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LIPOSUCTION REDUCES ARM LYMPHEDEMA WITHOUT SIGNIFICANTLY ALTERING THE ALREADY IMPAIRED LYMPH TRANSPORT

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ABSTRACT

In a prospective study, 20 patients with arm lymphedema after breast cancer treatment underwent liposuction combined with Controlled Compression Therapy (CCT) or CCT alone. Indirect lymphoscintigraphy (ILS) was used to study lymph kinetics before and after intervention. Lymphoscintigrams from the contralateral, non-edematous arm were characterized by prompt transit of the radiotracer (^{99m}Tc-albumin nanocolloid) to the axillary nodes, whereas tracer accumulation as dermal backflow characterized tracer transport in the lymphedematous arm. Neither liposuction with CCT nor CCT alone, changed this ILS profile. Liposuction combined with CCT reduced arm edema volume by (median) 115% (range 92-179%), whereas CCT alone decreased arm edema volume by only 54% (range 7-81%) (p=0.008). Because liposuction in conjunction with CCT was not associated with further impairment to an already restricted lymph transport, we recommend this therapy (liposuction with external compression) for chronic arm lymphedema, as it reduces edema volume safely, rapidly, and more efficiently than external compression alone. Moreover, it does not worsen an already impaired lymph transport in the lymphedematous upper extremity.

Previously, we demonstrated that liposuction combined with Controlled Compression Therapy (CCT) completely corrected chronic arm lymphedema that followed treatment of breast cancer (1), and, moreover, that this combination was significantly more effective than CCT alone (2). Removal of the lymphedematous soft tissue by liposuction accounts for the immediate clinical benefit, while sustained edema reduction is maintained by garment compression as increased hydrostatic pressure restricts net capillary filtration rate (lymph formation).

Increased skin capillary blood flow observed after liposuction for arm lymphedema tends to promote a greater turnover of the tissue fluid (3). Liposuction also may theoretically through operative trauma further damage already compromised lymphatic pathways, thereby further diminishing lymphatic transport capacity that in the long run may jeopardize the initially good surgical outcome in reducing edema volume (4). Based on these considerations, we carried out a prospective study of lymphatic transport in the lymphedematous arm before and after definitive treatment using either liposuction combined with CCT or using CCT alone. To ascertain whether possible changes with compression are immediate or long-term, we also studied the 2-day effect. For this purpose, we used indirect lymphoscintigraphy (ILS), which has replaced direct contrast lymphangiography as an imaging tool for evaluating lymphatic (dys)function (5).

MATERIAL AND METHODS

Patients

Twenty consecutive patients referred to our unit during an 18-month period were recruited for participation in this prospective study, which was approved by the Isotope Committee at Malmö University Hospital. Each patient had developed arm lymphedema after mastectomy and axillary lymph node excision combined with postoperative irradiation for breast cancer. Arm lymphedema was uniformly firm, with clinical signs of fibrosis (non-pitting; grade II). No patient had an ongoing local wound complication or systemic disease when entering the study. Indications for treatment intervention included subjective discomfort due to a heavy arm, and dissatisfaction of outcome after previous treatment with manual drainage or pneumatic compression therapy. No intensive treatment had recently preceded entry into the study.

Eleven patients were selected for liposuction combined with CCT, and 9 for CCT alone. Selection was made so that the distribution of edema volumes in the two groups was comparable. The matching procedure was done gradually throughout the trial as the study was conducted while patients were in urgent need of care, and treatment could not be postponed for ethical reasons. Demographic data on the two groups are shown in *Table 1.*

After initial recordings of arm volumetry (water displacement) and ILS, patients were treated and followed according to the protocol described below with repeat measurements at 3 and 12 months. Two patients developed a cancer recurrence during the study period. One patient in the liposuction and CCT group had to discontinue participation in the study just before 12 months and died soon afterwards. Due to poor general health, ILS was omitted in one patient at 12 months in the CCT group, although the volumetric measurements were completed. In 2 patients in the CCT group, the 12-month ILS had to be postponed because of persistent pain at the injection site in one and pregnancy in the other. Twenty patients had arm edema volume measured at 3 months and 19 at 12 months. Twenty patients underwent ILS at 3 months and 18 at 12 months. The numbers of paired observations are shown in each table. The reduced pairs is partly due to patients lost for follow-up at 12 months and partly due to unsatisfactory technical quality of the ILS. Of 1590 pairs of the ILS studies, 1483 were of high quality and were able to be interpreted properly. Thus, only 107 were rejected.

Controlled Compression Therapy: CCT

The rigorous method of compression therapy, instituted in both groups, is referred to as 'Controlled Compression Therapy' (CCT) and has been described in detail previously (2). Briefly, measurements are taken for a custom-made compression sleeve-and-glove garment that provides a compression force in the range of 32 to 40 mmHg (Jobst®-Elvarex; compression class 2 and 3; Beiersdorf AB, Sweden). For temporary use, an interim dressing is worn for 2 weeks; thereafter a custom-made garment is fitted. The custom-made compression garment is adjusted or replaced when needed and worn continuously. Compression is most important during the first 3 months when the most notable changes in arm volume occurs, particularly in the liposuction group. The garments are renewed at least three times during the first year. Because each patient always has two sets of sleeve-and-glove garments, they are worn continuously.

