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Axillary Reverse Mapping in Breast Cancer

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1. Introduction

Axillary lymph node dissection represents the standard surgical treatment for breast cancer patients with clinically or histologically involved axillary lymph nodes. However, it is associated with significant morbidity, including postoperative arm lymphedema and neuropathy of the involved extremity, and seroma formation in the axilla (Noguchi et al., 1997). Particularly, arm lymphedema develops in 7%- 77% of patients who undergo axillary lymph node dissection (Blanchard et al., 2003; Leidenius et al., 2005; Haid et al., 2002; Mansel et al., 2006; Ronka et al., 2005; Schijven et al., 2003; Schrenk et al., 2000; Swenson et al., 2002). At present, sentinel lymph node biopsy is accepted as the standard method of surgical staging for axillary lymph nodes in breast cancer. It can avoid unnecessary axillary lymph node dissection in node-negative patients, thereby minimizing arm lymphedema. Nevertheless, node-positive patients who undergo axillary lymph node dissection do not benefit from sentinel lymph node biopsy. Moreover, sentinel lymph node biopsy does not completely eliminate arm lymphedema. Several cooperative group trials have shown lymphedema rates in range of approximately 7% with sentinel lymph node biopsy alone (Sakorafas et al., 2006; Wilke et al., 2006).

Recently, the axillary reverse mapping technique has been developed to map and preserve arm lymphatic drainage during axillary lymph node dissection and/or sentinel lymph node biopsy (Nos et al., 2007; Thompson et al., 2007). This technique is based on the hypothesis that the lymphatic pathway from the arm cannot be involved by metastasis of the primary breast cancer. The assumption is that the lymphatic drainage from the upper arm is different from that of the breast, allowing safe removal of only the lymphatics of the breast and protection of the lymphatic channels draining the upper extremity during axillary lymph node dissection or sentinel lymph node biopsy, thereby preventing arm lymphedema. However, several studies have shown that there are limits to the principle of non-overlap between breast and arm nodes, including: (a) the axillary reverse mapping nodes may be involved with metastatic foci in patients with extensive axillary lymph node metastases (Bedrosian et al., 2010; Kang et al., 2009; Noguchi et al., 2010b; Nos et al., 2008; Ponzone et al., 2009), and (b) the sentinel lymph node draining the breast may be the same as the axillary reverse mapping node draining the upper extremity in some patients (Boneti et al., 2009; Britton et al., 2009; Kang et al., 2009; Noguchi et al., 2010b). Therefore, the oncological safety of this procedure has not yet determined. This article presents a review of current knowledge regarding in the axillary reverse mapping procedure, and discusses its practical applicability and relevance.

2. Lymph nodes and lymphatics from the breast and the upper extremity

Knowledge of the lymphatic pathway from the breast tissue is essential for the diagnosis and treatment of axillary lymph node metastases in breast cancer. Sappey's classic studies of the lymphatic anatomy of the chest wall are familiar to most physicians (Sappey, 1874) **(Fig. 1)**. Sappey distinguished a superficial group of lymphatics originating in the skin over the breast (subcutaneous lymphatics) and a deep group draining the mammary gland itself (intramammary lymphatics). The superficial and intramammary lymphatics anastomose extensively in the breast, and flow from the two lymphatic groups moves centrifugally toward the axillary and internal mammary nodes. Particularly, the axillary lymph nodes constitute the major regional drainage site for breast cancer. Sappey reported that the lymphatics of the breast collected in a subareolar plexus and then drained toward the axilla *via* lymph collecting vessels. Rouviere (1932), Grant et al. (1953), and Borgstein et al. (2000) supported Sappey's concept of the subareolar plexus for the breast lymph drainage. However, Turner-Warwick (1959), Spratt (1979), Tanis et al. (2001), and Suami et al. (2008) observed that lymphatic pathways from the breast drained directly into the axilla without first passing through the subareolar plexus. Thereby, two potential routes of lymphatic connections from the breast parenchyma to the axilla have been suggested: (a) direct lymphatic connections from the breast parenchyma to the axilla and (b) drainage of parenchyma *via* the subareolar complex into the axillary lymph nodes **(Fig. 2)** (Noguchi, 2009). This knowledge is important with regard to the optimal injection site for identifying sentinel lymph node in breast cancer, because subareolar injection may not always identify the same sentinel lymph node as peritumoral injection (Noguchi et al., 2009).

