



Axillary reverse mapping (ARM): where to go

Xuan Shao¹ · Bo Sun² · Yanwen Shen²

Received: 3 May 2018 / Accepted: 26 June 2018 / Published online: 30 June 2018
© The Japanese Breast Cancer Society 2018

Abstract

In the past decades, breast surgeons have changed the clinical practice in the surgical treatment of breast cancer, by performing sentinel lymph node biopsy (SLNB) instead of performing axillary lymph node dissection (ALND) in axillary lymph node clinically negative breast cancer patients. ALND can also be avoided in SLN-positive patients who meet the Z-0011 criteria. However, the postoperative complications of SLNB and ALND, such as the secondary upper extremity lymphedema, are common and need effective solutions to prevent as soon as possible. The axillary reverse mapping (ARM) technique has been developed to map and preserve arm lymphatic drainage during ALND and/or SLNB, thereby minimizing arm lymphedema. However, the success of ARM in reducing lymphedema has not been exactly determined. If ARM can be confirmed to be both effective and oncologically safe in preventing lymphedema, this technique should be recommended in the management of breast cancer treatment.

Keywords Axillary reverse mapping · Axillary lymph node dissection · Sentinel lymph node biopsy · Lymphedema · Breast cancer

Introduction

Breast cancer is the most common malignancy among women in the world and is the second only to lung cancer as a cause of cancer death [1]. With the prevalence of early detection and the emergency of more effective treatments, breast cancer mortality appears to be declining in spite of the incidence of breast cancer has increased steadily over the past few decades [2]. Receiving surgery is the main treatment method for breast cancer. From the radical mastectomy proposed by Halsted to the extended radical operation introduced by Marogottini and Urban [3], and then modified mastectomy initiated by Patey and Dyson in 1948 [4], the surgical treatment of breast cancer has evolved from more extensive procedure to less invasive breast-conserving

surgery in the last decades. Meanwhile, with the increased detection rate of early breast cancer, 50% of breast cancer patients do not involve in axillary lymph node metastasis, it will lead to overtreatment if they all receive axillary lymph node dissection (ALND). We, therefore, change the concept that breast cancer tissues and related lymphonodus must be extensively removed in the management of breast cancer. ALND can be avoided in sentinel lymph node (SLN)-negative patients. What is more, Z-0011 study suggested that ALND could also be avoided in SLN-positive patients who undergo breast-conserving surgery with whole-breast irradiation and systemic therapy [5]. More recently, the AMAROS trial, which included breast cancer patients treated with mastectomy, demonstrated that axillary radiation therapy provided effective locoregional control and survival benefit equivalent to ALND for patients with cT1-2N0 and one or two positive sentinel nodes [6]. However, the secondary upper extremity lymphedema still damages the life quality of patients who underwent axillary surgery no matter SLNB or ALND. As previously reported, ALND was associated with 7–77% risk of lymphedema [7], and SLNB, although only removes few axillary nodes, was also associated with 3–13% risk of lymphedema [8]. The axillary reverse mapping (ARM) technique, which can identify and preserve

Xuan Shao, Bo Sun and Yanwen Shen contributed equally to this work.

✉ Xuan Shao
surg2000@sina.com

¹ Department of Surgical Oncology, Second Affiliated Hospital of Zhejiang University, Hangzhou 310009, Zhejiang, China

² Institute of Translational Medicine, Zhejiang University School of Medicine, Hangzhou 310029, Zhejiang, China

lymphatic drainage from the arm during ALND/SLNB, came into being and is expected to solve this dilemma.

Axillary lymph node dissection (ALND) and sentinel lymph node biopsy (SLNB)

More than 100 years ago, Halsted introduced the radical mastectomy for breast cancer patients [9]. It was necessary to perform ALND during radical mastectomy, which could significantly benefit the survival [10–12]. However, ALND is associated with substantial morbidities, including arm lymphedema, seroma, upper limb dysfunction, sensory loss and discomfort [13]. The reported incidence of lymphedema after ALND ranged from 7 to 77% [14–16]. Hence, many authors had questioned this radical procedure [11], and altered interest to the SLNB technique. SLNB is based on the theory that sentinel lymph node is the first node where the primary tumor cells should drain to and it may function as a filter for tumor cells [17]. The procedure of SLNB was first described by Donald L. Morton and Alistair J. Cochran and colleagues in 1992 [18]. It was then introduced into the treatment of breast cancer after proven useful in malignant melanoma [19]. Consequently, a number of clinical trials proved that SLNB was a safe and accurate procedure to detect malignant cells in axillary lymph nodes, as even leaving unremoved positive nodes did not significantly increase the rate of distant recurrence or breast-cancer-related mortality [5, 14, 20–22]. As a result, SLNB alone with no further ALND in patients with negative clinically lymph nodes was accepted oncologist [23]. While receiving ALND remains the recommended treatment for patients with axillary metastases identified on SLNB [24]. Importantly, the IBCSG 23-01 trial suggested that axillary dissection might be overtreatment in patients who have micrometastases only in the sentinel node [25]. Consequently, 2011 St Gallen Consensus Conference had already recommended that micrometastases in a single sentinel node should not be an indication for axillary dissection irrespective of the type of breast surgery given [26]. A landmark study named Z-0011 trial reported that the regional recurrence rate was not significantly different in these patients with primary T1–T2 breast cancer and one positive sentinel node undergoing breast-conserving surgery to complete ALND or no ALND [27]. What is more, the information of total axillary nodal involvement was redundant, ignoring the extent of total node involvement appeared to have no major impact on the administration of adjuvant therapy [28, 29]. Hence, the updated 2014 American Society of Clinical Oncology (ASCO) guidelines recommended that “clinicians should not recommend axillary lymph node dissection (ALND) for women with early-stage breast cancer who have one or two sentinel lymph node

metastases and will receive breast-conserving surgery with conventionally fractionated whole-breast radiotherapy” [30].

Axillary reversing mapping (ARM)

ALND is associated with several morbidities, including arm lymphedema, seroma, upper limb dysfunction and sensory loss [13]. Even after SLNB, there is still much risk of having lymphedema. A newly systematic review included 28 articles, representing 9588 patients undergoing SLNB, showed the overall incidence of lymphedema in these patients ranged from 3 to 13%, which means lymphedema is still a serious problem in SLNB patients [31]. Whereas the incidence of lymphedema in patients who undergo ALND was reached as high as 7–77% [7]. The main reason of lymphedema after ALND or SLNB is because of the disruption of the lymphatic drainage of upper extremity. The axillary reverse mapping (ARM) technique is developed for identifying and preserving lymphatic drainage from the arm during ALND or SLNB, thereby expecting to minimize arm lymphedema [32]. ARM is based on the theory that those lymphatics and nodes draining the breast are distinct from those draining the arm, so preserving those axillary nodes draining from the arm can prevent the existence of lymphedema without concerning the spared ARM nodes harboring cancer cells. Suami et al. used hydrogen peroxide to image the lymphatic vessels of upper limb and showed that most lymph vessels were seen to flow into one main (sentry) lymph node in the axillary region; although some of the lymph vessels ran along the posterior forearm, bypassing the “sentry” node to reach other smaller nodes [33]. In 2007, Hama et al., utilized two-color spectral fluorescence lymphangiography to identify the different lymphatic flows draining the breast and the upper extremity [34]. This new technique ARM was then described in the same year [35], and pioneered in the US by Klimberg [36]. Currently there are mainly three kinds of tracers, namely, blue dye, radionuclide and fluorescent dyes, used in identification of ARM.

