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Simplified LYMPHA for Prevention of Breast Cancer-Related Lymphedema After Axillary Dissection: Initial Feasibility Experience from South Asia

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ABSTRACT

Objective: Breast cancer-related lymphedema is an important survivorship concern after axillary lymph node dissection. Conventional LYMPHA and immediate lymphatic reconstruction can reduce this risk, but adoption in low- and middle-income settings is limited by the need for microsurgical personnel, equipment, additional operating time, and cost. This study reports an initial feasibility assessment of simplified LYMPHA (S-LYMPHA) performed by breast surgical oncologists using indocyanine green guidance.

Materials and Methods: This was a prospective, single-arm feasibility cohort study. Consecutive eligible patients undergoing planned axillary lymph node dissection or completion axillary dissection after a positive intraoperative sentinel node assessment were enrolled from July 2024 to September 2025. Arm circumferences were measured preoperatively and at 3 and 6 months, at three fixed points. After confirmation that axillary dissection was required, methylene blue and indocyanine green were injected into the ipsilateral upper limb. Arm lymphatics were identified, preserved, and invaginated into a suitable axillary venous tributary after nodal dissection. The primary outcomes of this interim report were technical feasibility, short-term safety, and clinical lymphedema at 6 months.

Results: Thirty-seven patients underwent attempted S-LYMPHA. The median age was 51 years. Nineteen patients (51.4%) received neoadjuvant chemotherapy and 26 patients (70.3%) underwent mastectomy. Sixteen patients (43.2%) required axillary dissection after nodal metastasis was detected on intraoperative sentinel node assessment. Arm lymphatics were identified in all patients. The mean number of lymphatics identified was 2.6 (range 1–5), and the mean number of lymphovenous anastomoses created was 1.5 (range 1–3). More than one anastomosis was performed in 16 (43.2%) patients. At a uniform 6-month follow-up, one patient had clinical lymphedema, corresponding to an observed incidence of 2.7% (exact 95% confidence interval, 0.07–14.16). No dye-related adverse reaction or local complication attributable to the lymphatic reconstruction was observed.

Conclusion: S-LYMPHA was technically feasible and safe in this initial South Asian feasibility cohort. These early data should be interpreted as evidence of implementability and short-term safety rather than proof of lymphedema prevention. Larger comparative cohorts with longer follow-up are required to define efficacy, durability, and oncologic safety.

Keywords: Breast cancer; breast cancer-related lymphedema; LYMPHA; S-LYMPHA; axillary lymph node dissection; immediate lymphatic reconstruction; low-resource setting

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KEY POINTS

- Simplified LYMPHA (S-LYMPHA) is feasible in resource constrained settings.
- S-LYMPHA can reduce potential breast cancer-related lymphedema.

Introduction

Breast cancer is the most common malignancy among women in India, and improvements in survival have made long-term treatment-related morbidity increasingly important. Breast cancer-related lymphedema (BCRL) remains one of the most feared sequelae of axillary treatment, especially after axillary lymph node dissection (ALND) and regional nodal irradiation (1, 2). BCRL may present months to years after treatment, with progressive arm swelling, heaviness, pain, cellulitis, functional limitations, psychosocial distress, and financial burden.

Immediate lymphatic reconstruction, commonly referred to as LYMPHA, was developed to preserve lymphatic drainage at the time of axillary dissection by creating lymphovenous bypasses between transected arm lymphatics and adjacent venous tributaries (3, 4). Early series and institutional experiences have reported low lymphedema rates after LYMPHA, but implementation remains difficult in many South Asian and other low-resource settings because conventional LYMPHA usually requires microsurgical expertise, an operating microscope, specialized instruments, additional operative time, and added cost (3-5).

Simplified LYMPHA (S-LYMPHA) was subsequently described as a less resource-intensive adaptation that can be performed by an oncologic surgeon using loupe magnification and an invagination technique rather than formal supermicrosurgical suturing (6). This manuscript reports our early prospective experience with S-LYMPHA. In response to the preliminary nature of the data, the present report is framed as an IDEAL Phase IIa feasibility study, with emphasis on technical success, early safety, and short-term clinical outcomes rather than on definitive efficacy.