On the other hand, superficial and deep lymphatics from the upper extremity always flow into the axillary lymph node (called the "sentry node") **(Fig. 3)** (Suami et al., 2007a, 2007c).In the upper extremity, there is usually no communication between the superficial and deep lymphatics except in the epitrochlear region (Suami et al., 2007b). The superficial and deep lymphatics differ in that the former go straight to the axillary lymph nodes, whereas the

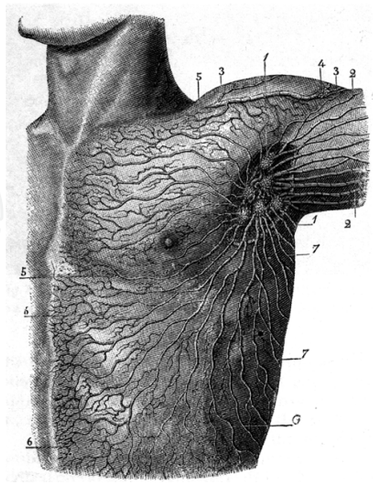


Fig. 1. **Sappey's drawing of the superficial lymphatics of the upper torso.** [Reprinted from Sappey, M.P.C. In A. Delahaye and E. Lecrosnier (Eds.), Anatomie, Physiologie, Pathologie des Vaisseaux Lymphatiques Consideres Chez l'Homme et Les Vertebres. Paris: Adrien Delahaye, 1874].

latter first pass through several interval lymph nodes before reaching the axilla. Thereafter, the lymphatics pass through several lymph nodes before merging into one vessel to reach the subclavian vein (Suami et al., 2007b). In the axilla, however, there are lymphatic interconnections between lymph nodes draining the upper extremity and nodes draining the breast (Suami et al., 2007a).

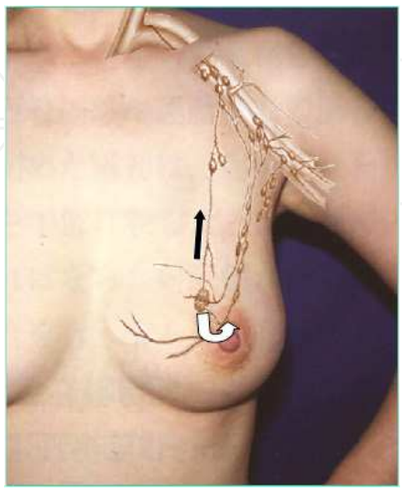


Fig. 2. **Lymphatic flow from the breast tumor to the axilla.** The black arrow shows a direct lymphatic connection from the breast parenchyma to the axilla and the white arrow shows drainage of the parenchyma *via* the subareolar complex into the axillary lymph nodes.

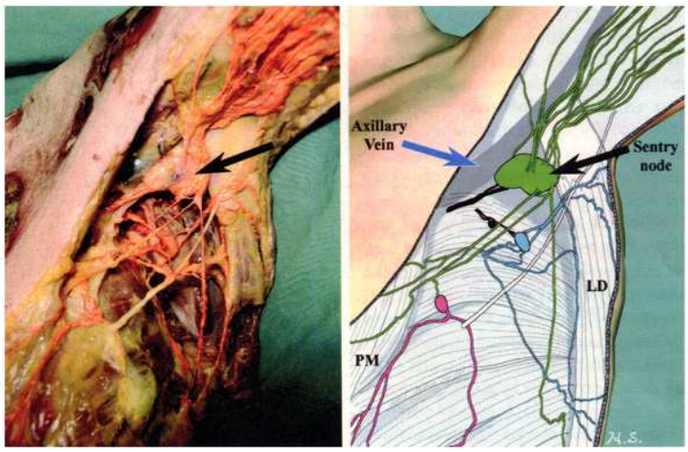


Fig. 3. **Lymphatic anatomy in the axilla.** Left: The left axilla region of the dissected male specimen; Right: a schematic diagram of the same area. The sentry node (black arrow) was connected with the lymphatics from both the upper limb and the upper torso (green). (Reprinted from Suami H: Plast Reconstr Surg 122: 1231-1239, 2008).

3. Axillary reverse mapping

The concept of axillary reverse mapping involves mapping the drainage of the arm with blue dye to determine the anatomical variation in these lymphatics and thus to provide a

roadmap for their preservation (Klimberg, 2008). Five variations of axillary reverse mapping lymphatics have been identified: (1) above or below the axillary vein; (2) a sling pattern that may come as much as 4 cm below the axillary vein; (3) a lateral apron; (4) a medial apron; and (5) a twine of cord-like pattern of multiple small nodes. All of these usually emanate from the arm just lateral to the thoracodorsal vessels just under the axillary vein—the so-called axillary ring (Klimberg, 2010). Variations in arm lymphatic drainage put the arm lymphatics at risk for disruption during axillary lymph node dissection or sentinel lymph node biopsy. If arm lymphedema is caused by cutting axillary lymphatics, then being able to see and identify them would allow their preservation. In effect, "axillary reverse mapping is the reverse of sentinel lymph node mapping that serves to map and then remove the lymph nodes draining the breast; axillary reverse mapping involves mapping the arm drainage to allow its preservation" (Klimberg, 2008) **(Fig. 4)**. This procedure is based on the hypothesis that the lymphatic pathway from the arm is not involved by metastasis of the primary breast cancer (Ponzone et al., 2008). However, the preservation of axillary reverse mapping nodes and/or lymphatics is not always possible, because oncological radicality with complete lymphatic preservation may be difficult (Ponzone et al., 2008).

