Published in final edited form as:

World J Surg. 2012 September ; 36(9): 2239–2251. doi:10.1007/s00268-012-1623-z.

The false-negative rate of sentinel node biopsy in patients with breast cancer: a meta-analysis

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Abstract

Background/Purpose—In sentinel node surgery for breast cancer, procedural accuracy is assessed by calculating the false-negative rate. It is important to measure this since there are potential adverse outcomes from missing node metastases. We performed a meta-analysis of published data to assess which method has achieved the lowest false-negative rate.

Methods—We found 3588 articles concerning sentinel nodes and breast cancer published from 1993 through mid-2011; 183 articles met our inclusion criteria. The studies described in these 183 articles included a total of 9306 patients. We grouped the studies by injection material and injection location. The false-negative rates were analyzed according to these groupings and also by the year in which the articles were published.

Results—There was significant variation in the false-negative rate over time with a trend to higher rates over time. There was significant variation related to injection material. The use of blue dye alone was associated with the highest false-negative rate. Inclusion of a radioactive tracer along with blue dye resulted in a significantly lower false-negative rate. Although there were variations in the false-negative rate according to injection location, none were significant. This meta-analysis also indicates a significant change over time in the false-negative rate.

Discussion/Conclusions—The use of blue dye should be accompanied by a radioactive tracer to achieve a significantly lower false-negative rate. Location of injection did not have a significant impact on the false-negative rate. Given the limitations of acquiring appropriate data, the false-negative rate should not be used as a metric for training or quality control.

Introduction

The false-negative rate (FNR) of the sentinel node (SN) biopsy procedure is an important measure of procedural accuracy in the surgical management of breast cancer. Potential adverse outcomes from missing node metastases include under-staging the patient and an increased risk of cancer recurrence. The FNR is measured by comparing the pathological status of the SNs to the remainder of the axillary nodes present in a completion axillary node resection (ANR).

A large randomized trial has demonstrated that when cancer has not metastasized to the SN, survival and recurrence are equivalent in either SN biopsy only and ANR[1]. Since the morbidity is lower with SN biopsy only, ANR is not typically justifiable in the SN-negative case. The era of gathering new data on FNR is essentially over.

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Potential conflict of interest: Dr David Krag has a financial interest in treeofmedicine.com

There are many different methods for removing SNs. These have been devised to achieve practical and theoretical advantages such as decreased pain, increased success rate, and ease of performing the procedure. Many of these outcomes can be reliably evaluated with the number of patients typically seen in a single center. However, establishing an accurate FNR involves observations on a very large number of patients. For example, to establish a 5% FNR for a single surgeon between a range of 0% and 7% would take about 300 patients with positive axillary nodes[2]. Comparing the differences in FNR between different SN biopsy methods requires a very large number of patients. Few if any published reports on single patient populations can define with sufficient statistical certainty what the FNR is for any given SN biopsy method.

We present here a meta-analysis of the FNR observed with different SN biopsy methods. The FNR analysis was based upon grouping published data according to the type of material injected and the location of injection. Only the axillary nodes were considered for this analysis; non-axillary nodes were not included.

Materials and Methods

Search Strategy

An information service provided a manually categorized list of the 3588 published articles related to SNs and breast cancer that were listed in PubMed from 1993 through mid-2011 (Sentinel Nodes and Breast Cancer, www.treeofmedicine.com). Of the 3588 articles, 302 were categorized as having reported a FNR. These 302 articles were reviewed for inclusion in this meta-analysis. Additionally, a PubMed search was performed for meta-analyses that have already addressed SN biopsy in breast cancer and FNR.[3–8] Citations from these meta-analyses were also reviewed.

Selection Criteria

To be included in the meta-analysis, articles must have contained groups or sub-groups of patients who had pathologically negative SN biopsy followed by an ANR. Injection material(s) and injection location(s) must have been clearly specified. A FNR reported for a group of patients must have been from a group that had the same injection material(s) and injection location(s) for each patient in the group. An article could have more than one group of patients and be included in our study. The number of patients with positive axillae and number of patients with false-negative SNs had to be described separately for each group in the article.

Articles that reported results largely based on the same group of patients as a previous article were excluded. Articles that were not available in English were also excluded.

Data Collection

A false-negative event is when a patient has a pathologically negative SN and has at least one pathologically positive non-SN. For each article, the number of false-negative cases and the number of cases with positive axillary nodes were recorded for each group of patients that met our inclusion criteria.

Patients were grouped according to the injection location and the injection material. Injection material was classified as dye alone, radioactive tracer alone, and combined dye and tracer. Dyes included isosulfan blue, methylene blue, patent blue, indocyanine green, indigocarmine, and Evan's blue. Tracers included ^{99m}Tc -colloidal albumin, technetium sulfur colloid, ^{99m}Tc tin, ^{99m}Tc phytate, ^{99m}Tc dextran, antimony sulfide, and ^{99m}Tc rhenium colloid.

Location of injection was classified as around the tumor (including peritumoral and subcutaneous over the tumor), areolar or periareolar, intratumoral, and intradermal. Combinations of injection locations were classified as around the tumor and areolar; around the tumor and intradermal; and intradermal and areolar. The classification of multiple injection locations were based on groups of patients in whom data were available and that met our inclusion criteria.

Statistical Analysis

For a set of patients who had a successful SN biopsy, the FNR was defined as the number of false-negative cases divided by the number of cases with any axillary nodal metastases ($FNR = FN/(TP + FN)$). The reported FNRs were in the form of sample proportions ($p = x/n$) where n = the number of cases with axillary dissections and x = the number of false-negative cases from each citation. This sample proportion p can be viewed as being an estimate of an unknown binomial parameter that represents the true study FNR (π) for a given study. It is known that the variance of the sample proportion p as an estimate of the binomial parameter π is equal to $(\pi)(1-\pi)/n$ and that the usual method of estimating this sampling variance is to substitute the observed proportion p for π . However, in the two extreme cases where the observed FNR proportion value p equals zero or 1.0, such a substitution can result in a zero value for the sampling variance. Such a simple substitution scenario does not provide a reasonable estimate for the sampling variance of p that reflects the influence of the sample size n . The arc sine transformation of the sample proportion p (x/n) does provide a method that reflects the sample size in the transformed data scale. The arc sine transformation is the result of taking the arc sine of the square root of (x/n) . [9] On the transformed arc sine scale, the transformed FNR has a sampling distribution with a variance of approximately $1/(4*n)$. Thus, the sample size n from each citation can be included to reflect the precision of the reported data. Formal meta-analysis of the transformed proportions ($p=x/n$) can be conducted and then the use of the appropriate back transformation allows summary effect size estimates to be converted back to the original FNR scale.

The arc sine-transformed FNR and sample size for each citation were entered into a data file with the corresponding covariate information, such as year of publication (broken down into approximate quartiles), the injection agents, and the locations used for injections. Furthermore, citations were divided into 17 possible groups by the combination of injection agent and location of injection used. Each covariate was examined relative to variation among the transformed FNR data with the use of a mixed model where citations within any given covariate subgroup were assumed to represent a random effect and the covariate subgroups were assumed to be a fixed effect. Summary forest plots for each of the three covariates subgroups were created based upon the random effects models. Forest plots of the transformed FNR data were created for those covariate groups, which showed reasonable mixed model statistical heterogeneity based upon the Q-test. [10] Significant Q-statistic values were followed with pairwise comparisons to isolate the source of the FNR heterogeneity. The summary effect sizes and 95% confidence limits within covariate subgroups were back transformed to create summary covariate specific subgroup FNR point estimates and their 95% confidence intervals. A sensitivity analysis was conducted by deleting those citations with FNR equal to zero to determine if any of the primary results were altered.

