Original Scientific Report

Experimental Basis and First Application of Clinical Lymph Vessel Transplantation of Secondary Lymphedema

Rüdiger G.H. Baumeister, M.D., Jürgen Seifert, M.D., Baldur Wiebecke, M.D., and Dietbert Hahn, M.D.

Department of Surgery, Institute for Surgical Research, Institute for Pathology, and Department of Radiology, University of Munich, Klinikum Grosshadern, Munich, West Germany

Lymphedemas due to a blockage of the lymph vessels in the root of the extremities were treated experimentally and clinically by autotransplantation of lymph vessels under the operating microscope. In experimental lymphedema of the hind leg of 10 dogs, an increased circumference of about 50% was reduced to 10% within 7 weeks by lymph vessel transplantation. After removal of the transplants, the circumferences returned to pre-transplantation values. The pre-transplantation elevated intralymphatic pressure of 12.5 torr (controls: 2.5 torr) was reduced to the normal range of 3.5 torr after the transplantation. In 8 of 10 dogs, the patency of the transplants could be demonstrated by inspection, lymphography, and isotope injections. In all 10 dogs, patency could be proved by histologic examination. The data indicate that lymph vessel transplantation can restore the diminished lymph-transporting capacity brought on by lymphedema.

In 2 patients, it was possible to prepare lymph collectors about 25 cm long. After the transplantation, the circumferences diminished. By isotopes improved lymphatic transport could be demonstrated after the operation. Autologous transplantation of lymph vessels is a promising method for the treatment of secondary lymphedema especially in the early stages.

Secondary lymphstatic edema of an extremity is usually caused by destruction of the lymph vessels in the root of the extremities and by the inability of the lymph vessels to regenerate. The diminished lymph-transporting capacity is unable to handle the normal lymphatic load and, therefore, edema develops [1]. Restoration of the lymph-transporting capacity is the only therapy to deal directly with the cause of lymphedema. Microsurgical techniques allows an operation on single lymph vessels. The restoration of the lymphatic pathways, lymph collectors that are especially adapted to the transport of the lymph, appears to be the most promising way to achieve an adequate lymph flow.

Reprint requests: R.G. Baumeister, M.D., Chirurgische Klinik der Universität München, Klinikum Grosshadern, Marchioninistrasse 15, D-8000 Munich 70, Federal Republic of Germany.

Materials and Methods

Experimental lymphedema was produced in mongrel dogs with an average weight of 28 kg. One hind limb was operated on, the contralateral limb serving as control. According to the method of Clodius and Wirth [2], the hind limb was totally transected except the femur, the femoral artery, vein and nerve, and the ischial nerve. The transection of the femoral vessels was performed with the aid of the operating microscope to clean the vessels of all lymphatic tissue and to ligate and mark the transected lymph vessels. In order to prevent spontaneous regeneration of the lymph vessels, a polyurethane-Teflon sheet (Epigard) was interposed. Only the skin was sutured. This method leads to a total blockage of the deep and superficial lymphatic

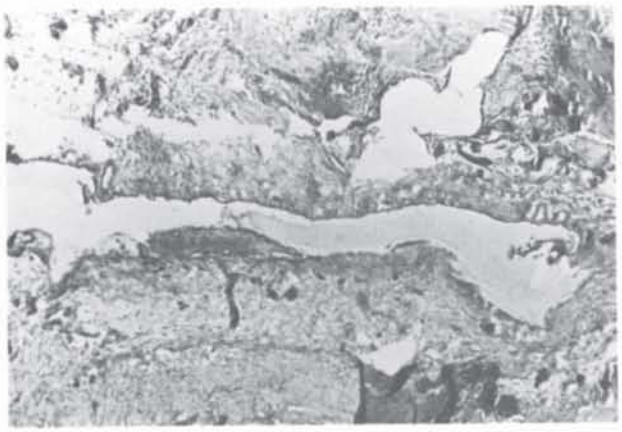


Fig. 1. Patent lymph vessel transplant 4 weeks after the autologous transplantation in dog (H-E. Objective 4 ×).

