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META-ANALYSIS

^{99m}Tc-labeled colloid SPECT/CT versus planar lymphoscintigraphy for sentinel lymph node detection in patients with breast cancer: a meta-analysis

Natale Quartuccio[1] · Pierpaolo Alongi[1] · Priscilla Guglielmo[2] · Rosaria Ricapito[1] · Gaspare Arnone[1] · Giorgio Treglia[3,4,5]

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Abstract

Background The aim of this meta-analysis was to compare single-photon emission computed tomography (SPECT/CT) and planar lymphoscintigraphy (PL) in patients with primary breast cancer, undergoing lymphoscintigraphy at initial staging. Specifically, we assessed the detection rate (DR) for sentinel lymph node (SLN), the absolute number of detected SLNs by each technique, and the proportion of patients with additional SLNs detected by one technique compared to the other one. Finally, we aimed to evaluate the impact of SPECT/CT on the surgical approach.

Methods Original articles, providing a head-to-head comparison between SPECT/CT and PL, including patients with primary breast cancer at first presentation, were searched in PubMed/MEDLINE and Scopus databases through March 31st, 2022. The DR of the imaging techniques was calculated on a per-patient analysis; studies were pooled on their odds ratios (ORs) with a random-effects model to assess the presence of a significant difference between the DRs of SPECT/CT and PL. The number of additional SLNs, calculated as relative risk (RR), and the pooled proportion of patients with additional SLNs using one imaging technique rather than the other one were investigated. The pooled ratio of surgical procedures (SLN harvesting) influenced by the use of SPECT/CT, according to the surgeons, was calculated.

Results Sixteen studies with 2693 patients were eligible for the calculation of the DR of SPECT/CT and PL. The DR was 92.11% [95% confidence interval (95% CI) 89.32–94.50%] for SPECT/CT, and 85.12% (95% CI 80.58–89.15%) for PL, with an OR of 1.96 (95% CI 1.51–2.55) in favor of SPECT/CT. There was a relative risk of detection of larger number of SLNs (RR: 1.22, 95% CI 1.14–1.32; 12 studies; 979 patients) for SPECT/CT ($n = 3983$) compared to PL ($n = 3321$) and a significant proportion of patients with additional SLNs detected by SPECT/CT, which were missed by PL (18.88%, 95% CI: 11.72%-27.27%; 13 studies). Four articles, with a total number of 1427 patients, revealed that 23.98% of the surgical procedures benefited from the use of SPECT/CT.

Conclusions This meta-analysis favors SPECT/CT over PL for the identification of SLN in patients with primary breast cancer at staging due to higher DR, more SLNs depicted, and a significant proportion of subjects with additional detected SLNs by SPECT/CT compared to PL. Furthermore, SPECT/CT positively influences the surgical procedure. However, PL remains a satisfactory imaging option for imaging departments not equipped with SPECT/CT due to its good patient-based DR.

Keywords Sentinel lymph node · Single photon emission computed tomography · Lymphoscintigraphy · ^{99m}Tc-labeled colloids · Nuclear medicine · Breast cancer · Meta-analysis

Introduction

The rationale for identifying the sentinel lymph node (SLN), namely the lymph node directly draining the primary tumor, relies on the low likelihood of the presence of cancer cells in the subsequent lymph nodes in the case of a non-metastatic SLN [1]. SLN biopsy (SLNB) is indicated as the gold standard technique for the axillary staging of patients with

✉ Giorgio Treglia
Giorgio.Treglia@eoc.ch

Extended author information available on the last page of the article

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breast cancer and no clinical evidence of metastatic nodes [2–4]. SLNB does not increase the risk of axillary recurrence in patients with breast cancer and reduces the risk of lymphedema compared to complete lymph node dissection (CLND) [5, 6].

SLNB reflects the status of the axillary cavity in over 97% of patients with breast cancer [7]. Radionuclide localization of SLN using ^{99m}Tc-labeled colloids in patients with breast cancer is a well-established procedure [8]. Nowadays, planar lymphoscintigraphy (PL) is currently a routine, simple and reliable procedure, performed in most nuclear medicine departments, for the identification of SLN and lymphatic disorders [9, 10]. The inclusion of nuclear medicine procedures for the detection of SLN in the diagnostic workup reduces the false-negative rate of SLNB in patients with breast cancer evaluated at first presentation [11]. Over the last decades, the use of single-photon emission computed tomography/computed tomography (SPECT/CT) has gained wider diffusion in nuclear medicine departments. Indeed, the use of hybrid scanners, providing complementary scintigraphic and morphological data, enables nuclear medicine physicians to offer more accurate information regarding the SLN (e.g. location, number, and surrounding anatomical structures) to the surgeons compared to PL, according to the results of a previous meta-analysis by our group involving patients with melanoma [12].

