

# Dermal Oedema in Lipodermatosclerosis: Distribution, Effects of Posture and Compressive Therapy Evaluated by High-frequency Ultrasonography

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Although leg oedema is believed to contribute to the pathogenesis of lipodermatosclerosis and leg ulcer, little is known about the cutaneous distribution of water in lipodermatosclerosis. In lipodermatosclerosis accompanied by leg ulceration, a subepidermal low echogenic band is seen in the high-frequency echograms of the skin at the boundary of the wound. Since skin echogenicity is inversely related to the amount of water contained, it has been assumed that the subepidermal low echogenic band corresponds to oedema in the papillary dermis. In this study we evaluated dermal oedema in lipodermatosclerosis by quantifying changes of skin echogenicity in 20 patients with lipodermatosclerosis and 20 age- and sex-matched controls. In order for us to evaluate the influence of the upright posture on skin water content, echogenicity was determined three times a day in various regions of the lower and upper extremities. