Autologous Lymph Node Transfer: Update On A Clinical Trial

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Introduction

There are over 2.5 million women with a history of breast cancer alive in the United States today. Of these survivors, recent prospective studies estimate that 15-54% will develop upper extremity lymphedema (UEL) within 3 years of breast cancer treatment. The remaining women have an ongoing risk of about 1% a year for at least 20 years. Post-mastectomy UEL can be disfiguring and painful, and it can also cause long-term physical, psychological, social, and financial problems. Recently, we have been investigating autologous lymph node transfer (ALNT), an innovative technique pioneered in France by Dr. Corinne Becker that has shown promise for treatment of UEL. Dr. Becker reports prospectively collected data on 1500 patients suggesting that ALNT results in >50% improvement of post-mastectomy UEL in 68% of patients with chronic disease resistant to physiotherapy. In these preliminary studies, 40% of patients with early disease are eventually able to stop complex decongestive therapy (CDT), the current standard of care.

In order to determine the efficacy of ALNT in treating chronic UEL, we developed an evaluator-blinded randomized controlled clinical trial to evaluate the efficacy of ALNT into the axilla for treatment of post-mastectomy UEL. Inclusion criteria include women aged 18-65 years who have undergone treatment for breast cancer resulting in chronic recalcitrant UEL refractory to conventional physiotherapy. Eligible patients are randomized to receive: 1) deep inferior epigastric artery perforator (DIEP) flap breast reconstruction with ALNT into the axilla; 2) DIEP flap breast reconstruction without ALNT into the axilla; or 3) ALNT into the axilla alone. A nurse researcher (blinded to randomization) records pre- and post-treatment measurements. The aims of the study were as follows:

1. To evaluate the efficacy of ALNT by collecting anthropometric and radiological measurements before and after surgery.
2. To determine changes in quality of life (QOL) after surgery by collecting patient-reported outcomes (PRO) data before and after surgery.

The ALNT technique used in this study involves harvesting 3-4 lymph nodes in subcutaneous fat from the superficial groin and anastomosing the vascular pedicle (artery and vein, no lymphatics) of the lymph nodes to a recipient artery and vein in the axilla. When the ALNT is performed in conjunction with DIEP, the lymph nodes (in their subcutaneous fat) are harvested en bloc with the DIEP. Unlike lymphaticovenous anastomosis (LVA), there is no direct connection between the lymphatic and vascular systems; we hypothesize that new lymphatic channels form de novo by lymphangiogenesis.

After surgery, patients are expected to undergo intensive manual lymphatic drainage for 3-6 months, but the goal is to eventually stop all physiotherapy. Interestingly, nearly all patients subjectively report an improvement in their UEL symptoms in the immediate postoperative period. Since it is unlikely that the lymph nodes transferred were functional within hours of surgery, we surmised that the axillary scar release and transfer of healthy vascularized tissue might have contributed to the rapid improvement in UEL symptoms.

The following is a description of two typical patients with chronic recalcitrant UEL after mastectomy treated with ALNT.

Patient #1

Patient #1 is a 41-year-old woman with a 3-year history of right upper extremity lymphedema that has failed conservative treatment. (Figure 1) The patient underwent right partial mastectomy and radiation in...
April 2007 for a 2.5 cm tumor with 15/37 positive lymph nodes that was complicated by a seroma. She underwent postoperative radiation therapy and developed mild lymphedema one year later, which worsened over time. She was hospitalized multiple times for cellulitis and infection from minor trauma to her right upper extremity. She underwent complete decongestive therapy with lymphatic massage, a compressive sleeve, and used a compression pump at home. She was 5’11” and 155 pounds (BMI 21.6), and her preoperative lymphoscintigraphy demonstrated delayed lymphatic migration of the radiotracer in the right upper extremity with accumulation within the subcutaneous tissues of the forearm, consistent with lymphedema (Figure 2).

Prior to surgery, infrared perometry assessment for LV revealed a LV of 2588 ml in her affected right arm vs a LV of 2233 ml in her non-affected left arm for a LV difference of 355 ml. The circumferential differences were observed in the affected right arm for three points from forearm to elbow (2.4 cm, 4.0 cm, and 2.9 cm) in comparison to the non-affected left arm. Bioimpedance (L-Dex U400) measurements for fluid level was L-Dex 8.6. In addition to swelling, the patient reported additional 8 symptoms (pain, heaviness, tightness, tenderness, limited limb movement, numbness, limb fatigue, and limb weakness).

On 25 May 2011, 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 significant decrease in swelling and a feeling of heaviness in her right hand and arm. Within two weeks, she reported that her right arm pain, tightness, and heaviness was gone, and there was a dramatic reduction in the difference between her preoperative and postoperative right and left arm volumes by infrared perometry from 355 ml to 55 ml. By two months, her right arm volume was stable despite the fact that she had been lifting heavy boxes, and she was able to wear clothes that she had not been able to wear since she developed lymphedema. She described the postoperative feeling of lightness in her right arm as if a chronic “headache” had disappeared. Throughout this time, the patient underwent manual lymphatic massage with a lymphedema therapist, and her arm also felt significantly softer.

Eight months postoperatively, infrared perometry assessment for LV revealed an absolute decrease in LV of 237 ml (9.1%) in her affected right arm. The LV of her affected right arm was 2351 ml vs a LV of 2176 ml in her non-affected left arm for a LV difference of 175 ml. The circumferential differences in the affected right arm of the three points from forearm to elbow were 1.6 cm, 1.9 cm, and 1.8 cm in comparison to the non-affected left arm. Bioimpedance (L-Dex U400) for fluid level was now L-Dex 2.8. The patient reported a significant decrease in swelling and occasional limb fatigue, but reported no symptoms whatsoever of pain, heaviness, tightness, tenderness, numbness, or limited limb movement. (Figure 3)

Figure 2. Preoperative lymphoscintigraphy of patient #1 demonstrated delayed lymphatic migration of the radiotracer in the right upper extremity with accumulation within the subcutaneous tissues of the forearm, consistent with lymphedema.

Patient #2

Patient #2 is a 55-year-old woman with an 8-year history of right upper extremity lymphedema that had failed conservative treatment B. Preoperative photograph of patient with recurrent skin cancer involving left naso-jugal junction.

Figure 4. Patient #2 is a 55-year-old woman with an 8-year history of right upper extremity lymphedema that has failed conservative treatment B. Preoperative photograph of patient with recurrent skin cancer involving left naso-jugal junction.

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Prior to surgery, the patient felt defeated and had largely stopped self-massage, and only wore her compression stocking at night. Her symptoms included significant right upper extremity swelling and heaviness. She was 5’ and 126 pounds (BMI 24.6), and her preoperative lymphoscintigraphy demonstrated obstruction to lymphatic flow with significant dermal backflow and formation of alternative channels of drainage into the right axilla. Even at three hours post-injection, there was very slow clearance of the tracer from the lower arm to the upper arm and right axilla consistent with lymphatic obstruction (Figure 5).

On 17 October 2011, patient #2 underwent ALNT alone from her left groin to her right axilla. She had an uneventful

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Figure 3. Eight months postoperatively, the arm for patient #1 continues to do well.