Whereas an overall superior SLN detection rate (DR) has been reported for SPECT/CT compared to PL in patients with cervical cancer [13] and melanoma [14], such evidence has not been systematically collected for patients with breast cancer.

The aim of this meta-analysis was to perform a head-to-head comparison of the DR of PL and SPECT/CT in patients with breast cancer. Furthermore, as secondary aims, we assessed whether there is a significant difference in the number of detected SLNs, and a significant proportion of patients with additional detected SLNs based on SPECT/CT rather than PL findings or vice versa. Finally, we assessed the ratio of surgical procedures (SLN harvestings) for which SPECT/CT proved a beneficial impact, according to the surgical team.

Materials and methods

The meta-analysis was conducted following the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [15]. Before starting the literature search, a protocol was developed to define the research question, search methods, inclusion criteria, quality assessment, data extraction, and statistical analysis. The protocol was registered in the International Prospective Register of Systematic Reviews, Prospero, (www.crd.york.ac.uk/prospero/;protocol CRD42022307723).

Literature search and inclusion criteria

PubMed/MEDLINE and Scopus databases were interrogated independently by two researchers to retrieve prospective or retrospective single or multicenter studies, carrying out PL and SPECT/CT with ^{99m}Tc-labeled colloids in patients with primary breast cancer at initial diagnosis before the surgical staging of the axilla.

For our primary outcome (comparison of DRs), we selected articles reporting both the DR of PL and SPECT/CT for SLN (at least 1 lymph node per patient). For our secondary outcomes, we selected articles reporting information on (1) the number of SLNs detected by SPECT/CT and PL, (2) the number of patients with additional SLNs detected by SPECT/CT and/or PL, (3) the ratio of surgical SLN harvestings influenced by SPECT/CT.

The search string was designed to capture the concepts of breast cancer, SLN, SPECT/CT, and PL within the title and article abstracts; for PubMed, the search string was Breast AND ("Sentinel Lymph Node"[Mesh] OR sentinel) AND ("Single Photon Emission Computed Tomography Computed Tomography"[Mesh] OR SPECT). For Scopus, the search string was Breast AND ("Sentinel Lymph Node" OR sentinel) AND ("Single Photon Emission Computed Tomography Computed Tomography" OR SPECT).

No date limit or language restriction was applied. The literature search was updated until March 31st, 2022. All identified references were exported to a reference management software (Endnote v. X7.5, Clarivate Analytics).

Study selection

Two investigators independently screened the titles and abstracts of the records retrieved by the search strings. Only original articles were selected. For each outcome of the present meta-analysis, articles from the same author with the risk of patients' overlap were also excluded, selecting only the study with the largest number of patients. Duplicates were identified in Endnote and deleted.

After excluding duplicates and non-original articles, the full text of the remaining articles was retrieved to verify the inclusion criteria for this meta-analysis: (1) a study cohort or a subset of a minimum of 10 patients with breast cancer at initial staging undergoing both SPECT/CT and PL in the same day for the identification of the SLN before surgery; (2) injection of ^{99m}Tc-nanocolloids; (3) no evidence of other malignancies.

Articles in languages other than English had been planned for translation into English by native speakers before performing the meta-analysis. The references of the retrieved

articles were also screened for eventually retrieving additional studies.

Data extraction

Data of all included studies in the meta-analysis were independently extracted by two researchers and any disagreement was resolved in a consensus meeting. Bibliographical and technical data extracted from the articles included: authors, publication year, country, journal, number of patients, sex, and age (mean and range).

For each article, the following data were also retrieved for statistical analysis: the absolute number of patients with at least 1 SLN depicted by SPECT/CT and/or PL, the total number of SLNs detected by SPECT/CT and/or PL, the number of patients with additional SLNs detected by SPECT/CT or PL, the number of patients evaluated for the assessment of the impact of SPECT and PL on the surgical procedure and the number of procedure influenced by the nuclear medicine examination according to the surgeons.

