Appropriate Concept of Prevention of Lymphedema at the Initial Treatment

Zisun Kim

Department of Surgery, Soonchunhyang University Bucheon Hospital, Soonchunhyang University College of Medicine, Korea
Introduction

• Lymphedema
  ✓ Abnormal accumulation of protein-rich fluid in the interstitial space
  ✓ A progressive disorder
  ✓ Treatment-induced mechanical insufficiency of the lymphatic system
Breast cancer associated treatments: the most common causes of upper extremity lymphedema

The overall incidence of lymphedema: 17%
- systematic review (72 studies, 29,612 women)

Risk factors for breast cancer related lymphedema (BCRL)
- axillary lymph node dissection (ALND)
- radiation therapy (RT)
- local infection, hematoma-seroma
- obesity, medication effects (taxane)

• 1,794 patients, Stage 0-3 breast cancer, median 10 yrs f/u
• 5 yr cumulative incidence of BCRL: 9.1% [95% CI 7.8–10.5%]
• 5 yr incidence of BCRL: 5.3% (SLNB) vs. 15.9% (ALND) ($p<0.001$)
• Breast/chest wall RT: 3.5% (surgery) vs. 9.5% (surgery+RT) ($p=0.01$)
BCRL is related to multimodal treatment, and not surgery alone.

tightness of surgical incision scar

decreased extensibility of pectoral muscle

decreased extensibility of latissimus muscle

axillary cording
Adverse impact

- Secondary shoulder dysfunction
  - Myofascial syndrome
  - Impingement syndrome
  - Pain and decreased muscle strength

- Psychological morbidity

- Diminished quality of life/lower patient reported outcome

- Higher medical costs and more productive days lost

Prevalence and time of onset

• Insidious onset, slowly progressive swelling of the upper extremity
• Most patients become symptomatic within 8 months of surgery.
• 23.1%: waxing and waning lymphedema symptoms in the first 3yrs
• The greatest risk for developing lymphedema: ≤2yr after treatment
• Freedom from progression: 79% (1yr), 66% (3yr), and 52% (5yr)
• Higher risk of progression: morbidly obese, positive axillary lymph nodes, supraclavicular irradiation

BCRL prevention 1: SLNB
## Incidence of BCRL after ALND

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>No. of patients</th>
<th>Measurement</th>
<th>Lymphedema, %</th>
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<td>Sackey</td>
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<td>194</td>
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<td>Schrenk</td>
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<td>35</td>
<td>NR</td>
<td>57</td>
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</table>

12 studies
5,354 patients
Pooled incidence: **22.3%**

### Incidence of BCRL after SLNB

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</table>

17 studies
6,711 patients
Pooled incidence: 6.3%

New anatomical classification of the axilla with implications for sentinel node biopsy

K. B. Clough, R. Nasr, C. Nos, M. Vieira, C. Inguenault and B. Poulet

The Paris Breast Centre (L'Institut du Sein), 7 Avenue Bugeaud, 75116 Paris, France
Correspondence to: Dr K. B. Clough (e-mail: krishna.clough@orange.fr)
<table>
<thead>
<tr>
<th>Zone</th>
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<th>Zone C</th>
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<td>80</td>
<td>10</td>
<td>1</td>
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<td>91 (40.1)</td>
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<tr>
<td>UIQ</td>
<td>27</td>
<td>6</td>
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<td>16</td>
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<td>1</td>
<td>0</td>
<td>18 (7.9)</td>
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<tr>
<td>LOQ</td>
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<td>0</td>
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<td>0</td>
<td>0</td>
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<td>8</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>9 (4.0)</td>
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<tr>
<td>JIQ</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>5 (2.2)</td>
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<tr>
<td>SLN location</td>
<td>197 (86.8)</td>
<td>26 (11.5)</td>
<td>4 (1.8)</td>
<td>0 (0)</td>
<td>11.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>A 86.8%</td>
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BCRL prevention 2: ARM
Axillary Reverse Mapping (ARM)

