review

High-resolution lymphoscintigraphy is essential for recognition of the significance of internal mammary nodes in breast cancer

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Background: Sentinel node biopsy (SNB) of internal mammary nodes (IMNs) in breast cancer is controversial. Most centers rarely identify IMN on lymphoscintigraphy but others report up to 45% of cases. Controversy relates to the technique of lymphatic mapping, safety of IMN SNB, the significance of positive IMN, and potential to impact survival.

Methods: Assessment of drainage rates from two unrelated nuclear medicine departments’ databases. Review of related literature.

Results: High-resolution lymphoscintigraphy results in IMN drainage in one-third of breast cancers. There is a learning curve for the technique. In 1754 consecutive cases, internal mammary drainage occurred in 53% of medial tumors, 37% midline tumors and 24% of lateral tumors (overall 34%). Extended radical mastectomy series also demonstrate the (approximately) 1/3 ratio when comparing IMN positivity rates to axillary node positivity rates (18.8% : 48.3%) and in node-positive patients (31% : 100%). The management altering potential of IMN assessment and potential survival impact are discussed.

Conclusions: IMN mapping gives information that alters management in up to one-third of cases. These rates of IMN drainage are reproducible and reflect lymphatic density and anatomy of the breast. A priority need exists to establish a collaborative clinical trial to clarify the value of IMN assessment.

Key words: breast cancer, internal mammary nodes, lymphoscintigraphy, sentinel node biopsy

introduction

The extended radical mastectomy (ERM) experience from the 1950s until the 1980s has provided compelling evidence that the presence of internal mammary node (IMN) metastasis in breast cancer is a prognostic factor of similar importance to axillary node positivity. The combination of positive nodes in both areas was shown to be indicative of doubly worse prognosis in nearly all these studies [1–16]. These studies were from a time when the concept of adjuvant therapy was in its infancy. In the 1960s, a large prospective, randomized trial of the International Cooperative Group comparing ERM and radical mastectomy demonstrated no statistical difference in overall survival, relapse-free survival or local-regional recurrence between the two treatment groups at 10-year follow-up [11]. The practice of IMN biopsy then largely fell into irrelevance. The issue of anatomical inaccessibility and logistics of IMN biopsy has seen it become a neglected aspect of breast cancer staging and thus have minimal impact on management decisions over the last 20–30 years. More recently, sentinel node biopsy (SNB) has replaced axillary dissection for staging the axilla [17–22]. Depending on the lymphoscintigraphy technique used and the interest of the nuclear medicine physicians (and the surgeons) involved, the advent of SNB and implementation of lymphatic mapping has seen the documentation of a wide variation in rates of IMN drainage on lymphoscintigraphy. This ranges from not doing lymphatic mapping preoperatively and thus 0% to 45% [23–25]. In centers where the lymphoscintigraphy IMN drainage rate is low then it would clearly have very little impact on clinical practice. In comparison, if surgeons and other members of the multidisciplinary team are working in an environment where the rate of IMN drainage is high, where more than one in three patients have IMN drainage, it is difficult to ignore the information forthcoming.

The relevance of IMN is reviewed starting with the lymphatic anatomy of the breast as this is central to question as to what is the true rate of IMN drainage which has implications on clinical relevance. Previous reviews by authors from Memorial Sloan Kettering Cancer Center [26, 27] and more recently by Chen et al. [28] underestimate the likely potential impact of the IMN on breast cancer management.
technical issues of lymphatic mapping and rates of IMN drainage