Methodological quality assessment

The methodological quality of the studies was assessed by two investigators using version 2 of the "Quality Assessment of Diagnostic Accuracy Studies" tool (QUADAS-2) [16], which comprises four domains: patient selection, index test, reference standard, flow and timing. The concerns about the risk of bias or applicability were described as low, high, or unclear.

Statistical analysis

Statistical analysis was carried out using MedCalc Statistical Software version 19.1.3 (MedCalc Software, Ostend, Belgium; https://www.medcalc.org; 2020). Publication bias was assessed by visual inspection of funnel plots. The I^2 statistic was used to measure the degree of inconsistency across the studies, with I^2 values of 25%, 50%, and 75% representing thresholds for low, moderate, and high heterogeneity. Interpretation of heterogeneity was carried out at a significance level of $p = 0.05$. A random-effects model was used for statistical pooling.

DR was defined based on the detection of at least one SLN in a single patient. Overall pooled DRs were calculated for SPECT/CT and PL on a per-patient-based analysis and presented using forest plots. To assess any statistically significant difference between the two pooled DRs of SPECT/CT and PL, studies were pooled on their odds ratios (ORs) with an inverse variance-weighted random effects model. Pooled data were presented with 95% confidence interval values (95% CI). A statistical difference of pooled DR among SPECT/CT and PL was present if there was no overlap among the 95% CI values.

The number of SLNs detected by SPECT/CT and PL were compared by pooling the ORs with an inverse variance-weighted random effects model. If the value 1 was not within the 95% CI, then the pooled OR is statistically significant at the 5% level ($p < 0.05$).

The weighted proportion of patients with additional SLNs detected by each technique compared to the other one, and the impact of SPECT/CT on surgery were pooled across the studies and presented in the form of pooled percentages on a per-patient analysis.

Results

Literature search and eligibility assessment

The comprehensive computer literature search from PubMed/MEDLINE and Scopus databases revealed 362 articles (Fig. 1). One-hundred thirty items were duplicates and excluded leading to 232 articles. After excluding non-original articles ($n = 110$), further 102 abstracts were excluded because they were not in the field of interest of the meta-analysis. The full text of the remaining 20 studies was searched; for two studies, the full text was not available despite contacting the corresponding authors. The characteristics of the retrieved 18 studies [17–34] are presented in Table 1, whereas methodological information concerning the acquisition of PL and SPECT/CT in the studies is summarized in Table 2.

The risk of bias for the studies included in the meta-analysis was scored low using the QUADAS-2. No publication bias was detected (Fig. 2).

Sixteen studies, with a total number of 2693 patients, were available for the calculation of the pooled DR of SPECT/CT and PL.

Twelve studies were eligible for the comparison of absolute number of SLNs detected by the two techniques.

Thirteen studies were eligible for calculation of proportion of patients with additional SLNs in one of the two techniques.

Four studies (1427 patients) were eligible for the assessment of the average percentage of patients for whom surgical management was influence by one of the two techniques.

Detection rate of SPECT/CT and PL

In a per-patient analysis, the pooled DR for SLN of SPECT/CT was 92.11% [95% confidence interval (95% CI) 89.32–94.50%], whereas the DR for SLN of PL was 85.12% (95% CI 80.58–89.15%) (Figs. 3 and 4, respectively).

