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ORIGINAL ARTICLE – BREAST ONCOLOGY

Single Institution Experience with Lymphatic Microsurgical Preventive Healing Approach (LYMPHA) for the Primary Prevention of Lymphedema

Sheldon Feldman, MD[1], Hannah Bansil, MD[1], Jeffrey Ascherman, MD[2], Robert Grant, MD[2], Billie Borden, BA[3], Peter Henderson, MD[2], Adewuni Ojo, MD[1], Bret Taback, MD[1], Margaret Chen, MD[1], Preya Ananthakrishnan, MD[1], Amiya Vaz, BA[1], Fatih Balci, MD[1,5], Chaitanya R. Divgi, MD[4], David Leung, MD[4], and Christine Rohde, MD[2]

[1]Division of Breast Surgery, Columbia University Medical Center, New York-Presbyterian Hospital, Columbia University, New York, NY; [2]Division of Plastic Surgery, Columbia University Medical Center, New York-Presbyterian Hospital, Columbia University, New York, NY; [3]Columbia University College of Physicians and Surgeons, New York, NY; [4]Department of Radiology, Columbia University Medical Center, New York-Presbyterian Hospital, Columbia University, New York, NY; [5]Department of Surgery, Atakent Hospital, Acibadem University, Istanbul, Turkey

ABSTRACT

Background. As many as 40 % of breast cancer patients undergoing axillary lymph node dissection (ALND) and radiotherapy develop lymphedema. We report our experience performing lymphatic–venous anastomosis using the lymphatic microsurgical preventive healing approach (LYMPHA) at the time of ALND. This technique was described by Boccardo, Campisi in 2009.

Methods. LYMPHA was offered to node-positive women with breast cancer requiring ALND. Afferent lymphatic vessels, identified by injection of blue dye in the ipsilateral arm, were sutured into a branch of the axillary vein distal to a competent valve. Follow-up was with pre- and postoperative lymphoscintigraphy, arm measurements, and (L-Dex®) bioimpedance spectroscopy.

Results. Over 26 months, 37 women underwent attempted LYMPHA, with successful completion in 27. Unsuccessful attempts were due to lack of a suitable vein ($n = 3$) and lymphatic ($n = 5$) or extensive axillary disease ($n = 1$). There were no LYMPHA-related complications. Mean follow-up time was 6 months (range 3–24 months). Among completed patients, 10 (37 %) had a body mass index of $\geq$30 kg/m^2 (mean 27.9 $\pm$ 6.8 kg/m^2, range 17.4–47.6 kg/m^2), and 17 (63 %) received axillary radiotherapy. Excluding two patients with preoperative lymphedema and those with less than 3-month follow-up, the lymphedema rate was 3 (12.5 %) of 24 in successfully completed and 4 (50 %) of 8 in unsuccessfully treated patients.

Conclusions. Our transient lymphedema rate in this high-risk cohort of patients was 12.5 %. Early data show that LYMPHA is feasible, safe, and effective for the primary prevention of breast cancer-related lymphedema.

Increasing use of sentinel lymph node biopsy has led to a decreased incidence of secondary lymphedema among women with breast cancer, with reported rates of 1–7 % after biopsy. Axillary lymph node dissection (ALND) is now performed more selectively on the basis of such studies as ACOSOG Z0011 and ACOSOG Z1071.[1–7] Still, secondary lymphedema remains a major source of morbidity among those who require ALND, with rates ranging from 20 to 45 %—four times that seen after sentinel lymph node biopsy.[1,8–10] A particularly high-risk group is women undergoing both ALND and nodal radiotherapy.[11,12] Factors shown to increase risk for secondary lymphedema include number of nodes dissected, extended nodal radiotherapy, and a body mass index (BMI) of $\geq$30 kg/m^2.[8,9,11–14] Current management focuses on alleviating the symptoms of secondary lymphedema through manual lymph drainage with massage, compression garments, and physical therapy but requires ongoing compliance with treatment.[15]

Breast cancer survivors with lymphedema report long-term decrease in their quality of life as well as chronic pain, depression, and anxiety.[16] They have higher medical costs

