cases and discussed the important points regarding these patients. Table 1 shows the characteristics of these two cases.

CASE PRESENTATION

CASE 1

A 17 year old female with the history of an ulcer in the external genital area was referred to the gynecology department. The location of the lesion was the right labium major at 3cm distance of the midline. After excisional biopsy of the lesion, the clear cell carcinoma of the vulva was confirmed. Clinical examination of the patient didn't show any abnormal finding and no inguinal lymph node was palpable. The patient was scheduled for hemi-vulvectomy and sentinel node mapping. The day of surgery, the patient received two sub-cutaneous peri-tumoral injection of 0.5 mCi/0.2cc Tc-99m-Antimony sulfide colloid. Five minutes post injection the anterior/posterior and lateral lymphoscintigraphy images of the pelvis was done (5 min/image, low energy high resolution collimator, Tc-99m photopeak using a dual head gamma camera: E.CAM Siemens [17]). The lymphoscintigraphy images did not show any sentinel node in the inguinal regions (Figure 1). The patient underwent surgery and immediately after anesthesia induction, two injection of Methylene blue was done in the same fashion of the radiotracer injections (0.5cc each). Intra-operatively, one blue/hot sentinel node was detected in the right inguinal basin. Frozen section evaluation of the sentinel node was negative for metastasis and inguinal lymph node dissection was not performed. Permanent section H&E examination of the harvested sentinel node was however positive for a focus of metastasis.

Table 1. Characteristics of the vulvar cancer patients underwent sentinel node mapping.

	Age (yr)	Location of the tumor	Tumor size (cm)	radiotracer/blue dye	Lymphoscintigraphy results	Intraoperative sentinel node detection	Frozen section/H&E results of the sentinel nodes	Pathological involvement of the dissected non-sentinel nodes	Duration of follow up/events
1	17	Right labium major >2cm form the midline	2.4	Tc-99m antimony sulfide colloid/Methylene blue	No sentinel node detected	One blue/hot node on the right side	Negative/positive	Inguinal node dissection not performed	4 years/patient developed lung metastasis, still alive
2	77	Midline	4.1	Tc-99m Phytate/ Methylene blue	One sentinel node on the right side	One blue/hot node on both sides	Negative/Negative on both sides	Negative on both sides	6 months/no event patient still alive

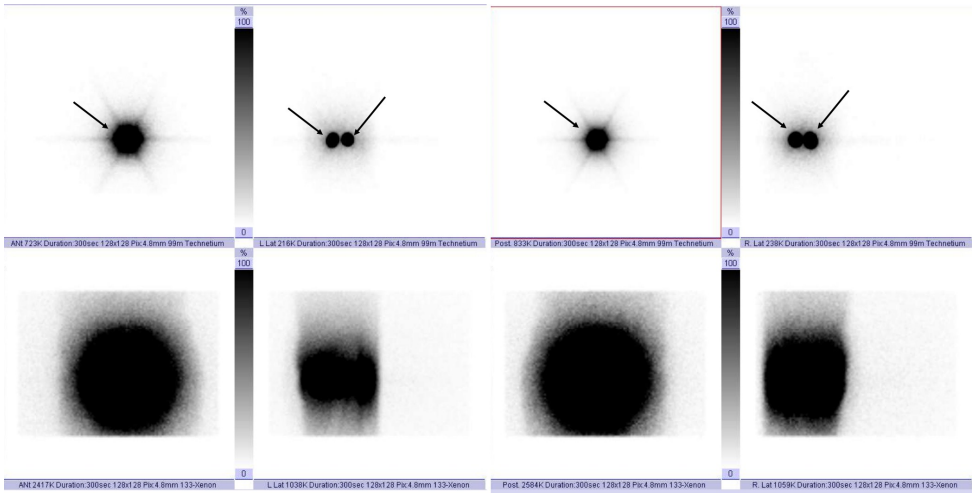

Fig 1. Anterior, Posterior, and lateral lymphoscintigraphy images of case 1. The arrows are injection sites. The lower row images are the corresponding scatterograms of the upper row lymphoscintigraphy views. No sentinel node was visualized.

The patients refused to undergo complete inguinal lymph node dissection and inguinal radiotherapy was performed to decrease the risk of regional lymph node recurrence. After one year of follow up, the patients developed lung metastasis which was treated by chemotherapy. The patient is still alive without any evidence of inguinal recurrence after 4 years of follow up.