Materials and Methods

Study Design and Setting

This was a prospective, single-arm feasibility cohort study of preventive lymphatic reconstruction in patients undergoing ALND for breast cancer. The study was conducted at participating breast surgical oncology centres following approval by the Saifee Hospital Ethics Committee (approval no: SH/DNB/SUR/07/2024/019, date: 30.07.2024). Written informed consent was obtained from all patients.

Participants

Consecutive adult patients with histologically confirmed breast cancer were eligible if ALND was planned preoperatively or if

it became necessary intraoperatively, after metastatic disease was identified during sentinel lymph node assessment. Patients undergoing completion ALND after a positive frozen-section or touch-imprint cytology were also eligible.

Exclusion criteria were: previous axillary surgery on the affected side; previous axillary radiotherapy; pregnancy or lactation; known allergy to methylene blue or indocyanine green; inability to complete follow-up measurements; and clinical inflammatory breast cancer requiring treatment pathways in which reliable arm lymphatic mapping or immediate reconstruction was judged unsuitable.

Perioperative Treatment and Physiotherapy

Recommendations for neoadjuvant chemotherapy, breast procedure, ALND, and adjuvant treatment were decided by the multidisciplinary team based on disease stage, receptor status, response to therapy, and institutional protocols. Radiotherapy was recommended when indicated by standard oncologic criteria, including nodal burden and receipt of breast-conserving surgery; however, data on completion of adjuvant radiotherapy and on radiation fields are not mature enough for analysis in this 6-month feasibility report. All patients received standard postoperative advice regarding shoulder and arm mobility. Overhead abduction was restricted until removal of the drain. Compression garments and formal physiotherapy were prescribed for symptomatic patients or those considered at higher risk after clinical review.

S-LYMPHA Technique

Procedures were performed by a two-surgeon team. Indocyanine green fluorescence imaging was performed using the Stryker SPY-PHI system. Before surgery, the baseline circumferences of both arms were recorded at three predefined points: at 10 cm above the elbow, at 5 cm below the elbow, and at the wrist.

After the decision for ALND had been confirmed, 1 mL of methylene blue was injected into the volar aspect of the ipsilateral upper arm, approximately 5 cm proximal to the axillary fold into the intradermal, subcutaneous, and deeper tissue planes. An additional 1 mL of indocyanine green was injected intradermally proximal to the methylene blue injection sites. After 15–20 minutes, the arm lymphatics were traced toward the axilla using fluorescence imaging. Identified lymphatics were dissected carefully, clipped distally, and preserved at the maximum feasible length.

Following standard ALND, a suitable venous tributary was selected and mobilized toward the lymphatics. The S-LYMPHA technique, as described by Ozmen et al. (6), was performed by invaginating one or more lymphatics into the venous tributary using a U-stitch and stay sutures with 6–0 polypropylene. When possible, intraoperative fluorescence imaging was used to confirm lymphatic flow into the venous tributary. When multiple suitable lymphatics were available, more than one lymphatic was invaginated into the same venous tributary or into separate tributaries, according to local anatomy (Figures 1 and 2).

A suction drain was placed in the axilla below the lymphovenous approximation, and a separate drain in the breast or chest wall was placed when required. Care was taken to avoid direct suction trauma to the anastomosis.

Outcome Definitions and Follow-up

The primary outcomes for this interim analysis were technical feasibility, defined as successful identification of arm lymphatics

and completion of at least one lymphovenous anastomosis, and short-term safety, defined as dye-related adverse events or local complications attributable to the reconstruction. Clinical lymphedema was assessed at 3 and 6 months.

Clinical BCRL was defined as an ipsilateral increase of more than 2 cm at any measured point compared with baseline and symptomatic BCRL as symptoms such as heaviness, tightness or functional discomfort; and absence of a comparable proportional increase in the contralateral arm.