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S. Feldman, MD
e-mail: sf2388@cumc.columbia.edu

and more productive days lost than women without lymphedema.[17] The significant impact on survivorship and requirement for lifelong therapy mandates that effective preventive strategies be explored. As early as 1988, Akimov and colleagues presented data on a surgical preventive approach being used in the USSR.[18,19] They described a technique of microsurgical lymphovascular anastomosis in the ipsilateral upper extremity of women undergoing radical mastectomy. Lymphoscintigraphy and intralymphatic pressure measurements demonstrated a return to normal microcirculation within 20 days of mastectomy. Despite early evidence of its effectiveness, the technique remained unused. Recently Boccardo et al. began using the axillary reverse mapping and lymphatic microsurgical preventive healing approach (LYMPHA) among women undergoing axillary dissection for breast cancer.[20–26] Arm lymphatics were identified and preserved at the time of axillary dissection, and microsurgical anastomosis to an axillary vein branch was performed. Among 74 patients undergoing LYMPHA, there was a 4.05 % secondary lymphedema rate at 4-year follow-up.

We report on the feasibility and short-term outcomes using this technique in a high-risk population at our institution.

METHODS

Female patients with breast cancer and documented axillary nodal metastasis undergoing planned axillary node dissection or modified radical mastectomy were offered LYMPHA. Exclusion criteria included those not undergoing complete axillary node dissection, allergy to Lymphazurin blue dye, and pregnancy. There was on-site training both in Genoa and from visiting faculty to our institution for mentoring on the technical aspects of the procedure. The experimental protocol was approved by our institutional review board.

Selection criteria differed from that of the Italian group.[26] In their cohort, patients were included on the basis of BMI >30 kg/m^2 or transit index >10 on preoperative lymphoscintigraphy. Among our patients, neither BMI nor preoperative lymphoscintigraphy were used as inclusion or exclusion criteria but were reported in final analysis. Patients deemed to be at high risk were selected on the basis of extensive nodal disease at presentation and the likely need for post-ALND radiotherapy.

Preoperative evaluation included examination with arm measurements as well as bilateral lymphoscintigraphy and L-Dex bioimpedance spectroscopy. Postoperatively, patients were seen in the clinic on a scheduled basis: 2 weeks, 4 weeks, 3 months, 6 months, 1 year, and 18 months. They had clinical examination, arm measurements, and L-Dex at all visits and underwent lymphoscintigraphy at 3 and 18 months. Patients who were enrolled but unable to undergo completed LYMPHA were followed with clinical examination and bioimpedance spectroscopy at the discretion of the attending surgeon, but they did not undergo postoperative lymphoscintigraphy.

Lymphoscintigrams were performed in the department of radiology. Approximately 2 millicuries of technetium was injected into the hand at the web spaces. A gamma camera was used to capture radiotracer images in the studied arm. Both arms were studied at all three time points for comparative purposes. Abnormal lymphoscintigram was defined as transit index of >10 or visualized obstruction or collateral formation in the ipsilateral arm.[27]

Arm measurements were performed at the five specified locations on the arm (wrist, midforearm, just above elbow, mid–upper arm, and axilla). Nursing staff was trained to perform arm measurements in order to limit interobserver variability. Arm measurements were considered to be abnormal if there was a more than 2 cm discrepancy in circumferential size measurements between the affected and unaffected arms or a change from baseline.

Any subject who developed clinical evidence or symptoms of lymphedema while participating in the study was referred for treatment with standard-of-care techniques, including compression sleeves, physical therapy, and lymphatic massage. Abnormal L-Dex findings or arm measurement alone in the absence of clinical findings or symptoms was not used as an absolute indication for referral. Choice to refer for therapy in these circumstances was left to the treating physician's discretion.

LYMPHA was performed at the time of planned axillary dissection. Before incision, Lymphazurin blue dye was injected into the volar surface of the upper third of the arm (3–4 ml intradermally, subcutaneously, and under muscle fascia). Standard level 1 and 2 axillary dissection was performed. Afferent blue lymphatics were identified from the arm and were clipped near the insertion to the nodal capsule. During dissection, a collateral branch of the axillary vein, with intact valve, was preserved with suitable length to reach the lymphatic vessels. Location and competence of the valve were determined by visual inspection and by the absence of back-bleeding before anastomosis. After completion of the axillary dissection and removal of the nodal packet, lymphatic–venous anastomosis was performed by a plastic surgeon trained in microsurgical technique. The anastomosis was performed using a "dunking" technique, with the identified lymphatics being inserted into the vein's cut end and sutured to the vein using 8-0 and 9-0 nylon sutures (Figs. 1, 2). A mean of 1.5 lymphatic vessels (range 1–3 vessels) were used. If multiple lymphatics were present, all were dunked into the same vein. A drain was placed in the axilla, and patients received standard postoperative care.