Importance of lymphoscintigraphy

Lymphoscintigraphy is an integral part of sentinel node mapping in surgical oncology [8, 18]. Lymphoscintigraphy may show the number and location of the sentinel nodes which can guide the surgeons before surgery and help them to harvest sentinel nodes more efficiently.

In our case, lymphoscintigraphy didn't show any sentinel node in the inguinal area despite successful sentinel node localization during surgery. This is most likely due to the time interval between injection and imaging. Despite very rapid movement of the radiotracers in the lymphatic system [19], the number of detected sentinel nodes can be less than the harvested sentinel nodes during surgery [20]. In our case delayed imaging likely would have shown the inguinal sentinel node.

Effect of excisional biopsy on sentinel node mapping

There is compelling evidence in the literature that excisional biopsy is not a contraindication for sentinel node mapping in breast cancer patients [21]. A recent systematic review on sentinel node mapping in vulvar cancer also showed that, excisional biopsy was not associated with higher sentinel node detection failure [13, 22].

Frozen section accuracy and importance of learning curve

For a successful sentinel node mapping, dedicated pathologists are needed who can perform frozen section efficiently. It is shown that frozen section accuracy is very high in breast cancer patients [23] with the sensitivity of about 87.5% in the hand of expert pathologists. The same results were also reported for sentinel node mapping in vulvar cancer [24] with 88.5% sensitivity. These sensitivities show that no matter how expert the pathologists are some patients would get false negative results.

An important strategy to decrease the false negative rate in sentinel node mapping is to establish a formal sentinel node teaching program before introduction of sentinel node mapping in a surgical oncology community [25]. This is also true for vulvar cancer as reported by Reade et al [26] and Sawicki et al [27]. Our case was the first vulvar cancer patient who underwent sentinel node mapping in our department. This can be the reason for false negative result in our case as all specialists involved in sentinel node mapping (including the pathologist) should have enough expertise.

CASE 2

A 77 year old female patient with extruding lesion from the vaginal opening was referred to the gynecological department. The lesion was highly

suspicious of vulvar squamous cell carcinoma. The patient was candidate for bilateral vulvectomy and sentinel node mapping.

The sentinel node mapping technique and lymphoscintigraphy imaging was the same as case 1. The only difference was the radiotracer as we shifted to Tc-99m-Phytate after several defective labelling by Tc-99m Antimony sulfide colloid [28].

Lymphoscintigraphy images showed an inguinal sentinel node on the right side (Figure 2). The lesion was excised and frozen section confirmed squamous cell carcinoma of the vulva. The surgeon then proceeded to sentinel node mapping. Intra-operatively two sentinel nodes were detected, one on each side of the pelvis in the inguinal region. Both sentinel nodes were blue and hot.

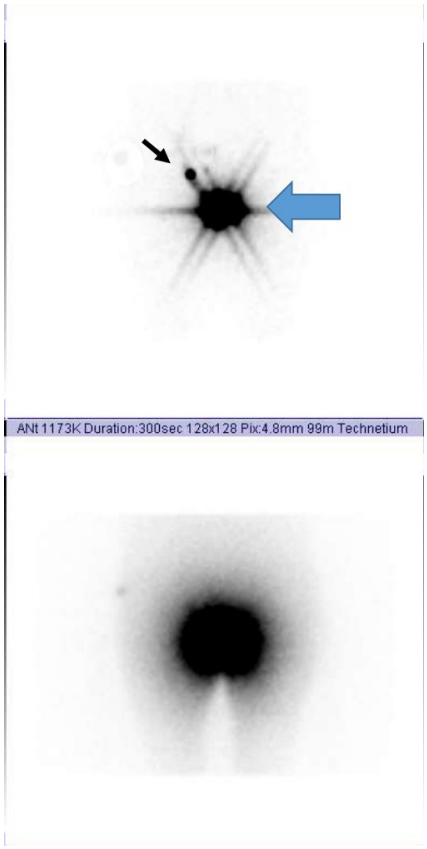

Fig 2. Anterior lymphoscintigraphy image of case 2. The large blue arrow in the injection site. The black arrow is the right inguinal sentinel node. Lower image is the corresponding scatterogram.

Frozen section examination of the harvested sentinel nodes was negative for lymph node metastasis. The surgeon continued to bilateral inguinal lymph node dissection. H&E examination of the sentinel and non-sentinel nodes didn't reveal any metastasis.

