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**Sentinel lymph node detection in patients with vulvar carcinoma;
Feasibility of intraoperative mapping with technetium-99m-labeled nanocolloid**

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Conflict of interest

The authors declare no conflict of interest

Abstract**Aims:**

Sentinel lymph node (SLN) mapping appears to be feasible in patients with primary vulvar cancer. Previous protocols describe the injection of the technetium-99m-nanocolloid at least 3 hours before surgery which involves two invasive procedures for the patient. In this study, we assessed the feasibility, safety, and accuracy of an intraoperative rather than preoperative SLN mapping in patients with primary vulvar cancer.

Methods:

Patients with histologically confirmed squamous cell vulvar cancer and clinically FIGO stage Ib disease underwent intraoperative SLN mapping by intradermal injection of the nanocolloid around the tumor. SLN were identified and removed before a complete inguino-femoral lymphnode dissection was performed. Surgical and pathologic data on all patients were prospectively entered into a database.

Results:

A SLN procedure was performed in 16 patients; 3 patients received unilateral lymphadenectomy, and 13 women underwent surgery on both groins. In all groins but 4 at least one SLN was clearly identified (detection rate 25/29, 86%). A median number of 2 SLN and 4 non-SLN per groin were removed. 3 of 16 patients (19 %) had metastatic disease in the lymph nodes. There was no false negative SLN result.

Conclusion:

Intraoperative SLN detection seems feasible in patients with early stage vulvar cancer. More patients need to be enrolled in this ongoing study before this more convenient technique can be considered safe.

Introduction

Current standard treatment for patients with squamous cell vulvar cancer (SCC) includes surgery followed by radiotherapy if indicated. For stage I disease, radical local excision without inguino-femoral lymph node dissection (ILND) is the treatment of choice in patients with less than 1 mm of stromal invasion, since the risk of inguinofemoral lymph node metastases is below 1 percent.¹ For lesions with stromal invasion more than 1 mm but less than 3 mm, the risk of inguinofemoral lymph node metastases is approximately 10 percent. In these cases of stage IB disease, radical local excision with ILND is recommended. The choice of unilateral or bilateral LND depends on the location of the lesion.²

These standards have led to an excellent 5-year survival rate of 98 % for stage I and of 85 % for stage II disease (1988 FIGO classification).³ However, a significant treatment-related morbidity has been observed concomitantly. The most frequently seen complications include postoperative wound healing problems, secondary wound infections, lymphocyst formation, chronic lymphedema of the lower extremities and psychosexual problems.^{4,5,6,7} Especially the latter complications may severely impact the patient's quality of life.⁸ Moreover, complications in either the vulva or groin delay a possibly indicated adjuvant radiation until the wounds have healed. Adjuvant radiation for vulvar cancer involves both pelvic and inguinal fields and is thought to exacerbate to lower extremity lymphedema.⁷ In stage I and II disease, the probability of a positive inguinal lymph node finding is 10 – 26 %, which suggests that approximately 80 % of these patients undergo unnecessary ILND.⁹ However, there is no doubt about the prognostic information of surgical lymph node staging since since the lymph node status is still the most important prognostic factor in vulvar malignancies.¹⁰

At present, no reliable noninvasive technique is available to discriminate between patients with and without microscopic inguinofemoral lymph node metastases. To obviate the negative side effects of full ILND, the application of the less extensive sentinel lymph node procedure is currently explored in patients with primary SCC.¹¹ The SLN identification by a technetium-99m-labelled nanocolloid (alone or with blue dye) appears to be the most accurate method, with a sensitivity of 97% as reported for pooled data published between 1979 and 2004.¹² Positive non-sentinel nodes (NSLN) in the presence of negative SLN (i.e. false-negative SLN) are rare.¹² The SLN procedure leads to a significant reduction in short term (wound breakdown, cellulitis) and long term morbidity (lymphedema, recurrent erysipeles) compared to ILND.¹³

Usually, the SLN detection in malignant melanoma is performed in two steps. First, preoperative injection of the radionuclids followed by imaging with a Gamma Camera to illustrate regional lymphatic drainage. Second, intraoperative identification of sentinel lymph nodes using a handheld probe. Tracer injection prior to surgery is an invasive procedure that can cause discomfort and anxiety which might lead to a high refusal rate of the procedure.¹⁴ To our knowledge, no published protocol has so far tested the feasibility of radionuclid injection and SLN removal in vulvar cancer patients when the patient is already anesthetized. In breast cancer patients, no difference in SLN detection rates between the intraoperative and preoperative protocols were found.¹⁵

The aim of this study was to evaluate the feasibility of a prospectively designed patient-convenient “short-protocol” in which ^{99m}-labelled nanocolloids are injected intraoperatively in already anesthetized patients with SCC.

