Autologous Lymph Node Transfer: An Update

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Disclaimer
The following article reports preliminary results from ongoing work in Lymph Node Transfer to address lymphedema resistant to CDT treatment. There are still no studies with large numbers of patients reporting good outcomes with long term follow-up. The NLN and the lymphedema community eagerly await that data.

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Statement of Financial Interest
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Background
Over the last several years, there has been increasing interest in a surgical treatment for lymphedema. Both upper and lower extremity LE, whether primary or secondary, is disfiguring and painful, and can cause enduring physical, emotional, social and economic problems. One potential surgical solution, autologous lymph node transfer (ALNT), has been performed in France by Dr. Corinne Becker for 20 years, but minimal clinical data has been published on the efficacy of the procedure. To answer questions about the effectiveness of ALNT, we have been collecting both anthropometric data and patient-reported outcome (PRO) measures on ALNT for the treatment of chronic LE.

To investigate the effectiveness of ALNT for chronic post-mastectomy lymphedema patients, we designed a double-blinded randomized controlled clinical trial. Very soon, however, it became evident that patients who had already exhausted conservative treatment were unwilling to be randomized. All patients undergoing surgery requested to be randomized to the treatment arm, even with the knowledge that the efficacy of the procedure remained in question. In addition, patients with different types of LE presented for treatment, including patients with upper extremity LE, lower extremity LE, primary LE, and secondary LE. Given this, the study design evolved to a prospective observational study of patients with upper or lower extremity LE who had exhausted conservative treatment.

We were comfortable proceeding with ALNT for both upper and lower extremity lymphedema, primary and secondary lymphedema, because we operated under the guidance of Dr. Corinne Becker. In order to ensure patient safety, Dr. Becker traveled to our hospital and was directly involved in patient evaluation and care. Over the last 20 years, Dr. Becker has performed approximately 4000 ALNT for all types of LE. Anecdotally, she has reported impressive results, but the paucity of published objective data has resulted in skepticism among many health-care providers in the LE community. By having Dr. Becker oversee the clinical aspect of the procedure, we felt confident that the technique and method employed was consistent with the best practices for ALNT. Since she developed the system for treatment, her technique could be considered the gold standard for ALNT. Furthermore, if our data did not reveal efficacy after treatment, we felt confident that it would not be due to inadequate execution of the ALNT technique.

With ALNT selected as a surgical intervention for objective evaluation, we attempted to systematically measure the results of treatment. In the lymphedema literature, there is controversy over the ideal method for measuring LE treatment outcomes. Traditionally, water displacement has been used, but it is messy, inconvenient, and imprecise. Lymphoscintigraphy has been used to map lymphatic channels, but the results are inconsistent and the subdermal injection is painful for patients. Infrared perometry may be considered the modern volumetric gold standard, and we were fortunate to work with a nurse researcher who was willing to conduct preoperative and postoperative limb measurements of patients with LE. The same researcher also obtained preoperative biimpedence measurements of fluid in limbs with LE. Preoperatively, we routinely obtained preoperative magnetic resonance angiography (MRA) of the affected limb. The NLI and the Breast Cancer and LE Symptom Experience Index (BCLSEI).

Funding limitations, however, precluded routine postoperative follow-up measurements using infrared perometry, biimpedence, MRA, and PRO measurements. Instead, the only measurements that could
be consistently obtained were preoperative and postoperative circumferential tape measurements of the affected and unaffected limb. In the future, with adequate research funding, we hope to supplement the circumferential tape measurements with postoperative infrared perometry, bioimpedence, MRA, and PRO measurements for more complete and sophisticated postoperative data.

Methods
This was a prospective observational study of 28 consecutive ALNTs performed between 2011 and 2012 at New York Eye & Ear Infirmary (NYEEI) for treatment of chronic recalcitrant lymphedema. Patients treated had upper extremity LE, lower extremity LE, primary LE, or secondary LE. All patients had exhausted conservative treatment with complete decongestive therapy (CDT). Dr. Corinne Becker supervised the clinical procedure to ensure standardization of the surgical technique. The successful revascularization of all ALNT flaps was confirmed intraoperatively with use of the SPY imaging device. Patient characteristics analyzed included age, body mass index (BMI), previous episodes of cellulitis, and iatrogenic causes of disease. The affected and unaffected limb was measured preoperatively and postoperatively using circumferential tape measurements. The difference in preoperative and postoperative measurements between the affected limb was compared and graphed. This was calculated by using the following formula:

\[(\text{postoperative measurement} - \text{preoperative measurement}) / \text{preoperative measurement}) \times 100 = \% \text{ change.}\]

Preoperative and postoperative photographs were also taken to document visual outcomes.

All patients were advised that ALNT was not a proven technique, and signed a detailed 8-page research informed consent in addition to the standard hospital surgical informed consent. Risks discussed with the patient included donor site lymphedema, donor and/or recipient site hematoma and/or seroma, postoperative infection, no improvement in LE, and need for further procedures. All patients underwent postoperative manual lymphatic drainage by a certified LE therapist within one month after surgery to encourage movement of lymphatic fluid toward the newly transplanted lymph nodes.