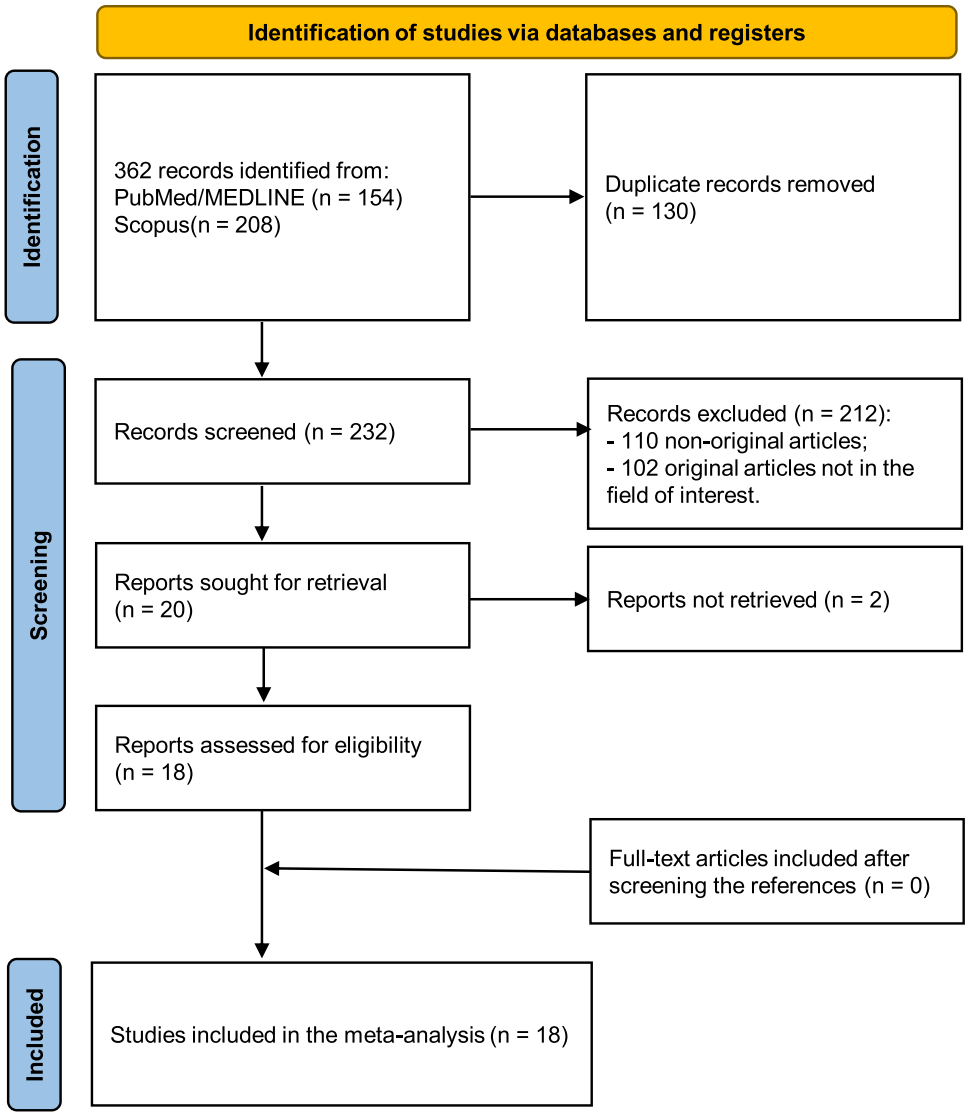


Fig. 1 Flow diagram of the literature search

The DR rate of SPECT/CT for SLN ranged from 77.78% to 100% across the studies. The DR rate of PL for SLN ranged from 59.70 to 100%. A marked statistical heterogeneity was found for SPECT/CT ($I^2 = 78.26\%$) and PL ($I^2 = 86.76\%$). A significant difference between the DRs was found with a pooled OR of 1.96 (95% CI 1.51–2.55) in favor of SPECT/CT ($I^2 = 33.66\%$).

Comparison of the number of SLNs detected by SPECT/CT and PL

SPECT/CT depicted a higher number (3978 vs. 3321) of SLNs compared to PL in 979 patients, with a statistically significant OR of 1.22 (95% CI 1.14–1.32). No study reported a larger number of SLNs depicted by PL compared to SPECT/CT.

Proportion of patients with additional SLNs detected by SPECT/CT or PL

Taking into account a total sample size of 2485 patients, the pooled proportion of patients in whom SPECT/CT depicted additional SLNs compared to PL was 18.88% (95% CI 11.72–27.27%).

The proportion of patients with additional SLNs detected by PL but missed by SPECT/CT was not significant (0.82%).

Impact on surgery of SPECT/CT

The pooled percentage of cases influenced by the use of SPECT/CT according to surgeons (4 studies enrolling 1427 patients) was 23.98% (95% CI 11.34–39.53%), whereas the corresponding proportion of case influenced by PL was 1.5% (95% CI 0.29–3.90%).