Liposuction

The surgical technique has been described in detail in a previous paper (1). Briefly, liposuction is done via 20-30, 3 mm long incisions and the hypertrophied and edematous fat is removed by vacuum aspiration as completely as possible. An interim dressing is worn temporarily for 2 weeks; thereafter CCT is maintained exactly as described for the nonoperative group.

Volume Measurements

Using the water displacement technique as described previously (1,3), arm edema volumes were measured before and 3 and 12 months after treatment. Besides an absolute value for each patient, the decrease in the arm edema volume was also calculated as a percentage. Thus:

$$\text{\% reduction of edema volume} = \frac{\text{initial edema volume - present edema volume}}{\text{initial edema volume}} \times 100$$

Indirect lymphoscintigraphy (ILS)

ILS was performed on three occasions at the time of arm volume measurements: before and at 3 and 12 months after instituting treatment. Both arms were studied. Two ILS were performed on each occasion with an interval of two days between studies (with and without the garment). For the initial studies, each patient wore a temporary compression garment that was adjusted to suit the arm as well as possible. After these initial studies, liposuction was performed without delay in the operated group, whereas in the CCT group the patients simply continued with external garment compression (see above).

The radiopharmaceutical was prepared from a lyophilized kit (Solco, Nanocoll, Sorin Biomedica S.p.A, Italy) containing 0.5 mg of human albumin as a nanocolloid (=HSA nanocolloid). The particle size was less than 80 nm for more than 95% of the labeled colloid. Labeling was performed by adding 1500 MBq ^{99m}Tc-pertechnetate from a dry column generator (Mallinckrodt Medical BV, The Netherlands) in a volume of 5 ml. The final product demonstrated a high labeling efficiency (96–99%) determined by thin-layer chromatography using ITLC paper as the stationary phase and normal saline 0.9% as the mobile phase. The patient rested comfortably in the supine position beneath the gamma camera with arms abducted about 15°. Injections were made subcutaneously into the second and third digital webspaces of each hand. Tuberculin syringes and needles 27 gauge (diameter 0.4 mm) were used; each injection emitted an activity of approximately 5 MBq in a volume of about 0.1 ml. The radioactivity in the syringes was measured before and after injection. The injection sites were gently massaged for 20 sec. Images were recorded with a gamma camera (Toshiba GCA-901A) equipped with a LEGP (Low Energy General Purpose) collimator and stored in the camera computer system for subsequent analysis.

Immediately following the injection and at 180 min, an image of the injection site was generated for 15 sec. After the initial imaging of the injection site the patient made pumping movements with the hand for 2 min while the arm was kept still and imaging of the arm began. Five-minute posterior images of the arm were obtained at 0, 5, 10, 15, 20, 25, 75 and 180 min after injection. Although the patient remained on the investigation table throughout the examination period, separate images were registered at 25, 75 and 180 min, using radioactive markers for orientation to ensure that the patient's position was unchanged. For this purpose, markers were placed in a standardized manner on the shoulder and at the elbow, and the contour of the arm was also outlined.

Guided by the markers, regions of interest (ROI) were drawn on the images to allow determination of the washout of the tracer from the injection site, as well as tracer uptake in the arm. Correction for background activity was made, as well as correction for decay of ^{99m}Tc. No correction for attenuation was applied, due to the uneven activity distribution seen in the lymphedematous arm in the planar images, as well as in a separate tomographic study in one patient.

The injection site, the proximal part of the forearm, the upper arm, and the axillary lymph node region were the ROIs studied separately in each arm. Uptake curves were approximated using linear regression and the constants were calculated and used for statistical analyses. Uptake activity at 180 min was recorded as a percentage both of the injected activity, and of the cleared activity. Analyses were made both to elucidate differences between the healthy and the lymphedematous arm, and also to reveal any scintigraphic changes in response to treatment. In the latter respect, we considered the comparisons between pretreatment recordings without compression, and those recorded at 3 and 12 months with compression garments as the most relevant, as they represented the clinical situation during the normal treatment regimen. Correction of lymph node uptake for attenuation of soft tissue thickness to characterize the grade of lymphedema as described by Weissleder et al (6) using corrected lymph node uptake and the appearance time of tracer in the lymph nodes was not feasible in our study due to the paucity of lymph nodes in the lymphedematous arm of these patients.

Calculations and Statistical Analyses

Volumes (ml) are presented as medians, ranges and quartiles unless otherwise specified. Tracer uptake activity (%) and uptake constants are presented as medians and quartiles. Each patient served as her own control, and the significance of differences was assessed with the non-parametric Wilcoxon signed rank test. The un-paired rank sum test was used to analyze volume differences between the two groups. Missing data and technical factors reduced the number of ILS values available for pairs testing. The number of paired observations (n) in each test is therefore the one shown in the Tables.

RESULTS

In the group that received CCT alone (n=9), the median volume of arm edema before treatment was 1415 ml (range 670-3245). After CCT, a gradual but substantial reduction was seen. At 12 months, the median volume of edema had decreased to 625 ml (range 340-1955).