High rates of IM mapping success have been attributed to peritumoral injection with technetium antimony sulfide colloid radioisotope [24, 29] (Figure 1). Review of the available literature indicates that this technical explanation is over simplified. It is clear that superficial injections into the subareolar area or dermis over the tumor have a very low chance of showing IMN drainage [25, 30]. However, even in nuclear medicine facilities that use peritumoral injections, there is still a very wide range of drainage rates (see Table 1). This is also the case when comparing groups who use peritumoral injections and the same radioisotope formulation (see Table 1). A good example is the rate of IMN drainage seen at two Australian institutions. Even though both groups use peritumoral injections of antimony sulfide colloid, the rate of IMN drainage reported at that time was 45% versus 6% [24, 31]. The only possible explanation for this is subtle differences in technique can account for large changes in demonstration of IMN drainage. In part, this will relate to the often small size of IMN and their tendency not to retain radioisotope as well as usually larger axillary nodes. This fickleness is compared with the robustness of lymphoscintigraphy for demonstrating axillary node drainage. This can be demonstrated easily when the radioisotope has been placed in all areas of the breast, including deep injection of radioisotope, sub- or intradermal injection, subareolar injection or even just blue dye mapping in experienced hands [20, 24, 25]. Under any of these circumstances, axillary sentinel nodes (SNs) can be demonstrated in >90% of cases. These findings have led many to conclude that IMN drainage is not real.

contemporary anatomy

For many years, the anatomical concept of breast lymphatic drainage was that there is a rich network of lymphatics all draining into a subareolar plexus and then directed to the axilla in larger lymphatic collectors. In addition, a deep lymphaticplexus was described which also drained to the axilla [45]. In 1959, Turner-Warwick [46] convincingly demonstrated that the subareolar plexus was not a key part of the lymphatic drainage of the breast. He found that the lymphatic collectors passed through the breast parenchyma or drained to more superficial collectors in the subcutaneous fat which then drained to the axilla. He also described collectors passing from the posterior surface of the breast to penetrate the pectoralis major muscle and deep fascia, which then passed through the intercostal spaces before coursing medially to reach the IMN [46]. Recent anatomical studies have further confirmed a model of breast lymphatic drainage that comprises superficial, deep and perforating systems [47]. These authors reported that the superficial system drains to the axilla, usually to a lymph node just behind the pectoralis minor muscle. The deep system drains to the axilla and also interacts with the perforating system which drains to the IMNs. In the publication by Suami et al. the authors found the perforating system does not interact with the superficial system [47]. Thus, the frequency of IMN drainage tends to reflect the method of lymphoscintigraphy, where peritumoral (deep lymphatic system) injections have a much higher frequency of IMN drainage than subareolar or subdermal (superficial lymphatic system) injections. This anatomical modeling corresponds precisely with the experience with high-quality lymphoscintigraphy and has been noted by us and other authors for many years now [29, 30]. These lymphatic anatomy concepts are demonstrated in Figure 2.

contemporary lymphatic anatomy as indicated by lymphoscintigraphy

Even in centers where peritumoral injections are used, the widely varying rates of IMN drainage on lymphoscintigraphy are central to the argument about the relevance of IMN biopsy. In a practice where ≤2% of tumors have lymphatic drainage to the IMN, this discussion seems ridiculous. However, as can be seen in Table 1 several authors report drainage up to 38%–45% of their cases. This magnitude of difference seems inexplicable. Ideally anatomy should answer the question of how often different areas of the breast drain to the IMNs. For technical reasons, the elegant demonstrations of Suami et al. [47] discussed above do not allow this type of data to be obtained by their direct visualization method (G. B. Mann, personal communication).

methods and results

We reviewed two unrelated nuclear medicine departments’ performance at demonstrating IMN lymphatic mapping over the periods of time they have carried out lymphoscintigraphy. Each facility’s prospective database was reviewed to document their yearly IMN drainage rates on lymphoscintigraphy over 15 and 7 years, respectively. Lymphoscintigraphy was done at both using a technique of peritumoral injection with technetium-labeled antimony sulfide colloid. In facility U, all patients had ultrasound-guided injection of radioisotope. In facility C, all nonpalpable lesions had ultrasound guidance especially in the later part of the series. The two facilities identified axillary SNs in 95.5% and 93.6% of cases, respectively. Facility U had a mean of 34% IMN drainage rate. The yearly IMN drainage rate varied between 28% and 48% over the 15-year period (overall first 9 years 316 cases at a rate of 33% while later 6 years 1438 cases at a rate of 33%) (Figure 3). Facility C had an overall IMN drainage rate of 29%. The initial drainage rate of 19% fluctuated up to 36% overall over the 7-year period (overall first 4 years 186 cases at a rate of 25% while later 3 years 421 cases at a rate of 31%) (Figure 3). The overall lymphatic drainage

