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A novel approach to the treatment of lower extremity lymphedema by transferring a vascularized submental lymph node flap to the ankle ☆

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ABSTRACT

Objective. Vascularized groin lymph node flaps have been successfully transferred to the wrist to treat post-mastecomy upper limb lymphedema. This study investigated the anatomy, mechanism and outcome of a novel vascularized submental lymph node (VSLN) flap transfer for the treatment of lower limb lymphedema.

Methods. Bilateral regional submental flaps were dissected from three fresh adult cadavers for histological study. A unilateral submental flap was dissected in another six fresh cadavers after latex injection. The VSLN flap was transferred to the ankles of seven lower extremities in six patients with chronic lower extremity lymphedema. The mean patient age was 61 ± 9.4 years. The average duration of lymphedema symptoms was 71 ± 42.2 months.

Results. There was a mean of 3.3 ± 1.5 lymph nodes around the submental artery typically at the junction with the facial artery, on the six cadaveric histological sections. Mean of 2.3 ± 0.8 sizable lymph nodes were dissected and supplied by the submental artery in six cadaveric latex-injected submental flaps. All seven VSLN flaps survived. One flap required re-exploration for venous congestion but was successfully salvaged. There was no donor site morbidity. At a mean follow-up of 8.7 ± 4.2 months, the mean reduction of the leg circumference was $64 \pm 11.5\%$ above the knee, $63.7 \pm 34.3\%$ below the knee and $67.3 \pm 19.2\%$ above the ankle.

Conclusion. The transfer of a vascularized submental lymph node flap to the ankle is a novel approach for the effective treatment of lower extremity lymphedema.

Introduction

Lymphadenectomy in uterine cancer is important for surgical staging and for cancer treatment by decreasing metastasis via lymphatic channels [1]. The incidence of lower extremity lymphedema post uterine cancer ablation, pelvic lymph nodes dissection and subsequent radiation treatments was reported from 1% to 48% [2–6]. Abu-Rustum reported that lower limb lymphedema mainly develops due to the pelvic lymph nodes dissection, especially when more than 10 nodes are removed [2–6]. The widely ranged incidence might result from the different diagnostic criteria of the lymphedema, numbers of pelvic lymph nodes excised, and the dosage of radiation therapy. The incidence is higher after cancer resection and lymph node dissection in vulva cancer followed by cervical and ovarian cancer [7]. Recently, sentinel lymph node biopsy was selectively applied in gynecological cancer surgery to reduce the lower limb lymphedema [8–10].

Treatments of lymphedema are aimed to control infection, to reduce the swelling of the extremity and to improve the quality of life. Basic treatments of lymphedema start with conservative physical therapy, including manual lymphatic drainage and compression bandage-centered decongestive lymphatic therapy. The efficacy of conservative physical therapy presents only when the patients are compliant with the treatment program. However, it also carries risks of intravascular cancer metastasis and thrombosis formation. When the conservative treatment fails, surgical treatments present as alternatives. Debulky surgery and circumferential suction-assisted lipectomy can be performed to reduce the severely, non-pitting lymphedematous extremity [11]. More technical demanding surgeries, such as lymphatico-lymphatic anastomosis [12] lymphatico-venous anastomosis were introduced in the past [13–20]. Although there were some good results from variable reports, the disadvantages of these techniques include: 1) difficulty finding the thin-walled minute

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lymphatic ducts, 2) the requirements of 12-0 nylon suture, supermicrosurgery instruments and high magnification microscope, 3) usually requiring 3 to 10 anastomoses, 4) difficulty to monitor the patency of anastomoses, and 5) the anastomosis is easily obstructed since the lumen cannot tolerate the positive interstitial pressure when the wound is closed.

Free vascularized lymph node transfer was initially described in 1990 by O'Brien and Chen [21,22] for the treatment of lymphedema in a canine model. In a sheep model, Tobbia et al. [23] addressed that the restoration of lymphatic function in vascularized lymph nodes transferred to the study animals was similar to sham controls and was significantly better than in the transferred avascular lymph nodes. Reports by Becker et al. [24] and Lin et al. [25] have demonstrated the clinical efficacy of vascularized groin lymph node flap transfer for the treatment of post-mastectomy upper extremity lymphedema using variable recipient sites. The basic physiologic mechanism of the vascularized submental lymph node flap is that lymph is absorbed by the transferred lymph nodes and drained into a donor vein through natural lymphaticovenous connections inside a flap. The arterial flow from the recipient artery to the vascularized lymph node flap provides the driving force for venous return and hence, continuous lymph drainage. Until recently, the groin flap with superficial inguinal lymph nodes was the flap of choice for vascularized lymph node transfer for upper extremity lymphedema. We report an innovated vascularized submental lymph node flap based on the findings from anatomic study in nine cadavers and the application of this flap in six patients with seven lower extremities with chronic lymphedema.