All primary data transformations and back transformations as well as recoding were conducted using SYSTAT (version 11). Mixed model meta-analysis calculations and graphical displays were obtained using Comprehensive Meta-Analysis (version 2.2).

Results

Of 302 articles that reported a FNR value, there were 183 articles that met inclusion criteria. Overall, these articles produced 202 unique patient groups for analysis. Seventeen articles had two clearly defined groups with either different injection materials or different locations and gave FNRs for each group. One article presented three separate groups. The total number of patients included in this study was 9220. The total number of patients with false-negative axillae was 794. The crude overall FNR was 8.61% (CI: 8.05–9.2%). Using a fixed effects model assuming homogeneity between studies, the overall FNR was calculated to be 7.5% (CI: 7.0–8.1%). Dropping the homogeneity assumption, it was estimated to be 7.0% (CI: 6.1–7.9%) using a random effects model.

By Year

The year of publication for the 202 groups shows growth from a few before 1997, with rapid growth from 1997 to a peak in 2000 and 2001, and a steady decline over the decade (Figure 1). The dates of publication for the 202 groups were divided into approximate quartiles by year of publication as follows: 1993–1999, 2000–2001, 2002–2004, and 2005–2011. The FNRs for these quartiles were 5.4% (CI 3.8–7.3%), 7.4% (CI 6.0–8.9%), 6.1% (CI 4.5–7.8%), and 8.9% (CI 7.1–11.5%), respectively. There was not significant variation between quartiles ($p=0.09$).

By Injection Material

FNRs were calculated for three categories of injection materials: dye-only, tracer-only, and dye-and-tracer. One study was excluded from this analysis because each patient received two different types of dye[11]. FNRs were 8.6% (CI 6.7–10.8%) for dye-only, 7.4% (CI 5.6–9.3) for tracer-only, and 5.9% (CI 4.8–7.1%) for dye-and-tracer (Figure 2 shows overall group data and Figure 3A–3C shows individual study data). All three groups were first compared to determine if their FNRs were equal. The Q-statistic for heterogeneity indicated that they were not all equal ($p = 0.050$). Subsequent pairwise comparisons indicated that there was a difference between the dye-only and the dye-and-tracer categories ($p=0.018$). However, there was no difference between tracer-only and dye-only ($p=0.370$), or tracer-only and dye-and-tracer ($p=0.178$).

By Location of Injection

There were seven categories based on location of injection. Four categories consisted of a single location site, while three categories represented a combination of locations. The intratumoral location had the lowest FNR at 2.5% (CI 0.2–12.6%), while FNRs at the other locations ranged from 4.9–8.3% (Figure 4). However, there was no statistically significant variation between these seven location categories ($p=0.95$).

By Location and by Injection Material

A total of 17 groups of patients could be identified based on the combination of materials injected and the location of injection (Table 1). The categories were first compared as a whole, and the Q-statistic indicated a statistically significant variation existed among the FNRs of the 17 categories ($p=0.034$).

There was significant FNR variation between the injection material categories for those injected around the tumor and those injected intradermally. In the patients that had injections restricted to around the tumor, there was a significant variation in the FNR depending on the injection material ($p = 0.0069$). The difference in FNR between the dye-only group (9.4%: CI 7.3–11.6%) and the dye-and-tracer group (5.4%: CI 4.2–6.9%) was statistically significant ($p = 0.002$). There was no significant difference in the FNR between the tracer-

only and the other two injection material categories. In the patients for whom the location of injection was intradermal, the FNR was significantly different between dye-only (14.3%: CI 6–25.3%) and tracer-only (0%: CI 0–10.3%) ($p=0.03$). However, there were only two groups of patients with injections restricted to this site.

There was no significant FNR variation detected between locations no matter the type of injection material(s) used.

Sensitivity Analysis

A sensitivity analysis was performed by dropping all groups that had a FNR of 0% from the analysis. After this, 166 groups remained. The resulting FNR was 8.7% (CI: 8.2–9.3%) using a fixed effects model and 8.5% (CI: 7.8–9.3%) using a random effects model. There continues to be no significant variation in FNR between the quartiles based on year of publication ($p=0.125$), or between injection locations ($p=0.450$). The significant variation between injection materials persists ($p=0.005$).

Conclusions

This meta-analysis includes data from over 9000 cases from 183 articles that met the inclusion criteria. As shown in Figure 1, the number of articles reporting FNR peaked in the year 2000 and declined at a rate similar to the ramp-up rate. There was a nonsignificant trend for the FNR to increase with the last time-period quartile, with the highest at 9.2%. It is unclear whether the most current quartile truly represents the stabilized rate (~9%) or whether the trend for even higher FNRs will continue.

We focused on injection materials and injection locations as the procedural variables most likely to impact the FNR. These are the variables that can be most easily modified to achieve the best results. There are too few cases available in the literature to make strong conclusions about how other variables impact the FNR, such as those related to institution, surgeon, and the patient. Injection materials were grouped into three categories: dye-only, tracer-only, and dye-and-tracer. There were insufficient cases to perform a more detailed analysis of materials within these categories. Figure 2 shows that dye-only had highest FNR of the three categories. No difference was observed between tracer-only and dye-and-tracer. These data support the inclusion of tracer when performing SN biopsy in order to achieve the lowest possible FNR.

Injection locations were grouped into 7 categories: four single-site injection locations and 3 multiple-site injection locations. There were no statistically significant variations between these seven location categories. Intra-tumor injections had the lowest numerical FNR but there were too few cases to establish that rate as statistically significant. Intradermal-only injections also had a low FNR but fewer cases resulted in an even wider confidence interval range. Despite the trends, no location stands out as a compelling choice to achieve the lowest FNR. In the absence of such information, the surgeon may consider other factors, such as convenience or success rate, when choosing the injection location.

More detailed analysis based on material injected and injection location allowed 17 groups of patients to be identified. The results from this more detailed analysis provided no new conclusions. When compared within individual injection materials, location did not make a difference in the FNR. Interestingly, injection material only made a difference when it was injected around the tumor and intradermally.

The results of this meta-analysis are limited to the cases available in the published literature. As a consequence, the potential for publication bias may exist due to the use of only English

language citations in peer reviewed journals. In addition, since many small studies may be prone to reporting of small FNR's and a true FNR of zero would be extremely unlikely in practice, the sensitivity analysis conducted excluded citations with FNR = 0. The subsequent analysis of this reduced set of citations did not impact on the basic conclusions based upon the full set of citations. Other limitations relate to results for the injection sites. Here, intra-tumor injection (with intra-dermal injection close behind) may have the lowest FNR but there are insufficient cases to determine this with certainty. The available data do not support any one injection location over another. There may also be a persistent trend of higher false-negative cases over time. This seemingly increasing trend however is not likely ever to be confirmed, since at this point confirmatory ANR is not tenable.

This meta-analysis was restricted to axillary nodes and the status of non-axillary nodes was not considered. There is considerable variation between the different SN biopsy methods to identify non-axillary SNs. For example, intratumoral or deep tracer injections identify non-axillary nodes in 15% or more of patients. About 1% of clinically node negative patients have extra-axillary metastases when there are no axillary metastases.[12, 13] Ignoring non-axillary nodes means that about 1% of SN metastases will be missed. An interesting question is whether this 1% of missed SN metastases should be added to the FNR of methods that are restricted to the axilla.