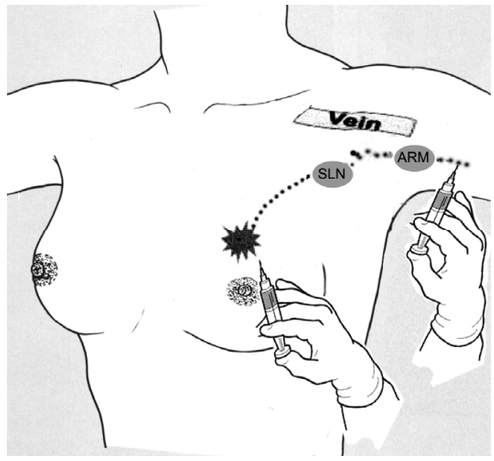


Fig. 4. **Concept of axillary reverse mapping.** Drainage from the breast sentinel lymph node and other lymph nodes from the breast rarely overlap with the lymphatics draining the arm. (Reprinted from Noguchi M : Breast Cancer Res Treat 119:529-535, 2010)

On the other hand, the extent of lymphatic channel disruption required to cause clinically significant lymphedema is unknown. However, it has been suggested that identification and preservation of axillary reverse mapping nodes and/or lymphatics are essential for decreasing postoperative lymphedema rates (Boneti et al., 2008). Boneti et al. (2008) observed the development of lymphedema in 2 of 12 patients in whom the axillary reverse mapping node and/or lymphatics were sacrificed, whereas no lymphedema occurred in patients in whom the axillary reverse mapping node was spared regardless of whether sentinel lymph node biopsy alone or axillary lymph node dissection was performed. In our previous study (Yokoi et al., submitted), 5 of 100 patients developed lymphedema after a mean follow-up of 8 months: 3 patients had undergone axillary lymph node dissection with removal of axillary reverse mapping nodes and lymphatics, and 2 patients had undergone sentinel lymph node biopsy with removal of axillary reverse mapping nodes because the SLN was the same as the axillary reverse mapping node. Although the follow-up has been

short in this study, no lymphedema occurred in the remaining patients who had undergone sentinel lymph node biopsy without removal of axillary reverse mapping nodes. As prevention is the key to avoiding lymphedema (Boneti et al., 2008), preservation of axillary reverse mapping nodes and/or lymphatics is worthwhile. If axillary reverse mapping can be confirmed to be both safe and effective in preventing lymphedema, this technique will become the most important technological advancement since sentinel lymph node biopsy.

4. Mapping of axillary reverse mapping node and lymphatics

4.1 Mapping by blue dye injection

Several investigators have reported feasibility studies of the axillary reverse mapping procedure using blue dye **(Fig. 5)** (Boneti et al., 2008; Casabona et al., 2008, 2009; Nos et al., 2007; Ponzone et al., 2008; Thompson et al., 2007). Thompson et al. (2007) injected 2.5 mL of blue dye intradermally or subdermally into the upper inner arm along the medial intramuscular groove of the ipsilateral arm. After injection, the site was massaged and the arm elevated for 5 min to enhance arm lymphatic drainage. Consequently, blue lymphatics and/or nodes in relation to axillary reverse mapping were identified in 11 of 18 (61%) patients, although no blue lymphatics or nodes were identified in the remaining 7 patients. In the same year, Nos et al. (2007) identified axillary reverse mapping nodes in 15 of 21 patients (71%) using a similar technique. Subsequently, several investigators identified axillary reverse mapping nodes using blue dye (Boneti et al., 2008, Casabona et al., 2008; Casabona et al., 2009; Ponzone et al., 2008).

However, identification rates of axillary reverse mapping nodes using blue dye alone were insufficient, ranging from 61% to 86% (Boneti et al., 2008; Casabona et al., 2009; Nos et al., 2007; Ponzone et al., 2008; Thompson et al., 2007) **(Table 1),** and the blue staining at the injection site may persist for up to 6 months after injection (Thompson et al., 2007). To use axillary reverse mapping, moreover, surgeons must use only isotope in the breast to use blue dye in the arm (Klimberg, 2008). This would not be acceptable for those surgeons who believe that the blue dye and radioisotope techniques are complementary for identifying sentinel lymph nodes (Albertini et al., 1996; Noguchi et al., 2000; Noguchi et al., 2009).