Methods

Anatomic study

The submental artery arises from the facial artery, deep to the submandibular gland and passes medially across the mylohyoid muscle and then superficially or deep to the digastric. The submental vein provides the venous drainage into the facial vein. The submental flap is an axial pattern flap that receives one to four cutaneous perforators traveling from the submental vessels to the skin overlying the platysma. The main perforator is typically found 3.2 cm in front of the facial artery, which pierces the platysma before dividing into several subdermal branches.

The first part of the regional anatomic dissection of the bilateral submental flaps was performed in three fresh adult cadavers, in collaboration with the University of Texas Southwestern Medical Center in Dallas, Texas, in July 2009. These six cadaveric submental flaps were sent for histological sectioning to evaluate the available lymph nodes supplied by the submental artery (Fig. 1, Left). In the second part, unilateral submental flap was dissected in six fresh cadavers at the 9th Duke Flap Course at Duke University Medical Center, Durham, North Carolina, in August 2011. These six latex-injected submental flaps were investigated to confirm the presence of visible lymph nodes (size greater than one cm) and to verify that they are vascularized by the submental artery (Fig. 1, Right).

Clinical applications

Between May 2010 and November 2011, six patients with a mean age of 61 ± 9.4 (range, 47 to 72) years developed lower extremity lymphedema and underwent a VSLN flap transfer to the ankle. The lymphedema in these patients was a result of sequelae from hysterectomies, lymph node dissections and subsequent radiation treatments. Three limbs were in stage II and four limbs were in stage III according to the International Society of Lymphology. The average duration of lymphedema symptoms was 71 ± 42.2 months (range, 36 to 120 months) with a mean of 3.9 ± 4.3 episodes (range, 0 to 10) of cellulitis that has failed to respond to conservative treatment (Table 1).

Surgical technique

Vascularized submental lymph node flap harvest (Supplemental Digital Video 1). The facial artery was palpated and marked. An elliptical skin paddle (10×5 cm) was designed with the upper margin along the lower border of the mandible, from the mandible angle to the symphysis. A pencil Doppler was used to detect the perforators from the submental artery. The incision was initiated at the upper margin and deep through the platysma layer. The distal facial artery above the mandible was identified at its junction with the submental artery. The submental artery was dissected from the proximal end to the distal end along its axis. The septocutaneous perforator from the submental artery to the skin paddle was carefully preserved. The soft tissue around the junction of the submental artery and the facial artery was included to ensure the preservation of the maximal number of submental lymph nodes. The anterior belly of the digastric muscle could be included to avoid injury to the septocutaneous perforators, and the marginal mandibular nerve was carefully preserved. The facial vessels were harvested with submental vessels for additional pedicle length, and the donor site was closed primarily with a suction drain.

Preparation of the lower extremity recipient site (Supplemental Digital Video 2). Based on our previous experience with vascularized groin lymph node transfer to the wrist for the treatment of upper limb lymphedema [25], the ankle was selected as the site of transfer on the lower extremity because of the easy drainage of lymph fluid by gravity and the catchment effect. An S-shaped incision was made on the dorsal ankle. The skin envelope was undermined to allow for the inset of the VSLN flap. The dorsalis pedis vessels were examined for adequate arterial spurting prior to the microanastomosis, and an

Fig. 1. (Left) Two lymph nodes were found in the histological sections in the dissected submental flap of a fresh cadaver. Please note that two submental lymph nodes were supplied by the submental artery, as observed on hematoxylin eosin stains under low-magnification histological examination. (Right) A submental lymph node flap supplied by the submental artery with two visible lymph nodes was dissected in a fresh cadaver post-latex injection.

Table 1
The outcomes of seven cases of lower limb lymphedema that underwent vascularized submental lymph node flap transfer to the ankle.