These results also are relevant to training and quality control. The number of cases needed to assess performance accuracy of an individual surgeon cannot be based on that surgeon's FNR. This has always been true, given the large number of cases necessary to establish an individual surgeon's FNR. Now, without the ability to perform confirmatory ANR, it will be impossible to determine a surgeon's FNR. For the same reasons, long-term surgeon performance also cannot be pegged to a FNR. Other metrics for gauging surgeon performance of SN biopsy will need to be established.

In conclusion, the results of this meta-analysis indicate that the material injected had an impact on FNR and that blue dye alone was associated with the highest FNR. Location of injection did not have a significant impact on FNR, indicating that any of the reported locations will achieve a similar FNR. There was a trend for higher FNRs over time and FNR for the population of surgeons currently performing this procedure is unknown. Lastly, FNR should not be used as a training or quality control metric.

Acknowledgments

Funding: Grant 4R01CA074137-12 Sentinel Node Versus Axillary Dissection in Breast Cancer

References

1. Krag DN, et al. Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. *Lancet Oncol.* 2010; 11(10):927–33. [PubMed: 20863759]
2. Tanis PJ, et al. The illusion of the learning phase for lymphatic mapping. *Ann Surg Oncol.* 2002; 9(2):142–7. [PubMed: 11888870]
3. Cox CE, et al. Lymphatic mapping and sentinel lymph node biopsy in patients with breast cancer. *Annu Rev Med.* 2000; 51:525–42. [PubMed: 10774480]
4. Fraile M, et al. Sentinel node biopsy as a practical alternative to axillary lymph node dissection in breast cancer patients: an approach to its validity. *Ann Oncol.* 2000; 11(6):701–5. [PubMed: 10942059]
5. Kim T, Giuliano AE, Lyman GH. Lymphatic mapping and sentinel lymph node biopsy in early-stage breast carcinoma: a metaanalysis. *Cancer.* 2006; 106(1):4–16. [PubMed: 16329134]

6. McMasters KM, et al. Sentinel-lymph-node biopsy for breast cancer--not yet the standard of care. *N Engl J Med.* 1998; 339(14):990–5. [PubMed: 9753717]
7. Miltenburg DM, et al. Meta-analysis of sentinel lymph node biopsy in breast cancer. *J Surg Res.* 1999; 84(2):138–42. [PubMed: 10357910]
8. Orr RK, Hoehn JL, Col NF. The learning curve for sentinel node biopsy in breast cancer: practical considerations. *Arch Surg.* 1999; 134(7):764–7. [PubMed: 10401830]
9. Dixon, W.; Massey, F. *Introduction to Statistical Analysis.* 3. New York: McGraw-Hill Book Company; 1969.
10. Borenstein, M., et al. *Introduction to Meta-Analysis.* United Kingdom: John Wiley & Sons; 2009.
11. Anan K, et al. Double mapping with subareolar blue dye and peritumoral green dye injections decreases the false-negative rate of dye-only sentinel node biopsy for early breast cancer: 2-site injection is more accurate than 1-site injection. *Surgery.* 2006; 139(5):624–9. [PubMed: 16701094]
12. Heuts EM, et al. Results of tailored treatment for breast cancer patients with internal mammary lymph node metastases. *Breast.* 2009; 18(4):254–8. [PubMed: 19515565]
13. Heuts EM, et al. Internal mammary lymph drainage and sentinel node biopsy in breast cancer - A study on 1008 patients. *Eur J Surg Oncol.* 2009; 35(3):252–7. [PubMed: 18684584]
14. Giuliano AE, et al. Lymphatic mapping and sentinel lymphadenectomy for breast cancer. *Ann Surg.* 1994; 220(3):391–8. discussion 398–401. [PubMed: 8092905]
15. Giuliano AE, et al. Sentinel lymphadenectomy in breast cancer. *J Clin Oncol.* 1997; 15(6):2345–50. [PubMed: 9196149]
16. Turner RR, et al. Histopathologic validation of the sentinel lymph node hypothesis for breast carcinoma. *Ann Surg.* 1997; 226(3):271–6. discussion 276–8. [PubMed: 9339933]
17. Guenther JM, Krishnamoorthy M, Tan LR. Sentinel lymphadenectomy for breast cancer in a community managed care setting. *Cancer J Sci Am.* 1997; 3(6):336–40. [PubMed: 9403045]
18. Flett MM, et al. Sentinel node localization in patients with breast cancer. *Br J Surg.* 1998; 85(7):991–3. [PubMed: 9692581]
19. Ratanawichitrasin A, et al. Experience with lymphatic mapping in breast cancer using isosulfan blue dye. *J Womens Health.* 1998; 7(7):873–7. [PubMed: 9785313]
20. Kapteijn BA, et al. Identification and biopsy of the sentinel lymph node in breast cancer. *Eur J Surg Oncol.* 1998; 24(5):427–30. [PubMed: 9800974]
21. Imoto S, Hasebe T. Initial experience with sentinel node biopsy in breast cancer at the National Cancer Center Hospital East. *Jpn J Clin Oncol.* 1999; 29(1):11–5. [PubMed: 10073145]
22. Cserni G. Estimating the overlap between sentinel lymph nodes and axillary node samples in breast cancer. *Pathol Oncol Res.* 1999; 5(2):129–33. [PubMed: 10393365]
23. Morgan A, et al. Initial experience in a community hospital with sentinel lymph node mapping and biopsy for evaluation of axillary lymph node status in palpable invasive breast cancer. *J Surg Oncol.* 1999; 72(1):24–30. discussion 30–1. [PubMed: 10477872]
24. Bobin JY, et al. Tagging sentinel lymph nodes: a study of 100 patients with breast cancer. *Eur J Cancer.* 1999; 35(4):569–73. [PubMed: 10492629]
25. Kern KA. Sentinel lymph node mapping in breast cancer using subareolar injection of blue dye. *J Am Coll Surg.* 1999; 189(6):539–45. [PubMed: 10589589]
26. Cserni G, Boross G, Baltas B. Value of axillary sentinel nodal status in breast cancer. *World J Surg.* 2000; 24(3):341–4. discussion 344. [PubMed: 10658070]
27. Motomura K, et al. Sentinel node biopsy guided by indocyanine green dye in breast cancer patients. *Jpn J Clin Oncol.* 1999; 29(12):604–7. [PubMed: 10721942]
28. Canavese G, et al. Sentinel lymph node mapping in early- stage breast cancer: technical issues and results with vital blue dye mapping and radioguided surgery. *J Surg Oncol.* 2000; 74(1):61–8. [PubMed: 10861612]
29. Altinyollar H, et al. Lymphatic mapping and sentinel lymphadenectomy in early stage breast carcinoma. *J Exp Clin Cancer Res.* 2000; 19(2):141–4. [PubMed: 10965808]
30. Ilum L, et al. Sentinel node localization in breast cancer patients using intradermal dye injection. *Acta Oncol.* 2000; 39(3):423–8. [PubMed: 10987241]