Mapping by dye injection

Thompson and colleagues first used blue dye to identify ARM lymphatics and nodes in 2007 [35]. 2.5 ml blue dye was injected into the upper inner arm dermally or subcutaneously. Then, massaged the injection site and raised the arm for 5 min until blue lymphatics were observed in the upper extremity. They identified 11 ARM lymphatics in 18 (61%) cases. Consequently, several investigators demonstrated the feasibility use of blue dye in ARM [37–39]. However, identification rates of ARM nodes using blue dye alone were insufficient, ranging from 33.7 to 94.7% (Table 1).

Table 1 The results of ARM mapping by dye injection

Author	No. of patients	SLNB	S–A	ALND	No. of ARM identified	No. of node	Crossover	Involved malignancy
Thompson et al. [35]	18	0	14	4	11/18 (61%)	–	0/11 (0%)	0% ^a
Nos et al. [37]	21	0	0	21	15/21 (71%)	1.7 (1–3)	–	0 ^b
Boneti et al. [38]	131	115	26	0	56/131 (42.7%)	–	5/128 (3.9%)	0/5 (0%) ^a
Casabona et al. [39]	72	63	9	0	27/72 (37.5%)	–	–	0 ^b
Han et al. [40]	97	14	83	0	10/14 (71%)	1.4 (1–4)	7/97 (7.2%)	2/7 (28.6%) ^a
Beek et al. [41]	112	0	0	112	98/112 (87.5%)	1.66 (1–9)	–	20/112 (17.8%) ^b
Deng et al. [42]	69	69	69	0	–	–	19/69 (27.5%)	6/19 (32%) ^a
Boneti et al. [36]	214	167	47	0	87/214 (41%)	2.5	6/214 (2.8%)	0/6 (0%) ^a
Bedrosian et al. [43]	30	0	3	27	15/30 (50%)	1 (0–3)	–	2/15 (13.3%) ^b
Ochoa et al. [44]	360	237	111	12	80/237 (33.7%)	–	15/348 (4.3%)	2/15 (14.3%) ^a
Boccardo et al. [45]	19	0	0	19	18/19 (94.7%)	(1–3)	–	0% ^b
Ponzone et al. [46]	49	0	20	29	27/49 (55.1%)	–	–	3/27 (11.1%) ^b
Gobardhan et al. [47]	93	0	43	50	36/43 (86%) SLNB 47/50 (94%) ALND	– –	– –	0 (0%) ^b 11/50 (52%) ^b
Eduardo et al. [48]	45	0	×	45	40/45 (88.9%)	1.9	–	10/40 (25%) ^b
Tausch et al. [49]	143	0	0	143	112/143 (78%)	–	55/112	14/55 (2.5%) ^a

ARM axillary reverse mapping, *No. of ARM* number of patients underwent ARM, *ALND* axillary lymph node dissection, *SLNB* sentinel lymph node biopsy, *S + A* complete ALND when SLN was positive, *No. of node* number of removed ARM nodes, *crossover* ARM nodes coincide with SLNs

^aCrossover nodes metastasis

^bMetastatic involvement of resected ARM nodes

Mapping by isotope injection

The ARM nodes often locate deeper than SLN nodes, which make it hard to identify the ARM node in the surgical field. To improve the identification rate of the ARM and reduce the tattoo left after injection of blue dye, isotopes have been used in ARM procedure. Isotope can be injected directly into the web space of the ipsilateral hand and then gamma probe is used to identify the radioactive ARM nodes, and the identification rate seems more attractive, ranging from 75 to 100% (Table 2). Other isotopes like dye, ¹¹¹In-human polyclonal immunoglobulin G can also be used to identify ARM nodes using a well-scintillation counter, and get a higher

identification rate [50]. Thus, radioisotope labeling seems to be more sensitive for detecting ARM nodes than using of blue dye alone. Radioisotopes improve node detection rate, but do not enable to visualize the lymphatic vessels. Combining two tracers to facilitate the detection and visualization of both nodes and lymphatic vessels may improve the results, which will be the object of a future study [51, 52].

Mapping by fluorescent

Although mapping by isotope improves the identification rate; however, this procedure is somewhat cumbersome and time-needed [54]. An invisible near-infrared fluorescence

Table 2 The results of ARM mapping by isotope injection

Author	No. of patients	SLNB	S–A	ALND	No. of ARM identified	No. of node	Crossover	Involved malignancy
Nos et al. [53]	23	0	0	23	21/23 (91%)	1.6	–	3/21 (14.3%) ^b
Britton et al. [50]	15	0	0	15	15/15 (100%)	–	2/15 (13.3%)	–
Gennaro et al. [51]	60	0	0	60	45/60 (75%)	–	–	–
Yue et al. [52]	138	0	0	138	129/138 (93.5%)	(1–3)	–	11/129 (8.53%) ^b

ARM axillary reverse mapping, *No. of ARM* number of patients underwent ARM, *ALND* axillary lymph node dissection, *SLNB* sentinel lymph node biopsy, *S + A* complete ALND when SLN was positive, *No. of node* number of removed ARM nodes, *crossover* ARM nodes coincide with SLNs

^aCrossover nodes metastasis

^bMetastatic involvement of resected ARM nodes

imaging system (Photo Dynamic Eye; Hamamatsu Photonics, Hamamatsu, Japan), by injecting 0.1 ml (0.25 mg) of indocyanine green (ICG) into the inner side of the wrist or the upper inner arm subdermally, is used for identifying the ARM nodes and lymphatics. During ALND or SLN biopsy, the light is occasionally switched off in the operating room, and shining fluorescent ARM nodes and lymphatics are observed in the axilla using the fluorescence imaging system [22]. The visualization rate of ARM nodes by fluorescence imaging system ranges from 32.3 to 88% (Table 3). The fluorescence imaging system makes it possible to carry out SLNB and ARM procedure in the same setting and same time. On the other hand, the cost of this technique is very low, and only few minutes are required to identify the lymphatic pathways. Moreover, identifying the pathways is very simple, and it can be performed at any institute who has a fluorescence imaging camera [55].