Table 1 Characteristics of the eighteen studies selected for the meta-analysis

Authors	Year	Country	Journal	Number of patients	Sex	Age (mean; range) in years
Arican	2013	Turkey	Turk J Surg	76	F	51; 33–87
Bennie	2015	South Africa	World J Surg	38	37 F; 1 M	60 (F), 79 (M)
Brouwer	2012	The Netherlands	Eur J Nucl Med Mol Imaging	50	F	56; 31–84
Frusciante	2016	Italy	Recenti Prog Med	73	F	56; 26–84
Giżewska	2017	Poland	Nucl Med Commun	153	F	58; 29–85
Husarik	2007	Switzerland	Semin Nucl Med	41	F	55; 26–80
Jankowska	2016	Poland	Pomerian J Life Sci	62	F	58
Jimenez-Heffernan	2015	Spain	J Nucl Med	1182	1175 F; 7 M	55
Kraft	2013	Czech Republic	Nucl Med Review	320	F	59
Lecoanet	2010	France	Médecine Nucléaire	51	F	62; 33–83
Lerman	2007	Israel	J Nucl Med	220	F	59; 23–83
Manca	2020	Italy	Clin Nucl Med	21	20 F; 1 M	64; 40–80
Mucientes Rasilla	2008	Spain	Rev Esp Med Nucl	25	F	56; 34–76
Pecking	2007	France	Cancer Treat Res	34	F	34–47
Siddique	2018	Kuwait	Asia Ocean J Nucl Med Biol	134	F	48; 26–82
Stanzel	2018	Austria	Nuklearmedizin	114	F	59; 29–84
van der Ploeg	2009	The Netherlands	Eur J Nucl Med Mol Imaging	134	F	54
Yoneyama	2015	Japan	Ann Nucl Med	56	F	56

F female; *SD* standard deviation; *M* male

Discussion

Radioisotope imaging has a lower false-negative rate than blue dye and there is no significant difference between indocyanine green (ICG) and radioisotope imaging for the SLN detection, according to a recent meta-analysis (a total of 30 studies, including 4,216 SLN procedures), which, nevertheless, did not analyze the impact of SPECT/CT in the detection performance [35].

In this meta-analysis, we focused on articles comparing SPECT/CT and PL in the same patients at initial staging rather including also studies with parallel data collection of SPECT/CT and PL, in keeping with our previous experience [14]. The reason of our choice is that head-to-head comparison provides a more accurate estimate of the outcome measures compared to matched-pair comparison [36]. We limited our analysis to patients at staging, because in case of breast cancer recurrence and previous axillary lymph node dissection (ALND), the repeat sentinel node biopsy has a significantly lower rate of harvesting and a much more aberrant lymphatic [37].

Very high rates of successful SLN detection in patients with breast cancer have been reported with either PL or SPECT/CT [24]. Nevertheless, the use of SPECT/CT has been encouraged by several authors due to substantial advantages over PL, including higher DR, better spatial resolution, more precise anatomical localization of the SLN [38] and efficient attenuation correction through the exploiting the CT data [13, 39, 40]. Conversely, the use of SPECT/CT increases the acquisition time and the radiation dose compared to PL, potentially reducing the patient workflow and bringing additional costs [41].

Our meta-analysis documented a superior DR for SPECT/CT compared to PL and a larger number of SLNs detected by SPECT/CT compared to PL. Higher DR and a larger number of SLNs identified by SPECT/CT in comparison with PL may also determine a meaningful impact on surgical decision-making. Nevertheless, the preoperative use of SPECT/CT for the identification of SLNs is not important only for the additional number of SLNs but also for the capability of providing anatomical information [42]. Indeed, SPECT/CT may also localize unspecific hot spots that could be mistaken as additional SLNs using PL only [43], for example in case of cutaneous contamination, skin fold, propagation from the injection site or leakage from the wire tract [27]. We found a 23.98% of change in surgical approaches in patients with breast cancer. A more precise localization of SLNs may lead to a more precise surgical procedure (due to a change in the location, size and accuracy of the incision), facilitating the surgical planning, reducing the morbidity, the duration of surgical operations and costs [44].