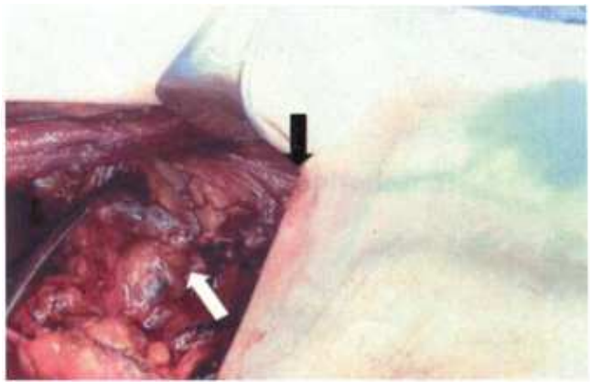


Fig. 5. **Blue axillary reverse mapping lymphatic.** The blue dye tattoo is shown on the inner aspect of the left upper arm in this patient. The white arrow shows a "lateral apron" of blue nodes well below the axillary vein, which is at the level of the black arrow (Reprinted from Klimberg VS: J Surg Oncol 97:563-564, 2008).

Method of ARM procedure Authors/Years	No. of ARM procedures	Identification rates of ARM (ALND field)	Identification rates of ARM (SLN biopsy field)
(a) Blue dye			
Thompson et al. (2007)	18	Nodes/lymphatics: 61% (11/18)	/
Nos et al. (2007)	21	Nodes: 71% (15/21)	/
Ponzone et al. (2007)	4	Nodes/lymphatics: 50% (2/4)	/
Boneti et al. (2008)	131	/	Lymphatics: 43% (56/131)
Casabona et al. (2009)	72	Lymphatics: 89% (8/9)	Lymphatics: 38% (27/72)
(b) Isotope			
Nos et al. (2008)	23	Nodes: 91% (21/23)	/
Britton et al. (2009)	15	Nodes: 100% (15/15)	/
(c) Fluorescence			
Noguchi et al. (2010b)	20	Nodes/lymphatics: 88% (7/8)	Nodes/lymphatics: 75% (9/12)
Yokoi et al. (submitted)	100	Nodes: 93% (25/27)	Nodes: 37% (27/73)

ALND: Axillary lymph node dissection; ARM: Axillary reverse mapping; SLN: sentinel lymph node.

Table 1. Results of Axillary Reverse Mapping Procedure

4.2 Mapping by isotope injection

To improve the identification rate of the axillary reverse mapping nodes and to prevent a persistent blue stain at the site of injection, Nos et al. (2008) injected an isotope into the web space of the ipsilateral hand. During axillary lymph node dissection, the radioactive axillary reverse mapping node was localized above the second intercostal brachial nerve, and then blue dye was injected directly into the node to visualize the efferent ducts constituting the lymphatic axillary reverse mapping chain. Consequently, the axillary reverse mapping nodes were identified in 21 of 23 patients (91%) **(Table 1)**. However, this procedure may be somewhat cumbersome and result in longer operating time. Moreover, direct injection into the axillary reverse mapping node using a syringe with high pressure may cause backflow into the sentinel lymph node, thereby increasing the rate of sentinel lymph node and axillary reverse mapping node confluence. On the other hand, Britton et al. (2009) injected ^{99m}Tc-human polyclonal immunoglobulin G into the breast to identify the sentinel lymph node and injected ^{111}In-human polyclonal immunoglobulin G into the hand to identify axillary reverse mapping nodes. In the specimen of axillary lymph node dissection, the axillary reverse mapping nodes were identified postoperatively in all of 15 patients (100%) using a well scintillation counter **(Table 1)**. Thus, radioisotope labeling seems to be more sensitive for detecting axillary reverse mapping nodes than use of blue dye alone. Identification rates of axillary reverse mapping nodes were improved by using radioisotope with or without blue dye (Britton et al., 2009; Nos et al., 2008). However, radioisotope alone does not permit the visual mapping of axillary reverse mapping lymphatics (Nos et al., 2008).