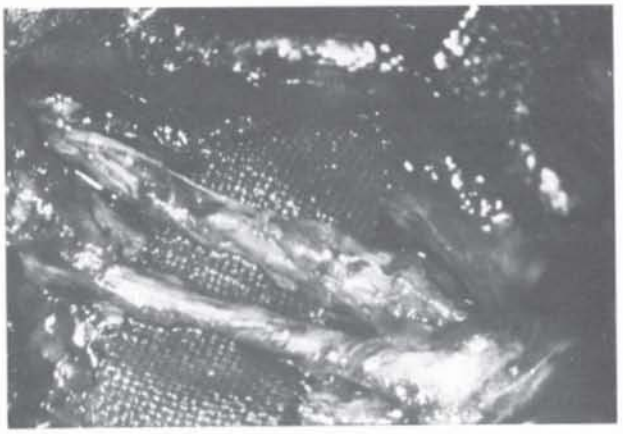


Fig. 2. Two transplanted patent lymph vessels under the operating microscope 4 weeks after transplantation.

system. After one week, the edema was fully developed.

Lymph collectors of the medial and superficial system of the contralateral thigh were removed from the length of the thigh. The enlarged distal and the proximal lymph vessels at the femoral vessels were prepared, and 2–3 transplants were interposed. End-to-end anastomoses were performed by a special tension-free anastomosing technique [3]. Under the operating microscope, the angle suture opposite to the surgeon is done first. The backwall is sewn with interrupted sutures, the wall being lifted only enough to allow the needle to pass. The anastomosis is finished with several interrupted sutures of the front wall. Throughout the anastomosing procedure, no transverse tension occurs. The operations were performed at the aid of a Zeiss operating microscope with a 40× magnification. Absorbable, atraumatic, and monofilament suture material was used [Polyglactin 910 (Vicryl)], the size ranging from 10-0 to 12-0.

After a therapeutic phase of about 7 weeks, the transplants were prepared again through a small longitudinal incision. Patency and function were tested and then the transplants were removed. The patency of the transplants was proved by visual examination, by lymphography using Lipiodol-Ultra Fluid, and by injecting isotopes (^{131}I-gamma globulin) at the paw and measuring the activity at the groin. The removed transplants were examined histologically.

The function of the transplanted lymph collectors was proved by measurements of the circumferences of the extremities at the paw, metatarsus, and lower leg. Furthermore, the function was examined by measuring the intralymphatic pressure as an end pressure [4]. A Statham element was used for the measurement. The zero baseline was at the level of the intralymphatic cannula.

Results

In 10 dogs, experimental lymphedema was treated by autologous transplantation of lymph collectors. In all 10 dogs, the patency could be proved by histologic examination (Fig. 1). In addition, in 8 of 10 animals, the patency of at least one transplanted lymph vessel could be proved by intraoperative inspection with lymphography and by isotopic investigation during the reoperation after the therapeutic phase. Two dogs could not be examined because of technical reasons. In Fig. 2, two transplanted lymph vessels are shown under the operating microscope 4 weeks after autologous transplantation.

Figure 3 shows an example of the evaluation of the patency by lymphography. One bigger and one smaller transplant filled with contrast medium can be seen. The lymph is transported along the transplants to the proximal lymph vessels. No collaterals could be seen. Injections of ^{131}I-gamma globulin were performed subcutaneously at the paw. After at least 5 minutes, in order to allow the absorption of the globulin into the lymph vessels and to exclude a false intravenous injection during that time, a quick rise in activity could be seen at the groin in both the controls and the transplanted legs and after standardized movements. After the induction of the edema before the transplantation, no rise in activity could be detected in the groin (Fig. 4).

The measurement of the circumferences at distinct levels of the operated hind leg compared with the contralateral leg served as a criterion for the function of the transplants in restoring the transport capacity of the totally blocked lymphatic outflow. Preoperatively, there was no difference in the circumferences between the two hind legs. After induction of the edema, the circumferences of the operated legs were significantly larger. After autol-

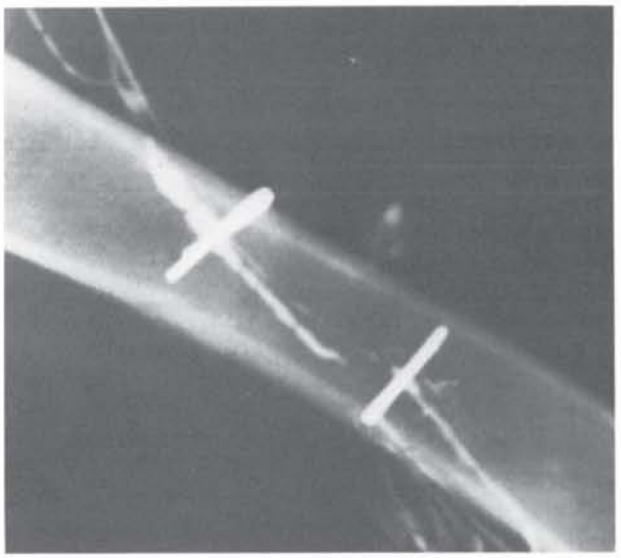


Fig. 3. Lymphographic patent transplants 4 weeks after autologous lymph vessel transplantation (marked by clamps).