Statistical Analysis

This feasibility analysis was descriptive. Continuous variables are presented as mean (range) or median, as appropriate. Categorical variables are presented as numbers and percentages. The observed incidence of lymphedema was reported with an exact binomial 95% confidence interval. No formal hypothesis testing was performed because the present report did not include a comparator arm and was not powered to evaluate efficacy.

Results

Patient and Treatment Characteristics

Thirty-seven patients underwent attempted S-LYMPHA during the study period. Baseline and treatment characteristics are summarized in Table 1. The median age was 51 years. Nineteen patients (51.4%) had received neoadjuvant chemotherapy. Twenty-six patients (70.3%) underwent mastectomy, including one who underwent bilateral mastectomy with ALND on the affected side and sentinel lymph node biopsy on the contralateral side. Sixteen patients (43.2%) initially underwent sentinel lymph node biopsy and subsequently required ALND after nodal metastasis was detected on intraoperative assessment.

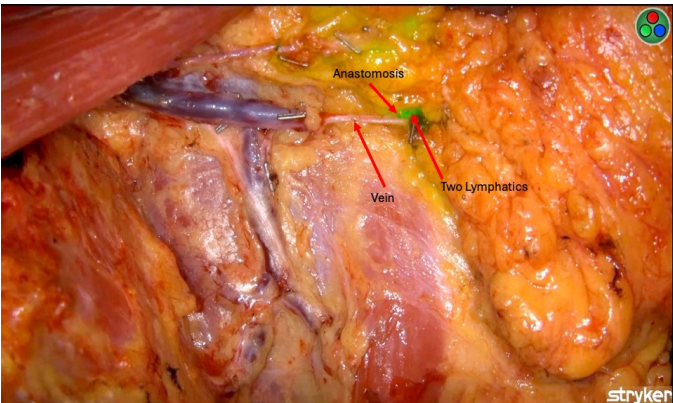


Figure 1. Two arm lymphatics invaginated into a single tributary of the axillary vein



Figure 2. Fluorescence imaging 30 minutes after the procedure demonstrating lymphatic flow into the venous tributary

Table 1. Baseline and treatment characteristics	
Variable	Value
Age	Median 51 years (30–65 years)
Neoadjuvant chemotherapy	19/37 (51.4%)
Breast operation	Mastectomy 26/37 (70.3%); breast conservation 11/37 (29.7%)
Indication for ALND	Planned ALND 21/37 (56.8%); ALND after positive intraoperative sentinel node assessment 16/37 (43.2%)
Mean lymph nodes removed	15 (range, 10–42)
Mean positive lymph nodes	3.1 (range, 0–24)
Body mass index mean	24.5+/-3.8
Radiotherapy	Incomplete
ALND: Axillary lymph node dissection	

Technical Feasibility and Short-term Safety

Arm lymphatics were identified using fluorescence guidance in all 37 patients. At least one lymphovenous anastomosis was completed in every patient. The mean number of arm lymphatics identified was 2.6 (range, 1–5), and the mean number of lymphovenous anastomoses created was 1.5 (range, 1–3). More than one anastomosis was performed in 16 patients (43.2%). No local complications attributable to the reconstructive step or no dye-related adverse reactions were observed (Table 2).

Lymphedema Outcomes

All patients included in this analysis had arm measurements available at the 6-month postoperative visit. Seventeen patients developed clinical lymphedema (>2 cm increase in arm circumference), corresponding to an observed 6-month incidence of 46%; one patient (2.7%) had symptomatic BCRL (Table 3). However 16 out of these 17 patients also showed increase in contralateral arm measurements. Hence it is actually weight gain and not true lymphedema.

Discussion and Conclusion

This initial prospective experience suggests that S-LYMPHA can be implemented in our breast surgical oncology setting with high technical success and no observed reconstruction-specific adverse events. Primary outcome feasibility: arm lymphatics were identified in all patients, and at least one lymphovenous anastomosis could be completed in every case by the operating team without reliance on a separate microsurgical service.

The observed 6-month symptomatic lymphedema incidence of 2.7% is encouraging but must be interpreted cautiously. BCRL often appears beyond the first postoperative year, particularly when regional nodal irradiation and higher body mass index are present (1, 2). A short follow-up interval can therefore underestimate the eventual incidence.