In the operated group (n=11), there were no major surgical complications. The median volume of edema before liposuction was 1610 ml (range 570-2950). The immediate effect of liposuction followed by CCT was a sharp reduction in arm volume and over the subsequent postoperative course, a gradual reduction was seen in the median volume of edema. After 12 months, it was -230 ml (from -655 to 235) (*Fig. 1*).

In summary, liposuction combined with CCT reduced the edema volume by a median of 115% (range 92-179%) (p=0.005), whereas CCT alone was associated with only a 54% (range 7-81%) volume decrease (p=0.008). Liposuction combined with CCT was more effective than CCT alone for reducing arm edema (p=0.0002).

ILS Before Treatment (Table 2)

The images of the non-edematous (healthy) arm showed a normal truncal pattern of lymph vessels with little or no uptake of the radiotracer in the soft tissues. Thus, the radiopharmaceutical was transported directly to the axillary nodes and radioactivity registered in the arm represented tracer in transit within the lymphatics. In the lymph nodes, a marked uptake was recorded.

In the lymphedematous arm, clearance rate from the injection site was similar among the patients. Lymph trunks were absent or barely detectable, and the tracer rarely reached the axilla where lymph nodes had been resected and in all but one patient also irradiated. Tracer transport was slow and marked dermal backflow was common with prominent accumulation of radiotracer in the soft tissues. Compared with the normal contralateral arm, uptake activity and uptake constants was significantly "depressed" *(Table 2)* as described by Ketterings and Zeddeman (4).

ILS After Liposuction and CCT (Table 3a,b)

The depressed lymph flow profile remained essentially unchanged after liposuction and CCT. With wearing of a compression garment at 12 months, there was slightly increased uptake activity in the upper arm as a % of cleared activity. Otherwise, there was no difference in ILS findings with and without compression at 3 and 12 months.

ILS After CCT alone (Table 4a,b)

The depressed lymph flow profile remained after treatment with CCT alone. With wearing of a compression garment, there was a slightly greater uptake in the arm at 3 months. At 12 months, tracer uptake in the upper arm was slightly lowered. Without wearing of compression, there also was slightly greater tracer uptake in the arm at 3 months.

Immediate Effect of Compression (Table 5a-c)

No effect of wearing the compression garment for 2 days before definitive treatment was detected (n=20). There also was no effect of not wearing the compression garment for 2 days at 3 or 12 months in either the operated or non-operated group.

DISCUSSION

The occurrence of arm lymphedema is roughly 25% of women treated for breast cancer (7) constitutes a significant additional burden for the patient. It is both a physical encumbrance and a social handicap. Concomitant complications such as recurring local infections are also often encountered. As nonoperative treatment is not uniformly satisfactory, an operative approach is sometimes deemed necessary. Many operative procedures previously recommended are relatively crude and although conceptually attractive, often entail considerable secondary drawbacks such as marked scarring and weeping of edema fluid. Liposuction as described here by comparison, is much less traumatic, although serious concerns persist about its potential deleterious effects on the microcirculation and especially lymphatic drainage of the soft tissues and skin of the lymphedematous arm (4). Thus, on the one hand, lymphatic transport capacity may further decrease in response to operative trauma to the subcutaneous lymph vessels. On the other hand, the early removal of hypertrophied fatty tissue may create a more optimal balance between lymphatic load and residual lymph flow competence. Previously, we found that skin capillary blood flow tends to increase after liposuction, a phenomenon which may augment the turnover of tissue fluid (3). Taking these considerations into account, we examined the effect of liposuction on the kinetics of lymph transport.

The lymphatic system for many years has been depicted primarily by direct lymphography. This method is useful for morphology but functional assessment of lymph dynamics is less precise (6). Injection is also often difficult and oily contrast media can cause local infection (8) or incite inflammation and fibrosis with damage to the endothelial lining of the lymphatics (9). Besides local complications, hypersensitivity reactions and pulmonary embolism can also ensue (10).

ILS using intradermal or subcutaneous injection of ^{99m}Tc -labeled microcolloid has nowadays replaced direct contrast lymphography as the preferred imaging tool for peripheral lymphedema (5,6). The technique is safe, minimally invasive and seemingly harmless to the lymph vessels, and is therefore particularly suited for studying patients with lymphedema where microcirculatory dynamics are already suboptimal. Another advantage is that repeated injections and therefore serial examinations are feasible. Various radiopharmaceuticals have been proposed for lymphoscintigraphy but in our facility we routinely use ^{99m}Tc-human serum albumin (HSA) nanocolloid.

Although ILS evaluation of lymph transport can be done in several ways, measurement of retention of the colloid at the injection site is straightforward (11, 12), as is measuring the time to appearance of tracer in the regional lymph nodes (5). A more detailed evaluation is possible by examining the distribution of the radioactivity in a scintigraphic image (5,8,13-15). In our study, repeated recordings allows for a dynamic evaluation by using tracer isotope uptake curves related to ROIs representing different parts of the limb (5,6,13,16,17). A more refined, yet simple analysis is calculation of a transport index taking the various characteristic findings of the scintigram into consideration (18-20).