- Klimberg and colleagues (2007)
- Modified lymph node mapping technique for identifying the SLN
- Preserve the functioning upper extremity lymphatics
- Hypothesis: the arm and breast has distinct lymphatic channels
- Blue dye (2~5mL) injected into the ipsilateral upper inner arm along the intramuscular groove

Improvement in lymphedema rates: 33% vs. 4~9% in ARM groups

A Prospective Study to Assess the Feasibility of Axillary Reverse Mapping and Evaluate Its Effect on Preventing Lymphedema in Breast Cancer Patients

Tao Yue, Dayong Zhuang, Peng Zhou, Luming Zheng, Ziyi Fan, Jian Zhu, Lei Hou, Fang Yu, Xuefeng Dong, Lei Xiao, Qingqing He

- 265 patients, ALND (n=127) vs. ALND+ARM (n=138)
- Identification rate of ARM node: 93.48% (129/138)
- 1 ARM node 75.2%, 2 ARM nodes 19.38%, 3 ARM nodes 5.43%
- FNAC assessment of ARM node metastasis
- ARM nodes metastasis: 8.53% (11/129)
- No nodal relapse during follow-up
- 20 month LE: 33% (ALND) vs. 5.93% (ALND+ARM) \( (p<0.001) \)
- ARM is a feasible technique to identify upper arm nodes.
- The incidence of LE can be decreased with ARM procedure.

Surgical Technique

Does Axillary Reverse Mapping Prevent Lymphedema After Lymphadenectomy?

Evan Tummel, MD,* Daniela Ochoa, MD,* Soheila Korourian, MD,† Richard Betzold, MD,* Laura Adkins, MS,* Maureen McCarthy, OCN, RN, Stephanie Hung, MD,* Kyle Kalkwarf, MD,* Kristalyn Gallagher, DO,* Jeannette Y. Lee, PhD,‡ and V. Suzanne Klimberg, MD*†

- 654 patients prospectively underwent ARM+SLNB and/or ALND
- **Objective LE:** 0.8% (SLNB) and 6.5% (ALND), 26-month median f/u
- Blue lymphatics identification: 29.2% (SLNB) and 71.8% (ALND)
- Crossover: 3.8% (18/472) of SLNB and 5.6% (12/213) of ALND
- Blue node metastases rate: 4.5% (2/44)
- Axillary recurrence rate: 0.2% (SLNB) and 1.4% (ALND)

- Lymphedema rates are dramatically reduced using ARM when compared with accepted standards.

Axillary Reverse Mapping (ARM)

- The ARM technique is applicable in surgical axillary staging, early breast cancer patients are better candidates.

- Preserving nodes using ARM decrease the occurrence of upper limb lymphedema after SLNB or ALND.

- Larger samples and longer follow-up times are needed to evaluate the oncological safety of ARM node (4~12% metastasis).

- Longitudinal studies using objective measurement could determine the primary benefit of ARM in LE prevention.
BCRL prevention 3: LYMPHA
Lymphatic microsurgical preventive healing approach (LYMHPA)

- Boccardo, et al. (2009)
- Surgical approach for the primary prevention of LE after ALND
- ALND + lympho-venous anastomosis

- Blue dye injected into the volar aspect of the ipsilateral upper arm
- The blue lymphatics are identified and the afferent lymphatics are clipped near insertion into the node.
- The afferent lymphatics are directly anastomosed into a collateral branch of the axillary vein with microsurgical technique.

- Significant reduction in LE at 18 months (30% vs 4.05%, p<0.01)

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

Sheldon Feldman, MD¹, Hannah Bansil, MD¹, Jeffrey Ascherman, MD², Robert Grant, MD², Billie Borden, BA³, Peter Henderson, MD², Adeolu Ojo, MD¹, Bret Taback, MD¹, Margaret Chen, MD¹, Preya Ananthakrishnan, MD¹, Amiya Vaz, BA¹, Fatih Balci, MD¹, Chaitanya R. Divgi, MD⁴, David Leung, MD⁴, and Christine Rohde, MD²