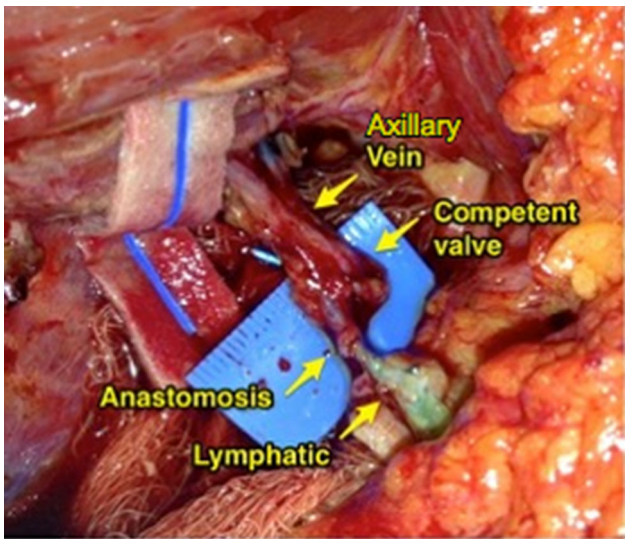

FIG. 1 Lymphovenous anastomosis

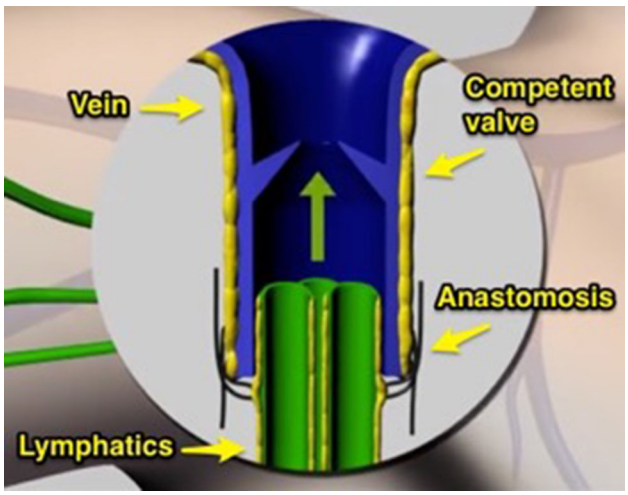

FIG. 2 Schematic of lymphovenous anastamosis with proximal valve

The quantitative variables—age, BMI, total nodes excised, and number of positive nodes—were compared between the completed and incomplete LYMPHA groups by the Student *t* test. Nominal variables (surgery type, radiotherapy, and chemotherapy) were compared by the Fisher exact test. Lymphedema rates in completed and incomplete groups and completed and historical groups were compared by the Fisher exact test. All reported *p* values are two sided.

RESULTS

Over a period of 29 months, beginning in December 2012, 40 women consented to the LYMPHA procedure. Three withdrew consent before surgery; two had preexisting lymphedema and were excluded from analysis. Of these 35 patients, 26 had successfully completed LYMPHA (Fig. 3). Two patients have yet to reach 3-month follow-up and are not included in analysis. Patient demographics and risk factors are provided in Table 1. Average additional surgical time required for completion of LYMPHA was approximately 45 min. All cases were treated by a breast surgeon and a plastic surgeon trained in microsurgical techniques. Four breast surgeons and three plastic surgeons participated in the study. Twenty-four of the 37 nodal dissections were performed by one breast surgeon. There was a nearly even split of completed LYMPHA cases, 15 and 12, between two of the plastic surgeons, with no significant difference in rates of unsuccessfully attempted LYMPHA between surgeons. The proportion of patients who consented to the procedure but who were unable to complete LYMPHA remained stable over the course of the study, with no evident learning curve in the rate of completion. The average size of the anastomosed lymphatics was 1–2 mm.

Median follow-up was 6 months (range 3–24 months). Three patients (12.5 %) developed lymphedema (95 % confidence interval [CI] 0.04–0.31). Onset was between 6 to 10 months after surgery. All had resolution within 6 months of onset, but two had recurrence requiring ongoing treatment at 18-month follow-up. All three had BMI of >30 kg/m^2, and two received external beam radiotherapy.