Factors influencing the success of ARM

The SLNs are located in the lower area of the axilla, while the ARM nodes are frequently located in the upper outer quadrant of the axilla, the visualization rate of ARM during SLND is significantly lower comparing that during ALND [39, 46]. Otherwise, the success of the ARM procedure was strongly associated with the time interval between the blue dye injection and the start of the surgery [60]. Actually, an interval less than 15 min or greater than 60 min indeed decreases the identification rate comparing with the optimal interval [46]. Besides, the volumes of blue dyes used in ARM would influence the visualization rates. Using 2–5 ml blues dye benefited the identification rate than using only 1 ml [35, 36, 46, 61]. Patients who received neoadjuvant chemotherapy might decrease the ARM node identification,

which could be explained by the reason that chemotherapy induced lymphatic fibrosis [62]. A trend was observed with high BMI index being associated with decreased ARM identification, although this observation did not reach statistical significance. Patient age, tumor size, the presence of extensive nodal metastases and concurrent SLNB were all not associated the identification rate of ARM [46, 49, 60]. The experience of surgeon was important when performing the ARM procedure; increasing surgical exposure increased the detection rates of ARM nodes [36, 37, 63].

Complications of ARM

Although the operation of ARM is not complicated, there are still many non-cancer-related complications occurring after operation. The most common complication is the blue tattooing that occurs at the injection site, the tattooing may disappear in a few days or persist to many years [35, 36]. Pain occurring at the injection site is the other common complication of ARM, and most patients suffer just mild pain [46]. Besides, systemic allergic or anaphylactic reactions may occur after dye injection [64].

Locations of ARM nodes

Pavlista et al. have mapped the lymphatic anatomy of upper extremities in health individuals and cadavers by lymphography images and blue dye [65, 66]. They found that numerous lymphatic drainage from the upper arm passed through the central, and some would toward or directly into the SLN field [65]. Most studies reported that ARM lymphatics were located below the axillary vein level [43, 53]. The identified rate of ARM node is much higher during ALND than

Table 3 The results of ARM mapping by fluorescent

Author	No. of patients	SLNB	S–A	ALND	No. of ARM identified	No. of node	Crossover	Involved malignancy
Noguchi et al. [56]	131	81	16	34	42/96 (43%)SLNB	1.7 (1–3)	27/96 (28%)	0/27 (0%) ^a
					29/34 (85%)ALND	5.4 (1–17)	–	11/29 (37.9%) ^b
Ikeda et al. [57]	98	0	51	47	80/98 (82%)	–	–	17/76 (22.4%) ^b
Noguchi et al. [58]	20	12	2	6	9/12 (75%)SLNB	1.2 (1–2)	2/12 (17%)	0/2 (0%) ^a
					7/8 (88%)ALND	2.7 (1–7)	–	3/7 (42.8%) ^b
Ikeda et al. [59]	60	0	35	25	26/35 (74%)SLNB	1.2	–	1/35 (2.9%) ^b
					22/25 (88%)ALND	1.4	–	6/25 (24%) ^b
Sakura et al. [55]	372	372	0	0	120/372 (32.3%)	–	77/372 (20.7%)	–

ARM axillary reverse mapping, *No. of ARM* number of patients underwent ARM, *ALND* axillary lymph node dissection, *SLNB* sentinel lymph node biopsy, *S + A* complete ALND when SLN was positive, *No. of node* number of removed ARM nodes, *crossover* ARM nodes coincide with SLNs

^aCrossover nodes metastasis

^bMetastatic involvement of resected ARM nodes

SLNB [39, 40, 56], which may be the reason that the majority of lymphatics draining the ARM are anatomically located deeper than the SLN. Five ALND fields have been described as follows: field A, the area between the axillary vein and the second intercostobrachial nerve, and close to the anterior edge of the latissimus dorsi muscle; field B, the area medially adjacent to field A and close to the anterior serratus muscle; field C, the area below the second intercostobrachial nerve and close to the anterior serratus muscle; field D, the area below the second intercostobrachial nerve and close to the anterior edge of the latissimus dorsi muscle; and field E, the area above the axillary vein [59]. Importantly, about 63–97% of ARM nodes are located in field A [40]. No upper extremity lymphatics are present at the caudal side of the second intercostobrachial nerve [55]. The important landmark in the operative field when performing ARM is the axillary vein and the second intercostobrachial nerve. There are no studies to systematically analyze the association between metastatic ARM nodes and its locations. We are not clear if there will exist some fixed locations that metastatic ARM nodes are much more prone to site.

Identification rate of ARM node during SLND and ALND

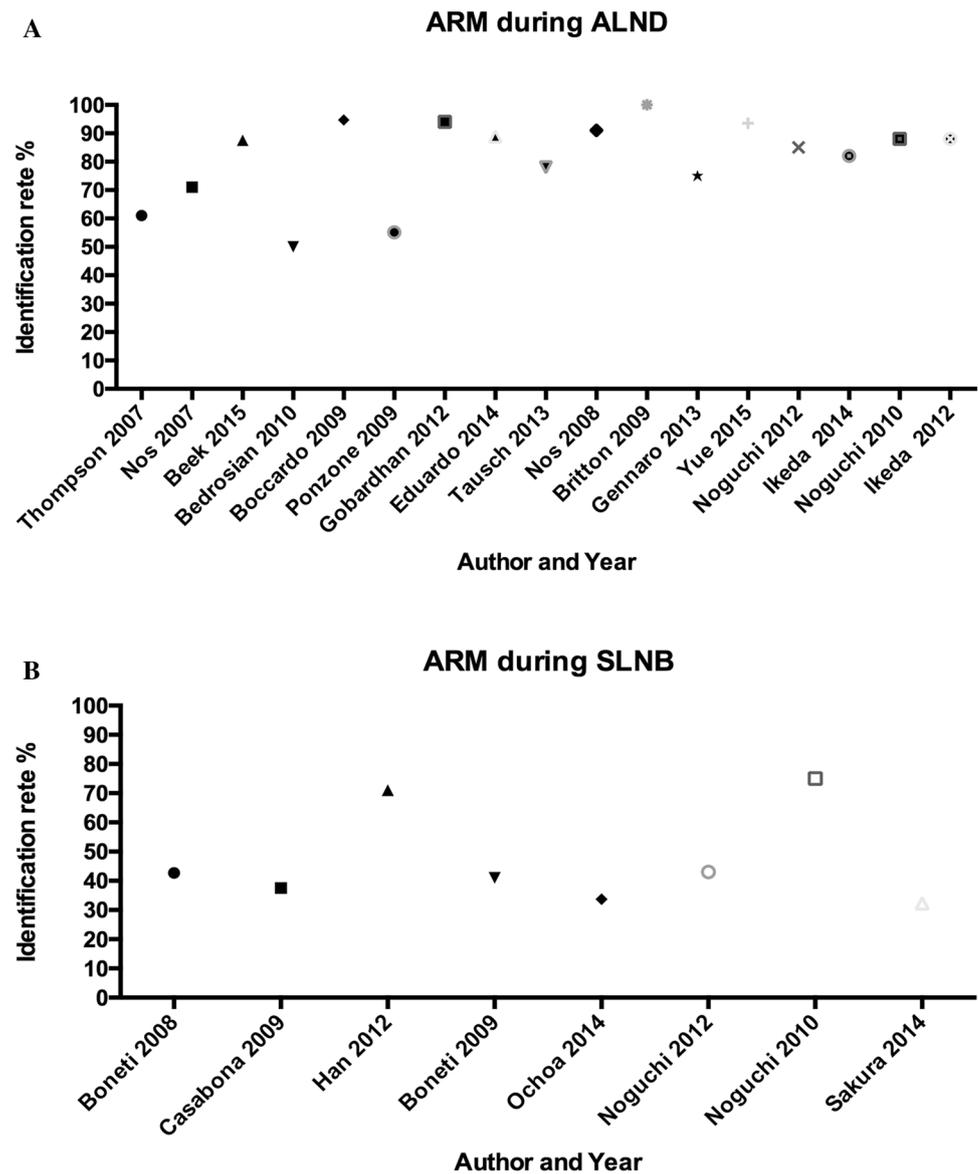
Thompson [35] and Nos [37] first introduced the ARM technique using blue dye and radioisotope to map arm lymphatic drainage to distinguish them from the breast lymphatic in breast cancer patients who were undergoing ALND; their identification rates of ARM lymph nodes and/or lymphatic were 61 and 91%, respectively. Subsequent studies reported that ARM node and/or lymphatic identification rates ranged from 55 to 100% during ALND (Fig. 1a). Otherwise, the identification rates for ARM during SLND were fewer than that during ALND. Boneti et al. first reported that 42.7% of the patients were identified to have blue ARM lymphatic channels in the SLNB field [38]. Then, subsequent reports showed a 33–75% identification rate for ARM nodes and lymphatics during SLNB (Fig. 1b).