Accuracy of sentinel node mapping in vulvar cancer

Vulvar cancer was among the first malignancies in which sentinel node mapping concept was evaluated. The bulk of literature shows very high sensitivity of this technique for inguinal lymph node staging in vulvar cancer [29-31]. Table 2 shows the characteristics of the studies on sentinel node mapping in vulvar cancer. A recent meta-analysis also showed 94.4% pooled detection rate and 92% pooled sensitivity for sentinel node mapping in vulvar squamous cell carcinoma [13]. Our second case also showed the reliability of sentinel node mapping in vulvar squamous cell carcinoma as both sentinel nodes and non-sentinel nodes were pathologically negative.

Blue dye: to use or not to use?

There is a consensus in the literature that combination of blue dye with radiotracer is an effective way of increasing sentinel node detection rate and sensitivity [6, 7, 13]. On the other hand due to life threatening reactions to blue dyes and low detection rate, some groups do not recommend its use, especially in the hand of expert surgeons [10, 32-34]. Due to current low expertise of our some surgeons, we strongly recommend using blue dyes in addition to radiotracer for sentinel node mapping of gynecological cancers.

Laterality of the vulvar tumor and its implication on sentinel node mapping

Midline lesions are defined as lesions within 2 cm of midline and lateral lesions are defined as lesions >2 cm from the midline plane. For lateral lesions (same as case 1 of our study), only ipsilateral inguinal region needs to be mapped as involvement of the contra-lateral inguinal area is extremely rare. However for midline lesions, each groin should be considered separately. This means that detection failure on one side would invariably lead to inguinal lymph node dissection of the same side as the possibility of lymph node involvement is high [13, 35]. Coleman et al. reported that bilateral lymphatic drainage was seen in 69% patients with midline tumors. Contralateral groin lymph node metastases were found in 12% with midline tumors and unilateral lymphatic drainage [36]. Louis-Sylvestre et al. also showed the same findings in 3 midline patients with unilateral drainage [37].

CONCLUSION

Sentinel node mapping is a safe and effective method for inguinal lymph node staging in vulvar cancers.

Table 2. Characteristics of the studies on sentinel node mapping in vulvar cancer

First author	Year	Mapping method	Total number of patients-groins	SLN detection: patient-groin	FNR: per patient-per groin
Levenback	1994	Blue dye	7-10	5-5	0/1-0/1
DeCesare	1997	Radiotracer	10-20	10-20	0/3-0/4
Bowles	1999	Radiotracer	6-11	6-7	0/1-0/1
Ansink	1999	Blue dye	51-93	42-52	1/8-2/11
Echt	1999	Blue dye	12-23	9-15	0/2-0/2
Rodier	1999	Both	6-N/A	5-N/A	N/A-N/A
de Cicco	2000	Radiotracer	37-55	37-50	0/8-0/8
de Hullu	2000	Both	59-107	59-95	0/23-0/30
Sideri	2000	Radiotracer	44-77	44-77	0/13-0/14
Tavares	2001	Both	15-N/A	15-N/A	0/3-N/A
Trope	2001	Both	6-N/A	6-N/A	0/3-N/A
Molpus	2001	Both	11-16	10-N/A	0/2-0/2
Sliutz	2002	Radiotracer (in 8 patients both)	24-43	24-43	0/9-0/9
Zambo	2002	Both	8-11	8-11	N/A
Radziszewski	2003	Both	20-40	N/A-36	0/11-0/20
Moore	2003	Both	29-42	29-42	0/10-0/12
Boran	2003	Radiotracer	10-17	10-17	2/6-2/8
Hakam	2004	Radiotracer	14-N/A	14-N/A	2/7-N/A
Basta	2005	Both	39-N/A	38-N/A	0/12-N/A
Merisio	2005	Radiotracer	20-31	20-21	1/3-1/5
Carcopino	2005	Both	15-19	14-18	N/A
Louis-Sylvestre	2006	Radiotracer and in some blue dye	38-64	36-47	3/15-1/13
Terada	2006	Both	23-27	23-27	N/A
Vidal-Sicart	2007	Both	62-97	61-85	0/16-N/A
Rob	2007	Blue dye in 16 and both in 43 patients	59-86	54-74	1/19-1/19
Nyberg	2007	Blue dye in all, both in 40 patients	47-N/A	46-N/A	1/19-N/A
Johann	2008	Both	39-N/A	37-N/A	1/11-N/A
Hampl	2008	Both in 72, radiotracer 47, Blue dye 8	127-N/A	125-N/A	3/39-4/50
Klat	2009	Both	23-41	23-38	1/15-1/18
Achimas-Cadariu	2009	Both	N/A-55	N/A-52	N/A
Garcia	2009	Both	9-N/A	8-N/A	0/2-N/A
Li	2009	Blue dye in 11, radiotracer in 10	21-N/A	20-N/A	1/8-1/10
Sawicki	2010	Both	24-39	24-34	0/4-0/9
Radziszewski	2010	Both	56-107	N/A-106	N/A-8/46
Lindell	2010	17 Blue dye, 60 both	77-130	75-94	4/23-2/22
Crosbie	2010	Both	32-49	31-45	0/7-1/10
Akrivos	2011	7 blue dye, 27 both	34-64	34-52	N/A-4/19
Guedec-Ghelfi	2011	Radiotracer	8-N/A	8-N/A	N/A
Klar	2011	Radiotracer	16-29	12-25	0/3-0/3
Ennik	2011	Radiotracer 33, blue dye 2, both 30	59-91	56-73	4/15-N/A
Crane	2011	Both/In addition fluorescence imaging was also done	10-16	10-16	N/A
Devaja	2011	Both	60-N/A	59-N/A	0/21-N/A
Woelber	2012	Radiotracer	106-N/A	106-N/A	N/A
Hutteman	2012	Both/In addition fluorescence imaging was also done	9-12	9-11	N/A
Levenback	2012	Both	452-772	418-593	11/132-12/152
Zekan	2012	Radiotracer	25-35	25-28	1/9-0/11
Garcia-Iglesias	2012	Radiotracer 15, both 61	65-N/A	65-N/A	N/A
Schaafsma	2013	Both/In addition fluorescence imaging was also done	24-34	19-25	N/A