![Figure 1. Complex lymphoscintigraphic mapping demonstrated with clear resolution of axillary and internal mammary nodes using technetium-labeled antimony sulfide colloid.](image-url)
Table 1. Rates of lymphatic mapping to internal mammary nodes by lymphoscintigraphy technique

<table>
<thead>
<tr>
<th>First author</th>
<th>Number of patients</th>
<th>Percentage IM drainage</th>
<th>Radioisotope; dose; injection site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uren [24, 29]</td>
<td>159</td>
<td>45</td>
<td>Antimony sulfide; 10–28 MBq; 0.2 –0.4 ml; pt</td>
</tr>
<tr>
<td>Kollias [31]</td>
<td>117</td>
<td>6</td>
<td>Antimony sulfide; 40 MBq; 0.5–4 ml; pt</td>
</tr>
<tr>
<td>Roumen [32]</td>
<td>66</td>
<td>14</td>
<td>Colloidal albumin; 60 MBq; 2 ml; pt</td>
</tr>
<tr>
<td>Roumen [33]</td>
<td>85</td>
<td>11</td>
<td>Colloidal albumin; 60 MBq; 2 ml; pt</td>
</tr>
<tr>
<td>Reuhl [34]</td>
<td>96</td>
<td>2</td>
<td>Colloidal albumin; 54 MBq; 0.5 ml; pt</td>
</tr>
<tr>
<td>Borgstein [35]</td>
<td>130</td>
<td>16</td>
<td>Colloidal albumin; 40 MBq; 4 ml; pt</td>
</tr>
<tr>
<td>Estourgie [36]</td>
<td>691</td>
<td>22</td>
<td>Nanocolloid albumin; 115 MBq; 0.2 ml; it</td>
</tr>
<tr>
<td>Jansen [37]</td>
<td>113</td>
<td>15</td>
<td>Colloidal albumin; 40–60 MBq; 0.2 ml; it</td>
</tr>
<tr>
<td>Van der Ent [38]</td>
<td>256</td>
<td>25</td>
<td>Nanocolloid albumin; 570 MBq; 1 ml; pt</td>
</tr>
<tr>
<td>Moffat [39]</td>
<td>70</td>
<td>9</td>
<td>Sulfur; 37 MBq; 4–8 ml; pt</td>
</tr>
<tr>
<td>Hill [40]</td>
<td>35</td>
<td>7</td>
<td>Sulfur; 11 MBq; ni; pt</td>
</tr>
<tr>
<td>Johnson [41]</td>
<td>41</td>
<td>12</td>
<td>Albumin; 111 MBq; 0.3 ml; pt</td>
</tr>
<tr>
<td>Noguchi [42]</td>
<td>43</td>
<td>7</td>
<td>Tin or albumin; 30–50 MBq; 2.5 ml; pt</td>
</tr>
<tr>
<td>Imoto [43]</td>
<td>43</td>
<td>7</td>
<td>Tin colloid; 30–80 MBq; subtumoral</td>
</tr>
<tr>
<td>Shimazu [23]</td>
<td>40</td>
<td>38</td>
<td></td>
</tr>
</tbody>
</table>

Table modified significantly from Cserni and Szekeres [44].
IM, internal mammary; pt, peritumoral; it, intratumoral; ni, not indicated.

Figure 2. (Modified) Suami et al. model of breast lymphatic anatomy [47]. Tumor location in depth and medial versus lateral site relates to the observed lymphatic drainage pattern.

results at facility U in a consecutive series of 1754 patients’ IM drainage occurred in 53% of medial tumors, 37% midline tumors and 24% of lateral tumors (overall 34%). These data are described in more detail and are documented in Table 2.