From our analysis, it can be observed that heterogeneity indexes are high either for SPECT/CT ($I^2 = 78.26\%$) or PL ($I^2 = 86.76\%$), which is in contrast with our previous

Table 2 Methodological information of the eighteen studies selected for the meta-analysis

Authors	PL				SPECT/CT						Notes
	Early (min p.i.)	Late (h p.i.)	Views	Matrix	Early	Late	Matrix	Angle(°)	Sec/frame	Reconstruction	
Arican	5	no	A,L	256×256	yes	no	128×128	6	40	nr	SPECT/CT immediately after visualization of the SLN on PL
Bennie	30–45	2	A,O	128×128	yes	yes	128×128	6	25	FBP	SPECT/CT immediately after visualization of the SLN on PL
Brouwer	10	2 and 4	A,L	nr	no	yes	128×128	6	25	nr	SPECT/CT after PL, carried out 4 h p.i
Frusciante	10	no	A,L,O	nr	yes	no	128×128	6	25	OSEM 3D	SPECT/CT immediately after visualization of the SLN on PL
Giżewska	No	1.5–2	A,L	256×256	no	yes	128×128	6	30	OSEM	SPECT/CT immediately after visualization of the SLN on PL
Husarik	20	no	A,O	nr	yes	no	128X128	3	20	OSEM	SPECT/CT started 40 min p.i
Jankowska	No	2.5	A,L,O	256×256	no	yes	128X128	6	10	OSEM	
Jimenez-Heffernan	Time nr	no	A,L,O	256×256	yes	no	128×128	3–4.5	20–40	OSEM	SPECT/CT immediately after visualization of the SLN on PL
Kraft	Time nr	no	A,L	nr	yes	no	128×128	5.625	25	OSEM 3D	SPECT/CT immediately after visualization of the SLN on PL
Lecoanet	Time nr	no	A,L	256×256	yes	no	128×128	5.625	15	OSEM 3D	SPECT/CT immediately after visualization of the SLN on PL
Lerman	0–60	up to 24	A,L	nr	time nr	time nr	nr	nr	nr	nr	Planar images were obtained both before and after SPECT/CT
Manca	30	no	A,L,O	128×128	time nr	no	128×128	3	20	nr	SPECT/CT immediately after visualization of the SLN on PL
Mucientes Rasilla	No	1–1.5 (and up to 20 if needed)	A,L	128×128	yes	yes	128×128	6	20	FBP	SPECT/CT immediately after visualization of the SLN on PL
Pecking	No	16–20	A,L	nr	no	yes	128×128	3	20	OSEM	SPECT/CT started after PL
Siddique	Time nr	time nr	A,L,O	nr	time nr	time nr	128×128	6	25	OSEM 3D	SPECT/CT immediately after PL
Stanzel	No	1–24	A,L	nr	no	time nr	nr	nr	nr	nr	SPECT/CT started after PL
van der Ploeg	10	2 and 4	A,L	nr	no	4 h	128×128	6	25	nr	
Yoneyama	10	3–4	nr	256×256	no	after 3-4 h from PL	128×128	6	20	OSEM	

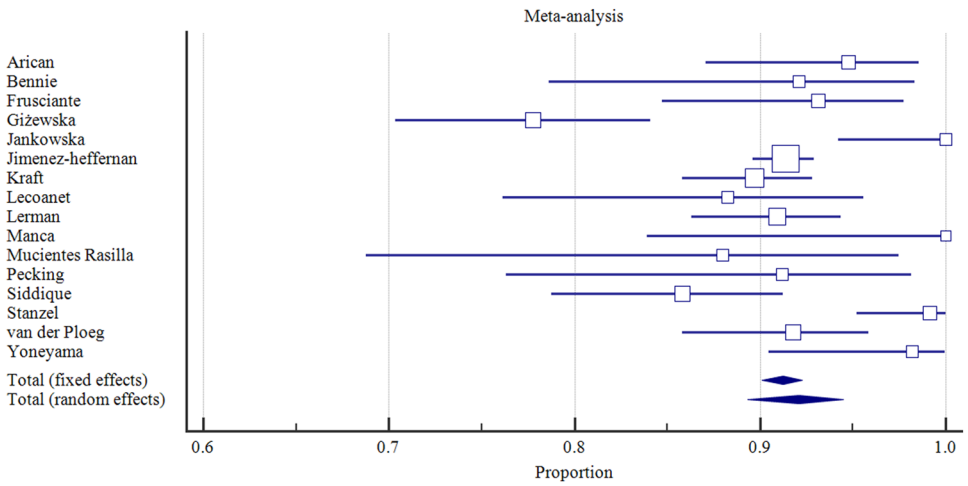
p.i. post-injection; *h* hours; *nr* not reported; *A* anterior; *L* lateral; *O* oblique; *sec* seconds; *FBP* filtered back projection; *OSEM* ordered subset expectation maximization

