

## FLUID TRANSLOCATION MEASUREMENT

### *A Method to Study Pneumatic Compression Treatment of Postmastectomy Lymphoedema*

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**ABSTRACT.** Tissue fluid translocation under the action of deformation was measured to study the pneumatic compression treatment of postmastectomy lymphoedema of the arm. Analysis of the results provides statistically significant parameters for characterization of the oedema. Mobility of the fluid in pitting oedematous tissue was significantly greater than that of normal tissue and decreased after pneumatic compression treatment. Oedematous fluid at the distal sites of the arm showed a greater mobility than that of the proximal sites. Improvement in the oedema due to pneumatic compression treatment was found to be greater at the distal sites than at the proximal sites. In addition, oedema recurred between the treatments and repeated treatments produced the best results. Measurement of fluid translocation is useful in selecting and evaluating the effectiveness of lymphoedema treatment, as well as in determining the viscoelastic properties of the oedematous tissues.

*Key words:* lymphoedema, fluid mobility, compressional force, oedema analysis.

The most common cancer among women is carcinoma of the breast, and a large group of these patients undergo some form of surgery. A frequent complication of surgery itself, or radiation therapy in which draining lymph nodes are damaged, is oedema of the arm. A small amount of protein leakage from the capillaries is normal, but the only means of returning the protein to the circulation is via the lymphatics. If an obstruction in the lymphatics occurs, the increased protein in the interstitium draws more fluid into this compartment and oedema occurs. The incidence of postmastectomy lymphoedema varies depending upon the conditions of surgery, irradiation therapy and other reasons (2, 11, 13). Lymphoedema is long lasting and causes swelling and functional disability because of poor oxygenation and tissue damage. The weight of the lymphoedematous arm often leads to aching and fatigue with impaired joint function. This tiresome,

cosmetically unsightly, mechanically embarrassing condition causes distress to the patients.

Various kinds of drugs (diuretics and anticoagulants), physical therapy (massage, pneumatic compression, tight bandaging, and elastic sleeve) and surgical therapy (procedures to increase lymph drainage, and excisions of the oedematous thickened subcutaneous tissue) are used to treat lymphoedema (1, 3, 5, 11, 14). Although pneumatic compression appears to be the most effective non-invasive physiotherapy technique for the treatment of lymphoedema of the arm (11), opinions differ regarding the selection of pneumatic machines because they (Jobst, Flowtron, Lympha press) employ different principles. Further clinical investigations are needed to determine the most effective treatment of lymphoedema. In addition, reliable and accurate measurement techniques are essential to evaluate the changes in the viscoelastic properties of tissues due to the treatment effectiveness.

Surface measurements and water displacement volumetry are common methods to assess limb volume increases due to oedema (1, 9, 13). Calculation of the volume based on surface measurements was compared with direct water displacement volumetry and a satisfactory correlation was shown (12). Swedborg (13, 14) pointed out the disadvantages and inaccuracies of surface measurement and found volumetry more efficient for evaluating the progress of lymphoedema treatment. However, volumetry like the surface measurements, determines only the degree of swelling in the limb, and therefore indicates nothing about the complex changes in the mechanical properties of the tissues due to oedema (4, 7, 8).

In most cases, subcutaneous pitting oedema can be qualitatively expressed using the classical clinical test, in which the tissue is indented with the tip of the physician's finger. Tissue is composed of a

fiber-reinforced solid matrix phase consisting of proteoglycan macromolecules and collagen fibers (about 20% by weight) and an interstitial fluid phase (about 80% by weight). Most of the fluid is free to move within the tissue under the action of applied loads. The pore size of the tissue ranges from 20 to 65 Å; thus, the tissue must be considered a micro-porous material (6). Under the action of compressive loading, the deformation of the solid matrix and the flow of interstitial fluid gives rise to relative motion between the two phases of the tissue. This relative motion exerts an action and reaction drag force that governs predominantly the observed viscoelastic properties of the tissue in compression (6). The translocation of fluid under compression differs between normal and oedematous tissues, depending on the resistance to outflow and the quantity of fluid stored. This flow is similar to that of compartment models of biological processes; resistance to outflow is directly proportional to fluid viscosity and inversely dependent on the dimension of the channel through which fluid flows. The increased fluid volume due to oedema is accompanied by lower viscosity of interstitial fluid, and decreased resistance to flow of interstitial fluid which also could be expressed as greater mobility for interstitial fluid (4, 7, 8). Therefore, the force needed to translocate interstitial fluid should be a suitable parameter to be used for evaluating the lymphoedema treatment. The aim of this study was to study the changes in the viscoelastic properties of oedematous tissues with treatment. We analyse the force curves which are proportional to fluid translocation under compressive deformation and study how the curve parameters change with the treatment of lymphoedema.

