



Incidental findings on single-photon emission computed tomography/computed tomography (SPECT/CT) lymphoscintigraphy in breast cancer: the proposed Westmead SPECT/CT incidental findings classification

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Introduction

Sentinel lymph node biopsy (SLNB) is performed in early invasive breast cancer to stage the axilla, by determining the presence or absence of lymph node metastasis. Lymphoscintigraphy is an imaging technique performed prior to SLNB to map the lymph node basins and identify sentinel lymph nodes. Single-photon emission computed tomography/computed tomography (SPECT/CT) is

Abstract

Background: The aim of this study is to determine the prevalence of incidental radiological findings detected on SPECT/CT performed as part of pre-operative lymphoscintigraphy for sentinel lymph node biopsy (SLNB) in patients undergoing breast cancer surgery and development of a modified classification to workup these lesions.

Methods: A retrospective audit was performed of all SPECT/CT performed in combination with lymphoscintigrams in breast cancer patients presenting with clinically node negative axillae and operated on by breast surgeons at the Westmead Breast Cancer Institute over a 12-month period.

Results: Four hundred and nineteen patients were included in the study. In 149 patients (35.6%), there was a total of 205 incidental findings. The most common findings were, pulmonary abnormalities (38.5%), abdominal findings (27.8%), thyroid nodules (14.6%), cardiac abnormalities (10.7%) and others (8.3%). Using our proposed Westmead SPECT/CT incidental findings (WSIF) classification, 7.8% were known, 17.6% were major findings, 48.3% were minor findings, 15.1% were minimal findings and 11.2% were equivocal findings. 17.6% ($n = 36$) underwent further workup and investigation and 3.4% of patients ($n = 5$) required therapeutic intervention, including chemotherapy for primary lung cancer ($n = 1$) and surgeries (thoracotomy, $n = 1$; thyroidectomy, $n = 2$; colonoscopy, $n = 1$). 93.8% ($n = 393$) had at least one SLN mapped, most commonly located in Level 1 of the axilla.

Conclusion: The incidental findings on SPECT/CT in combination with lymphoscintigraphy is within the range of previous studies (27.3–59.5%). A small proportion of patients required significant major interventions (3.4%). We propose that all incidental findings should be assessed according to our WSIF classification to aid in triaging need for further investigation and management.

incorporated together with lymphoscintigraphy to provide the anatomical location of the sentinel node and facilitate surgical exploration. The integration of low dose radiation CT with SPECT imaging improves image quantification and reduces attenuation artefact.^{1,2} Although the images obtained from low dose radiation CT are considered non diagnostic, they often reveal incidental findings unrelated to the initial diagnostic inquiry.^{1–3}

Incidental findings such as lymphoma⁴ and thyroid lesions⁵ have previously been published in case reports when lymphoscintigraphy is performed prior to SLNB for breast cancer. Although uncommon, these incidental findings require classification to determine which ones require further workup. In some cases, such as diagnosis of lymphoma, patients need further management and treatment. Previous studies have reported the rates incidental findings on SPECT/CT for myocardial perfusion imaging ranging from 27.3% to 59.5%.^{3,6}

An audit was conducted of all SPECT/CT scans performed in combination with lymphoscintigraphy for axillary staging in women undergoing surgery for invasive breast cancer operated on by four breast surgeons at the Westmead Breast Cancer Institute, New South Wales, Australia from September 2019 to September 2020, to investigate the incidental findings and their outcomes.

Methods

Study design

After obtaining approval from the Western Sydney Local Health District Human Research Ethics Committee, all patients who underwent lymphoscintigraphy in combination with SPECT/CT as part of their preoperative work up for axillary staging in the setting of early breast cancer surgery at the Westmead Breast Cancer Institute and surrounding private hospitals between September 2019 and September 2020 were identified from a prospectively maintained database. Patients who needed lymphoscintigraphy in combination with SPECT/CT scan were referred to a variety of public and private nuclear medicine practices, largely based on geography and insurance status.