31. Rodier JF, et al. Lymphatic mapping and sentinel node biopsy of operable breast cancer. *World J Surg.* 2000; 24(10):1220–5. discussion 1225–6. [PubMed: 11071466]
32. Noguchi M, et al. Dye-Guided Sentinel Lymphadenectomy in Clinically Node-Negative and Node-Positive Breast Cancer Patients. *Breast Cancer.* 1998; 5(4):381–387. [PubMed: 11091679]
33. Miyauchi M, et al. Computed Tomography for Preoperative Evaluation of Axillary Nodal Status in Breast Cancer. *Breast Cancer.* 1999; 6(3):243–248. [PubMed: 11091724]
34. Motomura K, et al. Sentinel Node Biopsy in Breast Cancer Patients with Clinically Negative Lymph-Nodes. *Breast Cancer.* 1999; 6(3):259–262. [PubMed: 11091726]
35. Motomura K, et al. Combination technique is superior to dye alone in identification of the sentinel node in breast cancer patients. *J Surg Oncol.* 2001; 76(2):95–9. [PubMed: 11223834]
36. Nos C, et al. Sentinel lymph node detection for breast cancer: which patients are best suited for the patent blue dye only method of identification? *Ann Surg Oncol.* 2001; 8(5):438–43. [PubMed: 11407519]
37. Mokbel K, Mostafa A. The role of subareolar blue dye in identifying the sentinel node in patients with invasive breast cancer. *Curr Med Res Opin.* 2001; 17(2):93–5. [PubMed: 11759188]
38. Shimazu K, et al. Comparison between periareolar and peritumoral injection of radiotracer for sentinel lymph node biopsy in patients with breast cancer. *Surgery.* 2002; 131(3):277–86. [PubMed: 11894032]
39. Cserni G, et al. Comparison of vital dye-guided lymphatic mapping and dye plus gamma probe-guided sentinel node biopsy in breast cancer. *World J Surg.* 2002; 26(5):592–7. [PubMed: 12098052]
40. Yu JC, et al. Sentinel node biopsy in early breast cancer in Taiwan. *World J Surg.* 2002; 26(11):1365–9. [PubMed: 12297929]
41. Ozmen V, et al. Increased false negative rates in sentinel lymph node biopsies in patients with multi-focal breast cancer. *Breast Cancer Res Treat.* 2002; 76(3):237–44. [PubMed: 12462384]
42. Nos C, et al. Macroscopic quality control improves the reliability of blue dye-only sentinel lymph node biopsy in breast cancer. *Ann Surg Oncol.* 2003; 10(5):525–30. [PubMed: 12794018]
43. Aihara T, Takatsuka Y. Dye-guided sentinel node biopsy revisited; validation and observational study from a single institute. *Breast Cancer.* 2003; 10(3):254–9. [PubMed: 12955039]
44. Meyer-Rochow GY, Martin RC, Harman CR. Sentinel node biopsy in breast cancer: validation study and comparison of blue dye alone with triple modality localization. *ANZ J Surg.* 2003; 73(10):815–8. [PubMed: 14525573]
45. D'Eredita G, et al. Subareolar injection may be more accurate than other techniques for sentinel lymph node biopsy in breast cancer. *Ann Surg Oncol.* 2003; 10(8):942–7. [PubMed: 14527915]
46. Shenoy V, Ravichandran D, Ralphs DN. Is massage following dye injection necessary in sentinel node biopsy in breast cancer? *Breast.* 2002; 11(3):273–4. [PubMed: 14965682]
47. Nour A. Efficacy of methylene blue dye in localization of sentinel lymph node in breast cancer patients. *Breast J.* 2004; 10(5):388–91. [PubMed: 15327490]
48. Radovanovic Z, et al. Blue dye versus combined blue dye-radioactive tracer technique in detection of sentinel lymph node in breast cancer. *Eur J Surg Oncol.* 2004; 30(9):913–7. [PubMed: 15498633]
49. Langer S, et al. Lymphatic mapping improves staging and reduces morbidity in women undergoing total mastectomy for breast carcinoma. *Am Surg.* 2004; 70(10):881–5. [PubMed: 15529842]
50. Deo S, et al. Sentinel lymph node biopsy assessment using intraoperative imprint cytology in breast cancer patients: results of a validation study. *Asian J Surg.* 2004; 27(4):294–8. [PubMed: 15564182]
51. Peintinger F, Reitsamer R, Ralph G. Implementation of sentinel lymph node biopsy with blue dye outside a specialized center: can we improve quality assurance? *Breast J.* 2005; 11(2):103–7. [PubMed: 15730455]
52. Ratanachaikanont T, Karalak A. Sentinel node localization in breast cancer using intradermal dye injection: results, influencing factors and learning curve. *J Med Assoc Thai.* 2005; 88(3):386–90. [PubMed: 15962649]

53. Gui GP, et al. Continued axillary sampling is unnecessary and provides no further information to sentinel node biopsy in staging breast cancer. *Eur J Surg Oncol.* 2005; 31(7):707–14. [PubMed: 15993028]
54. Asoglu O, et al. The role of sentinel lymph node biopsy with blue dye alone in breast cancer patients with excisional biopsy. *Acta Chir Belg.* 2005; 105(3):291–6. [PubMed: 16018523]
55. Kanwal S, Hussain R. Sentinel lymph node biopsy in early carcinoma breast with blue dye. *J Coll Physicians Surg Pak.* 2005; 15(8):515–6. [PubMed: 16202369]
56. Gurleyik G, et al. Accuracy of sentinel lymph node biopsy for the assessment of axillary status in patients with early (T1) breast carcinoma. *J Coll Physicians Surg Pak.* 2005; 15(11):697–700. [PubMed: 16300705]
57. Hung WK, et al. Randomized clinical trial comparing blue dye with combined dye and isotope for sentinel lymph node biopsy in breast cancer. *Br J Surg.* 2005; 92(12):1494–7. [PubMed: 16308853]
58. D'Eredita G, et al. A further validation of subareolar injection technique for breast sentinel lymph node biopsy. *Ann Surg Oncol.* 2006; 13(5):701–7. [PubMed: 16523366]
59. Lamichhane N, et al. Initial experience in a cancer hospital in Nepal with sentinel lymph node mapping and biopsy for evaluation of axillary lymph node status in palpable invasive breast cancer. *Nepal Med Coll J.* 2007; 9(1):22–6. [PubMed: 17593673]
60. Soares CT, Frederigue-Junior U, Luca LA. Anatomopathological analysis of sentinel and nonsentinel lymph nodes in breast cancer: hematoxylin-eosin versus immunohistochemistry. *Int J Surg Pathol.* 2007; 15(4):358–68. [PubMed: 17913942]
61. Kavallaris A, Camara O, Runnebaum IB. Subareolar blue dye only injection sentinel lymph node biopsy could reduce the numbers of standard axillary lymph node dissection in environments without access to nuclear medicine. *J Cancer Res Clin Oncol.* 2008; 134(6):667–72. [PubMed: 18026990]
62. Koukouraki S, et al. Is there any benefit from sentinel lymph node biopsy using the combined radioisotope/dye technique in breast cancer patients with clinically negative axilla? *Nucl Med Commun.* 2009; 30(1):48–53. [PubMed: 19020472]
63. Hirche C, et al. ICG fluorescence-guided sentinel node biopsy for axillary nodal staging in breast cancer. *Breast Cancer Res Treat.* 2010; 121(2):373–8. [PubMed: 20140704]
64. Yamashita K, Shimizu K. Evaluation of sentinel lymph node metastasis alone guided by three-dimensional computed tomographic lymphography in video-assisted breast surgery. *Surg Endosc.* 2009; 23(3):633–40. [PubMed: 18322737]
65. Chintamani, et al. Sentinel lymph node biopsy using dye alone method is reliable and accurate even after neo-adjuvant chemotherapy in locally advanced breast cancer--a prospective study. *World J Surg Oncol.* 2011; 9:19. [PubMed: 21396137]
66. Albertini JJ, et al. Lymphatic mapping and sentinel node biopsy in the patient with breast cancer. *JAMA.* 1996; 276(22):1818–22. [PubMed: 8946902]
67. Borgstein PJ, Meijer S, Pijpers R. Intradermal blue dye to identify sentinel lymph-node in breast cancer. *Lancet.* 1997; 349(9066):1668–9. [PubMed: 9186389]
68. Barnwell JM, et al. Sentinel node biopsy in breast cancer. *Ann Surg Oncol.* 1998; 5(2):126–30. [PubMed: 9527265]
69. O'Hea BJ, et al. Sentinel lymph node biopsy in breast cancer: initial experience at Memorial Sloan-Kettering Cancer Center. *J Am Coll Surg.* 1998; 186(4):423–7. [PubMed: 9544956]
70. Nwariaku FE, et al. Sentinel lymph node biopsy, an alternative to elective axillary dissection for breast cancer. *Am J Surg.* 1998; 176(6):529–31. [PubMed: 9926784]
71. Cox CE, et al. Sentinel lymphadenectomy: a safe answer to less axillary surgery? *Recent Results Cancer Res.* 1998; 152:170–9. [PubMed: 9928556]
72. Hill AD, et al. Lessons learned from 500 cases of lymphatic mapping for breast cancer. *Ann Surg.* 1999; 229(4):528–35. [PubMed: 10203086]
73. Carcoforo P, et al. Lymphatic mapping for the dissection of the sentinel node in the treatment of breast carcinoma. *J Exp Clin Cancer Res.* 1999; 18(1):75–7. [PubMed: 10374682]
74. Rehman S, et al. Sentinel lymph node mapping for staging breast cancer: preliminary results of a prospective study. *Md Med J.* 1999; 48(3):105–10. [PubMed: 10394225]