Case no.	Age (years)	Site	Stage of edema	Symptom duration	Reduction rate			Volume differentiation						Follow-up
					Above-knee 15 cm	Below-knee 15 cm	Above-ankle 10 cm	Above-knee 15 cm		Below-knee 15 cm		Above-ankle 10 cm		
				Months	%	%	%	Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op	Months
								%	%	%	%	%	%	
1*	66	R	III	72	81	100	75	14	7.3	6.5	1	5	6	22
2	47	R	III	84	46.2	100	73	32.5	10.9	42.2	6	53.3	23.3	19
3	65	R	III	120	62	31.6	51.9	24.2	10.8	23.8	17.6	37	20.3	8
4*	66	L	II	84	62.5	20	75	7.3	3.8	1.3	0	5.6	3	6
5	72	L	II	120	70	100	100	9.6	3.2	2.7	0	10.7	0	2
6	51	L	III	36	54.8	58.8	45.9	32.8	17.3	33	17.5	41	29.4	2
7	60	L	II	60	71.4	33.3	50	13	4.1	3.7	2.6	11.8	6.9	2
Mean ± SD %	61 ± 9.4			71 ± 42.2	64 ± 11.5	63.7 ± 34.3	67.3 ± 19.2	23.3 ± 9.1	8.4 ± 5.7	21.8 ± 14.4	6.3 ± 7.9	26.7 ± 16.9	11.6 ± 10.5	8.7 ± 4.2
p-value					$p<0.01$*	$p<0.01$*	$p<0.01$*	Pre-op vs. Post-Op $p<0.01$*		Pre-op vs. Post-Op $p=0.03$*		Pre-op vs. Post-Op $p=0.01$*		

* Cases 1 and 4 were the same patient.

adventitiectomy was required in patients with severe lymphedema. The arterial anastomosis was conducted in an end-to-end fashion with a 9-0 nylon suture. The double clamp was released to check for good venous backflow and flap perfusion before the venous anastomosis. A size discrepancy of the venous pedicles was not uncommon, but it was easily overcome with hand-sewn suturing. The flap was inset into the skin pocket. The wound was primarily closed over two Penrose drains. A split-thickness skin graft was needed in some cases on the sides of the flap because the flap thickness was usually too large to fit into the created skin pocket, which was typically fibrotic and tight. Care was taken not to compress the pedicle when the wound was closed. Postoperatively, the flap was monitored for signs of arterial insufficiency such as decreased temperature, paleness and slow capillary refill, as well as signs of venous insufficiency such as congestion, bluish discoloration and brisk capillary refill.

Statistics

The volume difference was defined as the circumference of the lesion limb minus the circumference of the healthy limb and divided by the circumference of the healthy limb. The reduction rate was defined as the preoperative difference between the circumferences of the lesion and healthy limbs minus the postoperative difference and divided by the preoperative difference; the circumference was calculated at 15 cm above the knee, 15 cm below the knee, and 10 cm above the ankle. The condition-specific quality of life assessment tool for lymphedema of the limbs (LYMQOL) was used for the assessment of the outcome [26]. The questionnaire was completed by face-to-face interviews. The LYMQOL contains four domains: function, appearance, symptoms, mood, as well as overall quality of life. Each subscale was standardized on a 1 to 4 scale and overall quality of life was score between 0 and 10; higher scores indicate better status. The Mann–Whitney *U* test was used for statistical comparisons. Statistical significance was defined as $p \leq 0.05$.

Results

Anatomic study

Mean of 3.3 ± 1.5 (range, 1 to 6) lymph nodes were found around the submental artery in the histological sections of six submental flaps (Fig. 1, Left). Mean of 2.3 ± 0.8 (range, 2 to 4) visible lymph nodes were around the submental artery on the six latex-injected cadaveric submental flaps (Fig. 1, Right). The length of the submental artery including the facial artery was approximately 6 cm.