In order to perform sentinel node mapping efficiently, paying attention to the details such as location of the tumor, expertise of the surgeons and pathologists, use of blue dye, etc is of utmost importance.

REFERENCES

1. Yousefi Z, Ahmadi S. A prospective study of female genital cancers at ghaem hospital in Mashad. J Sabzevar Univ Med Sci. 2002;4(22):8-15.
2. Yousefi Z, Homaei F, Sharifi N, Kadkhodayan S. Four cases of intraepithelial neoplasia of vulva: Case report. J Babol Univ Med Sci. 2004;3(23):59-63.

3. Balat O. Contemporary management of groin lymph nodes in early vulvar cancer: diagnosis and treatment. Eur J Gynaecol Oncol. 2002;23(5):378-82.

4. Walker KF, Day H, Abu J, Nunns D, Williamson K, Duncan T. Do surgical techniques used in groin lymphadenectomy for vulval cancer affect morbidity rates? Int J Gynecol Cancer. 2011 Nov;21(8):1495-9.

5. Gonzalez Bosquet J, Kinney WK, Russell AH, Gaffey TA, Magrina JF, Podratz KC. Risk of occult inguinofemoral lymph node metastasis from squamous carcinoma of the vulva. Int J Radiat Oncol Biol Phys. 2003 Oct 1;57(2):419-24.

6. Sadeghi R, Gholami H, Zakavi SR, Kakhki VR, Tabasi KT, Horenblas S. Accuracy of sentinel lymph node biopsy for inguinal lymph node staging of penile squamous cell carcinoma: systematic review and meta-analysis of the literature. J Urol. 2012 Jan;187(1):25-31.

7. Sadeghi R, Tabasi KT, Bazaz SM, Kakhki VR, Massoom AF, Gholami H, Zakavi SR. Sentinel node mapping in the prostate cancer. Meta-analysis. Nuklearmedizin. 2011;50(3):107-15.

8. Decesare SL, Fiorica JV, Roberts WS, Reintgen D, Arango H, Hoffman MS, Puleo C, Cavanagh D. A pilot study utilizing intraoperative lymphoscintigraphy for identification of the sentinel lymph nodes in vulvar cancer. Gynecol Oncol. 1997 Sep;66(3):425-8.

9. de Hullu JA, Doting E, Piers DA, Hollema H, Aalders JG, Koops HS, Boonstra H, van der Zee AG. Sentinel lymph node identification with technetium-99m-labeled nanocolloid in squamous cell cancer of the vulva. J Nucl Med. 1998 Aug;39(8):1381-5.