SLN-ARM (crossover) nodes and metastatic involved malignancy

The procedure of ARM is based on the anatomical knowledge that the lymph of breast and upper extremity drain to different nodes in the axilla; the oncologic safety of the procedure must be seriously concerned [67]. If the SLN draining the breast is the same node as the ARM node draining the upper extremity, it will be difficult to preserve the ARM node at SLN biopsy. The preliminary radiographic results of the lymphatic system of upper

torso indicated that the lymph vessels originating in the lower region of the upper extremity had close spatial association with the breast tissues [68]; about a quarter of patients had connection between lymphatic drainage of the upper extremity and breast [65]. When using two different methods to identify SLN nodes and ARM nodes in the same time, the same nodes identified by these two methods are called SLN-ARM nodes. The existence of SLN-ARM node means the SLN and the arm lymph node have common lymphatic channels, which should be highly concerned because of high risk of metastatic involvement. The occurrence of crossover nodes was about 4.3% in 348 patients according to a recent results [44]. Other investigators showed the crossover rates ranged from 0 to 28% [42, 50, 56]. SLN-ARM nodes have two different implications, first, removing of SLN nodes may somewhat disrupt the lymphatic drainage of up extremity [33], which may explain why SLNB still exists as the problem of lymphedema [54]. Second, if the SLN nodes contain metastatic breast cancer cells, these malignant cells may metastasis to SLN-ARM nodes. It will be difficult to preserve these ARM nodes. Case series have shown that patients with grossly involved nodal malignancy are at risk for alteration of normal lymphatic flow and back flow to the ARM nodes [69]. Deng and colleagues reported that all of the metastatic ARM nodes only occurred in patients with SLN-ARM nodes [42]. Only 0–32% of SLN-ARM nodes are involved with malignancy [36, 42, 44, 54, 56], and the metastatic rates for ARM nodes were positively associated with N stage [44]. Noguchi et al. [56] and Nos et al. [53] showed that patients with metastatic involvement of the ARM sampling were all pN3 stage. With the similar results, Ponzzone et al. reported that three patients with extensive nodal metastatic involvement (pN2a and pN3a) had metastatic cancer cells in ARM nodes [46]. Hence, N3 lymphatic invasion should be a contraindication for ARM procedure, not only because there exists a common lymphatic pathway, but also advanced breast cancer cells are much more prone to metastasis to juxtapose sites and impair axillary reverse mapping. However, positive ARM nodes were also observed in the patients with only a few positive or negative nodes [43, 59]. It is necessary to distinguish the metastatic nodes in SLN-ARM nodes, and remove them. Fine needle aspiration or biopsy of partial resection of SLN-ARM nodes may provide evidences to determinate which SLN-ARM node to dissect and which one to persevere. Ikeda et al. [59] used the FNA technique to evaluate the fluorescent ARM nodes when they were located in the ALND field showed no discordance between the cytological assessments by FNAC and the histological results. However, the sampling error mainly caused by deficient materials was 18% in with SLNB group and 26% in without SLNB group. Some variables appeared to

Fig. 1



predict a higher risk for ARM node's metastatic involvement, for example, young patient age and intensive axillary disease [48].

Microsurgical lymphatic venous anastomosis

ARM may be a promising technique to decrease the occurring of lymphedema during SLND or ALND, while we must notice that in a minority of patients the drainage pathway from upper limb and ipsilateral breast is through a common lymphatic channel [50]. It not only explains why such patients develop upper limb breast cancer-related lymphedema after SLN biopsy, but also warns that in these patients preserving the ARM lymph nodes may be at risk of

cancer recurrence because of these residual nodes. For these patients, especially with high N stages, the metastatic rate of ARM nodes is high and they should not be considered as the appropriate candidates to perform ARM procedure. To prevent these patients from lymphedema, therefore, lymphatic venous anastomoses (LVA) between arm lymphatics and collateral branches of axillary vein have been introduced to prevent lymphedema with low invasiveness [45]. This technique has been well-used in other medical area including pelvic lymphocyst [70] and primary peripheral lymphedema [71, 72]. Promisingly, the earlier the LVA were performed in peripheral lymphedema patients, the better were the outcome [72]. However, Danstra et al. [73] proceeded a prospective study and demonstrated that a minimal reduction in volume of lymphedema following LVA, non-operative treatment and elastic stockings were still preferred by most patients with

Table 4 Follow-up and evaluation of arm edema

Author	No.	Follow-up months	Lymphedema	
			(ARM removed)	(ARM reserved)
Han et al. [40]	83 ALND	3–24	1/13 (7.7%)	0/70 (0%)
Casabona et al. [39]	72 ALND	6–9	0/72 (0%)	–
Boneti et al. [36]	51 ALND	6	2/15 (13.3%)	0/36 (0%)
Gennaro et al. [51]	60 ALND	16 (6–36)	5/15 (33%)	4/45 (9%)
Ikeda et al. [57]	76 ALND	24 (12–36)	24/76 (32%)	–
Yue et al. [63]	265 ALND	20 (7–32)	42/127 (33%)	7/118 (5.93%)
Sakurai et al. [55]	321 SLNB	28	5/76 (6.6%)	0/245 (0%)
Noguchi et al. [56]	97 SLNB	12 (1–26)	2/28 (7.1%)	0/69 (0%)
Ochoa et al. [44]	158 SLNB	12 (3–48)	3/100 (3%)	1/58 (1.7%)

lymphedema [73]. Furthermore, post-mastectomy radiotherapy might compromise the effect of LVA because of the radiation-induced scar formation [74].