Two independent investigators (GQ and DG) retrospectively reviewed patient's medical records and relevant investigations. The following data were extracted using a standardized data extraction form: patient and operative characteristics including age, indication for surgery, type of surgery, hospital and nuclear medicine department where lymphoscintigraphy in combination with SPECT/CT scan was performed. The outcomes included number of incidental findings, relevance of incidental findings and outcome of findings.

Classification of incidental findings

All incidental findings were reviewed and classified by our radiologist (LJ) according to our modified version of the classification systems used by Goetze *et al.* in 2006³ and Coward *et al.* in 2014⁶ – the Westmead SPECT/CT incidental findings (WSIF) classification. In the original classification system used by Goetze³ and then adopted by Coward,⁶ incidental findings were divided into major, minor, minimal and equivocal. However, in these classification systems, there was no established follow up system of these incidental findings. In our proposed WSIF classification, incidental findings were divided into five categories as demonstrated in Table 1 – known, major, minor, minimal and equivocal with its proposed follow up system. Patients' medical records were reviewed and correlated with the incidental findings (known category). New incidental findings were classified as being major, minor, minimal or equivocal. Major findings were potentially clinically important findings requiring further investigation to be organized by treating team

or communicated appropriately to the patient's general practitioner (GP) in a timely fashion. Minor findings were most likely clinically unimportant but should be referred to patient's regular GP for monitoring and investigated appropriately if patients become symptomatic, for example findings such as cholelithiasis or non-obstructive renal stones. Minimal findings were classified as being thought to be of no clinical significance and not requiring further follow up or investigations. Equivocal findings were considered as having been incompletely worked up or unable to be characterized based on low dose CT scan requiring additional imaging workup with a modality such as ultrasound (US) for incidental thyroid nodules.

Statistics

Descriptive statistics were reported as mean and percentages. Categorical variables were reported as numbers and percentages, and continuous variables were reported as mean and ranges. Associations between categorical variables were evaluated using chi-square and Fisher's exact test, and t-test was used for continuous variables. A *P*-value of <0.05 was considered statistically significant.

Results

Patient and operative characteristics

Four hundred and thirty-three patients underwent SLNB for invasive breast cancer in the study period. Of those, 14 patients underwent blue dye only without preoperative lymphoscintigraphy in combination with SPECT/CT scan and were excluded from the study. Therefore, a total of 419 patients were included in the study. One hundred and seventy-five patients (41.6%) were operated in public hospitals and 246 patients (58.4%) in private hospitals. The mean age was 58.7 years. All patients underwent surgery for early-stage invasive breast cancer. Three hundred and nineteen patients underwent breast conserving surgery, and 100 patients had a mastectomy with or without reconstruction.

Majority of patients had their preoperative lymphoscintigraphy in combination with SPECT/CT scan in a private radiology centre (*n* = 246, 58.7%) and the remainder at the public hospital – Westmead Nuclear Medicine Department (*n* = 173, 41.3%).

Three hundred and ninety-three out of 419 patients (93.8%) had successful SLN mapping with a median of one SLN mapped. 93.4% (*n* = 367) mapped to Level 1, 5.1% (*n* = 20) to both level 1 and 2, 0.8% (*n* = 3) to level 2, 0.5% (*n* = 2) to the contralateral axilla and 0.3% (*n* = 1) to Level 1,2 and 3. A further 34 patients (8.7%) had lymphoscintigraphy mapping to the ipsilateral internal mammary chain and 11 patients (2.8%) to the supraclavicular lymph nodes.

Incidental findings

One hundred and forty-nine patients (35.6%) had incidental findings on the SPECT/CT scan, with a total of 205 incidental findings. The most common incidental findings were pulmonary (*n* = 79, 38.5%), followed by abdominal (*n* = 57, 27.8%), thyroid (*n* = 30, 14.6%), cardiac (*n* = 22, 10.7%), and others (*n* = 17, 8.3%).