discussion
improving lymphatic mapping IMN rates
The increasing IMN drainage rate at facility C was associated with increasing volume of cases and modifications in technique including increased use of ultrasound to localize the tumor. The practice also had upgrades of collimators and increasing awareness of the referring surgeons’ interest in this pathway of lymphatic drainage. These data indicate that the rate of IMN drainage is around one-third of the axillary drainage rate. Technical modifications have resulted in facility C converging on this parameter which has been maintained over many years by facility U. It is our opinion that in the absence of a reliable anatomical model, high-quality lymphatic mapping with peritumoral injections is the best known demonstrator of breast
lymphatic anatomy. An institution finding lower rates of IMN drainage reflects technical issues and not the anatomy of the breast. The remarkably constant rate of positive lymph nodes irrespective of the IMN drainage rate (discussed below) is supportive of these conclusions. Further supportive evidence is the rate of positive IMNs in the review of ERM series by Bevilacqua et al. [27] is 18.8% in unselected series compared with the axillary node positivity rate of 48%. This ratio approximates 39% which is similar to the high-quality lymphoscintigraphy rates of IMN drainage. Also in Bevilacqua’s review, the rate of IMN positivity in nonselective case series in the axillary node-positive cases was 31% [27]. This implies that SNs in both node fields were at some stage positive and thus the ratio of axillary to IMN positivity should be a reflection of the anatomical density of the lymphatics draining to each. Again, these data are in a consistent range similar to the lymphatic drainage rate from high-quality lymphoscintigraphy.

relevance of IMN biopsy

Transpectoral IM biopsy of SNs mapped on lymphoscintigraphy is of debatable relevance. This is principally due to the lack of conviction that it is a valuable addition to the staging information derived from standard histopathology and axillary assessment [26]. It is also due in part to the technical difficulty of surgical access, concern about potential complications of the procedure and a lack of technical expertise among many breast surgeons. Furthermore, many authors question the validity of IM biopsy in this day of early breast cancer diagnosis where most decisions on systemic therapy are made on primary tumor characteristics and increasingly on tumor genetic profiling. One publication recommended that by using a selection algorithm, IM biopsy should be reserved for tumors that are subcentimeter, medial location and proven to be axillary node negative. The authors argued that adjuvant treatments will not be changed otherwise [27].

Others have argued from clinical experience that the information from IMN biopsy changes management in a significant minority of patients [48, 49]. Higher level evidence of the contemporary relevance of IMN positivity can be extrapolated from two at first seemingly unrelated data sources. First, review of large databases has shown that medial tumors have a worse prognosis than lateral tumors [50–53]. This has been explained in all situations by the higher rates of IMN involvement being underrecognized (under staging) and therefore patients being effectively undertreated with adjuvant therapy. The second line of evidence is from a series of 604 early breast cancer patients including 104 who had IMN drainage but none of the IMNs were biopsied. The 5-year overall survival and recurrence-free survival outcomes were worse in those patients with IMN drainage. Axillary node-positive patients with lymphatic mapping to IMN had a 3.3-fold higher mortality risk (trending toward significance) [54]. This possibly indicates that even without the knowledge of the results of transpectoral IMN biopsy, the presence of anatomically identifiable IMN drainage may be enough prognostic evidence to influence management. For instance, from the ERM era, in circumstances where the patient is young, the tumor is large and medial, and the axilla is known to be positive then there maybe in excess of 40% chance of a positive result [3]. If you further select this case type by the demonstration of IMN lymphatic drainage, it is debatable whether transpectoral IMN biopsy is indicated as a strong case can be made for IMN radiotherapy in any case. These separate sources of data indicate relevance to doing lymphoscintigraphy with or without transpectoral SNB in all women including those with known positive axillary nodes.

**IMN positivity rates**

Even though the rates of IMN drainage vary widely on lymphoscintigraphy, there is evidence from a number of sources that there is a similar and significant frequency of positive IM sentinel lymph node metastasis. This rate ranges in a narrow band from 13% to 23.5% of the cases that have IMN drainage on lymphoscintigraphy who are able to be successfully biopsied (Table 3). This is in groups of patients who were clinically axillary node negative in the vast majority of cases and hence SNB was being done principally to stage the axilla. The ERM series mentioned above document several noteworthy points. First, the rate of IMN metastasis is significantly higher when the axilla is positive. Secondly, the rate of IMN metastases