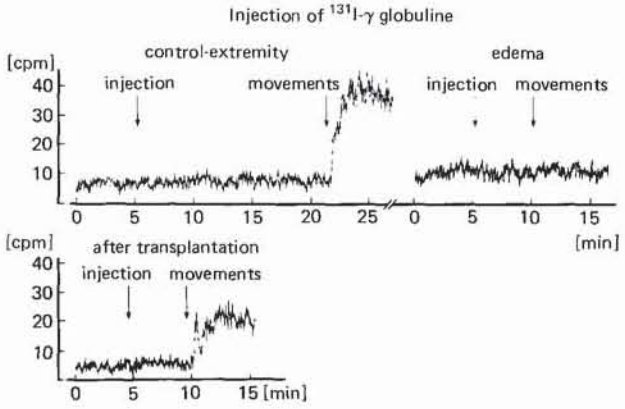
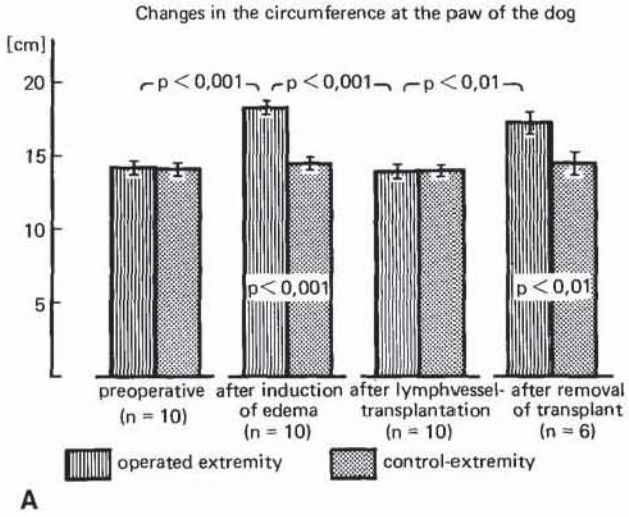
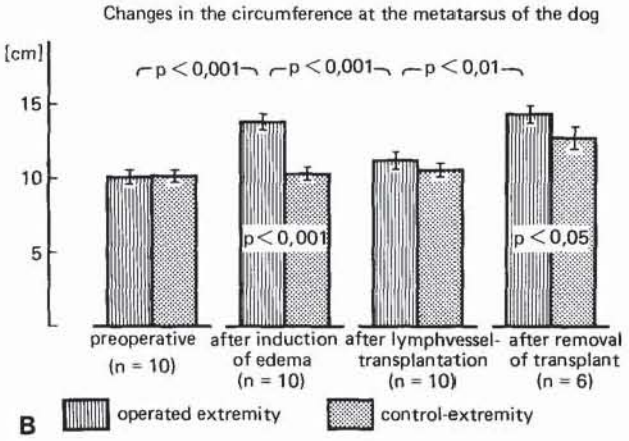


Fig. 4. Judgment of lymph flow of the hind leg of a dog was made by measuring activity at the groin after subcutaneous injection of ^{131}I-gamma globulin at the paw.

ogous lymph vessel transplantation, the circumferences of the operated legs went back to the range of the controls at the paw and at the metatarsus. Only at the lower leg were the circumferences somewhat larger than those of the control extremities. After removal of the transplants, the circumferences were again significantly elevated.

The comparison of the changes of the circumferences in the operated legs throughout the experiment showed a significant enlargement of the circumferences after induction of the edema, significant diminution after lymph vessel transplantation, and again a significant enlargement after removal of the transplants. This was true for all 3 measurement levels: the paw, metatarsus, and lower leg. The slight elevation of the circumference at the metatar-