## MATERIALS AND METHODS

Ten patients, who were being treated for advanced unilateral postmastectomy lymphoedema, participated in this study. The patients were between 39 and 67 years of age and had been operated upon from 2 to 8 years previously. A commercially available pneumatic compression device "Lympha Press" (10, 15) was used for lymphoedema treatment. The apparatus consists of a sleeve that is closely fitted over the limb with a series of individual inflatable cells, each overlapping the next. A pressure cycle is applied in such a way that they are inflated in turn from the finger tips upwards until all cells are distended. After 2 sec of complete inflation all cells are automatically deflated and the cycle begins again. The cycle is short enough to allow a pressure of 80–130 mmHg without

discomfort to transfer excess fluid to regions of normal circulation. Each patient had one compression treatment a day for 5 days or more; each treatment lasted 4 hours.

### Measurement of compressional force

For every patient four to six sites were measured on the oedematous arm before and after treatment. Similar locations on the contralateral, unaffected arm were found and assessed. The microcomputer based device for measurement of compressional force (8) rapidly indented the tissue to a depth of 4 mm by a cylindrical head with a diameter 15 mm and recorded the compressional force as the deformation was maintained. The measurement time was limited to 20 sec only, which reduced the risk of patient movement artifacts. The force  $F(t)$  decayed in proportion to the quantity of fluid translocated from the compressed site. The translocated fluid volume,  $V(t)$  was equal to the volume formed in the tissue by the cylinder and approximately equal to the product of the cylinder area,  $A$ , and the compression depth,  $h$ . Mridha & Ödman (1986) used this as an assumption in the equation:

$$V(t) = Ah(1 - F(t)/F(0)) = Ah(1 - F_n(t)) \quad (1)$$

where  $F(0)$  was the initial peak force. If  $V = Ah$ , was the real translocated volume then:

$$V(t) = V(1 - F_n(t)) \quad (2)$$

Volume normalization gives:

$$V_n(t) = V(t)/V = (1 - F_n(t)) \quad (3)$$

where  $V_n(t)$  is independent of the assumption that  $V = Ah$ . Hence, volume has been normalized in this study.  $V_n(t)$  gives normalized volume at time  $t$  and the slope is proportional to the rate of fluid flow, which is a measure of the mobility of the interstitial fluid. Integrating the function  $V_n(t)$  over the interval  $(0, T)$  and then dividing by  $T$  gives the mean value of all  $V_n(t)$  in the interval. This is also equal to the normalization in time and the value of the integral will be equal to or smaller than unity. The degree and reduction of oedema from translocation measurement,  $D_t$  and  $R_t$ , respectively is then defined as:

$$D_t = 1/T \int_0^T V_n(t) dt \times 100 \quad (4a)$$

$$R_t = D_{tb} - D_{ta} \quad (4b)$$

where indexes  $b$  and  $a$  mean before and after treatment respectively. A curve fitting procedure, least square method, was used to choose the right mathematical model to fit the experimental data and to interpret the results.

### Volumetry

The patients inserted the arm into a cylinder containing water filled up to an outlet. They slowly slid the arm against the cylinder wall and pressed the fist against the bottom of the cylinder. The displaced water was collected and weighed to obtain the volume. The degree of oedema from water displaced volumetry,  $D_v$  was calculated from eq. 5a, and the reduction of oedema,  $R_v$ , from eq. 5b.



Fig. 1. Oedematous tissue was compressed for 20 sec by a cylindrical head 15 mm in diameter to a depth of 4 mm. After withdrawal of the compression head, a depression remained due to the translocation of oedematous fluid.

$$D_v = 100(V_e - V_n)/V_n \quad 5(a)$$

$$R_v = D_{vb} - D_{va} \quad 5(b)$$

where

- $V_e$  = volume of the oedematous arm before treatment
- $V_n$  = volume of the contralateral normal arm
- $D_{vb}$  = degree of oedema before treatment
- $D_{va}$  = degree of oedema after treatment.