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

27 Completed LYMPHAs
- 3 excluded from analysis due to pre-op lymphedema or follow up <3 months

21/24 (87.5%) No Post-Op Lymphedema

3/24 (12.5%) Post-Op Lymphedema

10 LYMPHA Not Completed
- 2 excluded from analysis due to pre-op lymphedema or follow up <3 months

4/8 (50%) No Post-Op Lymphedema

4/8 (50%) Post-op Lymphedema

### TABLE 1 Patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Incomplete LYMPHA (n = 8)</th>
<th>Completed LYMPHA (n = 24)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55.8 ± 13.1 (33–71)</td>
<td>58.1 ± 11.8 (33–76)</td>
<td>0.63a</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>29.5 ± 7.1 (23.5–41.5)</td>
<td>28.7 ± 6.8 (17.4–47.5)</td>
<td>0.77</td>
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<tr>
<td>Total lymph nodes excised</td>
<td>14.0 ± 7.0 (4–28)</td>
<td>18.0 ± 8.0 (3–37)</td>
<td>0.26</td>
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<tr>
<td>Positive lymph nodes</td>
<td>5.0 ± 5.5 (1–16)</td>
<td>3.0 ± 3.0 (0–13)</td>
<td>0.26</td>
</tr>
<tr>
<td>Type of surgery (breast conservation)</td>
<td>1/8 (12.5)</td>
<td>4/24 (16.6)</td>
<td>1.0b</td>
</tr>
<tr>
<td>Adjuvant radiotherapy</td>
<td>6/8 (75)</td>
<td>15/24 (62.5)</td>
<td>0.68</td>
</tr>
<tr>
<td>Chemotherapy (yes/no)</td>
<td>7/8 (87.5)</td>
<td>23/24 (95.8)</td>
<td>0.44</td>
</tr>
</tbody>
</table>
• Updated data: more patients (n = 42), longer follow-up (22 months)
• LE rates: 7% (LYMPHA) vs. 31% (ALND)
• No significant complications
• 40 min of operating time
• Microsurgical technique (learning curve: 15)
• High-risk patients who require complete ALND

• LYMPHA is a promising technique for LE prevention, and should be explored further with appropriate patients.

NCCN Guidelines Version 1.2018
Invasive Breast Cancer

**SURGICAL AXILLARY STAGING** - T1-3, N0-1, M0 DISEASE

- Clinically node positive at time of diagnosis:
  - FNA or core biopsy positive
    - Axillary dissection level I/II
  - FNA or core biopsy negative
    - Sentinel node negative
      - No further axillary surgery (category 1)
    - Sentinel node positive
      - Only micrometastases seen in SLN
        - No further axillary surgery
      - Yes to all
        - No further axillary surgery
      - No
        - Axillary dissection level I/II
- Clinically node negative at time of diagnosis:
  - Sentinel node mapping and excision
    - Accurate SLNB
      - ARM
        - ARM+ALND
        - ARM+ALND+LYMPHA

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1. Consider pathologic confirmation of malignancy in clinically positive nodes using ultrasound-guided FNA or core biopsy in determining if a patient needs axillary lymph node dissection.
2. Sentinel lymph node mapping injections may be peritumoral, subareolar, or subdermal.
3. Sentinel node involvement is defined by multilevel node sectioning with hematoxylin and eosin (H&E) staining. Cytokeratin immunohistochemistry (IHC) may be used for equivocal cases on H&E. Routine cytokeratin IHC to define node involvement is not recommended in clinical decision-making.
4. See Axillary Lymph Node Staging (BINV-E).
5. For patients with clinically negative axilla who are undergoing mastectomy and for whom radiation therapy is planned, axillary radiation may replace axillary dissection level I/II for regional control of disease.
Conclusion

• Breast cancer treatment places survivors at lifelong risk for the development of lymphedema.

• The true incidence of BCRL is difficult to measure (symptoms variable onset, diagnosis not standardized)

• BCRL is related to multidisciplinary treatment; ALND, nodal radiation, and chemotherapy (treatment-related factors), and obesity (patient-related factor)

• Identification of high-risk patients and application of appropriate individualized surgical strategy (SLNB, ARM, and LYMPHA) could possibly prevent BCRL. (the highest risk of developing lymphedema: first 3 years)
Thank you for your attention