The effect of lymphedema prevention after ARM

Secondary upper extremity lymphedema is among the most deleterious chronic complication in breast patients who received axillary surgery. It has been estimated that one in five breast patients have suffered lymphedema [75]. Many factors, such as high body mass index (BMI > 25 kg/m²), postoperative radiotherapy, a history of wound infection or lymphangitis, the duration of axillary drainage, and residual lymph node disease after neoadjuvant chemotherapy were reported to relate with the occurrence of lymphedema after SLNB or ALND [57, 76, 77]. With the application of ARM procedure, the incidence of secondary upper extremity lymphedema was significantly decreased (Table 4). Boneti et al. recorded that there was no patient had lymphedema in the ARM nodes preserved group of 220 patients who had underwent ALND [36]. A recent study showed that ARM contributed to 23% lower incidence of lymphedema, and decreased the need for ongoing therapy [78]. While other report presented the contradictory results, after a median follow-up time of 19 months, preservation of ARM nodes did not benefit the incidence of lymphedema in 143 patients undergoing ALND [49]. Otherwise, tumor nodal staging also determined the benefit of ARM nodes preserving, it indeed benefited patients with N1 and N2, but not with N0 breast cancer [40]. On the other hand, the definition of lymphedema was not accurate and precise, we always defined lymphedema as a measurement change of > 2 cm of arm circumference; however, we ignored the subjective feeling of patients, although measurement change was less than 2 cm; if the patient felt discomforts, she might have lymphedema [40]. So a large, well-designed multicenter

randomized trial is required to exactly answer the question whether ARM benefits the prevention of lymphedema.

Conclusion

In clinical practice, in breast cancer patients with clinically negative axillary lymph node who meet the Z-11 criteria, ALND can be avoided even with positive SLNs. If they do not meet the Z-11 criteria, ALND with ARM procedure should be recommended. The ARM technique is feasible to prevent the occurrence of arm lymphedema for patients undergoing ALND; however, the unsatisfying identification rate limits its application in patients undergoing SLNB. Furthermore, the SLN-ARM (crossover) nodes are the possibility of metastatic ARM nodes, which we must prudent to preserve these nodes, but only a small proportion of SLN-ARM nodes are positive ARM node. We, therefore, need to make a series of criterion to identify the uninvolved malignance SLN-ARM nodes and spare them. We also need to investigate whether combining some factors, for example, the tumor size, the positive axillary nodes, the number of crossover nodes, can be effective predictors of ARM candidates. This needs a large number of studies and clinic trials to proceed. In addition, neoadjuvant chemotherapy reduces the risk of metastatic involvement of the ARM nodes, whether it is appropriate to preserve ARM node after neoadjuvant chemotherapy still needs further investigation.

Compliance with ethical standards

Conflict of interest The author reports no conflicts of interest in this work.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics 2017. *CA Cancer J Clin.* 2017;67(1):7–30. (PubMed PMID: 28055103. Epub 2017/01/06. eng).

2. Early Breast Cancer Trialists' Collaborative G. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. *Lancet*. 2005;365(9472):1687–717. (**PubMed PMID: 15894097**).
3. Kinoshita I, Fukami A, Nishi M, Kuno K, Kajitani T. An extended radical operation for breast cancer. *Shujutsu Oper*. 1969;23(3):281–90. (**PubMed PMID: 5805593**. **Epub 1969/03/01.jpn**).
4. Patey DH, Dyson WH. The prognosis of carcinoma of the breast in relation to the type of operation performed. *Br J Cancer*. 1948;2(1):7–13. (**PubMed PMID: 18863724**. **Pubmed Central PMCID: 2007539**).
5. Giuliano AE, Hawes D, Ballman KV, Whitworth PW, Blumenkrantz PW, Reintgen DS, et al. Association of occult metastases in sentinel lymph nodes and bone marrow with survival among women with early-stage invasive breast cancer. *Jama*. 2011;306(4):385–93. (**PubMed PMID: 21791687**. **Epub 2011/07/28**. **eng**).
6. Donker M, van Tienhoven G, Straver ME, Meijnen P, van de Velde CJ, Mansel RE, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981–22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. *Lancet Oncol*. 2014;15(12):1303–10. (**PubMed PMID: 25439688**. **Pubmed Central PMCID: PMC4291166**. **Epub 2014/12/03**. **eng**).
7. Ahmed M, Rubio IT, Kovacs T, Klimberg VS, Douek M. Systematic review of axillary reverse mapping in breast cancer. *Br J Surg*. 2016;103(3):170–8. (**PubMed PMID: 26661686**. **Epub 2015/12/15**. **eng**).
8. Lucci A, McCall LM, Beitsch PD, Whitworth PW, Reintgen DS, Blumenkrantz PW, et al. Surgical complications associated with sentinel lymph node dissection (SLND) plus axillary lymph node dissection compared with SLND alone in the American College of Surgeons Oncology Group Trial Z0011. *J Clin Oncol*. 2007;25(24):3657–63. (**PubMed PMID: 17485711**. **Epub 2007/05/09**. **eng**).