75. Burak WE Jr, et al. Routine preoperative lymphoscintigraphy is not necessary prior to sentinel node biopsy for breast cancer. *Am J Surg.* 1999; 177(6):445–9. [PubMed: 10414690]
76. Jaderborg JM, et al. The feasibility and accuracy of the sentinel lymph node biopsy for breast carcinoma. *Am Surg.* 1999; 65(8):699–703. discussion 704–5. [PubMed: 10432076]
77. Bass SS, et al. The role of sentinel lymph node biopsy in breast cancer. *J Am Coll Surg.* 1999; 189(2):183–94. [PubMed: 10437841]
78. Eary JF, et al. Sentinel lymph node mapping for breast cancer: analysis in a diverse patient group. *Radiology.* 1999; 213(2):526–9. [PubMed: 10551236]
79. Kollias J, et al. Reliability of sentinel node status in predicting axillary lymph node involvement in breast cancer. *Med J Aust.* 1999; 171(9):461–5. [PubMed: 10615338]
80. Molland JG, Dias MM, Gillett DJ. Sentinel node biopsy in breast cancer: results of 103 cases. *Aust N Z J Surg.* 2000; 70(2):98–102. [PubMed: 10711469]
81. Reintgen D, et al. The Role of Selective Lymphadenectomy in Breast Cancer. *Cancer Control.* 1997; 4(3):211–219. [PubMed: 10763020]
82. Doting MH, et al. Lymphatic mapping with intralesional tracer administration in breast carcinoma patients. *Cancer.* 2000; 88(11):2546–52. [PubMed: 10861432]
83. Borgstein PJ, et al. Functional lymphatic anatomy for sentinel node biopsy in breast cancer: echoes from the past and the periareolar blue method. *Ann Surg.* 2000; 232(1):81–9. [PubMed: 10862199]
84. Mariani G, et al. Mapping sentinel lymph node in breast cancer by combined lymphoscintigraphy, blue-dye, and intraoperative gamma-probe. *Cancer Biother Radiopharm.* 2000; 15(3):245–52. [PubMed: 10941531]
85. Lauridsen MC, et al. Sentinel lymph node biopsy in breast cancer--the Aarhus experience. *Acta Oncol.* 2000; 39(3):421–2. [PubMed: 10987240]
86. Villa G, et al. Localization of the sentinel lymph node in breast cancer by combined lymphoscintigraphy, blue dye and intraoperative gamma probe. *Tumori.* 2000; 86(4):297–9. [PubMed: 11016707]
87. Tsugawa K, et al. Dye- and gamma probe-guided sentinel lymph node biopsy in breast cancer patients: using patent blue dye and technetium-99m-labeled human serum albumin. *Breast Cancer.* 2000; 7(1):87–94. [PubMed: 11029778]
88. Ikeda T, et al. Sentinel lymph node biopsy using tin colloid RI and blue dye method. *Breast Cancer.* 2000; 7(4):284–6. [PubMed: 11114851]
89. Tafra L, et al. Multicenter trial of sentinel node biopsy for breast cancer using both technetium sulfur colloid and isosulfan blue dye. *Ann Surg.* 2001; 233(1):51–9. [PubMed: 11141225]
90. Mann BG, et al. High incidence of micrometastases in breast cancer sentinel nodes. *Aust N Z J Surg.* 2000; 70(11):786–90. [PubMed: 11147438]
91. Smith LF, Cross MJ, Klimberg VS. Subareolar injection is a better technique for sentinel lymph node biopsy. *Am J Surg.* 2000; 180(6):434–7. discussion 437–8. [PubMed: 11182393]
92. Boolbol SK, et al. Intradermal isotope injection: a highly accurate method of lymphatic mapping in breast carcinoma. *Ann Surg Oncol.* 2001; 8(1):20–4. [PubMed: 11206219]
93. Hodgson N, et al. A new radiocolloid for sentinel node detection in breast cancer. *Ann Surg Oncol.* 2001; 8(2):133–7. [PubMed: 11258777]
94. Frisell J, et al. Sentinel node in breast cancer--a Swedish pilot study of 75 patients. *Eur J Surg.* 2001; 167(3):179–83. [PubMed: 11316401]
95. Dupont E, et al. Learning curves and breast cancer lymphatic mapping: institutional volume index. *J Surg Res.* 2001; 97(1):92–6. [PubMed: 11319887]
96. McMasters KM, et al. Dermal injection of radioactive colloid is superior to peritumoral injection for breast cancer sentinel lymph node biopsy: results of a multiinstitutional study. *Ann Surg.* 2001; 233(5):676–87. [PubMed: 11360892]
97. Canavese G, et al. Technical issues and pathologic implications of sentinel lymph node biopsy in early-stage breast cancer patients. *J Surg Oncol.* 2001; 77(2):81–7. discussion 88. [PubMed: 11398158]
98. Smillie T, et al. Evaluation of feasibility and accuracy of sentinel node biopsy in early breast cancer. *Am J Surg.* 2001; 181(5):427–30. [PubMed: 11448435]