From the completed LYMPHA group, 16 patients have had 3-month lymphoscintigraphy. Five patients had 18-month lymphoscintigraphy. In only one was abnormal ipsilateral lymphatic drainage visualized. At most recent follow-up, 13 patients (54 %) had at least one ipsilateral arm measurement 2 cm above baseline, but only one patient with abnormal measurement had clinical lymphedema. The three patients with transient or ongoing lymphedema in the completed LYMPHA group each had at least one abnormal L-Dex measurement during their initial 6-month follow-up, coinciding with the time period of documented lymphedema. Despite this correlation, L-Dex had a calculated negative predictive value of 0.86 (95 % CI 0.56–0.97) and a positive predictive value of 0.44 (95 % CI 0.15–0.77) among our cohort. The majority of false-positive results occurred at the 2-week postoperative visit. This may be related to postsurgical fluid shifts causing differences in bioimpedance. Excluding the abnormal 2-week values gives a negative predictive value of 0.88 (95 % CI 0.60–0.97) and a positive predictive value of 0.57 (95 % CI 0.20–0.88).

Out of 35 patients, nine were unable to undergo LYMPHA at time of surgery. Among these, five had inadequate mapping with no suitable lymphatic identified. Three had no suitable vein for anastomosis. One had extensive

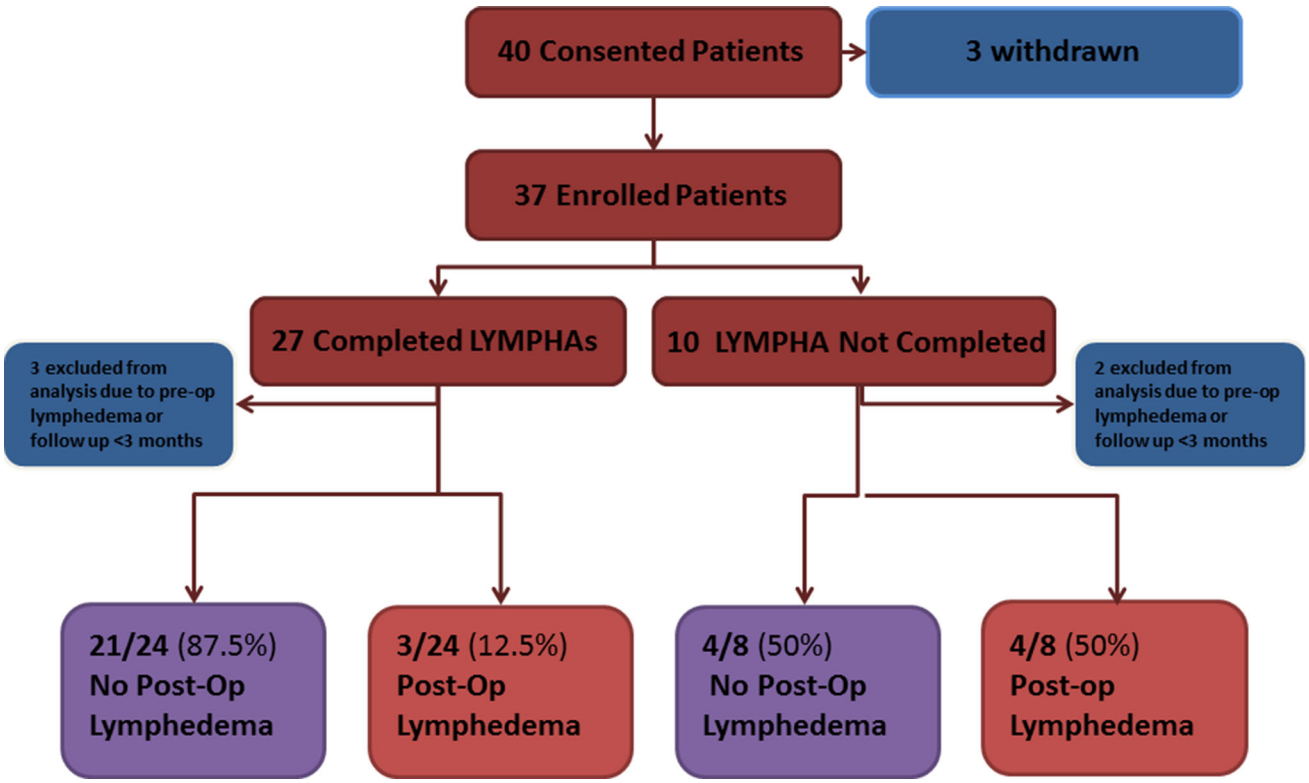

FIG. 3 Flow chart of enrolled patients and outcomes

TABLE 1 Patient characteristics

Characteristic	Incomplete LYMPHA ($n = 8$)	Completed LYMPHA ($n = 24$)	p
Age (years)	55.8 ± 13.1 (33–71)	58.1 ± 11.8 (33–76)	0.63[a]
Body mass index (kg/m^2)	29.5 ± 7.1 (23.5–41.5)	28.7 ± 6.8 (17.4–47.5)	0.77
Total lymph nodes excised	14.0 ± 7.0 (4–28)	18.0 ± 8.0 (3–37)	0.26
Positive lymph nodes	5.0 ± 5.5 (1–16)	3.0 ± 3.0 (0–13)	0.26
Type of surgery (breast conservation)	1/8 (12.5)	4/24 (16.6)	1.0[b]
Adjuvant radiotherapy	6/8 (75)	15/24 (62.5)	0.68
Chemotherapy (yes/no)	7/8 (87.5)	23/24 (95.8)	0.44

Data are presented as average ± SD (range) or as *n/N* (%)

[a] *t* test of independent samples, using two-tailed *p*

[b] Fisher's exact test, using two-tailed *p*

axillary disease that precluded completion of LYMPHA. Including only patients with at least 3-month follow-up, the median follow-up time in this group was 9 months (range 6–18 months). Of these, four patients, or 50 % (95 %CI 0.15–0.85), developed clinically apparent lymphedema. Three of the four required ongoing treatment for symptoms at most recent follow-up. These patients were overall comparable to the patients with completed LYMPHA, with no statistically significant differences in number of excised nodes, number of positive nodes, rates of radiotherapy, or BMI (Table 1).