Table 1 Westmead SPECT/CT incidental findings classification

Classification	Description	Thyroid	Pulmonary	Abdomen	Cardiac	Others
Known	Previously known findings or clinical conditions, which do not require further investigation or need to be referred back to primary treating team for further assessment.	Known thyroid nodule or multinodular goitre	Known lung lesions such as metastases, primary lung malignancy or lung nodules Known chronic lung diseases such as chronic obstructive pulmonary disease (COPD), bronchiectasis, tuberculosis (TB), idiopathic pulmonary fibrosis (IPF), sarcoidosis, previous asbestosis exposure	Known liver lesions such as metastases, cyst	Known coronary artery disease	Known contralateral breast lesion Nonspecific lymph nodes
Major	Potentially important finding and requires further investigation in view of clinical information and history. Treating team should be notified and investigation needs to be organized by treating team or communicated appropriately to regular General Practitioner (GP).	Multinodular goitre or enlarged thyroid +/- retrosternal extension +/- trachea deviation	Pulmonary nodule ≥ 6 mm Suspicious lung mass Pleural thickening/effusion	Suspicious liver lesion Suspicious adrenal mass Large right upper quadrant mass of uncertain origin Large exophytic renal lesions	Severe coronary calcification	—
Minor	Less significant than major findings; however, they may have clinical significance and requires follow up with GP in 3–6 months' time and investigated if symptomatic.	Small nodule Mildly enlarged thyroid with no trachea deviation	Pulmonary nodule < 6 mm Calcified granuloma Atelectasis	Benign liver cyst Hiatal hernia Cholelithiasis Non obstructive renal calculi Renal lesions, atrophic kidney Splenic granuloma	Mild to moderate coronary calcification	Spinal haemangioma
Minimal	Minimal or no clinical significance given patient history and does not require further investigations.	—	Lung base scarring	Splenunculus Hepatic steatosis Evidence of previous abdominal surgery	—	Non-specific sclerosis of spine Degenerative changes of spine Spondylosis
Equivocal	Findings unclear, will require appropriate imaging modality to investigate findings to be organized by GP.	Thyroid nodules unable to be characterized on CT	—	Most nonspecific liver lesions	—	—

The incidental findings were assessed using the WSIF Classification as demonstrated in Table 2. Upon correlation with patient's medical records, 7.8% ($n = 16$) of the findings were already known to the treating surgeon. 17.5% of the findings ($n = 36$) were in the major category and required further investigations. Almost half of the findings were in the minor category ($n = 100$, 48.5%) which may have some clinical significance and should be monitored or further investigated by the patient's GP. 11.2% ($n = 23$) were considered equivocal and required further appropriate investigations,

and 15.1% ($n = 31$) were in the minimal category and had no clinical significance.

Only 36 (17.6%) of the incidental findings were investigated in our study, as documented in the medical records. Of these, 20 were in the major category, 4 in the minor category, 5 in the equivocal category and 7 in the Known category. None of the findings in the minimal category were investigated.

Five patients (3.4%) in the major category received further intervention or treatment due to the incidental findings on SPECT/CT

Table 2 Incidental findings according to body regions

Classification	Thyroid	Pulmonary	Abdomen	Cardiac	Others	Total
Known	5	6	1	0	4	16 (7.8%)
Major	3	28	5	0	0	36 (17.6%)
Minor	4	41	31	20	3	99 (48.3)
Minimal	0	4	15	2	10	31 (15.1%)
Equivocal	18	0	5	0	0	23 (11.2%)
Total	30 (14.6%)	79 (38.5%)	57 (27.8%)	22 (10.7%)	17 (8.3%)	205