Clinical applications

All seven VSLN flaps survived, representing a 100% success rate. One flap required re-exploration for venous congestion and was successfully salvaged. At a mean follow-up period of 8.7 ± 4.2 (range, 2 to 22) months, the pre-operative volume differentiation was statistically higher than post-operative volume differentiation above the knee (23.3 ± 9.1% versus 8.4 ± 5.7%, $p<0.01$), below the knee (21.8 ± 14.4% versus 6.3 ± 7.9%, $p=0.03$) and above the ankle (26.7 ± 16.9% versus 11.6 ± 10.5%, $p=0.01$) (Table 1). The mean reduction rate of the circumference was 64 ± 11.5% (range, 46.2% to 81%) above the knee ($p<0.01$), 63.7 ± 34.3% (range, 31.6% to 100%) below the knee ($p<0.01$), and 67.3 ± 19.2% (range, 45.9% to 100%) above the ankle ($p<0.01$) (Fig. 2) (Table 1). There was no donor site morbidity such as wound disruption or infection or submandibular nerve injury. There was no complaint of donor site scar by all patients as the scar was inconspicuous and hidden in the submandibular area (Fig. 3). In all patients, compression garments and physical therapy were not routinely used in the postoperative period. The patients were allowed to ambulate after three weeks. All patients reported that their legs felt lighter and softer, and the range of motion also improved one week postoperatively. The episodes of cellulitis decreased from a mean of 3.9 ± 4.3 to 0.1 ± 0.4 post-VSLN flap transfer ($p=0.06$). The mean of preoperative LYMQOL score was 2.2 ± 0.8 and post-operative score was 7.5 ± 0.5 ($p<0.01$). All patients were satisfied with the improvement of quality of life (Table 2).

Case presentation

A 47-year-old female (Patient 2) suffered from chronic right lower limb lymphedema with three episodes of cellulitis post radical hysterectomy, bilateral pelvic lymph node dissection, and postoperative radiotherapy for cervical cancer treatment in 2003 (Fig. 4 left). Despite the placement of a right common iliac venous stent and aggressive conservative decongestive therapy, the patient did not show clinical improvement. The patient underwent a VSLN flap transfer using the ankle as a recipient site. The patient was placed on bridging intravenous anticoagulation therapy prior to surgery.

Postoperatively, the flap developed venous congestion requiring re-exploration, which was successfully salvaged. The patient was placed on maximal therapeutic heparin therapy after the results of a venous duplex of the right leg showed a partial thrombosis of the right GSV at the mid-calf level on day two. The flap subsequently recovered well with no further interventions. The patient was switched to oral anticoagulation after one week and was kept on lifetime therapeutic oral anticoagulation after hospital discharge.

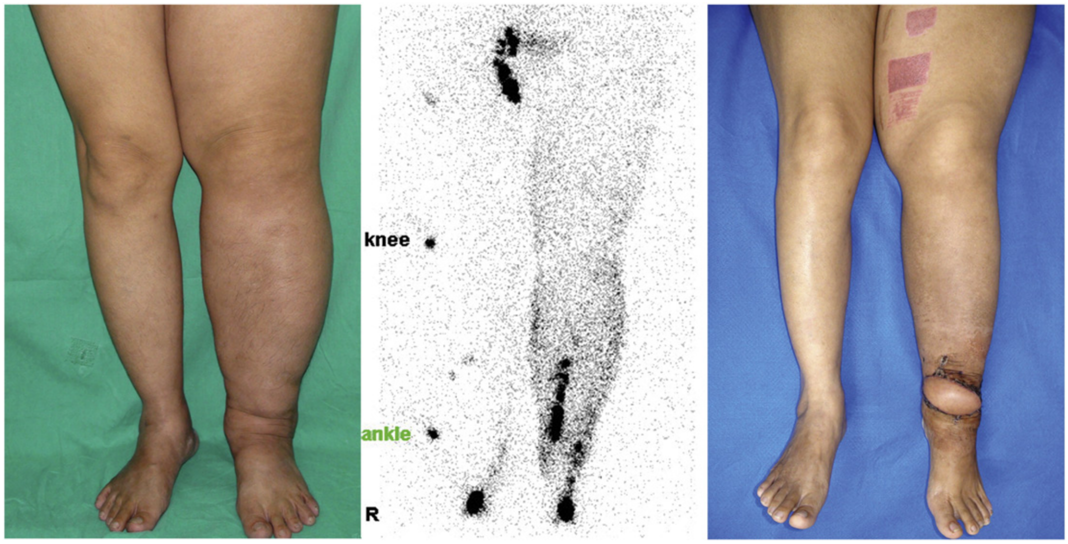

Fig. 2. A 51-year-old female (case no. 6) experienced left lower extremity lymphedema for 36 months post-radical hysterectomy, bilateral pelvic lymph node dissections, and post-operative radiotherapy (left). She underwent left vascularized submental lymph node flap transfer to the ankle. The preoperative lymphoscintigraphy revealed partial lymphatic obstructions at the right mid-calf and right mid-thigh levels (middle). At a follow-up of 2 months, the reduction rate of the lesion limb circumference was 54.8%, 58.8%, and 45.9% above the knee, below the knee and above the ankle, respectively (right).

