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Interaction between vascularized lymph node transfer and recipient lymphatics after lymph node dissection—a pilot study in a canine model

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ABSTRACT

Background: Vascularized lymph node transfer (VLNT) has become more widespread for surgical treatment of lymphedema. However, interaction between a transferred lymph node and the recipient lymphatic system in relieving lymphedema has not been identified. The aims of this study were to investigate anatomic changes in the lymphatic system in the forelimb of a canine after lymph node dissection and irradiation and to clarify the interaction between the transferred lymph node and recipient lymphatics.
Materials and methods: Two adult female mongrel canines were used for this exploratory study. The unilateral axillary and lower neck node dissections were performed, and 15-Gy irradiation was applied on postoperative day 3. After 1 y, a VLNT flap was harvested from the lower abdominal region and inset in the axilla with vascular anastomoses. The girth of each forelimb was determined with a tape measure at different time points. Indocyanine green fluorescence lymphography and lymphangiography were performed before and after each surgery to evaluate morphologic changes in the lymphatics.
Results: Both canines revealed identical changes in the lymphatic system, but only one canine developed lymphedema. After lymph node dissection, a collateral lymphatic pathway formed a connection to the contralateral cervical node. After VLNT, an additional collateral pathway formed a connection to the internal mammary node via the transferred node in the axilla.
Conclusions: The findings suggest that the lymphatic system has a homing mechanism, which allows the severed lymphatic vessels to detect and connect to adjacent lymph nodes. VLNT may create new collateral pathways to relieve lymphedema.

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Introduction

In developed nations, lymphedema is caused mainly by cancer treatment such as surgical ablation of regional lymph nodes and radiation therapy. The incidence of breast cancer–related lymphedema varies between reports but is at least 20% in women who have undergone treatment for breast cancer.[1,2] Despite the well-known morbidity of iatrogenic lymphedema, our knowledge of the pathophysiology of secondary lymphedema is very limited, and animal experiments are therefore desperately needed.[3]

Although little is known about the etiology of secondary lymphedema, surgical treatment of lymphedema has been attracting increasing attention from plastic surgeons. The current surgical options for lymphedema are roughly divided into two categories: ablative and physiological.[4] Vascularized lymph node transfer (VLNT), one of the physiological procedures, is becoming more widespread and has produced promising outcomes.[5-10] Two theories have been proposed to explain the relationship between VLNT and lymphedema. The first theory maintains that the transferred lymph node is a rich source of lymphangiogenic cytokines and facilitates bridging between the proximal and distal stumps of the lymphatic channels (bridging theory).[8,9] The second theory posits that the lymph node possesses a native lymphovenous shunt and that a portion of lymph drains through the vascular pedicle, with the lymph node functioning like a suction pump (pumping theory).[6,10]

Mouse models have been used to investigate lymphatic recanalization between a nonvascularized lymph node graft and recipient lymphatics by using the molecular biological approach.[11,12] However, mice are not ideal for modeling VLNT in humans because their small size precludes vascular microanastomosis and tracing of lymphatic vessels.

We have investigated the comparative anatomy of the lymphatic system in different animals and humans.[13-16] We believe that large animal studies are imperative for understanding the biological mechanisms of VLNT. We used canines in this exploratory study because the lymphatic system in the canine forelimb is similar to the lymphatic system in humans in terms of the arrangement of lymph nodes and clear separation between the superficial and deep components of the lymphatic system.[13,15] The first aim of this study was to investigate anatomic alterations in the lymphatic system of the forelimb after radical lymph node dissection followed by irradiation of the surgical site. The second aim was to understand the interaction between the transferred vascularized lymph node and recipient site lymphatics. We hypothesized that VLNT would facilitate collateral formation of the lymphatic system; thus, VLNT would have the potential to treat lymphedema.

Materials and methods

All animal procedures were approved by The University of Texas MD Anderson Cancer Center's Institutional Animal Care and Use Committee, which is accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International including the National Institutes of Health. Two adult female mongrel canines (canine A and canine B, weighing 25.4 and 23.0 kg, respectively on arrival) were used. They underwent identical procedures (Fig. 1).

The left forelimb underwent all procedures, and the right forelimb served as a nonoperative control. A single examiner measured forelimb girth with a tape measure every 2-3 d during the first 2 wk after each surgery and every 2-4 wk thereafter. Girth was measured at the following four sites in both forelimbs with the animal in a standing position on an examination table: forepaw, wrist, elbow, and midlevel between the wrist and elbow.

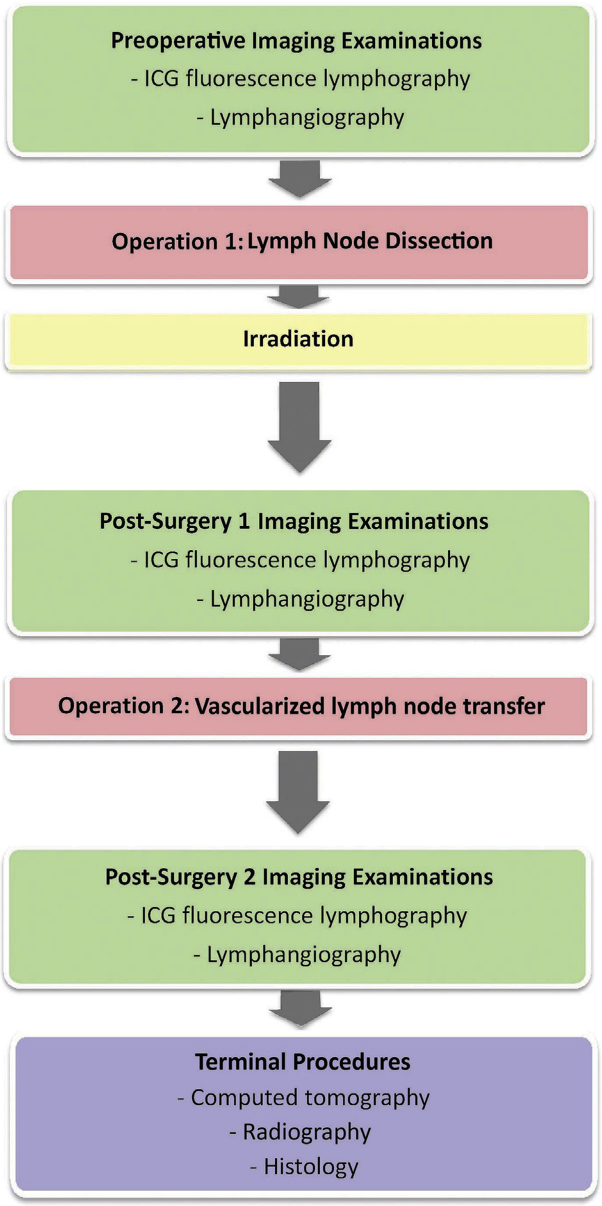

Fig. 1 – Experimental procedures. (Color version of figure is available online.)