4.3 Mapping by fluorescent imaging

We have used an invisible near-infrared fluorescence imaging system (PhotoDynamic Eye; Hamamatsu Photonics, Hamamatsu, Japan) for identifying the axillary reverse mapping

nodes and/or lymphatics **(Figs. 6 & 7)** (Noguchi et al., 2010b; Yokoi et al., submitted). Before the surgical prep, a smaller volume of indocyanine green (0.1 mL, 0.25 mg) (Diagnogreen; Daiichi Pharmaceutical, Tokyo, Japan) was injected into the forearm to decrease the risk of long-term tattooing, and the injection site was massaged until fluorescent axillary reverse mapping lymphatics were observed in the upper inner arm. During axillary lymph node dissection or sentinel lymph node biopsy, the light was occasionally switched off in the operating room and fluorescent axillary reverse mapping nodes and/or lymphatics were observed in the axilla using the fluorescence imaging system. Consequently, the axillary reverse mapping nodes were identified in 25 (93%) of 27 patients who underwent axillary lymph node dissection alone (Yokoi et al., submitted) **(Table 1).** Although the fluorescent axillary reverse mapping nodes and/or lymphatics were not observed in 2 patients, they were early cases in the study (Noguchi et al., 2010b). Thus, the fluorescence imaging technique is useful for detecting lymphatic drainage from the upper extremity, and it also permits differentiation of fluorescent axillary reverse mapping nodes and/or lymphatics from blue and/or hot sentinel lymph nodes (Noguchi et al., 2009).

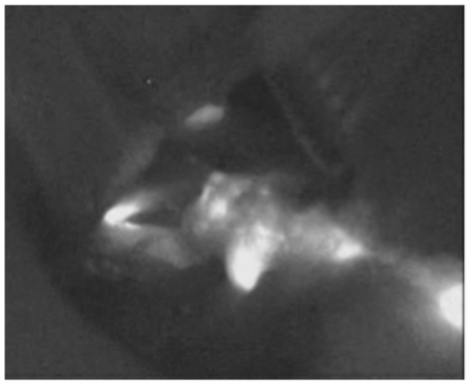


Fig. 6. Fluorescence imaging in the upper extremity.



Fig. 7. Fluorescence imaging in the axilla.

5. Mapping of axillary reverse mapping node and lymphatics in the fields of axillary lymph node dissection and sentinel lymph node biopsy

Generally, identification of the axillary reverse mapping nodes is not sufficient in patients undergoing sentinel lymph node biopsy alone (Boneti et al., 2008; Casabona et al., 2009;

Noguchi et al., 2010b). Boneti et al. (2008) reported that blue lymphatics draining the arm were visible from the sentinel lymph node biopsy incision, and so were located near or within the sentinel lymph node field in 56 (42.7%) of 131 patients. Casabona *et al.* (2009) also reported the blue lymphatics draining from the arm in the sentinel lymph node biopsy field in 27 of 72 patients (37.5%). Similarly, in our recent study, axillary reverse mapping nodes were identified in 27 (37%) of 73 patients who underwent sentinel lymph node biopsy. In the remaining 46 patients, however, the axillary reverse mapping node was not observed in the sentinel lymph node field (Yokoi et al., submitted), suggesting that the ARM nodes were located in different fields with respect to the sentinel lymph node area. In these studies (Boneti et al., 2008; Casabona et al., 2009; Noguchi et al., 2010b; Yokoi et al., submitted), a difference was observed in the identification rate of axillary reverse mapping nodes and/or lymphatics in the axillary lymph node dissection field and in the sentinel lymph node field **(Table 1)**. This may be because the majority of lymphatics draining the arm are anatomically located deeper than the sentinel lymph node (Casabona et al., 2009). This hypothesis is consistent with the higher incidence of lymphedema after axillary lymph node dissection than after sentinel lymph node biopsy (Celebioglu et al., 2007; Lucci et al., 2007; McLaughlin et al., 2008; Schrenk et al., 2000).

6. Metastases in axillary reverse mapping nodes

The concept of axillary reverse mapping is based on the hypothesis that the lymphatic pathway from the arm is not involved by metastasis of the primary breast cancer (Ponzone et al., 2008). Initial studies showed that no cancer cells were found in the ARM nodes even when the patients had many positive axillary nodes (Boneti et al., 2008; Casabona et al., 2009; Thompson et al., 2007) **(Table 2)**. Subsequently, they preserved the axillary reverse mapping nodes in patients in the later series (Boneti et al., 2008; Thompson et al., 2007).