At a follow-up of 18 months, the patient had reduction rates of 46.2%, 100%, and 73% for the right lower extremity lymphedema above the knee, below the knee, and above the ankle, respectively (Fig. 4). The volume differentiation in the right lymphedematous limb was 32.5% preoperatively versus 10.9% postoperatively above the knee, 42.2% versus 6% below the knee, and 53.3% versus 23.3% above the ankle (Fig. 4).

Discussion

This anatomic study confirmed a mean of 3.3 ± 1.5 submental lymph nodes that were vascularized and could be harvested with the submental flap. In our clinical cases, we have demonstrated the effectiveness of the VSLN flap for the treatment of chronic lower extremity lymphedema. To the best of our knowledge, this is the first report of the use of the VSLN flap in the treatment of lower extremity lymphedema.

The VSLN flap has favorable indications for the following reasons: in patients with lower extremity lymphedema, especially in bilateral cases where vascularized groin lymph node flap transfer is not ideal because of the possible risk of exacerbating the lower extremity lymphedema in the donor leg; the flap dissection is straightforward and rapid because the anatomy is fairly consistent; the flap is less bulky, making the inset easier; and the donor site is typically inconspicuous under the lower border of the mandible.

The mechanism of the lymph drainage in the vascularized lymph node flap transfer (Supplemental Digital Video 3) is as follows: first, the submental lymph nodes are perfused by the arterial inflow and act as the pumps to suction the lymph, which is drained into the donor vein via natural lymphaticovenous connections inside the flap. The lymph drainage via the transferred lymph nodes can be demonstrated by the quick uptake of indocyanine green into the recipient vein 10 minutes after its subdermal injection at the flap edge following the completion of the pedicle anastomosis (Supplemental Digital Video 2). This visualization provides direct evidence of lymph drainage from the transferred submental lymph nodes inside the flap, through the donor vein, and into the recipient vein. The improvement in the lymphedematous extremity is sustained and progressive because the VSLN flap continues to pump lymph drainage directly into the venous system. Second, as the subcutaneous interstitial pressure decreases, more lymph is recruited from the surrounding tissue in a "catchment" effect [25]. Third, with the effects of gravity, the lymph will gradually drain from the calf to the ankle, and from the thigh to the calf. Fourth, as the tissue compartment pressures normalize over time, old lymphatic channels may reopen, and lymphangiogenesis slowly recovers [27]. Because the number of transferred lymph nodes is limited, the effect on lymph drainage

Fig. 3. The minimal donor site morbidity post the vascularized submental lymph node flap transfer. Post-operative photographs of the patient 2 at a follow-up of 18 months, A–P and lateral views.

Table 2
The quality of life measurement for lymphedema of the limbs (LYMQOL) of seven cases of lower limb lymphedema that underwent vascularized submental lymph node flap transfer to the ankle.

Case no.	Stage of edema	Function		Appearance		Symptoms		Mood		Overall quality of life	
		Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op
1*	III	1	2	2	3	1	4	1	3	2	7
2	III	2	4	1	4	1	4	1	4	3	8
3	III	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing
4*	II	1	2	1	2	1	3	1	3	2	7
5	II	2	3	1	3	1	3	2	3	2	8
6	III	1	3	1	3	1	3	1	3	1	7
7	II	2	3	1	3	2	3	2	3	3	8
Mean $\pm$ SD %		1.5 ± 0.5	2.8 ± 0.8	1.1 ± 0.4	3 ± 0.6	1.2 ± 0.4	3.3 ± 0.5	1.3 ± 0.5	3.2 ± 0.4	2.2 ± 0.8	7.5 ± 0.5
p-value		Pre-op vs. Post-Op $p<0.01^{*}$		Pre-op vs. Post-Op $p<0.01^{*}$		Pre-op vs. Post-Op $p<0.01^{*}$		Pre-op vs. Post-Op $p<0.01^{*}$		Pre-op vs. Post-Op $p<0.01^{*}$	

*Cases 1 and 4 were the same patient.
LYMQOL questionnaire each subscale was standardized on a 1 to 4 scale, overall quality of life was score between 0 and 10; higher scores indicate more excellent status.

may not be dramatic, but its effect may be continuous with progressive improvement. Further investigations and long-term follow-up are needed.