10. Ansink AC, Sie-Go DM, van der Velden J, Sijmons EA, de Barros Lopes A, Monaghan JM, Kenter GG, Murdoch JB, ten Kate FJ, Heintz AP. Identification of sentinel lymph nodes in vulvar carcinoma patients with the aid of a patent blue V injection: a multicenter study. Cancer. 1999 Aug 15;86(4):652-6.

11. Echt ML, Finan MA, Hoffman MS, Kline RC, Roberts WS, Fiorica JV. Detection of sentinel lymph nodes with lymphazurin in cervical, uterine, and vulvar malignancies. South Med J. 1999 Feb;92(2):204-8.

12. Rodier JF, Janser JC, Routiot T, David E, Ott G, Schneegans O, Ghnassia JP. Sentinel node biopsy in vulvar malignancies: a preliminary feasibility study. Oncol Rep. 1999 Nov-Dec;6(6):1249-52.

13. Hassanzade M, Attaran M, Treglia G, Yousefi Z, Sadeghi R. Lymphatic mapping and sentinel node biopsy in squamous cell carcinoma of the vulva: systematic review and meta-analysis of the literature. Gynecol Oncol. 2013 Jul;130(1):237-45.

14. Oonk MH, van Hemel BM, Hollema H, de Hullu JA, Ansink AC, Vergote I, Verheijen RH, Maggioni A, Gaarenstroom KN, Baldwin PJ, van Dorst EB, van der Velden J, Hermans RH, van der Putten HW, Drouin P, Runnebaum IB, Sluiter WJ, van der Zee AG. Size of sentinel-node metastasis and chances of non-sentinel-node involvement and survival in early stage vulvar cancer: results from GROINSS-V, a multicentre observational study. Lancet Oncol. 2010 Jul;11(7):646-52.

15. Kakhki VRD, Jangjoo A, Tavassoli A, Asadi M, Sadri K, Masoom AF, Mehrabibahar M, Memar B, Ansari M, Sadeghi R. Sentinel node mapping for early breast cancer patients using 99mTc-phytate: Single center experience on 165 patients. Iran J Nucl Med. 2012;20(2):25-9.

16. Sadeghi R. Sentinel node biopsy in medical practice: more than 6 years of practice in Mashhad. Iran J Nucl Med. 2010;18(Suppl 1):56.

17. Momennezhad M, Zakavi SR, Dabbagh Kakhki VR, Jangjoo A, Ghavamnasiri MR, Sadeghi R. Scatterogram: a method for outlining the body during lymphoscintigraphy without using external flood source. Radiol Oncol. 2011 Sep;45(3):184-8.

18. Trifirò G, Travaini LL, Sanvito F, Pacifici M, Mallia A, Ferrari ME, Vertua A, Maggioni A, Paganelli G, Sideri MG. Sentinel node detection by lymphoscintigraphy and sentinel lymph node biopsy in vulvar melanoma. Eur J Nucl Med Mol Imaging. 2010 Apr;37(4):736-41.

19. Sadeghi R, Forghani MN, Memar B, Rajabi Mashhadi MT, Dabbagh Kakhki VR, Abdollahi A, Zakavi SR. How long the lymphoscintigraphy imaging should be continued for sentinel lymph node mapping? Ann Nucl Med. 2009 Aug;23(6):507-10.

20. Sadeghi R, Forghani MN, Memar B, Abdollahi A, Zakavi SR, Mashhadi MT, Raziee HR, Tavassoli A, Kakhki VR. Comparison of pre-operative lymphoscintigraphy with inter-operative gamma probe and dye technique regarding the number of detected sentinel lymph nodes. Hell J Nucl Med. 2009 Jan-Apr;12(1):30-2.

21. Javan H, Gholami H, Assadi M, Pakdel AF, Sadeghi R, Keshtgar M. The accuracy of sentinel node biopsy in breast cancer patients with the history of previous surgical biopsy of the primary lesion: systematic review and meta-analysis of the literature. Eur J Surg Oncol. 2012 Feb;38(2):95-109.

22. Woelber L, Grimm D, Vettorazzi E, Wisotzki C, Trillsch F, Jaenicke F, Schwarz J, Choschzick M, Mahner S. Secondary sentinel node biopsy after previous excision of the primary tumor in squamous cell carcinoma of the vulva. Ann Surg Oncol. 2013 May;20(5):1701-6.