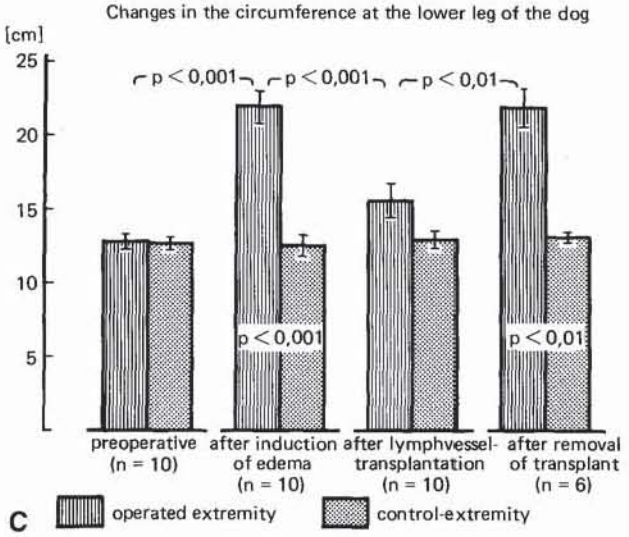


Fig. 5. The therapeutic effect of lymph vessel transplantation was evaluated by measuring several circumferences of the hind leg of the dog. **A.** Changes of the circumferences at the paw. **B.** Changes of the circumference at the metatarsus. **C.** Changes of the circumference at the lower leg.

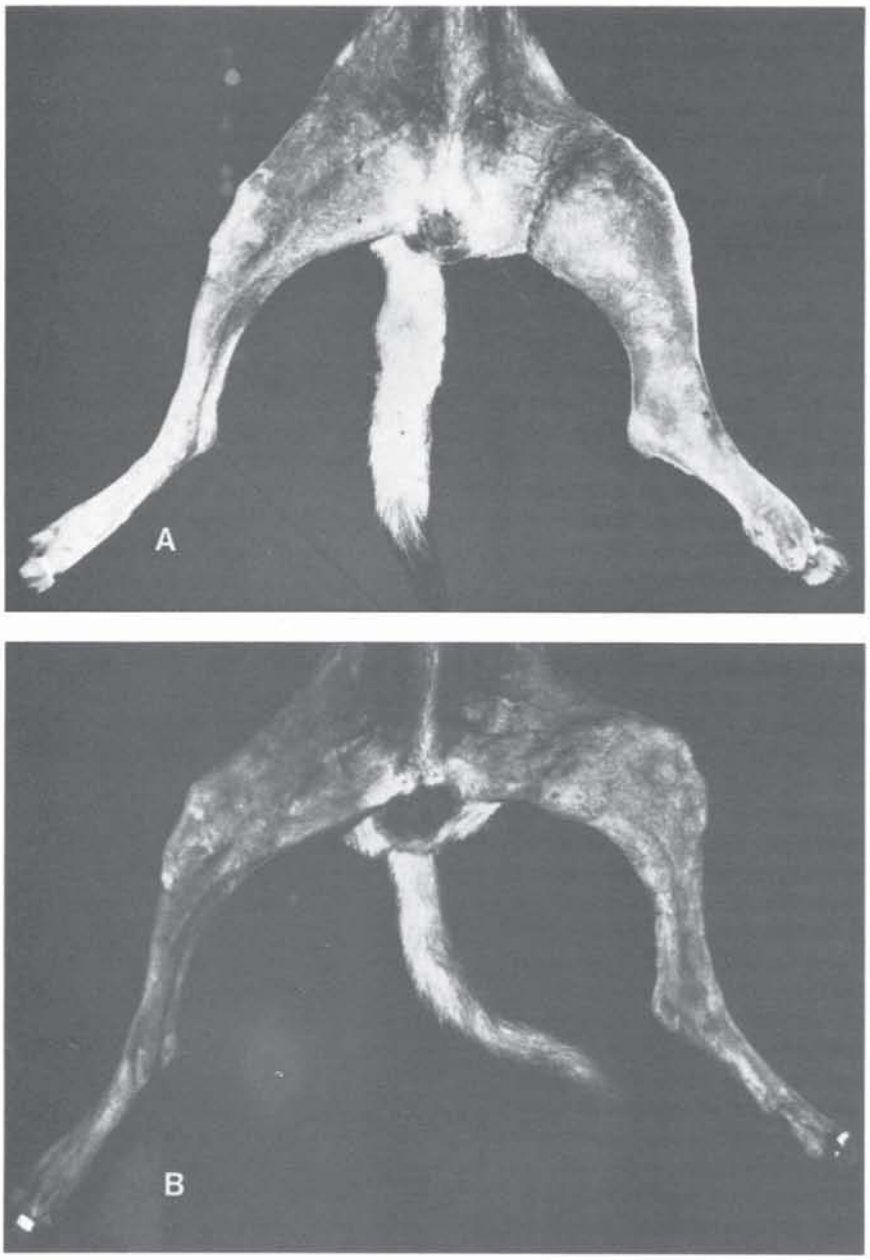


Fig. 6A. Lymphedema of the left hind leg of a dog. **B.** Four weeks after autologous lymph vessel transplantation.

sus of the control leg is probably due to the cannulation of the lymph vessels for pressure measurements (Fig. 5). Figure 6 shows an example of the therapeutic effect of the transplantation of lymph collectors on the experimental lymphedema of the dog.