### RESULTS

When the compression head was withdrawn from the oedematous skin a depression remained, as shown in Fig. 1. This indicates that oedematous

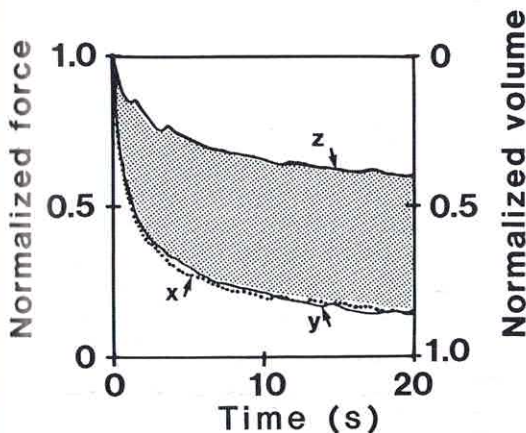


Fig. 2. Curves marked x and y represent repeated measurements on one oedematous site before treatment, with 1 hour intervals between measurements. Curve marked z was obtained from the same site after one pneumatic compression treatment.

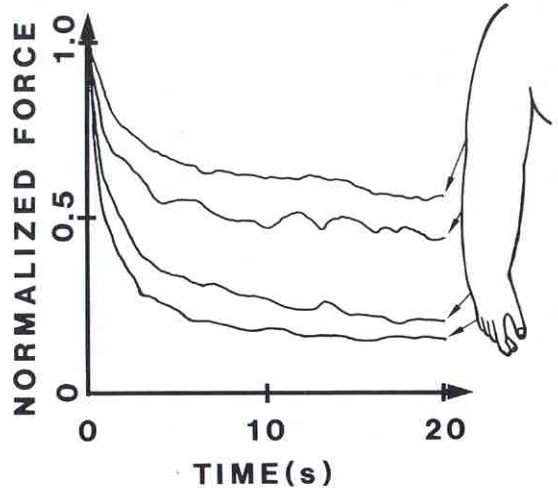


Fig. 3. Typical curves recorded from four different sites of an oedematous arm showing the differences in fluid translocation under compression.

tissue was deformed as indented due to fluid translocation. The depression was approximately equal to the translocated fluid volume or the product of cylinder surface area,  $A$ , and the indentation depth,  $h$ .

Curves marked x and y in Fig. 2 are from recordings of an oedematous site done one hour apart prior to treatment. These two curves demonstrated good measurement reproducibility. Curve z was recorded at the same site after treatment and showed lower rate of decay than the curves x and y. This indicated that tissue contained less mobile fluid after treatment than before treatment. The decrease in mobile fluid volume due to therapy is shown by the shaded area in Fig. 2.

Fig. 3 shows typical curves of normalized force, recorded at four sites on an oedematous arm before therapy. Curves from the distal sites decayed faster than proximal ones. This indicated that fluid from the distal sites was more mobile than that from the proximal sites. Reduction of oedema after treatment calculated according to eq. 4b and obtained from the recordings from four different points are shown in Fig. 4. Similar results were calculated for all ten patients. It was observed that a reduction in oedema took place at all four points, although the effect of treatment was not equal at all points. Greater reduction was obtained from the distal sites than from the proximal sites. Measurements made on the same sites before and after the compression

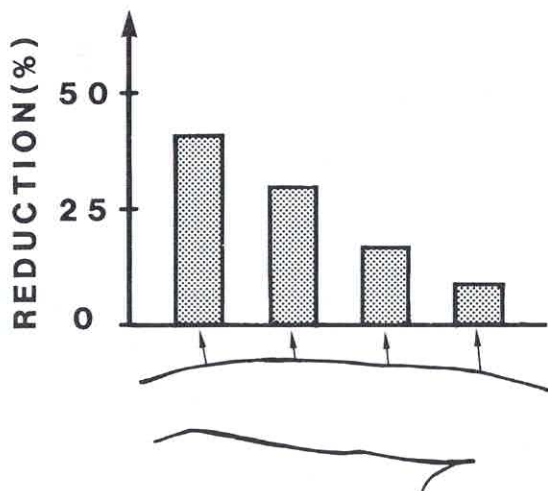


Fig. 4. Reduction of oedema at four sites, calculated according to eq. 6, from translocation curves due to repeated pneumatic compression therapy.

treatment showed different shapes. Fig. 5 shows results from measurements on the same site of one patient at various time intervals between the measurements. Fluid return after the withdrawal of compression increased as the interval between measurements became longer (Fig. 5). Similar behaviour was observed on patients too (Fig. 6). Normalized force curves from a typical patient are shown in Fig. 6 for: before treatment ( $t_0$ ); after the treatment ( $t_1$ ) and two days later ( $t_2$ ). Fluid translocated during