Interpretation of ILS is not always simple. There are multiple anatomical and physiological variations between individuals, and pathophysiologic changes may vary widely depending on the chronicity of the disease process. Technical factors relating to injection site, choice of radiotracer and imaging technique need also to be taken into account (21). Although visual interpretation is paramount, additional quantitative analysis of radiotracer uptake is desirable (13,15,22,23).

ILS was performed according to established departmental protocol utilizing subcutaneous injection of the radiopharmaceutical. Opinions differ as to whether the tracer should be injected subcutaneously or intradermally. The advantage of an intradermal injection is a more reliable uptake and better proximal transport, because lymphatics are more abundant within the dermis than in the subcutaneous tissue (14). This procedure, however, has an inherent risk of concomitant puncture of cutaneous microvessels in the deep dermis with rapid bloodstream uptake that may render findings difficult to interpret (6,21). Radioactive uptake over the liver may detect such unintended premature uptake by the bloodstream (4). Nonetheless, this drawback can be circumvented by subcutaneous injection of the tracer, which may be particularly important for dynamic and quantitative studies. The slower uptake, combined with a possible partial elimination via the venous system means, however, that tracer clearance from the hand may not reliably reflect lymph dynamics (11,12). This limitation was in fact observed in the present study where the clearance of the tracer from the injection site was similar in both arms (i.e., lymphedematous and non-edematous) *(Table 2)*. However, nodal uptake and transport constants were decidedly different with much slower tracer migration on the lymphedematous arm.

With CCT alone, there was a significant reduction in arm edema volume. Compression by the external garment allows gradual mobilization of the lymph fluid component while the tissue matrix remains constant. Like a squeezed sponge, the lymph capillaries are able to better absorb edema fluid. This pathophysiological reasoning is supported by our experience in patients in whom compression therapy was temporarily interrupted and which resulted in a significant increase in arm edema volume over a one-week period (2). This situation also favors increased radiotracer uptake (4), which was documented at 3 months *(Table 4a,b)*. Further compression by an external garment, however, is also associated with decreased lymph formation as heightened interstitial hydrostatic pressure restricts blood capillary filtration and further collapses lymph capillaries. These effects are supported by radioactivity dynamics at 12 months, which had returned to the initial levels and uptake constants were unchanged.

Liposuction before CCT promptly reduces arm edema volume. Not only is fluid removed by liposuction but, equally importantly, a notable amount of fat and tissue matrix is also removed. This phenomenon may explain (compared with the CCT group) why no increased radioactivity is detected at 3 months. Notable differences in radioactive uptake values or constants are also not seen at 12 months *(Table 3a,b)*, findings consistent with the response to CCT alone. Accordingly, it seems likely that limb compression determined lymph dynamics at this stage. Theoretically, liposuction exerts two effects. One is to decrease lymph fluid formation with a decrease in tissue load while the other is to directly damage and obliterate remaining lymphatics. Either way, the outcome appears to be incidental to the underlying pathophysiologic derangement of impaired lymph return. In other words, liposuction does not seem to reduce further the already impaired lymphatic transport. In view of the beneficial effect with markedly reduced arm edema volume, liposuction combined with CCT remains an attractive therapeutic option.

In conclusion, our results suggest that the primary treatment directed at controlling breast cancer is the principal determinant of later lymph flow dynamics of the arm. CCT alone gradually mobilizes the fluid component, but it does not do so promptly and as effectively as liposuction when the latter is combined with CCT. Neither of these therapies further reduce the already compromised lymph transport. This new operative technique when combined with CCT can therefore be recommended to patients in whom nonoperative treatment regimens such as complex physical therapy or pneumatic compression "pumping" are poorly tolerated or have less than a satisfactory outcome.

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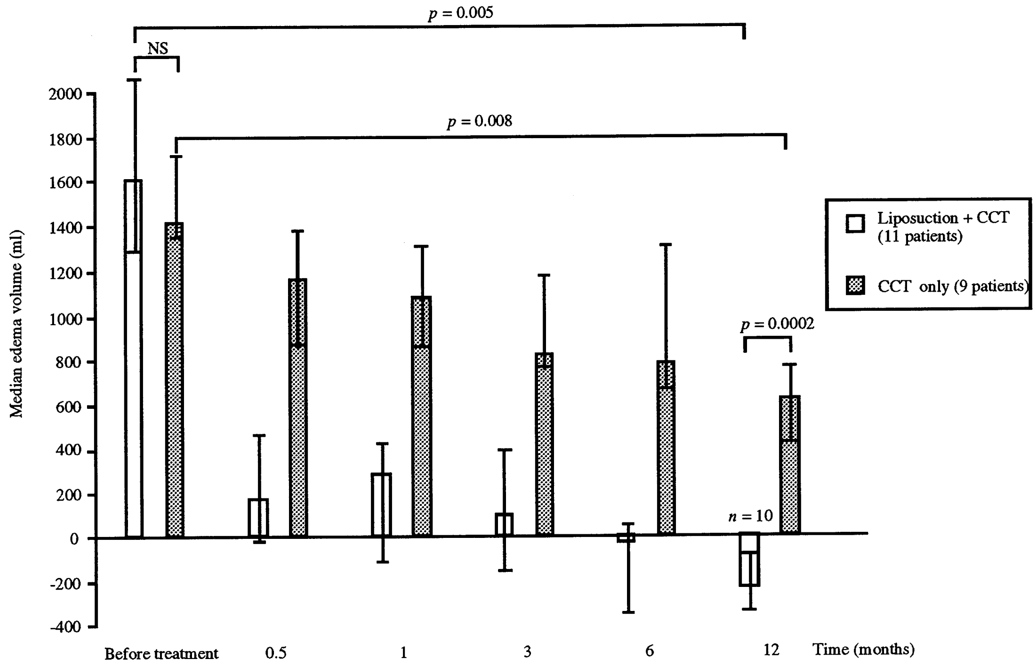