Materials and Methods

The ethics committee of the Medical Faculty of Freiburg gave approval for this study.

Patients with clinical stage Ib and II disease (2009 FIGO classification) were offered enrolment into this prospectively designed study. Patients were recruited from September 2007 to March 2010. A written informed consent was obtained from each patient.

Sentinel lymph node mapping

After induction of general anesthesia, 0.3 ml of 10 MBq (4x2.5) technetium-99m-labeled albumin-nanocolloid (GE Healthcare Buchler G,bH & Co.KG, Braunschweig, Germany; particle size < 80 nm (95%), microfiltration through Nucleopore filter) was injected intradermally at 12, 3, 6, and 9 o'clock around the tumor. Then the patient was prepped and draped in a sterile fasion. Afterwards SLNs were immediately identified using a handheld probe (Ethicon, Hamburg, Germany). After the removal of the first SLN, the groin was re-examined for radioactivity. If radioactivity was detected at a level greater than 10 % of the first excised sentinel lymph node, the dissection was continued in search of additional SLN. Subsequently, routine ILND was performed. The removed SLN and the ILND specimens were sent separately for histopathological examination.

Surgery

Surgical treatment consisted of radical excision of the primary tumor in combination with uni- or bilateral superficial as well as deep inguinofemoral lymphadenectomy via separate incisions. In general, bilateral lymphadenectomy was performed, except in patients with small unilateral lesions (table 1). A unilateral tumor was defined as a lesion that does not cross the midline, with the medial margin of the tumor more than 1 cm from the midline structures. The primary tumor was excised with a margin of at least 1 cm of normal skin.

All the procedures were performed by a trained gynaecologic oncologist (DD), with a significant experience in sentinel lymph node detection.

Histopathologic Examination

The pathologic assessment of the SLN(s) was performed according to a standard protocol. Briefly, the SLNs were cut in the middle for frozen section or cytologic specimen (both optional). Subsequently, four sections were cut from every half for hematoxylin and eosin (HE) staining (routine histopathologic examination). Ultrastaging was performed only on SLNs that were negative on routine histopathologic examination. For ultrastaging, additional pairs of sections were cut with three sections per millimeter. One section of each pair was

stained with HE, and the other section was immunostained with cytokeratin 1% AE1:AE3 antikeratin solution (Boehringer Mannheim, Mannheim, Germany). From the lymphadenectomy specimens, all lymph nodes were studied individually (one section per 0.5 cm for HE staining).

Statistics

Data were entered into a computerized database and analyzed using SPSS software (Version 14.0 for Windows, SPSS, Inc, Chicago, IL). Primary endpoint was the feasibility of the technique, which comprised the sensitivity of the technique (percentage of patients in which we were able to identify the SLN), including the number of these nodes. Secondary endpoint was a comparison between the SLN and NSLN in terms of metastasis, especially regarding the rate of false negative SLN.

Results

Patients

Initially, 20 patients were enrolled in this study. However, one patient had to be excluded because final pathology revealed a vaginal melanoma. Additionally, 3 patients were excluded because of macroscopic lymph node disease. Thus, a total of 16 patients with FIGO stage Ib vulvar cancer were finally eligible for statistical analysis.

The median age of all patients was 68 years (range 30 – 88 years). All patients were operated according to the prospectively designed protocol described above. In 8 patients, the primary tumor was <2cm in diameter (T1), and in the remaining 8 patients >2cm (T2) (table 1). No intraoperative complications occurred and no immediate postoperative complications were observed.

SLN detection

The accuracy of the SLN procedure according to the new protocol was assessed in all 16 patients. In total, 29 groins were dissected (13 bilateral, 3 unilateral). A total of 235 inguinal lymph nodes were removed. A total of 76 SLN were detected. The identification of the SLN was successful in 25 out of 29 groins (identification rate: 86 %). The detection rate per patient was 12/16 (75 %). In 4 cases the SLN was not found. SLN were histologically positive in 3 patients and in 3 groins. There was no further NSLN with histological proof of metastasis (negative predictive value, NPV: 100 %). In addition, immunohistochemical examination did not reveal further lymph node involvement, neither for SLN nor for NSLN in form of micrometastasis or isolated tumor cells (table 2).

We were not able to find a SLN in 4 patients. The median primary tumor size in these 4 patients was 1.7 cm (range: 1.1 – 4 cm) and therefore smaller than the median tumor size in all patients (table 1). In our study, thirteen patients had a central tumor localisation (table 1). All 4 patients in which the SLN was not found unilaterally, belong to this group, and were therefore supposed to drain bilaterally. In the first case, the SLN detection failed on the right side. In this case, the tumor was located at the introitus vaginae close to the urethral orifice making an additional partial urethral resection mandatory. In the three remaining cases, the SLN detection failed on the left side. The localizations in these cases were as follows: two times periclitoral and midline-perineal.

Discussion

Context

The SLN technique was introduced to reduce surgical related morbidity and to improve quality of life (QoL) in vulvar cancer patients. According to the GROINSS-V study from the Netherlands, vulvar cancer patients reported less treatment related morbidity after the SLN procedure compared to those who underwent bilateral ILND. However, less postoperative morbidity did not translate into an improved QoL score.¹⁶

Regarding the oncological safety of the SLN procedure, the data provided by a large German multicenter observational study on the accuracy and safety of SLN detection in early vulvar cancer, indicates that it appears safe to omit further lymph node dissection in case of a negative SLN from the groin.¹¹ However, the SLN technique in SCC contains many non-standardized variables. This includes the type of the radiocolloid (unfiltered or filtered particles), the use of combined tracers (combination with blue dye or nanocolloid alone), the method of injection (intratumorally or peritumorally) as well as the timing of administration (pre- or intraoperatively). These different methods can lead to heterogeneous results in SLN mapping in SCC.

SLN mapping in vulvar cancer patients

This is the first prospective trial designed to address the feasibility of intraoperative nanocolloid SLN mapping in the surgical management of vulvar cancer patients. The rationale of our trial was our observation of the high level of discomfort that patients express during the preoperative radiotracer injection. Indeed, in a different trial 4/15 (26.6 %) patients refused a preoperative injection without anesthesia. According to the authors, this finding “illustrates the anticipated burden (pain) by these patients of tracer administration without general anesthesia”.¹⁴ The preliminary results of this study support the intraoperative SLN mapping concept as a feasible technique since no false negative result was detected. These results are in concordance with those of other authors who were able to demonstrate that a preoperative lymphoscintigraphy did not enhance the detection rate of the SLN as compared to an intraoperative identification using a handheld probe only.¹⁶

Since the mortality from local relapse in the groin is high and the decision for adjuvant therapy in vulvar cancer is exclusively based on lymph node status, the determination of the lymph node status has to be highly accurate and errors are fatal and not acceptable. Successful

intraoperative detection of the SLN depends on the amount of radioactivity migrating to and being captured within the lymph nodes. The migration speed of the tracer correlates with the size of the nanocolloid particles used.^{17,18} The ideal particle size must be sufficiently large not to leak from lymphatic vessels and flow with lymph within the lymphatic vessels. Particles smaller than 4 nm in diameter may penetrate capillary membranes and increase blood background counts, which disturb the intra-operative probe detection of SLN. Particles less than 100 nm in diameter, as used in the current study, satisfy the requirements of rapid transfer into lymphatic vessels and remain for several hours in SLN. Larger colloid particles (0.5 to 1.0 μm) have a much slower rate of clearance from the interstitial space resulting in delayed accumulation into lymph nodes.

To our knowledge, intraoperative - in comparison to preoperative - nanocolloid injections protocols have so far been successfully tested in patients with malignant melanoma (identification 0.5 h after injection),¹⁹ colon (blue dye in addition),²⁰ stage I non-small cell lung cancer (identification 1 h and 0.5 h after injection)^{21,22} and breast cancer (identification 3 – 5 h after injection).¹⁵

Limitations of our findings

First, this study had a relatively small enrolment, which is often the case in vulvar cancer studies owing to the rareness of the disease. Additionally, 3 patients needed to be excluded because of enlarged lymph node in the groin. Any enlarged lymph node can cause disruption of the lymph flow and therefore negatively affect the SLN procedure. None of the remaining 16 patients had suspicious nodes at preoperative clinical examination.