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**Table 2.** Facility U lymphoscintigraphy rates for 1754 consecutive cases

<table>
<thead>
<tr>
<th></th>
<th>Medial tumors, n = 406</th>
<th>Central and midline tumors, n = 394</th>
<th>Lateral tumors, n = 943</th>
<th>All tumors, n = 1754</th>
</tr>
</thead>
<tbody>
<tr>
<td>AN</td>
<td>90.2</td>
<td>96.2</td>
<td>97.6</td>
<td>95.5</td>
</tr>
<tr>
<td>Not AN</td>
<td>9.9</td>
<td>3.8</td>
<td>2.4</td>
<td>4.5</td>
</tr>
<tr>
<td>IMN</td>
<td>52.7</td>
<td>37.8</td>
<td>24.4</td>
<td>33.9</td>
</tr>
<tr>
<td>Not IMN</td>
<td>47.3</td>
<td>62.2</td>
<td>75.6</td>
<td>66.1</td>
</tr>
<tr>
<td>Neither IMN nor AN&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.9</td>
<td>2.8</td>
<td>2.1</td>
<td>2.7</td>
</tr>
<tr>
<td>IMN, not AN&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5.9</td>
<td>1.0</td>
<td>0.3</td>
<td>1.8</td>
</tr>
<tr>
<td>Total&lt;sup&gt;b&lt;/sup&gt;</td>
<td>23.2</td>
<td>22.5</td>
<td>53.6</td>
<td>100.0</td>
</tr>
</tbody>
</table>

AN, axillary node lymphatic drainage; IMN, internal mammary node lymphatic drainage.
Table 3. Rates of internal mammary drainage and positivity compared with axillary status in contemporary series

<table>
<thead>
<tr>
<th>Author, total number of SNB cases</th>
<th>Year, country</th>
<th>% Ax positive</th>
<th>% IMN drainage</th>
<th>% IMN biopsied</th>
<th>% IMN positive</th>
<th>% IMN + if ALN negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Madsen [48], n = 506</td>
<td>2007, The Netherlands</td>
<td>41</td>
<td>22</td>
<td>78</td>
<td>24</td>
<td>N/A</td>
</tr>
<tr>
<td>Farrús [55], n = 225</td>
<td>2004, Spain</td>
<td>27</td>
<td>14</td>
<td>69</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Hong [49], n = 979</td>
<td>2005, Australia</td>
<td>32</td>
<td>15 (33°)</td>
<td>88</td>
<td>18</td>
<td>4</td>
</tr>
<tr>
<td>Paredes [56], n = 383</td>
<td>2005, Spain</td>
<td>N/A</td>
<td>14</td>
<td>73</td>
<td>25</td>
<td>20</td>
</tr>
<tr>
<td>Leidenius [57], n = 984</td>
<td>2006, Finland</td>
<td>40</td>
<td>14</td>
<td>88</td>
<td>15</td>
<td>44</td>
</tr>
<tr>
<td>Estourgie [56], n = 691</td>
<td>2003, The Netherlands</td>
<td>33</td>
<td>22</td>
<td>87</td>
<td>17</td>
<td>7</td>
</tr>
<tr>
<td>Dupont [58], n = 1273</td>
<td>2001, USA</td>
<td>N/A</td>
<td>2.4</td>
<td>N/A</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>Mansel [59], n = 707</td>
<td>2004, UK</td>
<td>26</td>
<td>10</td>
<td>45</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>Spillane [60], n = 100</td>
<td>2008, Australia</td>
<td>33</td>
<td>31</td>
<td>81</td>
<td>20</td>
<td>60</td>
</tr>
</tbody>
</table>

*Initial figure is surgeon reported; figure in parentheses is obtained after publication directly from nuclear medicine facility.