Figure 1. Median edema volume and 25 and 75 percentiles before and after treatment. Note the pronounced effect of surgery and that improvement continues significantly during the subsequent course. Median edema reduction at 12 months was 115% and 54% in the liposuction+CCT and CCT-only groups, respectively.

Table 1
Patient Profile

	CCT	Liposuction+CCT
Number of patients	9	11
Age at cancer operation (yr)		
mean	56	52
SD	14	11
range	28-71	40-70
Duration of lymphedema (yr)		
mean	7.1	7.5
SD	6.5	6.2
range	1-19	1-23
Age at treatment start (yr)		
mean	64	61
SD	14	9.9
range	30-79	46-74
Interval between breast cancer operation and treatment start (yr)		
mean	8.2	8.6
SD	6.6	5.9
range	1-19	1-24
Edema volume before treatment (ml)		
mean	1610	1720
SD	734	697
range	670-3245	570-2950

Table 2
ILS Findings in All Healthy and Lymphedematous Arms Before Definitive Treatment

	Healthy arm quartile				Lymphedema arm quartile				
		25%	75%	*n*		25%	75%	*n*	Wilcoxon
Clearance at 3 hours									
Hand	17	11	23	18	16	11	22	18	NS
Uptake activity at 3 hrs (% of injected activity)									
Forearm	0.17	0.15	0.21	20	0.95	0.42	1.6	20	p<0.001
Upper arm	0.43	0.30	0.58	20	1.1	0.58	2.6	20	p<0.01
Lymph Nodes	1.8	0.71	2.3	20	0.066	0.047	0.11	20	p<0.0001
Uptake activity at 3 hrs (% of cleared activity)									
Forearm	1.2	0.52	1.9	18	6.4	3.4	8.2	18	p<0.001
Upper arm	2.7	1.4	3.5	18	7.6	3.9	12	18	p<0.01
Lymph nodes	7.8	6.8	14	18	0.41	0.29	0.59	18	p<0.001
Uptake constants at 3 hrs									
Forearm	0.028	0.020	0.044	20	0.23	0.13	0.43	20	p<0.0001
Upper arm	0.074	0.043	0.13	20	0.28	0.16	0.50	20	p<0.001
Lymph nodes	0.37	0.20	0.73	20	0.018	0.013	0.027	20	p<0.0001

Clearance is recorded as % of injected activity (cpm/MBq) that has subsided by 3 hours. Uptake activity is recorded both as % of injected activity (cpm/MBq) and as % of the cleared activity (cpm/MBq) registered at 3 hours in the forearm, upper arm, and lymph nodes. Uptake constant of the different ROIs is the regression constant used to approximate uptake curves.

ILS=indirect lymphography

Table 3a
ILS Findings in Lymphedematous Arms With Compression Therapy in Operated Group After 3 and 12 Months

	Before operation (no compression) quartile				3 months (compression) quartile				12 months (compression) quartile				
		25%	75%	*n*		25%	75%	*n*		25%	75%	*n*	Wilcoxon
Clearance at 3 hours													
Hand	16	11	22	10	22	12	23	10					NS
	13	11	20	8					15	11	16	8	NS
Uptake activity at 3 hrs (% of injected activity)													
Forearm	0.78	0.51	2.8	11	1.0	0.55	1.6	11					NS
	0.78	0.53	2.2	8					2.0	1.1	2.6	8	NS
Upper arm	1.0	0.64	2.3	11	0.84	0.60	2.1	11					NS
	0.79	0.53	1.6	8					1.3	1.0	2.0	8	NS
Lymph Nodes	0.083	0.051	0.11	11	0.062	0.043	0.066	11					NS
	0.076	0.056	0.16	8					0.076	0.051	0.10	8	NS
Uptake activity at 3 hrs (% of cleared activity)													
Forearm	5.6	4.7	8.3	10	4.5	2.6	8.9	10					NS
	6.4	5.3	8.3	6					13	5.2	19	6	NS
Upper arm	6.7	3.9	12	10	5.7	3.3	10	10					NS
	5.9	1.7	11	6					8.7	7.8	20	6	p<0.05
Lymph nodes	0.51	0.29	0.63	10	0.39	0.27	0.42	10					NS
	0.45	0.29	0.81	6					0.40	0.38	0.73	6	NS
Uptake constants at 3 hrs													
Forearm	0.23	0.13	0.36	11	0.21	0.14	0.42	11					NS
	0.22	0.13	0.34	8					0.41	0.14	0.66	8	NS
Upper arm	0.27	0.17	0.42	11	0.22	0.18	0.48	11					NS
	0.22	0.15	0.29	8					0.35	0.28	0.50	8	NS
Lymph nodes	0.020	0.011	0.028	11	0.014	0.010	0.019	11					NS
	0.018	0.010	0.026	8					0.016	0.013	0.022	8	NS

Compression garments were worn at 3 and 12 months.