23. Memar B, Sadeghi R, Ayati NK, Aledavood SA, Tghizadeh A, Naseri S, Forghani MN, Homaee F, Abdollahi A. The value of touch imprint cytology and frozen section for intra-operative evaluation of axillary sentinel lymph nodes. Pol J Pathol. 2010;61(3):161-5.

24. Brunner AH, Polterauer S, Tempfer C, Joura E, Reinthaller A, Horvat R, Hefler L. The accuracy of intraoperative frozen section of the inguinal sentinel lymph node in vulvar cancer. Anticancer Res. 2008 Nov-Dec;28(6B):4091-4.

25. Abdollahi A, Jangjoo A, Dabbagh Kakhki VR, Rasoul Zakavi S, Memar B, Naser Forghani M, Mehrabibahar M, Sadeghi R. Factors affecting sentinel lymph node detection failure in breast cancer patients using intradermal injection of the tracer. Rev Esp Med Nucl. 2010 Mar-Apr;29(2):73-7.

26. Reade CJ, Jimenez W, O'Reilly D, Covens A. Sentinel lymph node biopsy in vulvar cancer: a health technology assessment for the canadian health care context. J Obstet Gynaecol Can. 2012 Nov;34(11):1053-65.

27. Sawicki S, Romanowicz G, Wydra D, Lass P. The usefulness of sentinel lymph node detection in vulvar cancer - a short communication. Nucl Med Rev Cent East Eur. 2010;13(2):81-3.

28. Sadri K, Ayati NK, Shabani G, Zakavi SR, Sadeghi R. Sentinel node detection failure due to defective labeling and large particle size of Tc-99m antimony sulfide colloid. Iran J Nucl Med. 2011;19(1):6-11.

29. Schaafsma BE, Verbeek FP, Peters AA, van der Vorst JR, de Kroon CD, van Poelgeest MI, Trimbos JB, van de Velde CJ, Frangioni JV, Vahrmeijer AL, Gaarenstroom KN. Near-infrared fluorescence sentinel lymph node biopsy in vulvar cancer: a randomised comparison of lymphatic tracers. BJOG. 2013 May;120(6):758-64.

30. Moore DH. Reflections on vulvar tumors, lymphatic drainage, and sentinel lymph node biopsy. Gynecol Oncol. 2013 Feb;128(2):153-4.

31. Zekan J, Mutvar A, Huic D, Petrovic D, Karelovic D, Mitrovic L. Reliability of sentinel node assay in vulvar cancer: the first Croatian validation trial. Gynecol Oncol. 2012 Jul;126(1):99-102.

32. Jangjoo A, Forghani MN, Mehrabibahar M, Sadeghi R. Anaphylaxis reaction of a breast cancer patient to methylene blue during breast surgery with sentinel node mapping. Acta Oncol. 2010 Aug;49(6):877-8.

33. Rob L, Robova H, Pluta M, Strnad P, Kacirek J, Skapa P, Taborska K. Further data on sentinel lymph node mapping in vulvar cancer by blue dye and radiocolloid Tc99. Int J Gynecol Cancer. 2007 Jan-Feb;17(1):147-53.

34. Levenback C, Coleman RL, Burke TW, Bodurka-Bevers D, Wolf JK, Gershenson DM.Intraoperative lymphatic mapping and sentinel node identification with blue dye in patients with vulvar cancer. Gynecol Oncol. 2001 Nov;83(2):276-81.

35. Fons G, ter Rahe B, Sloof G, de Hullu J, van der Velden J. Failure in the detection of the sentinel lymph node with a combined technique of radioactive tracer and blue dye in a patient with cancer of the vulva and a single positive lymph node. Gynecol Oncol. 2004 Mar;92(3):981-4.

36. Coleman RL, Ali S, Levenback CF, Gold MA, Fowler JM, Judson PL, Bell MC, De Geest K, Spirtos NM, Potkul RK, Leitao MM Jr, Bakkum-Gamez JN, Rossi EC, Lentz SS, Burke JJ 2nd, Van Le L, Trimble CL. Is bilateral lymphadenectomy for midline squamous carcinoma of the vulva always necessary? An analysis from Gynecologic Oncology Group (GOG) 173. Gynecol Oncol. 2013 Feb;128(2):155-9.

37. Louis-Sylvestre C, Evangelista E, Leonard F, Itti E, Meignan M, Paniel BJ. Sentinel node localization should be interpreted with caution in midline vulvar cancer. Gynecol Oncol. 2005 Apr;97(1):151-4.