9. Halsted WS. The results of operations for the cure of cancer of the breast performed at the Johns Hopkins Hospital. *Ann Surg*. 1894;20(5):497–555.
10. Axelsson CK, Mouridsen HT, Zedeler K. Axillary dissection of level I and II lymph nodes is important in breast cancer classification. The Danish Breast Cancer Cooperative Group (DBCG). *Eur J Cancer (Oxford, England: 1990)*. 1992;28a(8–9):1415–8. (**PubMed PMID: 1515262**. **Epub 1992/01/01**. **eng**).
11. Orr RK. The impact of prophylactic axillary node dissection on breast cancer survival—a Bayesian meta-analysis. *Ann Surg Oncol*. 1999;6(1):109–16. (**PubMed PMID: 10030423**. **Epub 1999/02/25**. **eng**).
12. Krag DN, Single RM. Breast cancer survival according to number of nodes removed. *Ann Surg Oncol*. 2003;10(10):1152–9. (**PubMed PMID: 14654470**. **Epub 2003/12/05**. **eng**).
13. Noguchi M, Miwa K, Michigishi T, Yokoyama K, Nishijima H, Takanaka T, et al. The role of axillary lymph node dissection in breast cancer management. *Breast Cancer (Tokyo, Japan)*. 1997;4(3):143–53. (**PubMed PMID: 11091589**. **Epub 2000/11/25**. **eng**).
14. Mansel RE, Fallowfield L, Kissin M, Goyal A, Newcombe RG, Dixon JM, et al. Randomized multicenter trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: the ALMANAC Trial. *J Natl Cancer Inst*. 2006;98(9):599–609. (**PubMed PMID: 16670385**. **Epub 2006/05/04**. **eng**).
15. Leidenius M, Leivonen M, Vironen J, von Smitten K. The consequences of long-time arm morbidity in node-negative breast cancer patients with sentinel node biopsy or axillary clearance. *J Surg Oncol*. 2005;92(1):23–31. (**PubMed PMID: 16180231**. **Epub 2005/09/24**. **eng**).
16. Swenson KK, Nissen MJ, Ceronky C, Swenson L, Lee MW, Tuttle TM. Comparison of side effects between sentinel lymph node and axillary lymph node dissection for breast cancer. *Ann Surg Oncol*. 2002;9(8):745–53. (**PubMed PMID: 12374657**. **Epub 2002/10/11**. **eng**).
17. Tanis PJ, Nieweg OE, Valdes Olmos RA, Th Rutgers EJ, Kroon BB. History of sentinel node and validation of the technique. *Breast Cancer Res BCR*. 2001;3(2):109–12. (**PubMed PMID: 11250756**. **Pubmed Central PMCID: Pmc139441**. **Epub 2001/03/16**. **eng**).
18. Morton DL, Wen DR, Wong JH, Economou JS, Cagle LA, Storm FK, et al. Technical details of intraoperative lymphatic mapping for early stage melanoma. *Arch Surg (Chicago, Ill: 1960)*. 1992;127(4):392–9. (**PubMed PMID: 1558490**. **Epub 1992/04/01**. **eng**).
19. Giuliano AE, Kirgan DM, Guenther JM, Morton DL. Lymphatic mapping and sentinel lymphadenectomy for breast cancer. *Ann Surg*. 1994;220(3):391–8. (**discussion 8–401**. **PubMed PMID: 8092905**. **Pubmed Central PMCID: 1234400**).
20. Fisher B, Wolmark N, Bauer M, Redmond C, Gebhardt M. The accuracy of clinical nodal staging and of limited axillary dissection as a determinant of histologic nodal status in carcinoma of the breast. *Surg Gynecol Obstet*. 1981;152(6):765–72. (**PubMed PMID: 7244951**. **Epub 1981/06/01**. **eng**).
21. Fisher B, Jeong JH, Anderson S, Bryant J, Fisher ER, Wolmark N. Twenty-five-year follow-up of a randomized trial comparing radical mastectomy, total mastectomy, and total mastectomy followed by irradiation. *N Engl J Med*. 2002;347(8):567–75. (**PubMed PMID: 12192016**. **Epub 2002/08/23**. **eng**).
22. Louis-Sylvestre C, Clough K, Asselain B, Vilcoq JR, Salmon RJ, Campana F, et al. Axillary treatment in conservative management of operable breast cancer: dissection or radiotherapy? Results of a randomized study with 15 years of follow-up. *J Clin Oncol*. 2004;22(1):97–101. (**PubMed PMID: 14701770**. **Epub 2004/01/01**. **eng**).
23. Krag DN, Anderson SJ, Julian TB, Brown AM, Harlow SP, Costantino JP, et al. Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. *Lancet Oncol*. 2010;11(10):927–33. (**PubMed PMID: 20863759**. **Pubmed Central PMCID: Pmc3041644**. **Epub 2010/09/25**. **eng**).
24. Lyman GH, Giuliano AE, Somerfield MR, Benson AB 3rd, Bodurka DC, Burstein HJ, et al. American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. *J Clin Oncol*. 2005;23(30):7703–20. (**PubMed PMID: 16157938**. **Epub 2005/09/15**. **eng**).
25. Galimberti V, Cole BF, Zurrada S, Viale G, Luini A, Veronesi P, et al. Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23-01): a phase 3 randomised controlled trial. *Lancet Oncol*. 2013;14(4):297–305. (**PubMed PMID: 23491275**. **Pubmed Central PMCID: Pmc3935346**. **Epub 2013/03/16**. **eng**).
26. Goldhirsch A, Wood WC, Coates AS, Gelber RD, Thurlimann B, Senn HJ. Strategies for subtypes—dealing with the diversity of breast cancer: highlights of the St. Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2011. *Ann Oncol*. 2011;22(8):1736–47. (**PubMed PMID: 21709140**. **Pubmed Central PMCID: Pmc3144634**. **Epub 2011/06/29**. **eng**).
27. Giuliano AE, McCall L, Beitsch P, Whitworth PW, Blumenkrantz P, Leitch AM, et al. Locoregional recurrence after sentinel lymph node dissection with or without axillary dissection in patients with sentinel lymph node metastases: the American College of Surgeons Oncology Group Z0011 randomized trial. *Ann*