Results
From 2011-2012 at NYEEI, 28 consecutive ALNTs were performed for treatment of chronic recalcitrant lymphedema. Of the 28 ALNTs, there were 13 ALNTs performed for upper extremity LE (46.4%), 15 ALNTs for lower extremity LE (53.5%), 3 ALNTs for primary LE (10.7%), 20 ALNTs for secondary LE (71.4%), and 5 ALNTs for LE of unknown etiology (17.9%). The mean age was 51.8 years (range 28-65 years). The mean BMI was 28.4 (range 18.2-51.4). Of the 28 ALNTs, 6 patients had experienced previous bouts of cellulitis due to their LE (21.4%). Of the 20 ALNTs performed for secondary LE, 13 ALNTs were performed for upper extremity LE due to treatment for breast cancer (65%), 4 ALNTs were performed for lower extremity LE due to treatment for cervical cancer (29%), 2 ALNTs were performed for lower extremity LE secondary to trauma (10%), and 1 ALNT was performed for lower extremity LE due to treatment for melanoma (5%). With regard to postoperative complications, 1 patient experienced a postoperative seroma (3.6%), 1 patient had postoperative cellulitis (3.6%), and 1 patient underwent an additional ALNT to the same affected limb to further reduce extreme girth due to lower extremity elephantiasis (3.6%).

For all patients, the affected limb was measured preoperatively and postoperatively using circumferential tape measurements. The difference in preoperative and postoperative measurements between the affected limb was compared and graphed. This was calculated by using the following formula:

\[(\text{postoperative measurement} - \text{preoperative measurement}) / \text{preoperative measurement}) \times 100 = \% \text{ change.}\]

Preoperative and postoperative photographs were also taken to document visual outcomes. Examples of preoperative and postoperative graphs and photo documentation for one upper extremity lymphedema patient and one lower extremity lymphedema patient are presented below.

Patient #1 (Upper Extremity LE)

![Patient #1 (Upper Extremity LE)](image1)

Figure 1. Patient #1 is a 43-year-old woman with a 2-year history of right upper extremity lymphedema that had plateaued on conservative treatment.

Patient #1 was a 43-year-old woman with a 2-year history of right upper extremity lymphedema that was not improving with conservative treatment (Figure 1). The patient underwent right partial mastectomy and chemotherapy in November 2008 followed by radiation therapy in March 2009. In February 2010, the patient cut her finger and developed right upper extremity swelling. She began seeing a LE therapist, and underwent complete decongestive therapy (CDT) every 6 months with lymphatic massage, bandaging, and compression garments. She was 5’8” and 202 pounds (BMI 30.7), and her preoperative MRA demonstrated edema in her forearm to her mid-humerous with dilated lymphatics consistent with LE. Her subcutaneous tissues in her right forearm were 2.8 cm in thickness compared to a maximum thickness of 1.5 cm in her left forearm (Figure 2).

On 3 July 2012, the patient underwent ALNT from her left groin to her right axilla. She had an uneventful postoperative recovery, and went home on POD#1. Within the first week, she noticed a decrease in swelling in her right hand. Within one month, the decreased swelling was noticeable throughout her right arm, and her entire arm felt softer and less fibrotic (Figure 3). By two
months, preoperative and postoperative tape measurements revealed a 5.6% reduction in the difference between her preoperative and postoperative affected arm circumferences. Throughout this time, the patient underwent manual lymphatic massage with a certified LE therapist. Overall, she reported a significant decrease in swelling, and stopped wearing her upper extremity compression garment except for rigorous activities.

Patient #2 (Lower Extremity LE)

Patient #2 was a 56-year-old woman with a 19-year history of right lower extremity lymphedema after minor trauma. The patient reported that she fell from a chair and sustained a contusion and possible laceration but no fractures. After her fall, her right lower leg swelled up and the swelling never subsided. She went to a physical therapist for her right lower extremity swelling and heaviness. She was 5’5” and 155 pounds (BMI 25.8), and her preoperative MRA demonstrated subcutaneous edema in her right calf and lower thigh, with no popliteal lymph nodes.

On 15 March 2012, the patient underwent ALNT from her left lateral thoracic region to her right knee. She had an uneventful postoperative recovery, and went home on POD#1. Within the first week, she stated that her right lower leg was tingling and felt like it was “waking up.” By six weeks, the patient stated that her right lower leg felt softer, less tight, and the girth had decreased. She was able to wear shoes that she was not able to fit into before surgery., Throughout this time, the patient continued wearing a lower extremity compression garment, and underwent manual lymphatic massage with a LE therapist. At five months, her preoperative and postoperative tape measurements revealed an 8.3% reduction in the difference between her preoperative and postoperative affected leg circumferences.

Discussion

In order to better understand the outcomes of ALNT, we attempted to quantify objective results with preoperative and postoperative anthropometric measurements of upper and lower extremity lymphedema after ALNT. In the short time period described, there was striking subjective improvement in symptoms described by the patient, which was contrasted with modest objective improvement in measurements collected by the researcher. Visual outcomes were sometimes less dramatic than the personal progress reported by the patient. The individual nature of LE symptoms and effects could make it difficult for a third party to fully understand improvements described by the patient.

In addition, the task of gathering outcome measures before and after ALNT for chronic recalcitrant LE proved to be gargantuan and humbling, as there was often resistance from patients, practitioners, and even fellow researchers with regard to data collection. Once patients experienced improvement, it was often difficult to convince them to return for follow-up. For patients who were from out of town, the economic realities of long-distance travel made frequent visits unrealistic. In addition, many patients experienced emotional ups and downs with regard to their progress. Significant leaps forward could be followed by plateaus in progress, and many patients required a significant amount of support during their recovery.

In sum, the improvements after ALNT for treatment for chronic recalcitrant lymphedema were often experienced by the patient in small private ways. For example, one patient described not being afraid of the summer season anymore, because she knew that she would not have to worry that her arm would “explode” with the heat. While the goal of ALNT for treatment of LE may be complete resolution of LE that obviates further need for compression garments and LE therapy, this did not seem to be a goal that was reached quickly after surgery. Despite this, all patients seemed to universally report improvement with LE in ways that affected their lives that were personally important. This was true even when their subjective experience of the disease was correlated with only modest improvements in objective measurements. In the long term, we will continue to observe how far ALNT can go in helping patients with upper and lower extremity LE in the hope that they can live their lives free from the burdens of disease.