Axillary reverse mapping for preventing lymphedema in axillary lymph node dissection and/or sentinel lymph node biopsy

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Axillary lymph node dissection (ALND) is a standard surgical treatment in patients with involved axillary lymph nodes. Unfortunately, arm lymphedema develops in 2.7–5.0% of patients treated by partial ALND (level I and II), in 3.1–9.6% of those undergoing total ALND, and in 26–38% of patients treated with ALND and radiotherapy [1]. The risk of lymphedema is often used as an argument against ALND. Currently, sentinel lymph node (SLN) biopsy has become a highly utilized and widely accepted method for surgical staging of axillary lymph nodes in breast cancer. It can avoid an unnecessary ALND in patients with node-negative breast cancer, thereby preventing arm lymphedema. Nevertheless, recent short-term studies demonstrated that lymphedema develops in 2–7% of patients even with SLN biopsy alone [2–4]. Transection of the arm lymphatics during ALND most likely results in lymphedema, but the ALND technique has changed little over the decades, and involves purely anatomical dissection. It is generally thought that the lymphatics reside juxtaposed to the vein, and the risk of lymphedema can be minimized if the surgeon takes care to avoid skeletonizing the vein. However, lymphatics with this positioning are rarely seen and SLN biopsy does not correct the problem of lymphedema, although it is less morbid than ALND [2].

Recently, the axillary reverse mapping (ARM) technique was developed to map and preserve arm lymphatic drainage during ALND and/or SLN biopsy. The arm and breast lymphatic drainage can be separated, allowing safe

removal of only the lymphatics of the breast (SLN or ALND) and protection of the lymphatic channels draining the upper extremity. This assumption is supported by a recent anatomical description of the lymphatic territories of the upper limb [5]. Several investigators have identified the lymphatics and/or nodes of the ARM using blue dye and/or isotope labeling [6–10]. Thompson et al. [6] injected 2.5 mL blue dye dermally or subcutaneously 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 with ARM 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. [7] identified ARM nodes in 15 of 21 patients (71%) with a similar technique.

However, a number of problems remain to be resolved in the practical use of this new concept derived from SLN biopsy for breast cancer. The limitations of this technique included insufficient identification rates of the ARM nodes (61–71%) as well as a persistent blue stain at the injection site [7]. To improve the identification rate of the ARM nodes and to prevent a persistent blue stain at the injection site, Nos et al. [9] injected an isotope into the web space of the ipsilateral hand in another study. During ALND, the radioactive ARM 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 ARM chain. Consequently, the ARM was identified in 21 of 23 patients (91%). However, this procedure may be somewhat cumbersome and result in longer operating time.

The fluorescence imaging technique with subcutaneous injection of indocyanine green (ICG) (Diagnogreen;

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Daiichi Pharmaceutical, Tokyo, Japan) was developed for detecting SLNs in Japan. In April 2009, we commenced a pilot study to investigate the feasibility of ARM using an invisible near-infrared fluorescence imaging system (PDE; Hamamatsu Photonics, Hamamatsu, Japan). Aliquots of 2 mL (5 mg) ICG were injected subcutaneously into the upper inner arm. During ALND, ICG-stained ARM nodes and/or lymphatics appeared green under visible illumination and fluorescent on fluorescence images several minutes after the first injection of ICG. PDE was highly sensitive for identification of fluorescent ARM nodes and/or lymphatics regardless of whether they were green or not under visible illumination, suggesting that this technique may be useful to improve the identification rate of the ARM (data not shown). This technique also permitted differentiation of green and fluorescent ARM nodes and/or lymphatics from blue SLNs in dye-guided SLN biopsy.

On the other hand, it is important to confirm that the ARM nodes are not involved with metastatic foci, even in patients at high risk of axillary nodal involvement [9]. The assumption is that the lymphatic drainage from the upper arm is different from that of the breast, and is uninvolved after metastatic involvement of the axillary nodes in relation to the breast. Boneti et al. [11] reported that blue lymphatics draining the arm were visible from the SLN incision, and so were located near or within the SLN field in 56 (42.7%) of 131 patients. This can explain why SLN biopsy does not correct the problem of lymphedema [2–4]. However, Boneti et al. [11] as well as Thompson et al. [6] found no cancer cells in the ARM nodes even when the patients had many positive axillary nodes in the initial series, and subsequently they preserved the ARM nodes in patients of the later series. Nevertheless, 3 of 21 patients (14%) in a study by Nos et al. [9] showed metastatic involvement of the ARM sampling, although the ARM nodes had no metastatic involvement in the remaining 18 patients. It is striking that metastatic involvement was found in the ARM nodes in 3 patients, even though these patients had significant axillary tumor burden (10 or more metastatic nodes) [9]. These findings constitute another limitation of the ARM technique.

Thus, the success of the ARM procedure in reducing lymphedema is yet to be determined. If ARM lymphatics join the common lymphatic pathway draining the breast when they exit the axillary vein, their preservation would likely be impossible [8]. In a study by Nos et al. [7], it was not possible to preserve the ARM node or lymphatic in 11 of 21 patients (53%), indicating a preservation rate of 47%. Boneti et al. also reported the development of lymphedema in 2 of 12 patients in whom the ARM node or lymphatic was sacrificed, whereas no lymphedema was

observed in patients in whom the ARM node was spared regardless of whether SLN biopsy alone or ALND was performed [11]. Therefore, the identification of ARM alone does not allow prevention of the closure of arm lymphatics because of the need to also remove ARM nodes [6–8]. To prevent arm lymphedema, Casabona et al. [10] performed microsurgical lymphatic-venous anastomosis using lymphatic collectors colored blue coming from the arm and one of the collateral branches of the axillary vein. This operation consisted of telescopic anastomosis, introducing lymphatics inside the vein, using microsurgical tools under magnification. Although lymphatic microsurgery techniques have been shown to be effective in the treatment of peripheral lymphedema [12], long-term follow-up studies are required before we can conclude that this microsurgical technique is effective to prevent arm lymphedema. Therefore, further studies are needed to determine whether the ARM technique can prevent arm lymphedema during ALND and/or SLN biopsy for breast cancer.

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