Second, the SLN detection rate in our study is rather low (86 %) as compared to the literature published to date (table 3). Potential explanations include the choice to use a radionuclid tracer only for the mapping procedure, the midline location of the primary tumor in the cases of SLN detection failure and the learning curve of the SLN technique:

Technetium-99m-labelled nanocolloid appears to be the most accurate technique to detect SLN in vulvar cancer patients. Lymphatic mapping with ^{99m}technetium labelled colloidal albumin either alone or in combination with blue dye yields generally better detection rates (89–100%) than the use of blue dye alone (56–95%).^{13,23-27} Other authors have used solely radioactive tracer for mapping and achieved high detection rates between 98% and 100% (table 3). According to these data the addition use of blue dye appears to be of limited benefit.

Taking this limited benefit into account combined with the described risk of developing severe allergic reactions by using blue dye, we decided to use technetium-99m-labelled nanocolloid only.

Some authors have described difficulties with the SLN technique in midline vulvar cancer. In a French study, in which 13 out of 17 patients (76 %) had a midline vulvar tumor, the SLN was only detected in one groin.²⁷ Of these 13 cases, three groins with no sentinel nodes identified contained in fact metastatic lymph nodes. In these three patients with central tumor location, the omission of a complete ILND would have been highly deleterious. The authors warrant relying on the sentinel node procedure in women with midline vulvar cancer only in case of unilateral spread confirmed by lymphoscintigraphy. The suitability of this procedure for midline tumors has been questioned by other authors as well.^{11, 28} Although we did not have false-negative results, our difficulties with the SLN procedures in patients with central tumor location highlight the need for further attention in future studies, especially in light of the increasing incidence of central SCC (38.4 %, in our study even 81.2 %) in Germany.²⁹ In view of these changes in localisation, a preoperative lymphoscintigraphy might be useful in the future for patients with midline lesion. Hampl et al. cite a panel's decision at the International Sentinel Lymph Node Society recommending that "...in case of a midline tumor, a SLN should be identified in both groins. If the SLN is not identified or any doubt exists regarding the correlation between a preoperative lymphoscintigram and the operative findings then the SLN biopsy procedure should be abandoned and a complete lymphadenectomy should be performed".¹²

It is moreover of note that any SLN procedure has a learning curve. A learning curve can be defined as the optimum number of SLN biopsies combined with ILND that the surgeon should perform to obtain a certain expertise. Hampl et al. and Levenback et al. report recommendations from the 6th Biennial International Sentinel Node Society Meeting in Australia (February 2008, personal communication) stating that gynaecologic oncologists should perform at least 10 groin dissections with successful identification of the SLN and no false negative before recommending SLN biopsy alone. At the University Medical Centre of Groningen, which enrolled 115 patients in the GROINSS-V study, only 2 of the 4 gynaecologic oncologists performed the SLN biopsies in order to ensure the quality of the procedure.^{12,25} The low incidence of vulvar carcinoma compared to other malignancies leads to the question on how much time it will take before gynaecologic oncologists, even in a reference centre, will pass the learning curve. Therefore, it might be of benefit if gynaecologic

oncologists augment their skills by collaborating with surgical oncologists treating breast cancer and / or melanoma on a regular base. In our study, a trained gynaecologic oncologist (DD) performed all the procedures. He has a significant expertise in sentinel lymph node detection since breast cancer in Germany is treated mainly by gynaecologists.

Conclusion

Regardless of these limitations, we believe that the new protocol provides a step forward towards less invasive, oncologically safe and more convenient procedures in the surgical management of stage I and II vulvar cancer patients. Our study indicates that an intraoperative SLN labelling and detection using Technetium is feasible and accurate.