Conventional LYMPHA has shown favorable outcomes in multiple early series, but implementation barriers are substantial in low-resource settings. Boccardo et al. (4) described primary preventive lymphovenous reconstruction after axillary surgery, and later reports showed durable feasibility (7). Feldman et al. (8) reported a low lymphedema incidence after LYMPHA in a single-institution experience. Ozmen et al. (6) described S-LYMPHA and reported lymphedema in 3% of patients undergoing S-LYMPHA compared with 19% after ALND alone. Our present data should be viewed as an early implementation experience, consistent with the technical feasibility reported elsewhere, not as proof that the same magnitude of benefit has been reproduced.

This distinction is particularly relevant for South Asia. Patients frequently present with larger tumours and more advanced nodal disease, and ALND remains common. In node-positive disease, level III nodal involvement may be encountered depending on burden in levels I and II (9). A feasible preventive strategy that breast oncologic surgeons can perform could therefore be valuable if its efficacy is confirmed in larger controlled studies. Further studies should also compare S-LYMPHA with other arm lymphatic preservation techniques such as axillary reverse mapping (10).

Study Limitations

This study has several important limitations. First, it is a single-arm feasibility cohort study without a comparison group; therefore, it cannot establish that S-LYMPHA reduces lymphedema. Second, the cohort is small. Third, the follow-up period analyzed is limited to 6 months, whereas BCRL commonly develops between 1 and 3 years after axillary treatment. Fourth, radiotherapy details are incomplete because most patients are still undergoing treatment. Validated patient-reported outcome measures, such as LYMPH-Q, were not administered. Fifth, the assessment relied on symptoms and circumference measurements rather than limb-volume calculation, perometry, or bioimpedance. Because of these limitations, the current report should be interpreted as evidence of feasibility and short-term safety.

S-LYMPHA was feasible and safe in this initial cohort of patients undergoing ALND for breast cancer. The procedure can be performed by trained breast surgical oncologists using indocyanine green guidance and an invagination technique. The short-term lymphedema rate was low, but the absence of a comparison group, a small cohort size, and a 6-month follow-up preclude drawing conclusions about efficacy. Longer follow-up periods and comparative evaluations are necessary before S-LYMPHA can be recommended as a proven lymphedema-prevention strategy.

Table 2. Technical and perioperative outcomes	
Outcome	Result
Successful arm-lymphatic identification	37/37 (100%)
Completion of at least one lymphovenous anastomosis	37/37 (100%)
Number of lymphatics identified	Mean 2.6 (range, 1–5)
Number of anastomoses created	Mean 1.5 (range, 1–3)
Dye-related adverse events	0/37
Local complications attributable to S-LYMPHA	0/37
S-LYMPHA: Simplified LYMPHA	

