Comprehensive Lymphedema Research: A Product Of Our Multi-Disciplinary Team
By Tara A. Russell, MPH

Through collaborative efforts to care for lymphedema patients, our team has enabled us to recognize the importance of a multi-disciplinary approach to lymphedema research. Through the incorporation of various team members’ personal insights on lymphedema, as well as the expertise from a variety of fields including medical, surgical and radiation oncology, as well as physical therapy and nursing, our team has evaluated various areas of research. Overall, this collaborative approach has fueled the Lymphedema Studies Team at Massachusetts General Hospital, allowing us to evaluate breast cancer-related lymphedema (BCRL) from a variety of angles.

Current research on BCRL, has provided the field with information about measurement, risk factors, management, and the impact of lymphedema on function and quality of life. Within our clinic, we have completed research on each of these components. This article will review findings from all of these areas of research and provide information on how our multi-disciplinary team has helped us to evaluate each of the areas of interest.

Measurement
Measurement of lymphedema is a field filled with a variety of tools, fraught with challenges and inconsistencies.\(^1\)\(^-\)\(^3\)\) Prior to initiating our research on lymphedema, we thoroughly reviewed the measurement tools available. In our busy clinic environment, we required a reliable, sensitive and valid instrument that could screen patients quickly and provide clinicians with useful information about changes in patient measurements as compared to previous visits or a baseline time point. The perometer, an optoelectric tool that quantifies arm volume by passing a frame composed of infrared light receiver pairs over the arm, was the optimal choice due to its speed of measurement and reliability\(^4\)\(^-\)\(^6\) (see Figure 1).

Through multi-disciplinary discussions about the use of perometry measurements in addition to our clinical experiences, our team collectively discussed the nuances of longitudinal screening. With the input of clinicians, each of whom plays a different role in the care of breast cancer patients, our team recognized the need to develop a standardized measurement protocol to easily evaluate lymphedema development and change. Through these discussions, informed by the perspective of various specialties, we developed a protocol that included a method for measuring changes in the affected arm while controlling for baseline limb asymmetry, as well as bilateral changes in arm volume. Utilizing this method, we have been able to screen over 750 patients prospectively throughout their treatment and follow-up, to evaluate changes in arm volume.

Risk Factors
In addition to lymphedema screening, our team is constantly aware of the need to improve our accuracy and...
efficiency in defining the natural history of lymphedema as well as risk factors that may increase a patient’s likelihood of developing this condition. In coordination with our screening program, we have also developed a clinical and pathological database to assist us in evaluating predictors of this condition. Some of our most recent research has been presented at the American Society of Breast Disease and American Society of Therapeutic Radiology and Oncology conferences. Utilizing the perspectives of our treating physicians as well as our clinical researchers we have been able to look at various predictors for the development of this condition. Our most current risk factor analyses are presented in Table 1.

Function, Quality of Life & Fear-Avoidance Behavior

BCRL has been clearly demonstrated in the literature to affect upper extremity function and quality of life. It has become clear to us that evaluating the function of patients during and after treatment for both breast cancer and lymphedema, is important. Following treatment for breast cancer many patients suffer from complications such as limited range of motion, post-operative infections, and delayed wound healing. As a team, we have been concerned about these many factors and their influence on lymphedema development. Furthermore, there is evidence that women avoid using their affected arm following treatment due to fear of developing lymphedema. Because our field emphasizes the efficacy and utility of exercise, we had concerns that such avoidance behavior might be more detrimental than protective.

Given these concerns, as well as those regarding changes in quality of life, our team utilized resources within our team and center—opinions and experiences of lymphedema research experts and various lymphedema and breast cancer surveys—to develop and pilot a new assessment tool within our center. The subsequent product of this collaborative effort is a survey tool called the Lymphedema Evaluation Following Treatment for Breast Cancer (LEFT-BC).

Management & Intervention

In addition to evaluating measurement, risk factors and other LE side effects, our team has been very active in the pursuit of a greater understanding of appropriate management and intervention strategies. We have attempted to establish a true threshold for LE intervention through evaluation of our own protocols and incorporating the viewpoints of our research staff and statisticians. While there is significant literature on BCRL, the definition of clinically significant lymphedema is an area of study that lacks consensus. As demonstrated by the work by Stout-Gergich, et al. who advocated for a 3% volumetric threshold for intervention, defining such a point can be difficult as the literature is full of different types of measurement values including volume change in milliliters or percent, bioimpedance values, as well as circumferential changes. In an effort to evaluate these different potential thresholds, our team has reviewed our lymphedema screening data to help establish a natural time course and progression of lymphedema. Utilizing the thresholds proposed by Stout-Gergich, et al. (3% volumetric change) as well as those that our team has advocated (5% and 10% volumetric change), natural history following these significant volume points was evaluated. We completed this evaluation by tracking natural changes in arm volume in a cohort of 468 patients that have been screened for at least six months post-operatively with the perometer. Additionally, we have been able to look at various factors and their influence on lymphedema healing. As a team, we have been concerned about these many factors and their influence on lymphedema development.

### Table 1

A sample of 336 patients were followed prospectively with the Perometer with at least 10 months post-operative follow-up. Treatment-associated risk factors were evaluated as compared to the control group (those who did not reach >10% difference in arm volume).

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>&gt;10% p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increasing # of Lymph Nodes Removed</td>
<td>0.001*</td>
</tr>
<tr>
<td>Increasing # of Positive Lymph Nodes</td>
<td>0.004*</td>
</tr>
<tr>
<td>Radiation (all fields)</td>
<td>0.764</td>
</tr>
<tr>
<td>Regional Lymph Node Radiation</td>
<td>0.001*</td>
</tr>
<tr>
<td>ALND + Radiation</td>
<td>0.012*</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>0.087</td>
</tr>
<tr>
<td>Sentinel Lymph Node Biopsy (SLNB)</td>
<td>0.804</td>
</tr>
<tr>
<td>Axillary Lymph Node Dissection (ALND)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mastectomy + ALND</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Lumpectomy + ALND</td>
<td>0.523</td>
</tr>
</tbody>
</table>

*Significant to <0.05
an increase in arm volume, and >90% of those reaching 10% continued to progress. Furthermore, comparison of the threshold groups (3%, 5% and 10%) by risk factors indicate that the 3% cohort does not differ significantly from the control group of patients who did not progress to a volumetric threshold of 3% or more, whereas the 5% and 10% cohorts demonstrate significant differences. Our research appears to support utilizing a 5% or 8% threshold for intervention, and suggests that patients with a 3% change in arm volume are not at significant enough risk for developing lymphedema to warrant a full course of intervention. However, further research, e.g. randomized control trials, is required to support these conclusions. It is the mission of our team to evaluate both the natural history of LE development as well as the efficacy of short-term intervention with long-term follow-up in a well-powered, prospective randomized trial.

**Future Steps for Our Team**

Through continued collaboration, our team hopes to contribute greatly to the understanding of breast cancer related lymphedema. Our next step is to evaluate the utility of screening and early intervention through a recently funded randomized control trial.

**References**


**Tara Russell is the Lymphedema Studies Clinical Research Program Manager at the Massachusetts General Hospital. Tara joined the MGH team in 2007 after graduating from Dickinson College in 2006 with a BS Biology & Sociology. She has since earned a Masters in Public Health and a concentration in Epidemiology & Biostatistics from Tufts University School of Medicine.**