Clearance is recorded as % of injected activity (cpm/MBq) that has subsided by 3 hours. Uptake activity is recorded both as % of injected activity (cpm/MBq) and as % of the cleared activity (cpm/MBq) registered at 3 hours in the forearm, upper arm, and lymph nodes. Uptake constant of the different ROIs is the regression constant used to approximate uptake curves.

ILS=indirect lymphoscintigraphy

Table 3b
ILS Findings in Lymphedematous Arms Without Compression in Operated Group After 3 and 12 Months

	Before operation (no compression)	quartile			3 months (no compression)	quartile			12 months (no compression)	quartile			
		25%	75%	*n*		25%	75%	*n*		25%	75%	*n*	Wilcoxon
Clearance at 3 hours													
Hand	16	11	22	10	13	12	15	10					NS
	15	11	19	9					14	10	16	9	NS
Uptake activity at 3 hrs (% of injected activity)													
Forearm	0.78	0.51	2.8	11	0.93	0.80	1.4	11					NS
	0.77	0.50	1.6	10					1.4	0.56	2.1	10	NS
Upper arm	1.0	0.64	2.3	11	0.90	0.58	1.9	11					NS
	0.98	0.63	1.3	10					0.94	0.77	2.3	10	NS
Lymph Nodes	0.083	0.051	0.11	11	0.061	0.047	0.086	11					NS
	0.076	0.045	0.11	10					0.087	0.074	0.14	10	NS
Uptake activity at 3 hrs (% of cleared activity)													
Forearm	5.6	4.7	8.3	10	6.7	4.4	7.9	10					NS
	5.0	4.6	6.6	9					9.4	5.9	11	9	NS
Upper arm	6.7	3.9	12	10	5.2	4.2	13	10					NS
	5.5	3.9	9.4	9					5.5	4.4	17	9	NS
Lymph nodes	0.51	0.29	0.63	10	0.53	0.30	0.69	10					NS
	0.59	0.29	0.65	9					0.58	0.40	0.92	9	NS
Uptake constants at 3 hrs													
Forearm	0.22	0.13	0.36	11	0.29	0.22	0.43	11					NS
	0.22	0.13	0.31	10					0.37	0.11	0.59	10	NS
Upper arm	0.27	0.17	0.42	11	0.23	0.14	0.62	11					NS
	0.26	0.17	0.33	10					0.27	0.23	0.65	10	NS
Lymph nodes	0.020	0.011	0.028	11	0.016	0.013	0.023	11					NS
	0.018	0.011	0.026	10					0.025	0.023	0.028	10	NS

At 3 and 12 months compression garments were removed for 2 days before investigation.

Clearance is recorded as % of injected activity (cpm/MBq) that has subsided by 3 hours. Uptake activity is recorded both as % of injected activity (cpm/MBq) and as % of the cleared activity (cpm/MBq) registered at 3 hours in the forearm, upper arm, and lymph nodes. Uptake constant of the different ROIs is the regression constant used to approximate uptake curves.

ILS=indirect lymphoscintigraphy

Table 4a
ILS Findings in Lymphedematous Arms With Compression Therapy in Non-Operated Group After 3 and 12 Months

	Before treatment (no compression)	quartile			3 months (compression)	quartile			12 months (compression)	quartile			
		25%	75%	*n*		25%	75%	*n*		25%	75%	*n*	Wilcoxon
Clearance at 3 hours													
Hand	15	11	22	8	18	14	21	8					NS
	18	15	22	7					16	13	21	7	NS
Uptake activity at 3 hrs (% of injected activity)													
Forearm	0.77	0.32	1.6	8	1.3	0.33	3.5	8					NS
	1.3	0.39	1.6	8					0.41	0.31	1.5	8	NS
Upper arm	0.95	0.46	1.9	8	1.4	0.36	4.4	8					p<0.05
	1.4	0.46	1.9	8					0.57	0.45	1.1	8	NS
Lymph Nodes	0.058	0.047	0.091	8	0.097	0.072	0.12	8					NS
	0.060	0.047	0.091	8					0.069	0.039	0.079	8	NS
Uptake activity at 3 hrs (% of cleared activity)													
Forearm	4.9	2.8	7.6	8	13	8.6	17	8					p<0.05
	7.2	4.9	8.0	7					4.2	2.4	10	7	NS
Upper arm	6.6	3.8	9.5	8	15	7.2	24	8					p<0.05
	8.5	5.0	11	7					4.9	2.4	8.4	7	p<0.05
Lymph nodes	0.46	0.37	0.55	8	0.72	0.52	0.95	8					NS
	0.40	0.30	0.46	7					0.52	0.17	0.81	7	NS
Uptake constants at 3 hrs													
Forearm	0.22	0.12	0.54	9	0.20	0.11	0.82	9					NS
	0.25	0.13	0.54	8					0.26	0.10	0.63	8	NS
Upper arm	0.29	0.14	0.51	9	0.26	0.084	0.95	9					NS
	0.36	0.13	0.63	8					0.37	0.13	0.81	8	NS
Lymph nodes	0.017	0.015	0.020	9	0.024	0.018	0.038	9					NS
	0.017	0.015	0.025	8					0.020	0.015	0.031	8	NS

Compression garments were worn at 3 and 12 months.