Fig. 2 QUADAS-2 results

Study	RISK OF BIAS				APPLICABILITY CONCERNS		
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Arican 2013	☺	☹	☺	☺	☺	☹	☺
Bennie 2015	☹	☹	☺	?	☹	☹	☺
Brouwer 2012	☺	☹	☺	☹	☹	☺	☺
Frusciante 2016	☺	☺	☺	☺	☺	☺	☺
Giżewska 2017	☹	☺	☺	☺	☹	☺	☺
Husarik 2007	☺	☺	☺	☺	☺	☺	☺
Jankowska 2016	?	☹	☺	☺	?	☺	☺
Jimenez-Heffernan 2015	☺	☹	☺	?	☹	?	☺
Kraft 2013	☺	☺	☺	☹	☺	☹	☺
Lecoanet 2010	☺	?	?	☺	☺	☺	?
Lerman 2007	☺	☺	☺	☺	☺	☺	☺
Manca 2020	☺	?	☺	☺	☺	☺	☺
Mucientes Rasilla 2008	☺	?	☺	☺	☺	☺	☺
Pecking	?	☺	☺	?	☺	☺	☺
Siddique 2018	☹	☺	☺	☺	☹	☺	☺
Stanzel 2018	☺	☺	?	☺	☺	☺	☺
van Der Ploeg 2009	?	?	☺	?	?	?	☺
Yoneyama 2015	☺	?	☺	☺	☺	☺	☺

☺ Low Risk ☹ High Risk ? Unclear Risk

Fig. 3 Forest plot of the DR for the SLN of SPECT/CT



results in melanoma patients [14], which suggested higher repeatability for SPECT compared PL, as highlighted by the lower heterogeneity index (I^2) obtained for SPECT/CT ($I^2 = 62.45\%$ vs. 78.96%).

van der Ploeg and coworkers suggested three main indications to perform SPECT/CT: (1) inconclusive PL due to unusual lymphatic drainage pattern, (2) difficulty in the interpretation of a lymphatic pattern, and (3) nonvisualization of SLN at PL [45], accounting approximately for a third

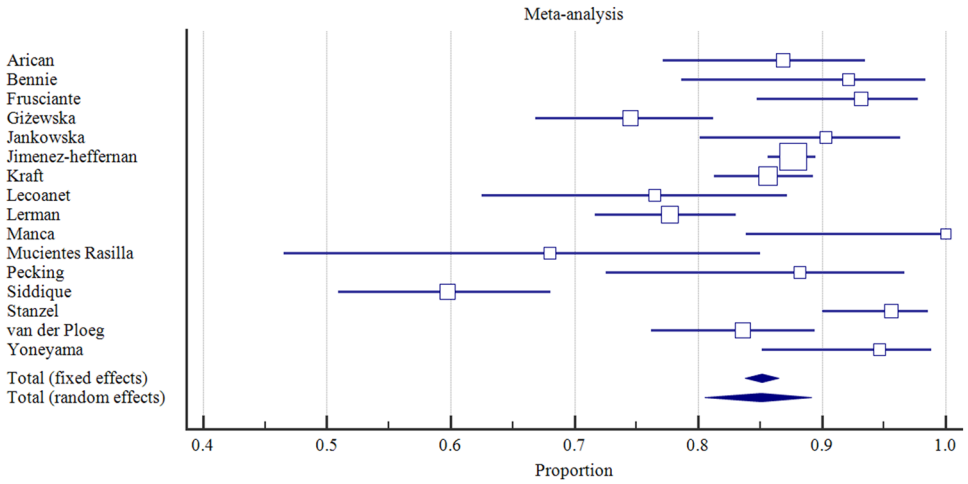


Fig. 4 Forest plot of the DR for the SLN of PL

of patients with breast cancer according to their experience [33]. Also, the recent systematic review of Ge et al., suggest to add SPECT/CT to the diagnostic work-up of patients with breast cancer recurrence when PL fails to detect the SLN, since SPECT/CT may increase the chance of detecting the lymph node also outside the axilla [37].