99. Sabel MS, et al. Accuracy of sentinel node biopsy in predicting nodal status in patients with breast carcinoma. *J Surg Oncol.* 2001; 77(4):243–6. [PubMed: 11473372]
100. Sato K, et al. Management of the axilla in breast cancer: a comparative study between sentinel lymph node biopsy and four-node sampling procedure. *Jpn J Clin Oncol.* 2001; 31(7):318–21. [PubMed: 11518744]
101. Martin RC, et al. Intradermal isotope injection is superior to intramammary in sentinel node biopsy for breast cancer. *Surgery.* 2001; 130(3):432–8. [PubMed: 11562666]
102. Xavier NL, et al. Sentinel lymph node identification and sampling in women with early breast cancer using 99m Tc labelled dextran 500 and patent blue V dye. *Nucl Med Commun.* 2001; 22(10):1109–17. [PubMed: 11567184]
103. Kim R, et al. Significance of lymphoscintigraphic mapping with Tc-99m human serum albumin and tin colloid in sentinel lymph node biopsy in breast cancer. *Int J Oncol.* 2001; 19(5):991–6. [PubMed: 11604999]
104. Tavares MG, et al. The use of 99mTc-phytate for sentinel node mapping in melanoma, breast cancer and vulvar cancer: a study of 100 cases. *Eur J Nucl Med.* 2001; 28(11):1597–604. [PubMed: 11702099]
105. Donahue EJ. Sentinel node imaging and biopsy in breast cancer patients. *Am J Surg.* 2001; 182(4):426–8. [PubMed: 11720685]
106. Manecksha R, et al. Value of sentinel node biopsy in the management of breast cancer. *Ir J Med Sci.* 2001; 170(4):233–5. [PubMed: 11918327]
107. Euhus DM, et al. Validating the performance of the mammary sentinel lymph node team. *J Surg Oncol.* 2002; 79(4):209–15. [PubMed: 11920777]
108. Shivers S, et al. Final results of the Department of Defense multicenter breast lymphatic mapping trial. *Ann Surg Oncol.* 2002; 9(3):248–55. [PubMed: 11923131]
109. Lloyd LR, Wesen CA, McCallum S. An analysis of filtration and volume of radionuclide in sentinel lymph node biopsy in breast cancer patients. *Am Surg.* 2002; 68(4):373–5. discussion 375–6. [PubMed: 11952249]
110. Sardi A, et al. The benefit of using two techniques for sentinel lymph node mapping in breast cancer. *Am Surg.* 2002; 68(1):24–8. [PubMed: 12467312]
111. Motomura K, et al. Patient age affects identification rate of sentinel nodes in breast cancer. *Biomed Pharmacother.* 2002; 56(Suppl 1):209s–212s. [PubMed: 12487284]
112. Motomura K, et al. Intradermal radioisotope injection is superior to subdermal injection for the identification of the sentinel node in breast cancer patients. *J Surg Oncol.* 2003; 82(2):91–6. discussion 96–7. [PubMed: 12561063]
113. Koizumi M, et al. Sentinel node detection using 99mTc-rhenium sulphide colloid in breast cancer patients: evaluation of 1 day and 2 day protocols, and a dose-finding study. *Nucl Med Commun.* 2003; 24(6):663–70. [PubMed: 12766602]
114. Classe JM, et al. Learning curve for the detection of axillary sentinel lymph node in breast cancer. *Eur J Surg Oncol.* 2003; 29(5):426–33. [PubMed: 12798745]
115. Yong WS, et al. Single institution's initial experience with sentinel lymph node biopsy in breast cancer patients. *ANZ J Surg.* 2003; 73(6):416–21. [PubMed: 12801341]
116. Hoar FJ, Stonelake PS. A prospective study of the value of axillary node sampling in addition to sentinel lymph node biopsy in patients with breast cancer. *Eur J Surg Oncol.* 2003; 29(6):526–31. [PubMed: 12875860]
117. Mahajna A, et al. Sentinel lymph node biopsy in early breast cancer: the first 100 cases performed in a teaching institute. *Isr Med Assoc J.* 2003; 5(8):556–9. [PubMed: 12929292]
118. Kennedy RJ, et al. Removal of two sentinel nodes accurately stages the axilla in breast cancer. *Br J Surg.* 2003; 90(11):1349–53. [PubMed: 14598413]
119. Hughes M, et al. Obesity and lymphatic mapping with sentinel lymph node biopsy in breast cancer. *Am J Surg.* 2004; 187(1):52–7. [PubMed: 14706586]
120. McIntosh SA, et al. Sentinel lymph node biopsy in impalpable breast cancer. *Breast.* 2001; 10(1):82–3. [PubMed: 14965566]

121. Snoj M, et al. Added value of blue dye in sentinel node biopsy for breast cancer. *J Exp Clin Cancer Res.* 2003; 22(4):551–5. [PubMed: 15053296]
122. Lauridsen MC, et al. Sentinel lymph node biopsy in breast cancer-experience with the combined use of dye and radioactive tracer at Aarhus University Hospital. *Acta Oncol.* 2004; 43(1):20–6. [PubMed: 15068316]
123. Peley G, et al. Subareolar injection of radioactive colloid for sentinel lymph node identification in breast cancer patients. *Am Surg.* 2004; 70(7):625–9. [PubMed: 15279188]
124. van Wessem KJ, Meijer WS. Sentinel lymph node biopsy in breast cancer: results of intradermal periareolar tracer injection and follow-up of sentinel lymph node-negative patients. *Breast.* 2004; 13(4):290–6. [PubMed: 15325663]
125. Goyal A, Newcombe RG, Mansel RE. Clinical relevance of multiple sentinel nodes in patients with breast cancer. *Br J Surg.* 2005; 92(4):438–42. [PubMed: 15672428]
126. Knox SM, Ley CA. Comparison of intraparenchymal and intradermal injection for identification of the sentinel node in patients with breast cancer. *Proc (Bayl Univ Med Cent).* 2002; 15(4):366–8. [PubMed: 16333465]
127. Krag DN, et al. Technical outcomes of sentinel-lymph-node resection and conventional axillary-lymph-node dissection in patients with clinically node-negative breast cancer: results from the NSABP B-32 randomised phase III trial. *Lancet Oncol.* 2007; 8(10):881–8. [PubMed: 17851130]
128. Canavese G, et al. Sentinel node biopsy compared with complete axillary dissection for staging early breast cancer with clinically negative lymph nodes: results of randomized trial. *Ann Oncol.* 2009; 20(6):1001–7. [PubMed: 19174453]
129. Moghimi M, et al. Accuracy of sentinel node biopsy in breast cancer patients with a high prevalence of axillary metastases. *Scand J Surg.* 2009; 98(1):30–3. [PubMed: 19447739]
130. Nakashima K, et al. Preoperative dynamic lymphoscintigraphy predicts sentinel lymph node metastasis in patients with early breast cancer. *Breast Cancer.* 2010; 17(1):17–21. [PubMed: 19466508]
131. Cheung TT, Suen DT, Kwong A. Is sentinel lymph node biopsy after neoadjuvant chemotherapy feasible in Chinese patients with invasive breast cancers? *ANZ J Surg.* 2009; 79(10):719–23. [PubMed: 19878167]
132. Nason KS, et al. Increased false negative sentinel node biopsy rates after preoperative chemotherapy for invasive breast carcinoma. *Cancer.* 2000; 89(11):2187–94. [PubMed: 11147588]
133. Martin RC 2nd, et al. Practical guidelines for optimal gamma probe detection of sentinel lymph nodes in breast cancer: results of a multi-institutional study. For the University of Louisville Breast Cancer Study Group. *Surgery.* 2000; 128(2):139–44. [PubMed: 10922983]
134. de Kanter AY, et al. Controlled introduction of the sentinel node biopsy in breast cancer in a multi-centre setting: the role of a coordinator for quality control. *Eur J Surg Oncol.* 2000; 26(7):652–6. [PubMed: 11078611]
135. Yalcin H, et al. Comparison of efficacy of Tc-99m HIG and Tc-99m nanocolloid on sentinel lymph node mapping in patients with breast cancer. *Nucl Med Commun.* 2010; 31(10):903–9. [PubMed: 20683362]
136. Dalus K, et al. Lymphoscintigraphy in breast cancer patients after neoadjuvant chemotherapy. Diagnostic value and the work-up of sentinel node negative patients. *Nuklearmedizin.* 2011; 50(1):33–8. [PubMed: 21336417]
137. Krag DN, et al. Surgical resection and radiolocalization of the sentinel lymph node in breast cancer using a gamma probe. *Surg Oncol.* 1993; 2(6):335–9. discussion 340. [PubMed: 8130940]
138. Pijpers R, et al. Impact of lymphoscintigraphy on sentinel node identification with technetium-99m-colloidal albumin in breast cancer. *J Nucl Med.* 1997; 38(3):366–8. [PubMed: 9074519]
139. Veronesi U, et al. Sentinel-node biopsy to avoid axillary dissection in breast cancer with clinically negative lymph-nodes. *Lancet.* 1997; 349(9069):1864–7. [PubMed: 9217757]
140. Roumen RM, Valkenburg JG, Geuskens LM. Lymphoscintigraphy and feasibility of sentinel node biopsy in 83 patients with primary breast cancer. *Eur J Surg Oncol.* 1997; 23(6):495–502. [PubMed: 9484918]