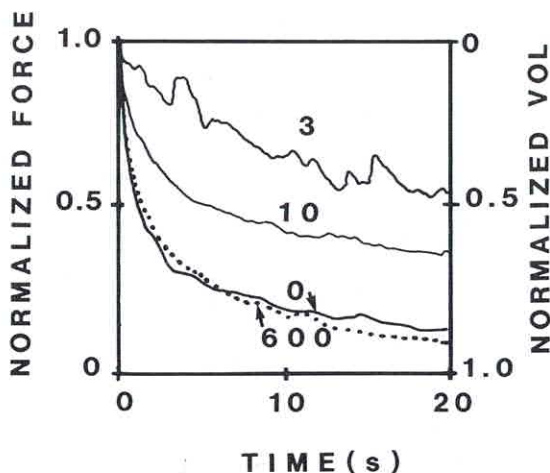


Fig. 5. Fluid recession increased after the withdrawal of compression as the interval between measurements (0, 3, 10, 600 s) became longer.

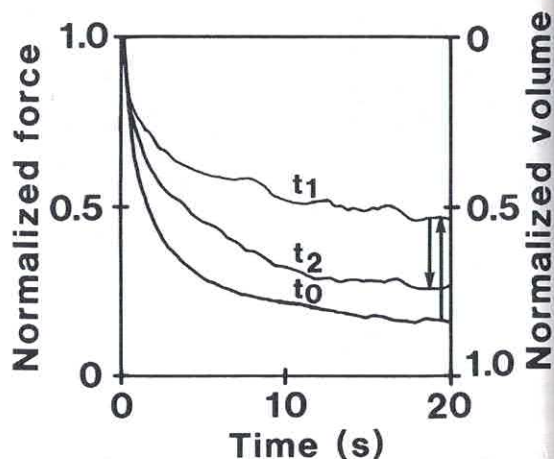


Fig. 6. Normalized force recorded before compressional treatment,  $t_0$ , immediately after treatment  $t_1$  and two days later  $t_2$ .

the treatment and is indicated by the change from  $t_0$  to  $t_1$ . Fluid returned toward the original level during the interval between treatments as indicated by the arrow from  $t_1$  to  $t_2$ .

The force curves,  $f_n(t)$ , from normal and oedematous tissues were found to fit best to a function of  $f(t)$ , the sum of two monoexponential terms (eq. 6). Each curve was represented by 32 measuring points. The sampling was done after every 0.05 s up to 0.5 s; 0.25 s up to 2.5 s; 0.5 s up to 5 s; 1.25 s up to 10 s, and 2.5 s up to 20 s. The sampling rate was higher in the beginning when the curves decayed more rapidly.

$$f(t) = A_1 \exp(-t/T_1) + A_2 \exp(-t/T_2) \quad (6)$$

The first term on the right hand side of eq. 6 represents the flow of low viscous water like fluid, and the second term represents the flow of gel like, higher viscosity fluid.  $A_1$  and  $A_2$  describe the fraction of the total displaced low and high viscosity fluid respectively.  $T_1$  and  $T_2$  are inversely proportional to the fluid mobility.

Table I shows the mean values with standard deviation of the parameters in eq. 6 for a group of normal subjects, lymphoedematous patients before treatment and after treatment. The values of  $T_1$  and  $T_2$  for oedematous curves,  $B$ , are significantly lower than the values of  $T_1$  and  $T_2$  for normal curves,  $N$ , and decrease significantly (paired  $t$ -test,  $p < 0.05$ ) after treatment.

Table I. Mean ( $\pm$ SD) of the parameters in eq. 6 estimated by fitting the response curves of lymphoedematous patients ( $n=10$ ) before treatment, B, after treatment, A, and normal subject ( $n=12$ ), N

Status	$A_1$	$T_1$	$A_2$	$T_2$
B	0.45 $\pm$ 1.00	1.05 $\pm$ 0.34	0.51 $\pm$ 0.12	26 $\pm$ 14.42
A	0.29 $\pm$ 0.07	1.58 $\pm$ 0.67	0.67 $\pm$ 0.07	115 $\pm$ 76.74
N	0.15 $\pm$ 0.04	1.39 $\pm$ 0.76	0.82 $\pm$ 0.05	124 $\pm$ 44.99

Linear regression between the reduction of oedema obtained from the volumetry  $R_v$  from eq. 5b, and the degree of swelling,  $D_v$  from eq. 5a, gave a correlation coefficient,  $r$ , equal to 0.54 for 14 patients. The parameters  $A_1$ ,  $A_2$ ,  $T_1$  and  $T_2$  of eq. 6, were correlated by linear regression to the degree of swelling,  $D_v$ , of eq. 5b which gave a poor correlation coefficient with  $r$  values of 0.167, 0.007, 0.49 and 0.40, respectively.