Authors/references	No. of patients	No. of patients with ARM involvement	% of ARM involvement
Thompson et al. (2007)	7	0	0%
Nos et al. (2007)	10	0	0%
Boneti et al. (2008)	7	0	0%
Nos et al. (2008)	21	3	14%
Ponzone et al. (2009)	27	3	11%
Kang et al. (2009)	101	9	8.9%
Bedrosian et al. (2010)	11	2	18%
Noguchi et al. (2010)	7	3	43%
Yokoi et al. (submitted)	25	11	44%

ARM: axillary reverse mapping

Table 2. The Involvement of Axillary Reverse Mapping Nodes in Patients who underwent Axillary Lymph Node Dissection with Removal of Axillary Reverse Mapping Nodes

However, recent studies have demonstrated involvement rates of axillary reverse mapping node ranging from 8.9% to 44% **(Table 2)**. In a study performed in France, Nos et al. (2008) reported that the axillary reverse mapping nodes showed metastatic involvement in 3 of 21 patients with N0-3 (14%). Ponzone et al. (2009) also found that three patients with extensive nodal metastatic involvement (*i.e.*, pN2a and pN3a) showed metastatic cells in the axillary reverse mapping nodes, although the ARM was clear of metastases in the remaining 24 (89%) of 27 patients. In a large study, Kang et al. (2009) reported that ARM node metastases were found in 9 (8.9%) of 101 patients who underwent axillary reverse mapping procedure. In our recent study (Yokoi et al., submitted), on the other hand, the axillary reverse mapping nodes were positive in 11 (44%) of 25 patients with a clinically positive node who underwent axillary lymph node dissection without sentinel lymph node biopsy. The fluorescence imaging system was highly sensitive for identification of the fluorescent axillary reverse mapping nodes, and the excised axillary reverse mapping nodes were cut into serial sections at 2 mm intervals for the histological examination (Noguchi et al., 2010b). This may increase the detection of metastatic axillary reverse mapping nodes. It is not surprising that the axillary reverse mapping nodes could be involved by metastasis of the primary breast cancer, because of anatomical interconnections between lymphatics draining from the upper extremity and lymphatics draining from the breast (Suami et al., 2007a). It has been suggested that effacement of nodes by the gross tumor may alter the pattern of lymph flow in these patients, allowing metastasis to the axillary reverse mapping nodes.

7. Convergence of axillary reverse mapping node and sentinel lymph node

The sentinel lymph node is most commonly located in the central nodal group, and it is possible that the axillary reverse mapping nodes are located in the central nodal group. If the sentinel lymph node draining the breast were the same node as the axillary reverse mapping node draining the upper extremity, it would be impossible to preserve the axillary reverse mapping node at sentinel lymph node biopsy. Boneti et al. (2009) reported that crossover (axillary reverse mapping node = sentinel lymph node) occurred in only 6 (2.2%) of 220 patients, although axillary reverse mapping lymphatics were near or within the sentinel lymph node biopsy field in 40.6% of patients. However, Britton et al. (2009) reported that sentinel lymph node from the breast was the same as the axillary reverse mapping node from the upper extremity in 2 (13%) of 15 patients, indicating convergence of the two drainage pathways through the same node. Kang et al. (2009) also reported a concordance rate of 18.9% (19/96) between axillary reverse mapping node and sentinel lymph node. Noguchi et al. (2010b) reported that the sentinel lymph node from the breast was the same as the axillary reverse mapping node from the upper extremity in 3 (21%) of 14 patients **(Fig. 8)**. In our recent study (Yokoi et al., submitted), the sentinel lymph node from the breast was the same as the axillary reverse mapping node from the upper extremity in 20 of 27 patients in whom axillary reverse mapping nodes were identified, but the axillary reverse mapping node was not observed in the sentinel lymph node field in the remaining 46 patients, yielding a concordance rate of 27% (20/73) between axillary reverse mapping node and sentinel lymph node **(Table 3)**. These findings were supported by a recent anatomical description of the lymphatic territories of the upper extremity (Suami et al., 2008). Removal of this common lymph node at sentinel lymph node biopsy will result in disruption of lymphatic drainage of the upper extremity and an increased risk of lymphedema, explaining why sentinel lymph node biopsy does not correct the problem of

lymphedema (Schrenk et al., 2000; Sener et al., 2001; Wilke et al., 2006). This is an important limitation of the axillary reverse mapping procedure (Khan & Lurie, 2009), although the axillary reverse mapping lymphatics vary significantly from patient to patient.