- Surg. 2010;252(3):426–32. (discussion 32–3. PubMed PMID: 20739842. Epub 2010/08/27. eng).
28. Straver ME, Meijnen P, van Tienhoven G, van de Velde CJ, Mansel RE, Bogaerts J, et al. Role of axillary clearance after a tumor-positive sentinel node in the administration of adjuvant therapy in early breast cancer. *J Clin Oncol*. 2010;28(5):731–7. (PubMed PMID: 20038733. Pubmed Central PMCID: 2834391).
 29. Savolt A, Musonda P, Matrai Z, Polgar C, Renyi-Vamos F, Rubovszky G, et al. Optimal treatment of the axilla after positive sentinel lymph node biopsy in early invasive breast cancer. Early results of the OTOASOR trial. *Orvosi hetilap*. 2013;154(49):1934–42. (PubMed PMID: 24292111. Epub 2013/12/03. Az axilla optimális kezelese pozitív orszemnyiroksomo eseten korai invaziv emlorkabban. Az OTOASOR vizsgalat elozetes eredmenyei. hun).
 30. Lyman GH, Temin S, Edge SB, Newman LA, Turner RR, Weaver DL, et al. Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol*. 2014;32(13):1365–83. (PubMed PMID: 24663048. Epub 2014/03/26. eng).
 31. Gebruers N, Verbelen H, De Vrieze T, Coeck D, Tjalma W. The incidence and time path of lymphedema in sentinel negative breast cancer patients: a systematic review. *Arch Phys Med Rehabil*. 2015;96:1131–1139. (PubMed PMID: 25637862. Epub 2015/02/01. Eng).
 32. Noguchi M. Z-11 trial and rethinking axillary reverse mapping. *Breast Cancer*. 2015;22(2):99–100. (PubMed PMID: 25577513. Epub 2015/01/13. eng).
 33. Suami H, Taylor GI, Pan WR. The lymphatic territories of the upper limb: anatomical study and clinical implications. *Plastic Reconstr Surg*. 2007;119(6):1813–22. (PubMed PMID: 17440362. Epub 2007/04/19. eng).
 34. Hama Y, Koyama Y, Urano Y, Choyke PL, Kobayashi H. Simultaneous two-color spectral fluorescence lymphangiography with near infrared quantum dots to map two lymphatic flows from the breast and the upper extremity. *Breast Cancer Res Treat*. 2007;103(1):23–8. (PubMed PMID: 17028977. Epub 2006/10/10. eng).
 35. Thompson M, Korourian S, Henry-Tillman R, Adkins L, Mumford S, Westbrook KC, et al. Axillary reverse mapping (ARM): a new concept to identify and enhance lymphatic preservation. *Ann Surg Oncol*. 2007;14(6):1890–5. (PubMed PMID: 17479341. Epub 2007/05/05. eng).
 36. Boneti C, Korourian S, Diaz Z, Santiago C, Mumford S, Adkins L, et al. Scientific Impact Award: axillary reverse mapping (ARM) to identify and protect lymphatics draining the arm during axillary lymphadenectomy. *Am J Surg*. 2009;198(4):482–7. (PubMed PMID: 19800452. Epub 2009/10/06. eng).
 37. Nos C, Lesieur B, Clough KB, Lecuru F. Blue dye injection in the arm in order to conserve the lymphatic drainage of the arm in breast cancer patients requiring an axillary dissection. *Ann Surg Oncol*. 2007;14(9):2490–6. (PubMed PMID: 17549570. Epub 2007/06/06. eng).
 38. Boneti C, Korourian S, Bland K, Cox K, Adkins LL, Henry-Tillman RS, et al. Axillary reverse mapping: mapping and preserving arm lymphatics may be important in preventing lymphedema during sentinel lymph node biopsy. *J Am Coll Surg*. 2008;206(5):1038–42. (discussion 42–4. PubMed PMID: 18471751. Epub 2008/05/13. eng).
 39. Casabona F, Bogliolo S, Valenzano Menada M, Sala P, Villa G, Ferrero S. Feasibility of axillary reverse mapping during sentinel lymph node biopsy in breast cancer patients. *Ann Surg Oncol*. 2009;16(9):2459–63. (PubMed PMID: 19506954. Epub 2009/06/10. eng).
 40. Han JW, Seo YJ, Choi JE, Kang SH, Bae YK, Lee SJ. The efficacy of arm node preserving surgery using axillary reverse mapping for preventing lymphedema in patients with breast cancer. *J Breast Cancer*. 2012;15(1):91–7. (PubMed PMID: 22493634. Pubmed Central PMCID: Pmc3318181. Epub 2012/04/12. eng).
 41. Beek MA, Gobardhan PD, Klompenhouwer EG, Rutten HJ, Voogd AC, Luiten EJ. Axillary reverse mapping (ARM) in clinically node positive breast cancer patients. *Eur J Surg Oncol*. 2015;41(1):59–63. (PubMed PMID: 25468747. Epub 2014/12/04. eng).
 42. Deng H, Chen L, Jia W, Chen K, Zeng Y, Rao N, et al. Safety study of axillary reverse mapping in the surgical treatment for breast cancer patients. *J Cancer Res Clin Oncol*. 2011;137(12):1869–74. (PubMed PMID: 21935615. Epub 2011/09/22. eng).
 43. Bedrosian I, Babiera GV, Mittendorf EA, Kuerer HM, Pantoja L, Hunt KK, et al. A phase I study to assess the feasibility and oncologic safety of axillary reverse mapping in breast cancer patients. *Cancer*. 2010;116(11):2543–8. (PubMed PMID: 20336790. Epub 2010/03/26. eng).
 44. Ochoa D, Korourian S, Boneti C, Adkins L, Badgwell B, Klimberg VS. Axillary reverse mapping: five-year experience. *Surgery*. 2014;156(5):1261–8. (PubMed PMID: 25444319. Epub 2014/12/03. eng).
 45. Boccardo F, Casabona F, De Cian F, Friedman D, Villa G, Bogliolo S, et al. Lymphedema microsurgical preventive healing approach: a new technique for primary prevention of arm lymphedema after mastectomy. *Ann Surg Oncol*. 2009;16(3):703–8. (PubMed PMID: 19139964. Epub 2009/01/14. eng).
 46. Ponzzone R, Cont NT, Maggiorotto F, Cassina E, Mininanni P, Biglia N, et al. Extensive nodal disease may impair axillary reverse mapping in patients with breast cancer. *J Clin Oncol*. 2009;27(33):5547–51. (PubMed PMID: 19826123. Epub 2009/10/15. eng).
 47. Gobardhan PD, Wijsman JH, van Dalen T, Klompenhouwer EG, van der Schelling GP, Los J, et al. ARM: axillary reverse mapping—the need for selection of patients. *Eur J Surg Oncol*. 2012;38(8):657–61. (PubMed PMID: 22607749. Epub 2012/05/23. eng).
 48. Schunemann E Jr, Doria MT, Silvestre JB, Gasperin P Jr, Cavalcanti TC, Budel VM. Prospective study evaluating oncologic safety of axillary reverse mapping. *Ann Surg Oncol*. 2014;21(7):2197–202. (PubMed PMID: 24599413. Pubmed Central PMCID: Pmc4047480. Epub 2014/03/07. eng).
 49. Tausch C, Baege A, Dietrich D, Vergin I, Heuer H, Heusler RH, et al. Can axillary reverse mapping avoid lymphedema in node positive breast cancer patients? *Eur J Surg Oncol*. 2013;39(8):880–6. (PubMed PMID: 23735162. Epub 2013/06/06. eng).
 50. Britton TB, Solanki CK, Pinder SE, Mortimer PS, Peters AM, Purushotham AD. Lymphatic drainage pathways of the breast and the upper limb. *Nucl Med Commun*. 2009;30(6):427–30. (PubMed PMID: 19319006. Epub 2009/03/26. eng).
 51. Gennaro M, Maccauro M, Sigari C, Casalini P, Bedodi L, Conti AR, et al. Selective axillary dissection after axillary reverse mapping to prevent breast-cancer-related lymphoedema. *Eur J Surg Oncol*. 2013;39(12):1341–5. (PubMed PMID: 24113621. Epub 2013/10/12. eng).
 52. Yue T, Zhuang D, Zhou P, Zheng L, Fan Z, Zhu J, et al. A prospective study to assess the feasibility of axillary reverse mapping and evaluate its effect on preventing lymphedema in breast cancer patients. *Clin Breast Cancer*. 2015;15(4):301–6. (PubMed PMID: 25776198. Epub 2015/03/18. eng).
 53. Nos C, Kaufmann G, Clough KB, Collignon MA, Zerbib E, Cusumano P, et al. Combined axillary reverse mapping (ARM) technique for breast cancer patients requiring axillary dissection. *Ann Surg Oncol*. 2008;15(9):2550–5. (PubMed PMID: 18618185. Epub 2008/07/12. eng).
 54. Noguchi M, Inokuchi M, Zen Y. Complement of peritumoral and subareolar injection in breast cancer sentinel lymph node biopsy.