scan. Three patients had pulmonary pathologies and two patients had thyroid pathology. The first patient had a large mass found in her right lower lobe of lung. She had further investigations including CT chest, CT guided core biopsy and PET scan, which confirmed diagnosis of malignant solitary fibrous tumour. She underwent surgery (Right thoracotomy and excision of tumour) and had an uneventful recovery. The second patient had a 3.3 cm mass in her right upper lobe of lung. CT chest and subsequent biopsy revealed primary lung squamous cell carcinoma. She was referred to the oncology team for further treatment (chemotherapy and radiotherapy). The third patient had multiple bilateral lung nodules measuring up to 7 mm. She had a dedicated CT chest and PET scan which revealed metabolic activity at the colon. Given her history of previous colorectal cancer, she was referred back to her colorectal surgeon who organized a colonoscopy. The colonoscopy revealed benign colon polyps and she was returned to routine surveillance. The fourth patient had a large goitre with retrosternal extension and tracheal compression, mediastinal lymphadenopathy and several small pulmonary nodules, concerning for metastatic disease. Her initial breast surgery was postponed allowing further workup of the thyroid and pulmonary findings, which included staging CT scans and biopsies. She was diagnosed with multinodular goitre with retrosternal extension and pulmonary sarcoidosis with benign mediastinal lymph nodes. She went on to have simultaneous total thyroidectomy and breast conserving surgery. The final patient had an incidental right thyroid nodule, and subsequent investigations confirmed thyroid cancer. She underwent right hemithyroidectomy and had an uneventful recovery.

The mean age of patients with incidental findings (61.9 years) was higher than patients with no incidental findings (57 years) ($P = 0.0002$). Private radiology departments ($n = 80$, 53.7%) were more likely to report a normal lymphoscintigraphy in combination with SPECT/CT compared with public radiology departments ($n = 69$, 46.3%) ($P = 0.0001$).

Discussion

Although there have been previous studies^{3,6,7} on incidental findings on SPECT/CT nuclear medicine studies such as in myocardial perfusion imaging, this is the first case series on incidental findings on SPECT/CT in combination with lymphoscintigraphy for management of breast cancer. Our study highlights the importance of recognizing the incidental findings on SPECT/CT and we propose that they should be managed according to the WSIF classification.

Of the 419 patients who were included in the study, 35.6% had incidental findings, with a total of 205 findings. 7.8% of the findings were known to patients previously. Of the remaining 189 findings, close to a third of the patients (28.8%) may have benefitted from further investigations either due to being classified as major important clinical findings or equivocal findings. A further 48.3% had findings which may be of clinical significance (minor category) and ideally should be monitored by the patient's GP.

The clinical dilemma that prompted this study, and which has been previously described^{1,8} is what to do with the incidental findings encountered on SPECT/CT – which findings are clinically significant and who is responsible for investigating these findings? Indeed, during our study period, only 36 (17.6%) of the incidental findings were documented to have been investigated as we had no established protocol to manage these findings. The incidental findings were mostly investigated after receiving a phone call from the reporting radiologist to alert the treating surgical team to the concerning incidental findings or the lymphoscintigram was being reviewed in our multidisciplinary team meeting. As a result of this study, we identified a further 34 findings (16.6%) which were recommended by our radiologist for further investigations or monitoring (16 in the major category and 18 in the equivocal category) that had not been acted on at the time of reporting as there was no previous established protocol in managing incidental findings in our institution.

The WSIF classification was modified from previously published classifications^{3,6} to aid in triaging and investigating these incidental findings. The main advantage of our modified version is that it provides a clear pathway for clinicians to prioritize which incidental findings should be subject to urgent investigations and which ones could be monitored by the patient's GP. We now recommend that clinically significant findings which may potentially be life threatening in the major category must be investigated by the treating team or communicated to patient's GP in a timely fashion to ensure diagnosis is not delayed (Table 1). 17.6% of findings in our study fall in the major category and 13.9% of patients had subsequent surgery significant pathologies, indicating that these important incidental findings should be worked up. We now recommend, equivocal findings should be investigated with appropriate workup, and this can be managed by the patient's GP. Most of the findings were in the minor category (48.3%) and we recommend that the presence of these findings be communicated to the patient's GP for noting and or action should they become symptomatic. For example, finding of cholelithiasis in a patient with no history of biliary colic.

Following the establishment of our WSIF classifications, we are in the process of retrospectively contacting our patients or their GPs who had the incidental findings in the major or equivocal category (16.6%) that were not initially investigated for further management.