Ax, axillary lymph node positive rate; ALN, axillary lymph node; N/A, not available.

is nearly double when assessing medial/central tumors versus lateral tumors. Clearly, the likelihood of metastases to these IMNs relates to the frequency of lymphatic drainage to IMN from these different regions of the breast. Thirdly, the overall rate of IMN positivity in the review of ERM series, when adjusted for selection bias, was 18.8% [27]. This is about three to four times the current SNB series range which ranges from ≤4% to 7% of all cases (20% of the ~34% of cases that have IMN mapping) (Table 3). The ERM series have ~50% of cases with positive axillary nodes often with clinically apparent disease, compared with more recent studies where most SNB series have axillary node positivity rates ranging from 26% to 41% but in patients who are clinically axillary node negative [24, 33, 59]. This significant stage migration in axillary node positivity and disease burden rates with earlier diagnosis would intuitively be expected to reflect in a similar quantum stage migration with the rate of IMN positivity. Even taking this into account, the current reported rates of IMN-positive nodes in units doing transpectoral SNB indicate that the rate of IMN positivity is still lower than you would expect from this extrapolation. This raises the question of a significant false-negative result from transpectoral IMN biopsy. Other confounding factors in interpretation of these data include the possibility of a selection bias in the current SNB series for medial cases where the information from the IMN SNB is thought to be more relevant and a separate surgical incision would not be necessary. This is not obvious from the publications but is possible. However, if this was happening, it would indicate a higher false-negative rate in the biopsy technique as the IMN-positive rates should be higher in medial sector tumors. On the other hand, another factor that may lead to underestimation of positivity rates in the old ERM series is the different pathology protocols used for assessing SNs compared with lymph node assessment before SNB. This may have lead to missed IMN micrometastatic disease in the ERM series. Although the rates of micrometastatic disease were not discussed in the ERM series, the ratios of IMN to axillary node positivity should remain an accurate reflection of breast lymphatic pathways and this should still be relevant today. In the ERM study by Veronesi et al. [3], the rates of IMN positivity ranged up to 44% in axillary node-positive women who were <40 years old and had medial tumors ≥2 cm in maximum diameter. Even in axillary node-negative younger women, it was up to 17% IMN positivity. This study, as did the others related to adjuvant therapy naive ERM, demonstrated very significant prognostic importance of this information equivalent to that derived from axillary node status if either was positive but doubly worse if both were positive [3, 5]. Again, it should be emphasized that this is not just information that confirms ‘node positivity’.

**Survival impact of IMN metastasis**

There is strong evidence that patients with IM metastasis have significant reduction in survival. Historical series of ERM demonstrated poor survival of these patients at all stages [3, 12, 61]. The ERM series are essentially observational in that the diagnosis of IMN disease did not change adjuvant systemic therapy. For the most part, chemotherapy and radiotherapy was not given. Certainly, the results of the IMNs did not lead to changes in management that have subsequently been shown to be effective in improving survival. Thus, in the randomized controlled trial of the International Cooperative Group, the survival equivalence was a test of surgery’s ability to improve survival, not a test of the information derived from IMN biopsy to alter the systemic and radiotherapy managements that are now known to improve survival [11, 12]. As will be discussed in the subsequent paragraph, a recent publication by Veronesi et al. [62] suggest an influence on survival from taking the results of IMN biopsy and giving IMN/supraclavicular radiotherapy for positive cases.

**IMN sampling**

Veronesi et al. have recently published their results of sampling from the upper intercostal spaces in medial breast cancers. In this series, 38% of cases were guided by the gamma probe after peritumoral injection of radioisotope. The positivity rate was 11% in these cases and 9.8% in the remaining women whose IMN biopsies were not guided by a gamma probe. Overall 68 of 663 patients had positive IMN. The patients with positive nodes all had IMN radiotherapy. The cohort’s excellent 5-year survival was in part attributed to this radiotherapy [62].
Exploring the second and third intercostal spaces would identify just over half of our IMN SN sites.