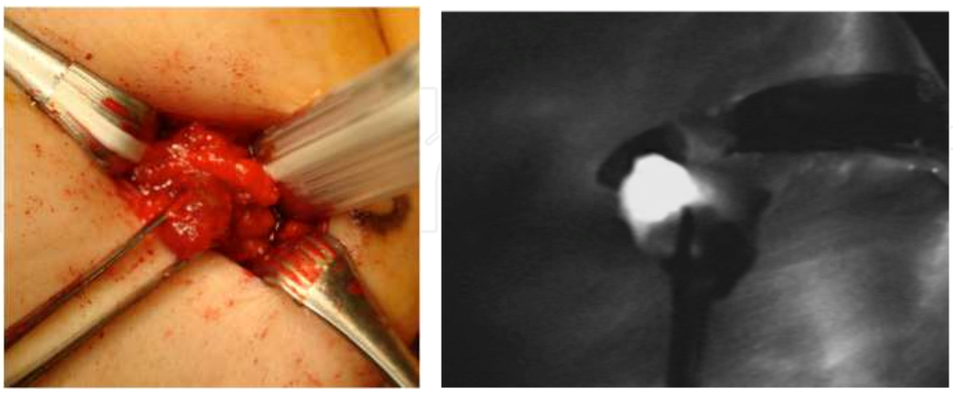


Fig. 8. **Sentinel lymph node and axillary reverse mapping node.** Left: sentinel lymph node biopsy: A hot and blue node was identified. Right: Fluorescence imaging by Photodynamic Eye: A fluorescent ARM node in the axilla, which is the same as the SLN.

Authors/references	No. of patients	No. of patients with converged sentinel lymph node – axillary reverse mapping node	Rates of convergence (%)
Boneti et al. (2009)	220	6	2.2%
Britton et al. (2009)	15	2	13%
Kang et al. (2009)	96	19	18.9%
Noguchi et al. (2010)	14	2	14%
Yokoi et al. (submitted)*	73	20	27%

*: This study included patients from the previous study (Noguchi et al., 2010).

Table 3. Concordance of sentinel lymph node and axillary reverse mapping nodes in patients who underwent sentinel lymph node biopsy and axillary reverse mapping procedure.

8. Preservation of axillary reverse mapping node and lymphatics

Several studies have demonstrated that the axillary reverse mapping nodes are involved with metastatic foci in some patients with extensive axillary lymph node metastasis (Bedrosian et al., 2010; Kang et al., 2009; Noguchi et al., 2010; Nos et al., 2008; Ponzone et al., 2009; Yokoi et al., submitted). Therefore, patients with suspected extensive nodal disease at clinical examination, ultrasonography of the axilla, or intraoperative pathologic assessment

should not be candidates for preservation of axillary reverse mapping nodes and lymphatics (Ponzone et al., 2009). On the other hand, the SLN draining the breast is the same node as the axillary reverse mapping node draining the upper extremity in some patients (Boneti et al., 2009; Britton et al., 2009; Kang et al., 2009; Noguchi et al., 2010; Yokoi et al., submitted). It is impossible to preserve converged sentinel lymph node – axillary reverse mapping node, although the excision of one converged node does not always translate into lymphedema, because multiple lymphatic channels drain the arm. Thus, there is no reliable separation of arm and breast lymphatic pathways, because there are lymphatic interconnections between lymph nodes draining the upper extremity and nodes draining the breast.

However, it has been suggested that patients with clinically uninvolved nodes might derive the most benefit from the axillary reverse mapping procedure (Ponzone et al., 2009). In a previous study by Boneti et al. (2009), 220 patients with clinically uninvolved nodes underwent sentinel lymph node biopsy and axillary reverse mapping procedure. Forty of these patients subsequently underwent axillary lymph node dissection because of positive sentinel lymph nodes. Consequently, axillary reverse mapping nodes were negative for malignancy. In our recent study (Yokoi et al., submitted), axillary reverse mapping node was identified in 27 of 73 patients with clinically uninvolved nodes who underwent sentinel lymph node biopsy, and it was the same as the sentinel lymph node in 20 patients. In 11 patients with a positive sentinel lymph node who subsequently underwent axillary lymph node dissection, however, axillary reverse mapping nodes were tumor-free as far as it was not the same as the positive sentinel lymph node. Therefore, it may be possible to spare the remaining axillary reverse mapping nodes during axillary lymph node dissection in patients with clinically negative node but positive sentinel lymph node.

To minimize prolonged seroma and prevent arm lymphedema, on the other hand, Kodama routinely performed lower axillary dissection without using either axillary reverse mapping or sentinel lymph node biopsy. The lower axillary dissection is defined as dissecting axillary lymph nodes only below the second intercostal brachial nerve. Consequently, they found that the 5-year overall and relapse-free survival rates were 95.3% and 88.3%, respectively, in 1043 clinically node-negative patients from 2001 to 2008 (Kodama et al., 2010). They were not significantly different from those of 1084 clinically node-negative patients who underwent total or partial axillary lymph node dissection from 1994 to 2000 (94.9% and 88.4%, respectively). Only 6 (0.6%) of 1043 patients developed axillary recurrence with a median follow-up of 72 months, while no lymphedema occurred. Although axillary reverse mapping nodes are usually localized above the second intercostal brachial nerve, therefore, it may be oncologically safe to spare axillary lymph nodes and lymphatics above the second intercostal brachial nerve in patients with clinically negative nodes. However, sentinel lymph node is not infrequently located above the second intercostal brachial nerve, and the axillary reverse mapping procedure is a more accurate means of preserving lymphatics from the upper extremity than partial axillary lymph node dissection. Therefore, sentinel lymph node biopsy followed by axillary lymph node dissection with axillary reverse mapping is oncologically more safe than the lower axillary dissection in patients with clinically negative nodes.