141. Borgstein PJ, et al. Sentinel lymph node biopsy in breast cancer: guidelines and pitfalls of lymphoscintigraphy and gamma probe detection. *J Am Coll Surg.* 1998; 186(3):275–83. [PubMed: 9510258]
142. Offodile R, et al. Minimally invasive breast carcinoma staging using lymphatic mapping with radiolabeled dextran. *Cancer.* 1998; 82(9):1704–8. [PubMed: 9576292]
143. Miner TJ, et al. Ultrasonographically guided injection improves localization of the radiolabeled sentinel lymph node in breast cancer. *Ann Surg Oncol.* 1998; 5(4):315–21. [PubMed: 9641452]
144. Crossin JA, et al. Gamma-probe-guided resection of the sentinel lymph node in breast cancer. *Am Surg.* 1998; 64(7):666–8. discussion 669. [PubMed: 9655279]
145. Gulec SA, et al. Sentinel lymph node localization in early breast cancer. *J Nucl Med.* 1998; 39(8): 1388–93. [PubMed: 9708514]
146. Krag D, et al. The sentinel node in breast cancer--a multicenter validation study. *N Engl J Med.* 1998; 339(14):941–6. [PubMed: 9753708]
147. Snider H, et al. Sentinel node biopsy in the staging of breast cancer. *Am J Surg.* 1998; 176(4): 305–10. [PubMed: 9817244]
148. Rubio IT, et al. Sentinel lymph node biopsy for staging breast cancer. *Am J Surg.* 1998; 176(6): 532–7. [PubMed: 9926785]
149. Feldman SM, et al. Limitation in gamma probe localization of the sentinel node in breast cancer patients with large excisional biopsy. *J Am Coll Surg.* 1999; 188(3):248–54. [PubMed: 10065813]
150. Winchester DJ, et al. Sentinel lymphadenectomy for breast cancer: experience with 180 consecutive patients: efficacy of filtered technetium 99m sulphur colloid with overnight migration time. *J Am Coll Surg.* 1999; 188(6):597–603. [PubMed: 10359352]
151. Miner TJ, et al. Sentinel lymph node biopsy for breast cancer: the role of previous biopsy on patient eligibility. *Am Surg.* 1999; 65(6):493–8. discussion 498–9. [PubMed: 10366201]
152. Bembenek A, et al. Sentinel lymph node dissection in breast cancer. *Swiss Surg.* 1999; 5(5):217–21. [PubMed: 10546520]
153. Moffat FL Jr, et al. Unfiltered sulfur colloid and sentinel node biopsy for breast cancer: technical and kinetic considerations. *Ann Surg Oncol.* 1999; 6(8):746–55. [PubMed: 10622502]
154. Zurrida S, et al. Radioguided sentinel node biopsy to avoid axillary dissection in breast cancer. *Ann Surg Oncol.* 2000; 7(1):28–31. [PubMed: 10674445]
155. Weaver DL, et al. Pathologic analysis of sentinel and nonsentinel lymph nodes in breast carcinoma: a multicenter study. *Cancer.* 2000; 88(5):1099–107. [PubMed: 10699901]
156. Kowolik JH, et al. Detection of micrometastases in sentinel lymph nodes of the breast applying monoclonal antibodies AE1/AE3 to pancytokeratins. *Oncol Rep.* 2000; 7(4):745–9. [PubMed: 10854537]
157. Casalegno PS, et al. Sentinel lymph node and breast cancer staging: final results of the Turin Multicenter Study. *Tumori.* 2000; 86(4):300–3. [PubMed: 11016708]
158. Gucciardo G, et al. The success rate of identification of the sentinel lymph node in breast cancer: our training series. *Tumori.* 2000; 86(4):312–3. [PubMed: 11016712]
159. Galli A, et al. Study of sentinel lymph node in breast cancer: our experience in 46 cases. *Tumori.* 2000; 86(4):317–9. [PubMed: 11016714]
160. Mechella M, et al. A study of sentinel node biopsy in T1 breast cancer treatment: experience of 48 cases. *Tumori.* 2000; 86(4):320–1. [PubMed: 11016715]
161. Paolo de Rubeis G, et al. The sentinel lymph node in T1N0 breast cancer. *Tumori.* 2000; 86(4): 327–8. [PubMed: 11016718]
162. Hsieh PP, et al. Histopathologic analysis of sentinel lymph nodes in breast carcinoma. *Zhonghua Yi Xue Za Zhi (Taipei).* 2000; 63(10):744–50. [PubMed: 11076431]
163. Sato K, et al. Effocacu and Significance of Sentinel Lymph Node Identification with Technetium-99m-labeled Tin Colloids for Breast Cancer. *Breast Cancer.* 1998; 5(4):389–393. [PubMed: 11091680]