In a retrospective review at our institution, 170 patients were identified who had undergone axillary node dissection during a 7-year period from November 2007 to November 2014, all performed by surgeons participating in the current study. Documented clinical lymphedema rate was 52 (30.6 %) of 170 (95 % CI 0.24–0.38).

Comparing patients with completed and incomplete LYMPHA with 3-month or longer follow-up, the odds ratio for development of lymphedema with LYMPHA versus no LYMPHA was 0.14 (95 % CI 0.02–0.90). The Fisher exact probability test provided a two-tailed p value of 0.05.

When we compared the completed LYMPHA patients with more than 3-month follow-up with the historical group at our institution, we found the calculated odds ratio for development of clinically apparent lymphedema provided completed LYMPHA to be 0.32 (95 % CI 0.09–1.13), with a Fisher exact probability test two-tailed p value of 0.09.

DISCUSSION

There are three major limitations to our current study: its nonrandomized study design, the difficulty of defining transient versus ongoing lymphedema, and the current limitations in knowledge on the significance and appropriate measurement of preclinical lymphedema.

Our study was designed as a pilot project to evaluate the feasibility of LYMPHA among our own high-risk patient population. As such, it had neither randomization nor a formal control group. Even so, our subset of patients unable to complete LYMPHA had clinical characteristics including age, BMI, type of surgery, nodal disease burden, and radiotherapy rates comparable to those of our completed group (Table 1). This group and the historical group from our own institution allowed us to make meaningful comparisons between patients treated with LYMPHA and those receiving standard management. In both comparisons, LYMPHA showed decreased odds for development of clinical lymphedema, and although limited by small sample size, this reached statistical significance in the completed versus incomplete groups. Because of decreasing rates of axillary node dissection, it is difficult to accrue sufficient patients for a randomized trial at a single institution, but further evaluation in a multicenter trial is warranted by these findings.