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References

1. Farias-Eisner R, Cirisano FD, Grouse D, u. a. Conservative and individualized surgery for early squamous carcinoma of the vulva: the treatment of choice for stage I and II (T1-2N0-1M0) disease. *Gynecol. Oncol.* 1994;53(1):55-58.
2. Hacker NF, Berek JS, Lagasse LD, Nieberg RK, Leuchter RS. Individualization of treatment for stage I squamous cell vulvar carcinoma. *Obstet Gynecol.* 1984;63(2):155-162.
3. Homesley HD, Bundy BN, Sedlis A, u. a. Assessment of current International Federation of Gynecology and Obstetrics staging of vulvar carcinoma relative to prognostic factors for survival (a Gynecologic Oncology Group study). *Am. J. Obstet. Gynecol.* 1991;164(4):997-1003; discussion 1003-1004.
4. Andersen BL, Hacker NF. Psychosexual adjustment after vulvar surgery. *Obstet Gynecol.* 1983;62(4):457-462.
5. Podratz KC, Symmonds RE, Taylor WF, Williams TJ. Carcinoma of the vulva: analysis of treatment and survival. *Obstet Gynecol.* 1983;61(1):63-74.
6. Gaarenstroom KN, Kenter GG, Trimbos JB, u. a. Postoperative complications after vulvectomy and inguinofemoral lymphadenectomy using separate groin incisions. *Int. J. Gynecol. Cancer.* 2003;13(4):522-527.
7. Rouzier R, Haddad B, Dubernard G, Dubois P, Paniel B. Inguinofemoral dissection for carcinoma of the vulva: effect of modifications of extent and technique on morbidity and survival. *J. Am. Coll. Surg.* 2003;196(3):442-450.
8. Carlson JW, Kauderer J, Walker JL, u. a. A randomized phase III trial of VH fibrin sealant to reduce lymphedema after inguinal lymph node dissection: a Gynecologic Oncology Group study. *Gynecol. Oncol.* 2008;110(1):76-82.

9. Knopp S, Holm R, Tropé C, Nesland JM. Occult lymph node metastases in early stage vulvar carcinoma patients. *Gynecol. Oncol.* 2005;99(2):383-387.
10. Burger MP, Hollema H, Emanuels AG, u. a. The importance of the groin node status for the survival of T1 and T2 vulval carcinoma patients. *Gynecol. Oncol.* 1995;57(3):327-334.
11. Hampl M, Hantschmann P, Michels W, Hillemanns P. Validation of the accuracy of the sentinel lymph node procedure in patients with vulvar cancer: results of a multicenter study in Germany. *Gynecol. Oncol.* 2008;111(2):282-288.
12. Selman TJ, Luesley DM, Acheson N, Khan KS, Mann CH. A systematic review of the accuracy of diagnostic tests for inguinal lymph node status in vulvar cancer. *Gynecol. Oncol.* 2005;99(1):206-214.
13. Van der Zee AGJ, Oonk MH, De Hullu JA, u. a. Sentinel node dissection is safe in the treatment of early-stage vulvar cancer. *J. Clin. Oncol.* 2008;26(6):884-889.
14. de Hullu JA, Doting E, Piers DA, u. a. Sentinel lymph node identification with technetium-99m-labeled nanocolloid in squamous cell cancer of the vulva. *J. Nucl. Med.* 1998;39(8):1381-1385.
15. Dauphine CE, Khalkhali I, Vargas MP, u. a. Intraoperative injection of technetium-99m sulfur colloid is effective in the detection of sentinel lymph nodes in breast cancer. *Am. J. Surg.* 2006;192(4):423-426.
16. Oonk MHM, van Os MA, de Bock GH, u. a. A comparison of quality of life between vulvar cancer patients after sentinel lymph node procedure only and inguinofemoral lymphadenectomy. *Gynecol. Oncol.* 2009;113(3):301-305.
17. Rob L, Robova H, Pluta M, u. a. Further data on sentinel lymph node mapping in vulvar cancer by blue dye and radiocolloid Tc99. *Int. J. Gynecol. Cancer.* 2007;17(1):147-153.
18. Sato K, Krag D, Tamaki K, u. a. Optimal particle size of radiocolloid for sentinel node identification in breast cancer-electron microscopic study and clinical comparison. *Breast*

Cancer. 2004;11(3):256-263; discussion 264-266.

19. Morton DL, Thompson JF, Essner R, u. a. Validation of the accuracy of intraoperative lymphatic mapping and sentinel lymphadenectomy for early-stage melanoma: a multicenter trial. Multicenter Selective Lymphadenectomy Trial Group. *Ann. Surg.* 1999;230(4):453-463; discussion 463-465.

20. Terwisscha Van Scheltinga SEJ, Den Boer FC, Pijpers R, u. a. Sentinel node staging in colon carcinoma: value of sentinel lymph node biopsy with radiocolloid and blue staining. *Scand. J. Gastroenterol. Suppl.* 2006;(243):153-157.