Table 3. Six-month arm-circumference measurements

No.	Baseline arm circumference*	6-month arm circumference*	Increase >2 cm	Symptomatic BCRL
1	R 27/25/16; L 28/25/16	R 29.5/25/17; L 27/25/16.	Yes	Yes
2	L 33/29/18; R 32/30/18	L 31/25/16.6; R 31/25.5/16.5	No	No
3	L 33/24/15; R 33/25/15	L 34/25/15; R 33/25/15	No	No
4	L 35/28/19; R 35/28/19	L 33/28/18; R 30.4/25.4/17.7	No	No
5	L 35/26/18; R 34/21/17	L 34.2/27.9/16.5; R 33/27.9/17.7	No	No
6	R 26/24/15; L 26/24/15	R 26.5/20/12; L 26/20/12	No	No
7	R 26/21/16; L 24/21/16	R 25.5/22.8/15; L 25.5/22.8/15	No	No
8	L 30/23/15; R 31.5/22/15	L 27/22/17; R 26/23/18	Yes	No
9	R 27.5/23.5/16; L 27/23/16	R 23/22/16; L 23/22/16	No	No
10	L 29/21/15; L 28/20/15	L 31/29/15; R 31/29/15	Yes	No
11	L 30/24/15; R 28/24/15	L 33/27/19; R 33/26/19	Yes	No
12	L 29/24/16; R 28/24/16	L 28/24/16; R 28/24/16	No	No
13	L 19/17/13; R 19/17/13	L 18/17/13; R 18/18/13	No	No
14	L 28.5/24/16; R 27/23.5/16.5	L 30/25/16; R 31/25/17	No	No
15	L 25/21/16; R 24/22/17	L 35/26/18; R 34/26/19	Yes	No
16	L 27/21/14; R 27/21/14	L 25/23/16; R 25/23/16	Yes	No
17	R 36/26/17; L 34/25/16	R 35/26/17; L 33/24/16	No	No
18	L 24/20/15; R 24/20/15	L 26.5/21/14.5; R 26.5/21/14.5	Yes	No
19	L 26/23/16; R 26/22/16	L 26/22/16; R 27/23/16	No	No
20	R 28/24/16; L 27/24/16	R 29/25/16.5; L 28/24/16	No	No
21	L 29/24/15; R 26/24/15	L 27/24/16; R 27/25/17	No	No
22	L 29/23/17; R 27/23/17	L 32/26/17; R 31/26/17	Yes	No
23	R 28/22/16; L 27/22/16	R 26/24/16; L 26/24/16	Yes	No
24	L 26/23/18; R 27/23/18	L 31/22/15; R 31/24/15	Yes	No
25	R 28/23/16; L 28/23/16	R 32.5/24.5/16.5; L 31/24.5/15.5	Yes	No
26	L 30/25/14; R 32/26/15	L 30/25/16; R 31/26/16	Yes	No
27	L 33/28/18; R 32/26/18	L 34/28/18; R 32/26/18	No	No
28	R 28/21/14; L 28/22/14	R 29/22/16; L 28/21/16	No	No
29	R 30/25/16; L 30/24/16	R 28/25/17; L 27/24/17	No	No
30	L 28/22/15; R 28/22/14	L 26.5/22/13; R 25.5/22/13.5	No	No
31	L 25/22/15; R 25/23/15	L 27/23/16; R 27.5/23/16	Yes	No
32	R 29/24/15; L 29/24/15	R 32/25/16; L 33/25/16	Yes	No
33	R 26/24/15; L 27/24/15	R 29/25/16.5; L 30/26/17	Yes	No
34	R 28/23/15; L 26/23/15	R 27/22/16; L 27/23/17	No	No
35	L 28/23/15; R 28/23/15	L 30/26/16; R 30/26/16	Yes	No
36	L 35/26/15; R 35/26/15	L 37/27/17; R 36/26/16	Yes	No
37	R 32/24/15; L 31/24/15	R 32/22/15; L 32/22/15	No	No

*: Measurements are shown as 10 cm above the elbow, 5 cm below the elbow, and at the wrist. The affected side is listed first. BCRL: Breast cancer-related lymphedema

Ethics

Ethics Committee Approval: The study was conducted at participating breast surgical oncology centres following approval by the Saifee Hospital Ethics Committee (approval no: SH/DNB/SUR/07/2024/019, date: 30.07.2024).

Informed Consent: Written informed consent was obtained from all patients.

Footnotes

Authorship Contributions

Surgical and Medical Practices: N.R.G., J.R.A., I.R., E.T., N.C.; Concept: N.R.G., J.R.A., I.R., E.T., N.C., E.K., A.G., R.S., E.A.; Design: N.R.G., J.R.A., I.R., E.T., N.C., R.S., E.A.; Data Collection and/or Processing: N.R.G., J.R.A., I.R., E.T., R.S.; Analysis and/or Interpretation: N.R.G., J.R.A., I.R., E.T., E.K., A.G., R.S., E.A.; Literature Search: N.R.G., J.R.A., I.R., E.T., E.K., R.S., E.A.; Writing: N.R.G., J.R.A., I.R., E.T., E.K., R.S., E.A.

Conflict of Interest: The authors have no conflicts of interest to declare.

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