Unsurprisingly, most of the incidental findings were pulmonary (38.5%), like previous studies.^{6,7} The position of the lungs in relation to the breasts meant that SPECT/CT performed to aid lymphoscintigraphy in breast cancer treatment will inevitably include a low dose CT chest. This gives us a unique opportunity to screen for lung metastases in the setting of breast cancer and primary lung tumours. The National Lung Screening Trial in 2002 demonstrated that mortality from lung cancer is reduced from using low dose CT chest as a screening tool.⁹ The WSIF classification adopted the revised 2017 Fleischner Society guideline¹⁰ where pulmonary nodules ≥ 6 mm were classified in the major category and a dedicated CT chest was recommended. Following this algorithm, 35.4% with incidental pulmonary findings in our study were recommended to have a dedicated CT chest and 7.1% of those so far required urgent major intervention.

One of the challenges of incidental findings in SPECT/CT is the high rate of false positives as previously reported by Coward *et al.*^{1,6} This is due to low dose radiation CT scan performed at time of imaging without intravenous (IV) contrast, leading to poor quality of attenuation-correction CT image.^{1,6} We were unable to calculate the false positive findings in our study as only a small proportion of the findings were further investigated, and some incidental findings were still under investigation. Incidental findings on SPECT/CT can lead to over diagnosis of benign tumours which otherwise may not have become symptomatic in a patient's lifetime.^{1,7} Once incidental findings are detected, clinicians may feel obliged to investigate them further, particularly with findings in the major and Equivalent categories. This exposes patients to increased radiation risk, especially if repeated CT scans are required, such as monitoring of pulmonary nodules. On top of this, false-positives incidental findings can increase patient's anxiety and can have a significant negative psychological effect. Over diagnosis and false positives also create an increased financial burden on the healthcare system.¹ With the WSIF classification, we recommend that only incidental findings in the major and Equivalent category be investigated to minimize the potential negative impact on patients and the healthcare system alike. This would roughly amount to only a quarter (28.8%) of our study population. A further 48.3% fall in the minor category and should only be investigated if patients become symptomatic and 15.5% in the minimal category did not require any further follow up or investigations.

There are several limitations to our study. Firstly, some private radiology SPECT/CT films were not available for review and could only be assessed by our radiologist based on the original reports. This is a retrospective study and some incidental findings in the major and Equivalent categories (16.6%) were still being investigated at the time of data collection. Some findings may have been investigated by the patient's GP or by the medical or radiation oncologists later and documented in medical record systems that we did not have access to. We were not able to calculate the false positive rate due to missing data. This is also a relatively short study period of 1 year and certain findings such as pulmonary

nodules require ongoing monitoring for definite diagnosis. A further prospective follow up study to calculate the false positive rates in the incidental findings and assessing the validity of our WSIF classification is planned. We also recommend that the incidental findings are reviewed at an appropriate setting, such as postoperative multidisciplinary meetings.

Conclusion

The prevalence of incidental findings on SPECT/CT in combination with lymphoscintigraphy for SLNB in early breast cancer patients, in our study is 35.6%, with higher clinically significant findings (17.6%) compared with previous studies.^{3,7} 3.4% of our study population underwent major intervention due to these unexpected findings. We propose that all incidental findings should be reviewed and investigated based on our WSIF classification to ensure clinically significant findings are worked up appropriately while minimizing financial and emotional impacts on patients and the health care system.

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Author contributions

Gaik Si Quah: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; visualization; writing – original draft; writing – review and editing. **James R. French:** Conceptualization; methodology; project administration; supervision; validation; visualization; writing – review and editing. **Damon J. Gordon:** Data curation; formal analysis; investigation. **Laximi Y. Juvarkar:** Formal analysis; investigation. **Farid Meybodi:** Writing – review and editing. **Jeremy Hsu:** Validation. **Elisabeth Elder:** Conceptualization; supervision; writing - review and editing.

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