164. Rink T, et al. Lymphoscintigraphic sentinel node imaging and gamma probe detection in breast cancer with Tc-99m nanocolloidal albumin: results of an optimized protocol. *Clin Nucl Med*. 2001; 26(4):293–8. [PubMed: 11290886]
165. Watanabe T, et al. Sentinel node biopsy with technetium-99m colloidal rhenium sulphide in patients with breast cancer. *Br J Surg*. 2001; 88(5):704–7. [PubMed: 11350445]
166. Krag DN, et al. Radiolabeled sentinel node biopsy: collaborative trial with the National Cancer Institute. *World J Surg*. 2001; 25(6):823–8. [PubMed: 11376422]
167. Rink T, et al. Results of a standardized protocol for sentinel node imaging in breast cancer with Tc-99m labeled nanocolloidal albumin. *Nuklearmedizin*. 2001; 40(3):80–5. [PubMed: 11475077]
168. Ishida M, et al. Detection of micrometastasis in the sentinel lymph nodes in breast cancer. *Surgery*. 2002; 131(1 Suppl):S211–6. [PubMed: 11821813]
169. Quan ML, et al. Biology of lymphatic metastases in breast cancer: lessons learned from sentinel node biopsy. *Ann Surg Oncol*. 2002; 9(5):467–71. [PubMed: 12052758]
170. Fonti R, et al. Sentinel lymph node identification in breast cancer patients. *Radiol Med*. 2002; 103(4):370–7. [PubMed: 12107387]
171. Xu M, et al. Sentinel lymph nodes lymphoscintigraphy and biopsy in breast cancer. *Chin Med J (Engl)*. 2002; 115(8):1137–40. [PubMed: 12215277]
172. Mariotti S, et al. Minimal sentinel node procedure for staging early breast cancer. *Tumori*. 2002; 88(3):S45–7. [PubMed: 12365388]
173. Fernandez A, et al. Sentinel node localization in patients with non-palpable breast cancer. *Nucl Med Commun*. 2002; 23(12):1165–9. [PubMed: 12464780]
174. Maza S, et al. Peritumoural versus subareolar administration of technetium-99m nanocolloid for sentinel lymph node detection in breast cancer: preliminary results of a prospective intra-individual comparative study. *Eur J Nucl Med Mol Imaging*. 2003; 30(5):651–6. [PubMed: 12612811]
175. Bourgeois P, et al. How 'hot' is the pathologically positive sentinel lymph node in breast cancer patients? *Nucl Med Commun*. 2003; 24(5):513–8. [PubMed: 12717067]
176. Pargaonkar AS, et al. Evaluation of immunohistochemistry and multiple-level sectioning in sentinel lymph nodes from patients with breast cancer. *Arch Pathol Lab Med*. 2003; 127(6):701–5. [PubMed: 12741893]
177. Veronesi U, et al. A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. *N Engl J Med*. 2003; 349(6):546–53. [PubMed: 12904519]
178. Zavagno G, et al. Sentinel node biopsy in breast cancer. *Breast*. 2000; 9(3):139–43. [PubMed: 14731837]
179. Ellis RL, et al. Periareolar injection for localization of sentinel nodes in breast cancer patients. *Breast J*. 2004; 10(2):94–100. [PubMed: 15009034]
180. Lamichhane N, et al. Sentinel lymph node biopsy in breast cancer patients after overnight migration of radiolabelled sulphur colloid. *Postgrad Med J*. 2004; 80(947):546–50. [PubMed: 15356357]
181. Classe JM, et al. Prospective comparison of 3 gamma-probes for sentinel lymph node detection in 200 breast cancer patients. *J Nucl Med*. 2005; 46(3):395–9. [PubMed: 15750149]
182. Kebudi A, et al. The safety and accuracy of sentinel-node biopsy in early-stage invasive breast cancer--Turkish experience. *J Invest Surg*. 2005; 18(3):129–34. [PubMed: 16036784]
183. Bajen MT, et al. Subdermal re-injection: a method to increase surgical detection of the sentinel node in breast cancer without increasing the false-negative rate. *Eur J Nucl Med Mol Imaging*. 2006; 33(3):338–43. [PubMed: 16307292]
184. Namwongprom S, et al. Breast lymphoscintigraphy for sentinel node identification in breast cancers with clinically-negative axillary nodes. *Singapore Med J*. 2005; 46(12):688–92. [PubMed: 16308641]
185. Lo YF, et al. Radioguided sentinel lymph node biopsy in early breast cancer: experience at Chang Gung Memorial Hospital. *Chang Gung Med J*. 2006; 29(5):458–67. [PubMed: 17214389]

186. Song XY, et al. Different criteria for radioactive sentinel lymph nodes has different impact on sentinel node biopsy in breast cancer patients. *J Surg Oncol.* 2007; 95(8):635–9. [PubMed: 17252554]
187. Yen RF, et al. Radio-guided sentinel lymph node biopsy using periareolar injection technique for patients with early breast cancer. *J Formos Med Assoc.* 2007; 106(1):44–50. [PubMed: 17282970]
188. Zavagno G, et al. Clinical impact of false-negative sentinel lymph nodes in breast cancer. *Eur Surg Oncol.* 2008; 34(6):620–5.
189. Seok JW, et al. Sentinel lymph node identification with radiopharmaceuticals in patients with breast cancer: a comparison of 99mTc-tin colloid and 99mTc-phytate efficiency. *Breast Cancer Res Treat.* 2010; 122(2):453–7. [PubMed: 20532977]
190. Veronesi U, et al. Sentinel lymph node biopsy in breast cancer: ten-year results of a randomized controlled study. *Ann Surg.* 2010; 251(4):595–600. [PubMed: 20195151]
191. Seok JW, et al. Comparison of subareolar injection lymphoscintigraphy with the 1-day and the 2-day protocols for the detection of sentinel lymph nodes in patients with breast cancer. *Ann Nucl Med.* 2009; 23(5):465–9. [PubMed: 19452250]
192. Mudun A, et al. Comparison of different injection sites of radionuclide for sentinel lymph node detection in breast cancer: single institution experience. *Clin Nucl Med.* 2008; 33(4):262–7. [PubMed: 18356664]
193. Gimbergues P, et al. Sentinel lymph node biopsy after neoadjuvant chemotherapy is accurate in breast cancer patients with a clinically negative axillary nodal status at presentation. *Ann Surg Oncol.* 2008; 15(5):1316–21. [PubMed: 18311507]

Figure 1.
Number of articles published per year that report false negative rate.

Figure 2.
The false negative rate according to injection material of dye only, tracer only, or combination of dye and tracer.

Figure 3.

False negative rates for individual studies according to dye only (graph 3A), combination of dye and tracer (graph 3B), and tracer only (graph 3C).

Figure 4.
The false negative rate according to injection location.

Table 1

False negative rate according to injection material and site of injection.

Material	Location	Number of Groups	False-Negative Rate (%)	95% Confidence Interval (%)
Dye-Only	Around Tumor	39	9.38	7.33–11.6
Dye-Only	Areolar	10	4.65	0.88–11.2
Dye-Only	Intratumoral	1	0	0–9.30
Dye-Only	Intradermal	1	14.3	6.01–25.3
Dye-Only	Around Tumor & Areolar	1	27.3	6.31–55.9
Dye-Only	Intradermal & Areolar	1	6.25	0.0001–22.8
Tracer-Only	Around Tumor	50	7.25	5.31–9.47
Tracer-Only	Areolar	5	9.75	4.61–16.5
Tracer-Only	Intradermal	1	0	0–10.3
Tracer-Only	Around Tumor & Intradermal	2	7.61	3.11–13.9
Tracer-Only	Around Tumor & Areolar	1	5.88	0.0001–21.5
Dye-and-Tracer	Around Tumor	66	5.44	4.18–6.86
Dye-and-Tracer	Areolar	3	13.8	6.73–23.0
Dye-and-Tracer	Intratumoral	1	5.10	0.994–12.1
Dye-and-Tracer	Around Tumor & Intradermal	11	6.21	3.78–9.18
Dye-and-Tracer	Around Tumor & Areolar	7	6.80	3.29–11.5
Dye-and-Tracer	Intradermal & Areolar	1	9.38	1.90–21.7