21. Melfi FMA, Lucchi M, Davini F, u. a. Intraoperative sentinel lymph node mapping in stage I non-small cell lung cancer: detection of micrometastases by polymerase chain reaction. *Eur J Cardiothorac Surg.* 2008;34(1):181-186.

22. Liptay MJ, Grondin SC, Fry WA, u. a. Intraoperative sentinel lymph node mapping in non-small-cell lung cancer improves detection of micrometastases. *J. Clin. Oncol.* 2002;20(8):1984-1988.

23. Oonk MHM, van de Nieuwenhof HP, van der Zee AGJ, de Hullu JA. Update on the sentinel lymph node procedure in vulvar cancer. *Expert Rev Anticancer Ther.* 2010;10(1):61-69.

24. Levenback C, Coleman RL, Burke TW, u. a. Intraoperative lymphatic mapping and sentinel node identification with blue dye in patients with vulvar cancer. *Gynecol. Oncol.* 2001;83(2):276-281.

25. Ansink AC, Sie-Go DM, van der Velden J, u. a. Identification of sentinel lymph nodes in vulvar carcinoma patients with the aid of a patent blue V injection: a multicenter study. *Cancer*. 1999;86(4):652-656.

26. Radziszewski J, Kowalewska M, Jedrzejczak T, u. a. The accuracy of the sentinel lymph node concept in early stage squamous cell vulvar carcinoma. *Gynecol. Oncol.* 2010;116(3):473-477.

27. de Hullu JA, Hollema H, Piers DA, u. a. Sentinel lymph node procedure is highly accurate in squamous cell carcinoma of the vulva. *J. Clin. Oncol.* 2000;18(15):2811-2816.
28. Louis-Sylvestre C, Evangelista E, Leonard F, u. a. Sentinel node localization should be interpreted with caution in midline vulvar cancer. *Gynecol. Oncol.* 2005;97(1):151-154.
29. Hampl M, Deckers-Figiel S, Hampl JA, Rein D, Bender HG. New aspects of vulvar cancer: changes in localization and age of onset. *Gynecol. Oncol.* 2008;109(3):340-345.

characteristics	no of patients (%)
<u>Mean age of the patients in years (SD):</u>	
65.6 (36 - 88)	
<u>Location of primary tumor:</u>	
lateral	3 (18.8)
median	13 (81.2)
<u>Disease</u>	
unifocal	16 (100)
<u>Tumor size:</u>	
T 1	8 (50)
T 2	8 (50)
Median (Range) in cm: 2.2 cm (0.7-9.8)	
<u>Grading:</u>	
1	2 (12.5)
2	11 (68.6)
3	3 (18.8)
<u>Patients with nodal metastasis</u>	3 (18.8)

Table 1:

Summarized tumor and treatment characteristics of the patients

characteristics	value
Total no of removed lymph nodes	235
Total no of lymph node metastasis	3
<u>SLN:</u>	
total	76
Median number per patient (range)	4.75 (0 - 18 [*])
Median number per groin (range)	3 (0 - 18 [*])
<u>NSLN:</u>	
total	159
Median number per patient (range)	10 (0 - 14)
Median no of NSLN per groin (range)	6.3(0 - 14)
<u>Metastasis identified in SLN</u>	
by H&E staining	3
by IHC staining	0
<u>Metastasis identified in NSLN</u>	
by H&E staining	0
by IHC staining	0
<u>Accuracy data:</u>	
Total no of false-negative SLN	0
Sensitivity per patient (%)	12/16 (75 %)
Sensitivity per groin (%)	86
NPV (%)	100

Table 2:

SLN and NSLN characteristics and accuracy of intraoperative SLN mapping in patients with primary SCC.

^{*} In one case we submitted a 15 mm piece of lymphatic tissue that was delineated to contain 18 small lymph nodes after final review of the pathologist.

Study	No of patients	Detection rate	False-negative rate
1. Bowles et al., 1999 ³¹	6	100 %	0
2. De Chicco et al., 2000 ³²	37	100 %	0
3. Merisio et al., 2005 ³³	20	100 %	1
4. Vidal-Sicart et al., 2007 ³⁴	50	98 %	0
5. Present study	16	86 %	0

Table 3:

Comparison of detection and false negative rates for protocols using radioactive tracer alone either applied preoperatively (1-4) or intraoperatively (5).