As a further parameter for the function of the transplants, the intralymphatic pressure was measured during the edematous state, after the transplantation, and in controls. The end pressure was found to be 2.5 torr in the control extremities. In the edematous leg, it was elevated to 12.5 torr. After transplantation, the pressure subsided to the range of the controls at 3.5 torr (Fig. 7).

Clinical Use

The experimental data indicated a therapeutic effect of autologous lymph vessel transplantations for the treatment of a secondary lymphedema. Therefore, this promising method was also used in humans.

Our first patient was operated on in June 1980. After a traumatic injury at the right groin with severe infection, he developed an edema of the right leg within one year. The maximal difference in the circumference was 6 cm. No changes in the venous system at the groin were seen by phlebography. Conservative therapy showed no success, so we decided to perform a lymph vessel transplantation.

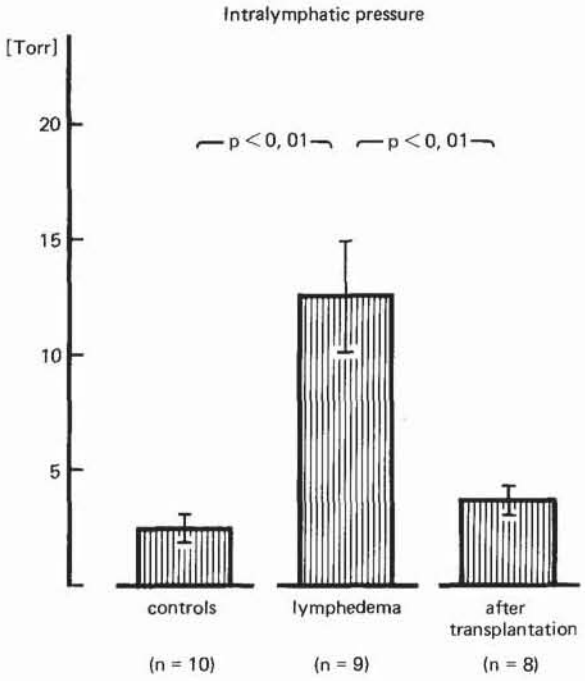


Fig. 7. The function of lymph vessel transplants was evaluated by measuring the intralymphatic end pressure.

We were able to prepare lymph collectors of the superficial medial system for the full length of the left thigh. Two collectors with a length of 25 cm were transposed to the right side via the symphysis (Fig. 8). At the right groin, two end-to-end anastomoses with a superficial and a deep lymph vessel of the edematous leg were performed using the tension-free anastomosing technique. Within one week, the difference in the circumference war reduced to a maximum of 1 cm. After a period of over 9 months, this result remains unchanged. Technetium-99m-albumin (Tecemin) was injected in the right foot to establish patency. Afterwards, groin activity showed a rise in both groins with a delay in the left groin. After massage of the affected leg, an extra rise could be detected in both groins (Table 1). With the aid of the gamma camera, the path of the transplants could be followed to the symphysis. There is an overlapping with the activity in the bladder (Fig. 9).

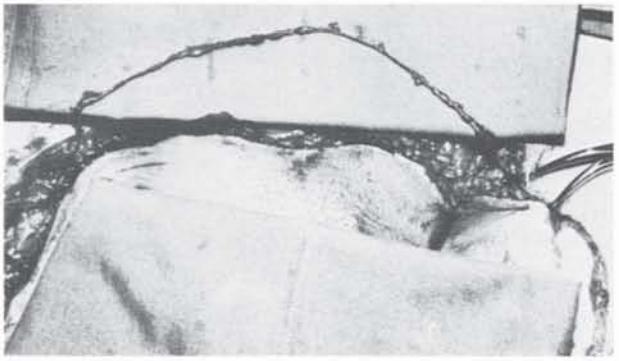


Fig. 8. Lymph collectors of the left thigh transposed via the symphysis.