Table II shows values of  $A_1$ ,  $T_1$ ,  $A_2$  and  $T_2$  from one patient with pitting oedema.  $T_1$  and  $T_2$  increase with treatment and approach the values of the  $T_1$  and  $T_2$  for the contralateral normal arm after multiple treatments. The increase of  $T_1$  and  $T_2$  values agree well with the decrease of the arm volume measured by volumetry.

## DISCUSSION

The analysis of parameters  $A_1$ ,  $T_1$ ,  $A_2$ ,  $T_2$  and  $D_i$  showed  $D_i$  to be the best parameter to represent the oedema status. It was defined as the mean of the

Table II. Parameters in eq. 6 estimated by fitting curves of pitting oedema of one patient before treatment, B; after a single treatment,  $A_1$ ; after three treatments,  $A_3$ , to illustrate the increase of  $T_1$  and  $T_2$  values with repeated treatments as the volume of the arm decreases

$T_1$ ,  $T_2$  and  $V$  values tend to change towards the normal values of N

Type	$A_1$	$T_1$	$A_2$	$T_2$	$V$ (ml)
B	0.37	0.65	0.62	9.92	3 096
$A_1$	0.51	1.15	0.47	65.45	2 856
$A_3$	0.31	2.54	0.68	214.76	2 631
N	0.34	2.57	0.65	217.08	1 642

Table III. Table III shows the correlation coefficient for linear correlation, between each of the parameters  $A_1$ ,  $T_1$ ,  $A_2$ ,  $T_2$  and  $D_i$  when correlated with the volumes of the oedematous arm before, after one and after repeated treatments

Mean and standard deviation for the five patients are calculated

No	$r_{A_1}$	$r_{T_1}$	$r_{A_2}$	$r_{D_i}$
1	0.27	0.96	0.26	0.96
2	0.05	0.98	0.10	0.74
3	0.97	0.37	0.98	0.30
4	0.98	0.63	0.99	0.89
5	0.98	0.48	0.98	0.99
Mean	0.65	0.68	0.66	0.77
$\pm$ SD	0.45	0.28	0.44	0.28

normalized volume  $V_n(t)$  during the registration time  $T$ . The integration over the time  $T$  in eq. 4 serves as a low pass filter and reduces the influence of small variations in force curve due to, for example, blood circulation and movement artifacts. The values of  $T_1$  and  $T_2$  are inversely proportional to the fluid mobility. Analysis of the curves shows that  $T_1$  and  $T_2$  provide statistically significant parameters for characterizing oedema. The values of  $T_1$  and  $T_2$  (in Table I) of oedematous tissues are significantly lower than those of normal tissues (paired  $t$ -test,  $p<0.05$ ) and significantly increases after treatment of oedema (paired  $t$ -test,  $p<0.05$ ).

In cases of patients with pitting oedema the volume of the oedematous arm decreased with treatment and agreed with the corresponding decrease of tissue fluid mobility (i.e. the increase of  $T_1$  and  $T_2$  values). An example in Table II shows that the volume of an oedematous arm decreases from 3 096 ml to 2 856 ml after a single treatment and then to 2 631 ml after some repeated treatments. This is in agreement (almost linearly correlated with  $r>0.90$ ) with the decrease of fluid mobility, i.e. increase of  $T_1$  and  $T_2$  values. Table III shows, for five pitting oedematous patients, the coefficient of correlation,  $r\pm$ SD values for the parameters  $A_1$ ,  $A_2$ ,  $T_1$ ,  $T_2$  and  $D_i$  when correlated with the volumes of the oedematous arm before treatment, after a single treatment and after repeated treatments. Among all the parameters,  $D_i$  shows over all the best linear relation ( $r=0.94$ ) with the decrease of the volume.

Reduction of oedema,  $R_v$  calculated from the

volumetry (eq. 5a) did not show any strong linear correlation ( $r=0.54$ ) with the degree of oedema,  $D_v$  (eq. 5b). This indicates that the reduction of oedema obtained by compression treatment is not dependent on the degree of swelling. However, the reduction,  $R_t$  depends to a greater extent (linear correlation,  $r=0.80$ ) on the degree of oedema,  $D_t$  which is dependent on the mobility of the fluid. Thus  $D_t$  provides a clinically important parameter for the treatment of oedema.