**false-negative rates of IMN biopsy**
IMN biopsy is a technically challenging procedure in some instances. This is particularly in the lower intercostal spaces where the gap between the ribs is smaller. When identified on lymphoscintigraphy, the rates of successful IMN SN retrieval reported in the literature range from 45% to 88% [36, 49, 59]. This is from centers interested in the procedure. The difficulties not often discussed include if a lymphoscintigraphy indicates hot spots in multiple intercostal space levels, are they all SNs or are some second tier lymph nodes? It is known that IMNs are less efficient at retaining radiocolloids than are axillary nodes. A single collector may thus radiolabel a string of IMNs but only the lowest node directly receiving the draining collector is the true SLN. Thus, how many spaces need to be explored? Removing a lymph node from the indicated space does not necessarily mean it was the SN as there are often multiple lymph nodes at each level. The use of peritumoral injections for lymphoscintigraphy in medial tumors may have a shine through effect making lymphatic mapping less reliable. The hot and/or blue node may also be under the rib and not retrievable in some cases. Lateral tumors with IMN drainage may not be explored because of the concern about having to make a cosmetically unpleasant separate incision. These factors all add to the potential for a false-negative transpectoral IMN biopsy.

**IMN biopsy and minimal access breast surgery**
A number of authors have now documented that the majority of IMN SNB can be done through the breast incision and there is no need for a separate parasternal incision in the majority of cases [63]. In a series of 100 cases of attempted minimal access breast surgery for axillary and IMN SNB, only 1 of 21 IMN SNBs required a separate incision. That patient had augmentation implants [60].

**management altering potential of IMN biopsy results**
If the IMN is positive after transpectoral biopsy, there is a strong indication from the literature that most radiation oncologists will recommend radiotherapy to that area [48, 49, 62]. Conversely, if the IMN is not positive, many radiation oncologists use that information to guide them against giving radiotherapy to that area. If it is a high-risk case for loco-regional relapse, then the absence of IMN drainage on lymphatic mapping may be used by some centers as a guide to indicate no probability of additional benefit to IMN radiotherapy. Depending on the axillary node status, the decision to give postmastectomy radiotherapy or not may be determined by any additional IMN involvement. Until results from current clinical trials are available many centers use three or more axillary nodes as their threshold for postmastectomy radiotherapy.

In light of our concerns regarding the false-negative rate of both IMN sampling and IMN SNB, there may be a reasonable argument to give radiotherapy to high-risk patients who demonstrate IMN mapping on good quality lymphoscintigraphy. However, more research would be needed if IMN mapping were used as a surrogate marker to guide adjuvant radiotherapy decisions. There is growing evidence that good quality chest wall radiotherapy alone confers a survival benefit and this maybe in part due to inadvertent treatment of these nodes [64]. The exact role of IMN radiotherapy in any situation is still controversial as was fully discussed in Bevilacqua’s review [27]. This is unlikely to be resolved by the European Organization for Research and Treatment of Cancer Trial (EORTC-22922) as cases were not selected using information from high-quality lymphoscintigraphy.

As also pointed out by Bevilacqua et al. [27], the decision on whether to give chemotherapy or not is not often solely based on having a positive IMN. This is because many such decisions are made on primary tumor characteristics. Another reason cited is that most cases of IMN positivity also have axillary lymph node positivity [27]. However, a positive IMN result may contribute information that alters the amount of chemotherapy given, particularly if working in a center that escalates the number of cycles of chemotherapy based on the degree of lymph node positivity. An underrecognized factor, when making adjuvant therapy decisions in this situation, is that axillary and IMN positivity has been associated with a doubly worse prognosis in the past. In the small tumors with negative axillary SNB but positive IMN SNB, this information maybe crucial to determining whether to have chemotherapy.

**conclusions**
IMN drainage on lymphoscintigraphy is more difficult to demonstrate than axillary node drainage. This is due to technical reasons and not the absence of anatomically real lymphatics to the IMN. There are multiple sources of data indicating that IMN drainage occurs in about one-third of breast cancers but is more common in medial tumors. There is evidence now that therapy is altered in a substantial proportion of patients by the knowledge of IMN drainage and biopsy of IMN by transpectoral SNB. There is evidence that survival is worse in patients who have IMN drainage ignored when planning adjuvant therapy. The best way to clarify the situation is to design a clinical trial designed for assessing these areas of controversy. This would be the only way to resolve the importance of IMN in a contemporary population of breast cancer patients.

**funding**
The Mater Hospital to AJS; Cancer Institute of NSW to FN.

**references**