Certain patient characteristics may also lead to add SPEC/CT to the radioisotope mapping. Increased body mass index (BMI) is a major risk factor for the development of severe lymphedema after ALND [46] and, along with breast size, is also an important factor affecting negatively lymphoscintigraphic and intraoperative SLNs detection [47, 48]. On the other hand, Lerman et al. demonstrated the superior performance of SPECT/CT in identifying SLNs in overweight and obese breast cancer patients, even in case of intraoperative blue dye technique failure, suggesting the indication to routinely perform SPECT/CT in case of high BMIs [27].

The 2013 joint EANM and SNMMI guidelines do not indicate SPECT or SPECT/CT as mandatory, but as optional or alternate imaging, suggesting its use in the case of non-visualization of SLN on PL, obese patients, and SLNs outside the axilla. Otherwise, the execution of SPECT/CT may be justified by the difficulty in the interpretation of PL due to unexpected or unusual lymphatic patterns (e.g. multiple sites of drainage or the appearance of the intramammary lymph node chain, SLN in the contralateral axilla, previous breast surgery, the presence of a SLN near the injection area, or suspicion of contamination) [49]. Conversely, the Chinese Society of Breast Surgery in 2021 attributed a level B (weak) strength of recommendation to lymphoscintigraphy as a mapping method of the SLN, not even mentioning SPECT/CT [50].

The current use of PL as the elective method for radioisotope mapping of the SLN relies on its high detection rate [41]. There are still few data to demonstrate that the addition of SPECT/CT improves staging, since only a few studies reported the histologic data of the SLNs depicted by SPECT/CT but missed by PL [33]. Additionally, there are still no sufficient data to confirm that a higher number of SLN identified by SPECT/CT and removed result in an improvement of control disease. Nevertheless, SPECT/CT is strongly recommended for selected indications, especially when PL fails to detect the SLN, in case of abnormal lymphatic drainage pattern, and for overweight patients.

Some limitations may affect our meta-analysis. The selected studies provided markedly variable sample sizes. Another source of bias may derive from the high heterogeneity of the DR across the studies. Further sources of bias may arise from some differences across the studies including the number of radiotracer injections, and methodology of PL and SPECT/CT execution. As suggestions for further studies, cost-effectiveness analyses should evaluate whether the use of preoperative SPECT/CT compared with PL for SNL detection in breast cancer is associated not only with higher detection of metastatic involvement but also with a significant cost reduction.

Conclusions

The present meta-analysis favors the use of SPECT/CT with ^{99m}Tc-labeled colloids over PL in patients with breast cancer for the identification of SLN due to its superior DR. Further advantages of SPECT/CT over PL are an overall larger number of depicted SLNs, a significant proportion of patients with additional SLNs detected by SPECT/CT but missed by PL, and an impact on surgical strategy on a significant percentage of patients. Nonetheless, in institutions where SPECT/CT is not available, PL remains a good option due to its good DR for the SLN on a patient-based analysis.

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Declarations

Conflict of interest All the authors (Natale Quartuccio, Pierpaolo Alongi, Priscilla Guglielmo, Rosaria Ricapito, Gaspare Arnone, and Giorgio Treglia) declare that have nothing to disclose and did not receive any funding.

Human and animal rights This article does not contain any studies with human or animal subjects performed by the any of the authors.

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Authors and Affiliations

Natale Quartuccio[1] · Pierpaolo Alongi[1] · Priscilla Guglielmo[2] · Rosaria Ricapito[1] · Gaspare Arnone[1] · Giorgio Treglia[3,4,5]

[1] Nuclear Medicine Unit, A.R.N.A.S. Ospedali Civico, Di Cristina e Benfratelli, Palermo, Italy

[2] Nuclear Medicine Unit, IOV-IRCCS, Castelfranco Veneto, TV, Italy

[3] Imaging Institute of Southern Switzerland, Ente Ospedaliero Cantonale, Bellinzona, Switzerland

[4] Faculty of Biology and Medicine, University of Lausanne, Lausanne, Switzerland

[5] Faculty of Biomedical Sciences, Università Della Svizzera Italiana, Lugano, Switzerland