The fluid flow from compressed oedematous skin was different at various sites and this was observed in all patients. Distal sites showed greater mobility (lower resistance to fluid flow) than proximal sites (Fig. 3). On the same patient, oedema was reduced to a greater extent at distal sites than at the proximal ones (Fig. 4). This phenomenon may be attributed to the presence of a greater amount of free, low-viscosity fluid at distal sites, and/or a larger dimension of the channels through which fluid flow takes place.

From this study it may be recommended that the fluid mobility should be measured so that the pressure in the sleeve sections could be adjusted to the mobility of the fluid underneath in order to obtain more effective treatment. However, pressure adjustments within different sections of the sleeve were not possible, with the pneumatic compressor used. From our experience with pneumatic compression treatment, it may be suggested that pneumatic compression devices be improved to allow pressure adjustment for each section of the sleeve. Sleeve pressure, duration of treatment at each session, and the number of sessions may vary from patient to patient depending on the mobility and volume of the oedematous fluid, and thus must be taken into account.

Fluid return after the withdrawal of compression increased as the interval between measurements became longer (Fig. 5). Similar phenomena were observed between the treatments, when oedema translocated during treatment, but returned between treatments (Fig. 6). Fluid return greatly increased during weekends when no treatment was given and when the patients did not use any elastic sleeve. In some patients, whose treatment was interrupted for about 3 months, oedema recurred almost to the pretreatment value. The repeated sessions of pneumatic compression appeared to improve treatment.

The method of measuring fluid translocation ap-

peared to be rapid, convenient, and reproducible. It also gives information as to whether compression treatment is applicable to a patient and if so, how effective the treatment is. However, the method and its interpretation rely on the empirical best fit applied to the experimental results. Therefore, a mathematical model of the tissue flow/displacement is being developed. The flow of oedematous fluid as described by eq. 6 can be explained by a two-compartment system separated by a membrane enclosed in a rigid container with an inflow and outflow. The elastic membranes permit the volume change. Any change in tissue resistance values cause the changes in flow rates and the changes in the volume of the compartments. The electrical analogy is that the compliance of the membrane is represented as a capacitance, and thus the changes in the volume of the compartment is analogous to the charge stored on the capacitance. The viscoelastic property of tissue varies in different stages of oedematous condition to give different flow rates and volume flow. A quantitative analysis of the tissue resistance and capacitance is being performed with the help of its electrical counterpart in order to obtain the values mathematically by simulating the electrical model of the tissue flow/displacement.

## CONCLUSION

The fluid mobility in subcutaneous pitting oedematous tissue is significantly different from that in normal tissue. The measurement of mobility and analysis of the parameters provide  $D_t$  to be a clinically important parameter for treatment control of oedema. The distal sites of the lymphoedematous arm have softer oedema than that of the proximal sites. Effectiveness of pneumatic compression treatment did not depend on the degree of swelling but depended on the mobility of the oedematous fluid. Greater reduction of oedema was obtained at the distal sites of the arm. The advantage of the method used in this study is the ability to apply at any site for measurement of fluid translocation, to determine the degree of oedema and reduction of oedema with treatment.

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## ANNOUNCEMENT

### *The Volvo Awards for Low Back Pain Research 1990*

In order to encourage research in low back pain, the Volvo Company of Göteborg, Sweden, also this year has sponsored three prizes of US\$ 8 000 each. Awards will be made competitively on the basis of scientific merit, in one or more of the following three areas:

- Clinical studies
- Bioengineering studies
- Studies in other basic science areas

Papers submitted for the contest must contain *original* material, not previously published or submitted for publication. A multiple authorship is acceptable. The manuscripts should be in the form of a complete report, including original illustrations, not exceeding 30 typewritten pages, double-spaced, and in a form suitable for submission to a scientific journal. One original and 5 copies of each paper submitted in full

should reach the address given below not later than November 19, 1989.

One of the authors should be prepared, at his own expenses, to come to Boston, USA, at the time of the meeting of the International Society for the Study of the Lumbar Spine, June 13–17, 1990, to present the paper and to receive the award.

The board of referees will be chaired by the undersigned and will contain members from the fields of clinical medicine, bioengineering and biochemistry.

Please direct all correspondence to:

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