9. Microsurgical lymphatic-venous anastomosis

It is not always possible to preserve ARM nodes and/or lymphatics during axillary lymph node dissection or sentinel lymph node biopsy. Therefore, Casabona et al. (2008, 2009)

performed microsurgical lymphatic-venous anastomosis using lymphatic collectors coming from the arm and one of the collateral branches of the axillary vein. Lymphatic collectors were introduced inside the vein and the inferior edge of the lymphatics introduced into the vein lumen acted as valves to avoid backflow of blood into the lymphatics (Campisi et al., 2007), thus preventing the occurrence of thrombosis. In fact, lymphatic microsurgery techniques have been shown to be effective in the treatment of peripheral lymphedema (Campisi et al., 2007). To perform lymphatic-venous microanastomosis, however, the axillary reverse mapping lymphatics must be visible and preserved as much as possible during axillary lymph node dissection, while maintaining oncological radicality.
On the other hand, postmastectomy radiotherapy is currently accepted as a standard adjuvant treatment in patients with more than 4 positive axillary nodes (Noguchi et al., 2002; Recht et al., 2001). According to the Guidelines of the American Society of Clinical Oncology (Recht et al., 2001), the chest wall as well as the supraclavicular region should be irradiated, whereas full axillary radiotherapy should not be performed routinely in patients undergoing axillary lymph node dissection. In postmastectomy radiotherapy, the lymphatic-venous microanastomosis in the axilla can be exposed to non-negligible irradiation as tangents with chest wall irradiation. It is well known that arm lymphedema can be caused by scar formation from surgery and/or radiation therapy. Therefore, long-term follow-up studies are required before we can conclude that this microsurgical technique is effective for prevention of arm lymphedema even after postmastectomy radiotherapy.

10. Conclusions

The axillary reverse mapping procedure is not completely accurate in differentiating between the arm and breast lymphatic pathways. The ARM node is involved with metastatic foci in some patients with extensive axillary lymph node metastasis. Moreover, the sentinel lymph node draining the breast is the same node as the axillary reverse mapping node draining the upper extremity in a minority of patients. It is oncologically unacceptable to preserve a metastatic axillary reverse mapping node in axillary lymph node dissection or converged sentinel lymph node – axillary reverse mapping node in sentinel lymph node biopsy. In patients with a positive sentinel lymph node who subsequently underwent axillary lymph node dissection, however, remaining axillary reverse mapping nodes are tumor-free as far as it is not the same as positive sentinel lymph node. Therefore, it may be oncologically safe to spare the axillary reverse mapping nodes during axillary lymph node dissection only in patients with clinically uninvolved nodes. Further studies are needed before this technology can be accepted as a standard procedure in the surgical management of breast cancer. On the other hand, it is not always possible to preserve ARM nodes and/or lymphatics during axillary lymph node dissection. Therefore, microsurgical lymphatic-venous anastomosis may be effective for prevention of arm lymphedema in patients who underwent axillary lymph node dissection with removal of axillary reverse mapping nodes. However, long-term follow-up studies are required before we can conclude that it is effective for prevention of arm lymphedema even after postmastectomy radiotherapy.

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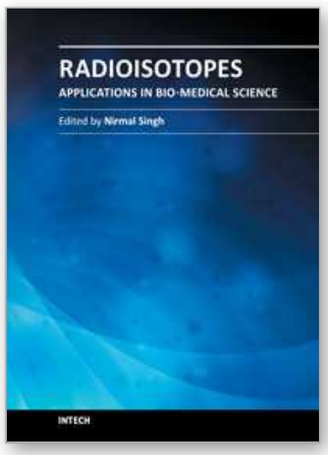
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The book Radioisotopes - Applications in Bio-Medical Science contains two sections: Radioisotopes and Radiations in Bioscience and Radioisotopes and Radiology in Medical Science. Section I includes chapters on medical radioisotope production, radio-labeled nano-particles, radioisotopes and nano-medicine, use of radiations in insects, drug research, medical radioisotopes and use of radioisotopes in interdisciplinary fields etc. In Section II, chapters related to production of metal PET (positron emission tomography) radioisotopes, 3-dimensional and CT (computed tomography) scan, SS nuclear medicine in imaging, cancer diagnose and treatments have been included. The subject matter will by highly useful to the medical and paramedical staff in hospitals, as well as researchers and scholars in the field of nuclear medicine medical physics and nuclear bio-chemistry etc.

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