Clearance is recorded as % of injected activity (cpm/MBq) that has subsided by 3 hours. Uptake activity is recorded both as % of injected activity (cpm/MBq) and as % of the cleared activity (cpm/MBq) registered at 3 hours in the forearm, upper arm, and lymph nodes. Uptake constant of the different ROIs is the regression constant used to approximate uptake curves.

ILS=indirect lymphoscintigraphy

Table 4b
ILS Findings in Lymphedematous Arms Without Compression in Non-Operated Group After 3 and 12 Months

	Before treatment (no compression)	quartile			3 months (no compression)	quartile			12 months (no compression)	quartile			
		25%	75%	*n*		25%	75%	*n*		25%	75%	*n*	Wilcoxon
Clearance at 3 hours													
Hand	16	11	21	9	9.6	7.5	18	9					NS
	17	14	22	8					15	12	19	8	NS
Uptake activity at 3 hrs (% of injected activity)													
Forearm	1.1	0.33	1.6	9	1.5	1.0	1.9	9					NS
	1.3	0.39	1.6	8					0.92	0.53	1.3	8	NS
Upper arm	1.2	0.47	1.6	9	0.64	0.51	2.7	9					NS
	1.4	0.46	1.9	8					0.62	0.50	1.0	8	NS
Lymph Nodes	0.059	0.047	0.077	9	0.083	0.067	0.097	9					NS
	0.060	0.047	0.091	8					0.053	0.038	0.073	8	NS
Uptake activity at 3 hrs (% of cleared activity)													
Forearm	6.9	2.9	7.6	9	11	8.5	19	9					$p<0.05$
	7.2	2.8	7.8	8					4.6	3.4	11	8	NS
Upper arm	7.3	4.2	8.9	9	11	5.9	19	9					$p<0.05$
	7.9	3.8	9.8	8					3.8	3.2	5.4	8	NS
Lymph nodes	0.41	0.33	0.51	9	0.85	0.44	1.4	9					$p<0.05$
	0.46	0.32	0.55	8					0.31	0.23	0.57	8	NS
Uptake constants at 3 hrs													
Forearm	0.22	0.12	0.54	9	0.36	0.26	0.69	9					NS
	0.25	0.13	0.54	8					0.29	0.23	0.48	8	NS
Upper arm	0.29	0.14	0.51	9	0.020	0.14	0.67	9					NS
	0.36	0.13	0.63	8					0.29	0.53	0.73	8	NS
Lymph nodes	0.017	0.015	0.020	9	0.029	0.020	0.033	9					NS
	0.016	0.015	0.025	8					0.020	0.015	0.022	8	NS

At 3 and 12 months compression garments were removed for 2 days before investigation.

Clearance is recorded as % of injected activity (cpm/MBq) that has subsided by 3 hours. Uptake activity is recorded both as % of injected activity (cpm/MBq) and as % of the cleared activity (cpm/MBq) registered at 3 hours in the forearm, upper arm, and lymph nodes. Uptake constant of the different ROIs is the regression constant used to approximate uptake curves.

ILS=indirect lymphoscintigraphy

Table 5a
ILS Findings in All Lymphedematous Arms Before and After Compression Before Definitive Treatment

	no compression quartile				compression quartile				
		25%	75%	*n*		25%	75%	*n*	Wilcoxon
Clearance at 3 hours									
Hand	16	11	23	17	18	8.5	25	17	NS
Uptake activity at 3 hrs (% of injected activity)									
Forearm	1.1	0.41	1.6	19	0.93	0.44	2.5	19	NS
Upper arm	1.1	0.55	2.3	19	1.3	0.61	3.2	19	NS
Lymph Nodes	0.063	0.046	0.11	19	0.080	0.060	0.18	19	NS
Uptake activity at 3 hrs (% of cleared activity)									
Forearm	6.6	3.0	8.3	17	7.7	5.0	11	17	NS
Upper arm	7.9	4.2	12	17	9.5	7.5	14	17	NS
Lymph nodes	0.43	0.29	0.60	17	0.67	0.39	0.86	17	NS
Uptake constants at 3 hrs									
Forearm	0.23	0.12	0.47	20	0.16	0.093	0.57	20	NS
Upper arm	0.28	0.12	0.51	20	0.36	0.15	0.62	20	NS
Lymph nodes	0.018	0.011	0.028	20	0.023	0.014	0.035	20	NS

ILS (indirect lymphoscintigraphy) was performed both with and without compression before definitive treatment.

Clearance is recorded as % of injected activity (cpm/MBq) that has subsided by 3 hours. Uptake activity is recorded both as % of injected activity (cpm/MBq) and as % of the cleared activity (cpm/MBq) registered at 3 hours in the forearm, upper arm, and lymph nodes. Uptake constant of the different ROIs is the regression constant used to approximate uptake curves.