Selection of the recipient site for the VSLN flap transfer is an important issue. The groin is not an ideal recipient site because the area is usually scared, radiated, with fibrosis, which makes recipient vessels dissection more tedious. Most importantly, it is difficult for the transferred lymph nodes to suction the lymph against the gravity, especially from the foot and leg. The popliteal fossa is also not a convenient recipient site since it requires additional change in position during surgery. There are less available recipient vessels as the popliteal vessels are not expendable. The ankle is the preferred option because the available recipient vessels (dorsalis pedis and posterior tibialis) are usually healthy without radiation damage. It is also the most dependent position where the most lymph is pooled from the effect of gravity.

The major drawback associated with this technique is the failure to include enough lymph nodes and soft tissue surrounding the lymph nodes to maximize the natural lymphaticovenous connections. In addition, the pedicle length for this flap is short, often requiring the inclusion of the facial vessels. Potential injury to the marginal mandibular nerve during flap dissection should be avoided.

Although the submental lymph nodes can be harvested without the skin, the skin paddle of the submental flap is important to achieve a tension-free wound closure of the fibrotic skin pocket. Small split-thickness skin grafts for the coverage of exposed subcutaneous areas of the flap may also be helpful to allow for further release of the wound tension and avoiding pedicle compression.

Recipient site morbidities are minimal. Since the ankle joint and tendons were not pre-operatively affected and intra-operatively injured, the function of the ankle and foot are not compromised. The difficulty of wearing shoes, besides the boots, was not reported by any patient. One concern is the appearance of the bulky flap on the ankle, which is not pleasing. The cosmesis of the bulky flap can be improved with de-epithelialization of the transferred flap at one year postoperatively.

Although the VSLN flap was used for the treatment of lower extremity lymphedema in this report, its application may be extended to other areas of lymphedema in the future. In chronic severe lymphedema, as expressed in patients in the present study, a complete cure of the lymphedema may not be possible with VSLN alone. Additional procedures, such as liposuction or wedge resection of the fibrotic and subcutaneous adipose tissue, may be required to further decrease the lymphatic load and improve the final cosmetic contours [11].

Conclusion

The transfer of a vascularized submental lymph node flap with a mean of 3.3 ± 1.5 lymph nodes to the ankle is a novel and effective approach for the treatment of lower limb lymphedema.

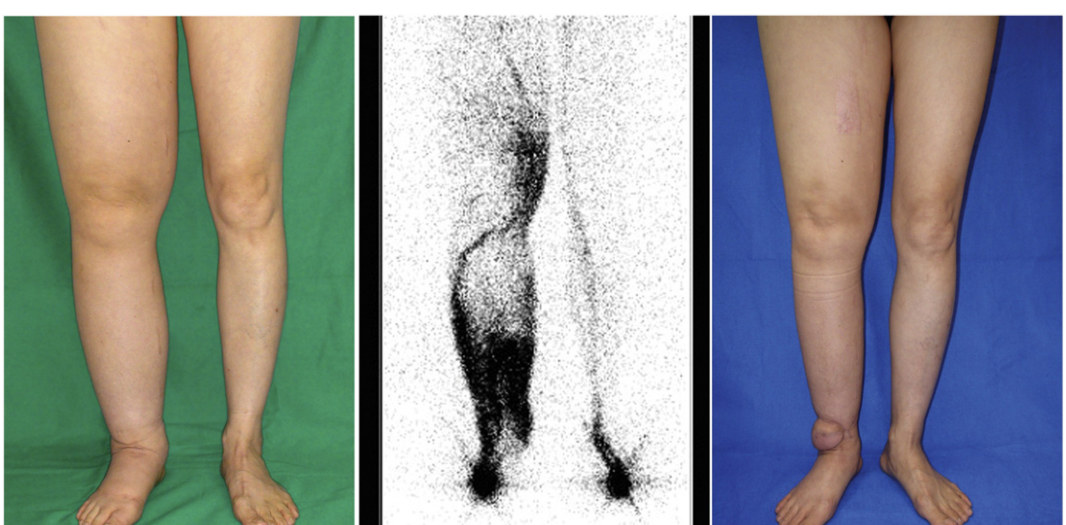

Fig. 4. A 47-year-old female (Patient 2) suffered from chronic right leg lymphedema post-radical hysterectomy, bilateral pelvic lymph node dissections, and postoperative radiotherapy for cervical cancer in 2003 (left). The preoperative lymphoscintigraphy revealed partial lymphatic obstructions at the right mid-calf and right mid-thigh levels (middle). At an 18-month follow-up, the reduction rate of the lesion limb circumference was 46.2%, 100%, and 73% above the knee, below the knee and above the ankle, respectively (right).

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