The second patient was a 57-year-old female. Two years ago, an anal carcinoma was treated by abdominoperineal extirpation of the rectum with consecutive lymph node extirpation at both groins, followed by radiation therapy. A progressive lymphedema developed over a 6-month period. Scintiscans with Technetium-99m-sulfur-colloid (Lymphoszint) showed no lymphatic flow to the iliac nodes in the right edematous leg. On the left side, there was no significant defect in lymph transportation. Surgically, two lymph collectors were transposed via the symphysis and anastomosed end-to-end with the superficial and deep lymphatic system. Within 3 weeks, the circumferences were markedly reduced especially at the lower leg (Table 2). This time, scintiscans showed a quick flow of the lymph out of the extremity.

Discussion

The restoration of a sufficient transporting capacity of the lymphatic system by transplantation of lymph vessels was experimentally accomplished in the most severe form of lymphedema. After the total blockage of the lymphatic system, a malignant lymphedema developed. Untreated, this leads to death from profuse loss of proteins through the skin. Our experiences with 5 dogs correspond to that of Clodius [5]. In clinical situations, the deficiency of transporting capacity is less severe than that of this experimental model.

Another important aspect is the development of

Table 1. Half-life period corrected simultaneous measurements of the activity in the right and left groin after subcutaneous application of Tecemin in the first patient's right foot [t (counts/sec)].

Measurement point (min)	50	100	150[1]	200	230	250
Right groin	200	260	240	280	270	260
Left groin	20	100	240	300	330	280

[1]Massage of the right lower leg was performed after measurement at 150 min.

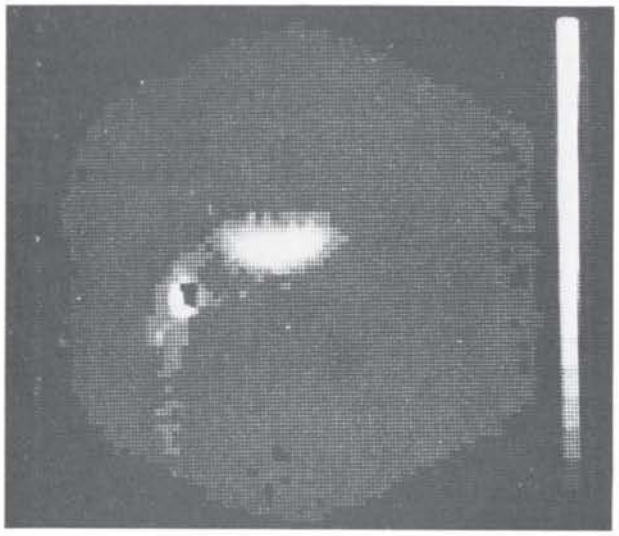


Fig. 9. Lymphatic scintiscan showing the course of the transplants to the symphysis.

an infection and a sclerosis of the edematous limb with a thickening of the basal membrane of the lymph capillaries and an accumulation of collagen fibers around the lymph vessel [6]. For a full rehabilitation by lymph vessel transplantation, it is therefore desirable to perform the operation in stage 1 of the lymphedema. As clinical experience shows, there is also lymph flow along fibrotic lymph vessels. Moreover, macrophages are able to destroy the interstitial proteins [7, 8]. Therefore, a diminution of the fibrosis might be possible after improvement of the lymph flow in stage 2.

An alternate method to the microsurgical lymph vessel transplantation is the creation of microlymphovenous shunts [9–11]. Since in edematous limbs spontaneous anastomoses have been seen [12], lymphovenous anastomoses are only a quantitative improvement of a compensation mechanism that is obviously working insufficiently.

The venous peripheral pressure is higher than the intralymphatic pressure, at least at rest [13]. Operations dealing only with the lymphatic system have the advantage that the risk of a thrombosis is diminished by the low coagulation parameters of the lymph [14].

The transplantation of lymph vessels could also be added to a resectional procedure for treating stage 3 lymphedema. Recurrent episodes [15] may be avoided by the improvement in the transporting capacity of the lymphatic system.

Acknowledgments

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Table 2. Preoperative and postoperative circumferences of the surgically treated right leg compared to those of the untreated left leg in the second patient.

	Left circumferences (cm)	Right circumferences (cm)	
		Preoperative	Postoperative
Thigh	57	63.5	61.5
Knee	41.5	46.0	42.5
Lower leg	38.0	42.0	39.0
Ankle	22.0	26.0	23.0
Metatarsus	23.0	25.0	23.0

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