In reporting 4-year follow-up on their cohort of 74 patients undergoing LYMPHA, Boccardo et al. reported a 4.05 % rate of ongoing lymphedema and if including transient lymphedema a total rate of 10.8 %.[26] The definition and significance of transient lymphedema remains unclear, and in our own population we had an 8.3 % rate of ongoing lymphedema and a total rate of 12.5 %. We defined transient lymphedema as clinically evident arm swelling, grade 1 or more at clinical examination, or patient-reported arm swelling or heaviness occurring more than 2 weeks after surgery and resolving completely within 6 months of onset, with or without physical therapy and compression treatment. In their prospective study of the natural history of lymphedema in breast cancer patients, Blaney et al. reported 27 patients identified over the 12-month course of the study as having lymphedema. Of these 27 patients, 14 (51.8 %) had spontaneous resolution of their lymphedema before being seen in the physical therapy clinic (average time to visit was 4.8 weeks). Of these 14 patients, 10 returned to the physical therapist for 6-month evaluation, and only three required further treatment for lymphedema.[28] Transient lymphedema may be related to many treatment and patient factors beyond simply lymphatic obstruction in the axilla; radiation effects, Taxol effect, and elevated BMI may all play a role.[29,30] In their prospective study of breast cancer survivors Norman et al. found that 23.1 % of women experienced mild waxing and waning lymphedema symptoms in the first 3 years after treatment.[31] Although symptoms for most were mild and transient, this group had three times the risk of progression to moderate or severe edema compared to those who never had symptoms. Both the Boccardo et al. cohort and our own patients had multiple risk factors for transient lymphedema, including high average BMI, high rates of Taxol use, and postoperative radiotherapy. With multiple potentially contributing factors and unclear significance of transient lymphedema, it is apparent that long-term follow-up of our patients is imperative.

Key to defining success is how we chose to follow and evaluate patients. Ultimately the most important outcomes are those of patient reported symptoms and satisfaction. Use of bioimpedance and arm measurement have shown little prognostic value in our patients, and if abnormal are of uncertain significance in asymptomatic patients. Although arm circumference measurements are logistically much easier than volumetric measurement, they require a very high degree of interuser reliability that may not be attainable. These evaluation difficulties are demonstrated among our own patients with significant fluctuation in arm measurements, L-Dex measurements, and transit index observed over time with limited correlation to development of clinically significant lymphedema. In addition, attempts to visualize anastomotic patency by lymphoscintigraphy were limited by lack of imaging resolution. Important future areas for evaluation of this technique are inclusion of patient-reported outcomes such as the Norman Questionnaire and newer imaging modalities such as single-photon emission computed tomography to visualize anastomotic patency.[32]

CONCLUSION

Early data in our high-risk cohort of patients suggest that LYMPHA is feasible, safe, and effective as a method for the primary prevention of clinical lymphedema. We believe this technique may serve to significantly improve the long-term quality of life in breast cancer patients. Follow-up is ongoing to evaluate the significance of transient lymphedema and subclinical measurement abnormalities in our patient population. Larger multi-

institutional and randomized trials are warranted to further evaluate the effectiveness of LYMPHA.

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DISCLOSURE The authors declare no conflict of interest.