- J Surg Oncol. 2009;100(2):100–5. (PubMed PMID: 19479943. Epub 2009/05/30. eng).
55. Sakurai T, Endo M, Shimizu K, Yoshimizu N, Nakajima K, Nosaka K, et al. Axillary reverse mapping using fluorescence imaging is useful for identifying the risk group of postoperative lymphedema in breast cancer patients undergoing sentinel node biopsies. *J Surg Oncol.* 2014;109(6):612–5. (PubMed PMID: 24310418. Pubmed Central PMCID: Pmc4263257. Epub 2013/12/07. eng).
 56. Noguchi M, Noguchi M, Nakano Y, Ohno Y, Kosaka T. Axillary reverse mapping using a fluorescence imaging system in breast cancer. *J Surg Oncol.* 2012;105(3):229–34. (PubMed PMID: 21913193. Epub 2011/09/14. eng).
 57. Ikeda K, Ogawa Y, Kajino C, Deguchi S, Kurihara S, Tashima T, et al. The influence of axillary reverse mapping related factors on lymphedema in breast cancer patients. *Eur J Surg Oncol.* 2014;40(7):818–23. (PubMed PMID: 24768416. Epub 2014/04/29. eng).
 58. Noguchi M, Yokoi M, Nakano Y. Axillary reverse mapping with indocyanine fluorescence imaging in patients with breast cancer. *J Surg Oncol.* 2010;101(3):217–21. (PubMed PMID: 20063370. Epub 2010/01/12. eng).
 59. Ikeda K, Ogawa Y, Komatsu H, Mori Y, Ishikawa A, Nakajima T, et al. Evaluation of the metastatic status of lymph nodes identified using axillary reverse mapping in breast cancer patients. *World J Surg Oncol.* 2012;10:233. (PubMed PMID: 23116152. Pubmed Central PMCID: Pmc3527301. Epub 2012/11/03. eng).
 60. Ponzzone R, Mininanni P, Cassina E, Sismondi P. Axillary reverse mapping in breast cancer: can we spare what we find? *Ann Surg Oncol.* 2008;15(1):390–1. (author reply 2–3. PubMed PMID: 17990039. Epub 2007/11/09. eng).
 61. Kuusk U, Seyednejad N, McKeivitt EC, Dingee CK, Wiseman SM. Axillary reverse mapping in breast cancer: a Canadian experience. *J Surg Oncol.* 2014;110(7):791–5. (PubMed PMID: 25053441. Epub 2014/07/24. eng).
 62. Rubio IT, Cebrecos I, Peg V, Esgueva A, Mendoza C, Cortadellas T, et al. Extensive nodal involvement increases the positivity of blue nodes in the axillary reverse mapping procedure in patients with breast cancer. *J Surg Oncol.* 2012;106(1):89–93. (PubMed PMID: 22258666. Epub 2012/01/20. eng).
 63. Yue T, Zhuang D, Zhou P, Zheng L, Fan Z, Zhu J, et al. A prospective study to assess the feasibility of axillary reverse mapping and evaluate its effect on preventing lymphedema in breast cancer patients. *Clin Breast Cancer.* 2015;15:301–6. (PubMed PMID: 25776198. Epub 2015/03/18. Eng).
 64. Klompenhouwer EG, Gobardhan PD, Beek MA, Voogd AC, Luiten EJ. The clinical relevance of axillary reverse mapping (ARM): study protocol for a randomized controlled trial. *Trials.* 2013;14:111. (PubMed PMID: 23782712. Pubmed Central PMCID: PMC3663653. Epub 2013/06/21. eng).
 65. Pavlista D, Eliska O. Relationship between the lymphatic drainage of the breast and the upper extremity: a postmortem study. *Ann Surg Oncol.* 2012;19(11):3410–5. (PubMed PMID: 22526910. Epub 2012/04/25. eng).
 66. Pavlista D, Eliska O. Analysis of direct oil contrast lymphography of upper limb lymphatics traversing the axilla—a lesson from the past—contribution to the concept of axillary reverse mapping. *Eur J Surg Oncol.* 2012;38(5):390–4. (PubMed PMID: 22336143. Epub 2012/02/18. eng).
 67. Pavlista D, Koliba P, Eliska O. Axillary reverse mapping—chance to prevent lymphedema in breast cancer patients. *Ceska gynecologie/Ceska lekárska společnost. J Ev Purkyne.* 2011;76(5):355–9. (PubMed PMID: 22132635. Epub 2011/12/03. Reverzni mapovani lymfatik v axile jako možnost prevence lymfedemu u pacientek s karcinomem prsu. cze).
 68. Suami H, O'Neill JK, Pan WR, Taylor GI. Superficial lymphatic system of the upper torso: preliminary radiographic results in human cadavers. *Plastic Reconstr Surg.* 2008;121(4):1231–9. (PubMed PMID: 18349641. Epub 2008/03/20. eng).
 69. Senofsky GM, Moffat FL Jr, Davis K, Masri MM, Clark KC, Robinson DS, et al. Total axillary lymphadenectomy in the management of breast cancer. *Archives of surgery (Chicago, Ill: 1960).* 1991;126(11):1336–41. (discussion 41–2. PubMed PMID: 1747046. Epub 1991/11/11. eng).
 70. Mihara M, Hayashi Y, Hara H, Todokoro T, Koshima I, Murai N. Lymphatic-venous anastomosis for the radical cure of a large pelvic lymphocyst. *J Minim Invasive Gynecol.* 2012;19(1):125–7. (PubMed PMID: 22196262. Epub 2011/12/27. eng).
 71. Campisi C, Bellini C, Campisi C, Accogli S, Bonioli E, Boccardo F. Microsurgery for lymphedema: clinical research and long-term results. *Microsurgery.* 2010;30(4):256–60. (PubMed PMID: 20235160. Epub 2010/03/18. eng).
 72. Campisi C, Boccardo F. Microsurgical techniques for lymphedema treatment: derivative lymphatic-venous microsurgery. *World J Surg.* 2004;28(6):609–13. (PubMed PMID: 15366754. Epub 2004/09/16. eng).
 73. Damstra RJ, Voesten HG, van Schelven WD, van der Lei B. Lymphatic venous anastomosis (LVA) for treatment of secondary arm lymphedema. A prospective study of 11 LVA procedures in 10 patients with breast cancer related lymphedema and a critical review of the literature. *Breast Cancer Res Treat.* 2009;113(2):199–206. (PubMed PMID: 18270813. Epub 2008/02/14. eng).
 74. Noguchi M. Axillary reverse mapping for breast cancer. *Breast Cancer Res Treat.* 2010;119(3):529–35. (PubMed PMID: 19842033. Epub 2009/10/21. eng).
 75. DiSipio T, Rye S, Newman B, Hayes S. Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. *Lancet Oncol.* 2013;14(6):500–15. (PubMed PMID: 23540561. Epub 2013/04/02. eng).
 76. Jammallo LS, Miller CL, Singer M, Horick NK, Skolny MN, Specht MC, et al. Impact of body mass index and weight fluctuation on lymphedema risk in patients treated for breast cancer. *Breast Cancer Res Treat.* 2013;142(1):59–67. (PubMed PMID: 24122390. Pubmed Central PMCID: Pmc3873728. Epub 2013/10/15. eng).
 77. Ugur S, Arici C, Yaprak M, Mesci A, Arici GA, Dolay K, et al. Risk factors of breast cancer-related lymphedema. *Lymph Res Biol.* 2013;11(2):72–5. (PubMed PMID: 23772716. Pubmed Central PMCID: Pmc3685313. Epub 2013/06/19. eng).
 78. Pasko JL, Garreau J, Carl A, Ansteth M, Glissmeyer M, Johnson N. Axillary reverse lymphatic mapping reduces patient perceived incidence of lymphedema after axillary dissection in breast cancer. *Am J Surg.* 2015;209(5):890–5. (PubMed PMID: 25796096. Epub 2015/03/23. eng).