Table 5b
ILS Findings in Lymphedematous Arms With and Without Compression in Operated Group at 3 and 12 Months

	3 months									12 months								
	no compression quartile				compression quartile					no compression quartile				compression quartile				
		25%	75%	*n*		25%	75%	*n*	Wilcoxon		25%	75%	*n*		25%	75%	*n*	Wilcoxon
Clearance at 3 hours																		
Hand	13	12	17	11	22	12	23	11	NS	12	10	15	9	15	9.3	16	9	NS
Uptake activity at 3 hrs (% of injected activity)																		
Forearm	0.93	0.80	1.4	11	1.0	0.55	1.6	11	NS	1.9	0.75	2.1	8	2.0	1.1	2.6	8	NS
Upper arm	0.90	0.58	1.9	11	0.84	0.60	2.1	11	NS	0.92	0.63	1.8	8	1.3	1.0	2.0	8	NS
Lymph Nodes	0.061	0.047	0.086	11	0.062	0.043	0.066	11	NS	0.082	0.064	0.10	8	0.076	0.051	0.10	8	NS
Uptake activity at 3 hrs (% of cleared activity)																		
Forearm	6.7	4.7	9.0	11	5.4	2.7	12	11	NS	11	7.7	43	7	15	7.2	19	7	NS
Upper arm	5.6	4.2	13	11	6.2	3.5	11	11	NS	5.5	4.8	23	7	8.9	8.0	24	7	NS
Lymph nodes	0.52	0.25	0.67	11	0.38	0.27	0.42	11	NS	0.58	0.36	0.76	7	0.43	0.29	0.71	7	NS
Uptake constants at 3 hrs																		
Forearm	0.29	0.22	0.43	11	0.21	0.14	0.42	11	NS	0.39	0.11	0.63	8	0.41	0.14	0.66	8	NS
Upper arm	0.23	0.14	0.62	11	0.22	0.18	0.48	11	NS	0.27	0.21	0.56	8	0.35	0.28	0.50	8	NS
Lymph nodes	0.016	0.013	0.023	11	0.014	0.010	0.019	11	NS	0.024	0.020	0.026	8	0.016	0.013	0.022	8	NS

ILS (indirect lymphoscintigraphy) was performed both with and without compression at 3 and 12 months.

Clearance is recorded as % of injected activity (cpm/MBq) that has subsided by 3 hours. Uptake activity is recorded both as % of injected activity (cpm/MBq) and as % of the cleared activity (cpm/MBq) registered at 3 hours in the forearm, upper arm, and lymph nodes. Uptake constant of the different ROIs is the regression constant used to approximate uptake curves.

Table 5c
ILS Findings in Lymphedematous Arms With and Without Compression in Non-Operated Group at 3 and 12 Months

	3 months									12 months								
	no compression	quartile			compression	quartile				no compression	quartile			compression	quartile			
		25%	75%	*n*		25%	75%	*n*	Wilcoxon		25%	75%	*n*		25%	75%	*n*	Wilcoxon
Clearance at 3 hours																		
Hand	10	7.8	19	8	18	14	21	8	NS	14	12	17	7	16	13	21	7	NS
Uptake activity at 3 hrs (% of injected activity)																		
Forearm	1.7	0.89	2.2	8	1.3	0.34	3.5	8	NS	0.93	0.54	1.3	8	0.41	0.31	1.5	8	NS
Upper arm	0.87	0.52	2.7	8	1.4	0.36	4.4	8	NS	0.62	0.50	1.0	8	0.57	0.45	1.1	8	NS
Lymph Nodes	0.086	0.070	0.10	8	0.097	0.072	0.12	8	NS	0.053	0.038	0.078	8	0.069	0.039	0.079	8	NS
Uptake activity at 3 hrs (% of cleared activity)																		
Forearm	11	7.5	16	8	13	8.6	17	8	NS	5.6	3.5	14	7	4.2	2.4	10	7	NS
Upper arm	8.7	5.8	14	8	15	7.2	24	8	NS	3.8	3.7	6.2	7	4.9	2.4	8.4	7	NS
Lymph nodes	0.69	0.43	1.2	8	0.72	0.52	0.95	8	NS	0.33	0.20	0.63	7	0.52	0.17	0.81	7	NS
Uptake constants at 3 hrs																		
Forearm	0.36	0.26	0.69	9	0.20	0.11	0.82	9	NS	0.29	0.23	0.48	8	0.26	0.10	0.63	8	NS
Upper arm	0.20	0.14	0.67	9	0.26	0.084	0.95	9	NS	0.29	0.13	0.49	8	0.37	0.13	0.81	8	NS
Lymph nodes	0.029	0.020	0.033	9	0.024	0.018	0.038	9	NS	0.017	0.015	0.022	8	0.02	0.015	0.031	8	NS

ILS (indirect lymphoscintigraphy) was performed both with and without compression at 3 and 12 months.

Clearance is recorded as % of injected activity (cpm/MBq) that has subsided by 3 hours. Uptake activity is recorded both as % of injected activity (cpm/MBq) and as % of the cleared activity (cpm/MBq) registered at 3 hours in the forearm, upper arm, and lymph nodes. Uptake constant of the different ROIs is the regression constant used to approximate uptake curves.