REFERENCES

1. Wilke L, McCall L, Posther K, et al. Surgical complications associated with sentinel lymph node biopsy: results from a prospective international cooperative group trial. *Ann Surg Oncol.* 2006;13:491–500.
2. Giuliano A, Hunt K, Ballman K, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis. *JAMA.* 2011;305:569–75.
3. Fleissig A, Fallowfiel L, Langridge C, et al. Postoperative arm morbidity and quality of life: results of the ALMANAC randomized trial comparing sentinel node biopsy with standard axillary treatment in the management of patients with early breast cancer. *Breast Cancer Res Treat.* 2006;95:279–93.
4. Veronesi U, Paganelli G, Viale G, et al. A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. *N Engl J Med.* 2003;349:546–53.
5. Mansel R, Fallowfield L, Kissin M, 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;98:599–609.
6. McLaughlin S, Wright M, Morris K, et al. Prevalence of lymphedema in women with breast cancer 5 years after sentinel lymph node biopsy or axillary dissection: patient perceptions and precautionary behaviors. *J Clin Oncol.* 2008;26:5220–6.
7. Boughey J, Suman V, Mittendorf E, et al. Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer. *JAMA.* 2013;310:1455–61.
8. DiSipio T, Rye S, Newman B, Hayes S. Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. *Lancet.* 2013;14:500–15.
9. Hayes S, Johansson K, Stout N, et al. Upper-body morbidity after breast cancer. *Cancer.* 2012;118:2237–49.
10. Hayes S, Disipio T, Rye S, et al. Prevalence and prognostic significance of secondary lymphedema following breast cancer. *Lymphat Res Biol*. 2011;9:135–41.
11. Chang D, Feigenberg S, Indelicato D, et al. Long-term outcomes in breast cancer patients with ten or more positive axillary nodes treated with combined-modality therapy: the importance of radiation field selection. *Int J Radiat Biol Phys.* 2007;67:1043–51.
12. Warren L, Miller C, Horick N, et al. The impact of radiation therapy on the risk of lymphedema after treatment for breast cancer: a prospective cohort study. *Int J Radiat Oncol Biol Phys.* 2014;88:565–71.
13. Ridner S, Dietrich M, Stewart B, Armer J. Body mass index and breast cancer treatment-related lymphedema. *Support Care Cancer.*2011;19:853–7.
14. Helyer L, Varnic M, Le L, Leong W, McCready D. Obesity is a risk factor for developing postoperative lymphedema in breast cancer patients. *Breast J.* 2010;16:48–54.
15. Vignes S, Porcher R, Arrault M, Dupuy A. Long-term management of breast cancer–related lymphedema after intensive decongestive physiotherapy. *Breast Cancer Res Treat.* 2007;101:285–90.
16. Pasket E, Dean J, Oliveri J, Harrop J. Cancer-related lymphedema risk factors, diagnosis, treatment, and impact. *J Clin Oncol.* 2012;30:3726–33.
17. Yah-Chen T, Ying Xu J, Cormier S, et al. Incidence, treatment costs, and complications of lymphedema after breast cancer among women of working age: a 2-year follow-up study. *J Clin Oncol.* 2009;27:2007–14.
18. Pronin V, Adamian A, Zolotarevsky V, Rozanov Y, Savchenko T, Akimov A. Lymphovenous anastamosis for the prevention of a post-mastectomy edema of the arm. *Sov Med.* 1989;4:32–35.
19. Pronin V, Adamian A, Zolotarevsky V, Rozanov J, Savchenko T, Akimov A. Lymphovenous anastamosis formation at an early stage after radical mastectomy. *Sov Med.* 1989;8:77–9.
20. Casabona F, Bogliolo S, 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;16:2459–63.
21. Stanton A, Modi S, Britton T, et al. Lymphatic drainage in the muscle and subcutis of the arm after breast cancer treatment. *Breast Cancer Res Treat.* 2009;117:549–57.
22. Thompson M, Korourian S, Henry-Tillman R, et al. Axillary reverse mapping (ARM): a new concept to identify and enhance lymphatic preservation. *Ann Surg Oncol.* 2007;14:1890–5.
23. Ochoa D, Korourian S, Boneti C, Adkins L, Badgwell B, Klimberg S. Axillary reverse mapping: five-year experience. *Surgery.* 2014;156:1261–8.
24. Boccardo F, Casabona F, De Cian F, et al. Lymphedema microsurgical preventive healing approach: a new technique for primary prevention of arm lymphedema after mastectomy. *Ann Surg Oncol.* 2009;16:703–8.
25. Boccardo F, Casabona F, Friedman D, et al. Surgical prevention of arm lymphedema after breast cancer treatment. *Ann Surg Oncol.* 2011;18:2500–5.
26. Boccardo F, Casabona F, DeCian F, et al. Lymphatic microsurgical preventing healing approach (LYMPHA) for primary surgical prevention of breast cancer–related lymphedema: over 4 year follow up. *Microsurgery.* 2014;34:421–4.
27. Kleinhans E, Baumeister R, Hahn D, Siuda S, Bull U, Moser E. Evaluation of transport kinetics in lymphoscintigraphy: follow-up study in patients with transplanted lymphatic vessels. *Eur J Nucl Med.* 1985;10:349–52.
28. Blaney J, McCollum G, Lorimer J, Bradley J, Kennedy R, Rankin J. Prospective surveillance of breast cancer-related lymphedema in the first-year post-surgery: feasibility and comparison of screening measures. *Support Care Cancer.* 2015;23(6):1549–59.
29. Lee M, Beith J, Ward L, Kilbreath S. Lymphedema following taxane-based chemotherapy in women with early breast cancer. *Lymphat Res Biol.* 2014;12:282–8.
30. Kilbreath S, Lee M, Refshauge K, et al. Transient swelling versus lymphoedema following surgery for breast cancer. *Support Care Cancer.* 2013;21:2207–15.
31. Norman S, Localio R, Potashnik S, et al. Lymphedema in breast cancer survivors: incidence, degree, time course, treatment, and symptoms. *J Clin Oncol.* 2009;27:390–7.
32. Norman S, Miller L, Erikson H, Norman M, McCorkle R. Development and validation of a telephone questionnaire to characterize lymphedema in women treated for breast cancer. *Phys Ther.* 2001;81:1192–205.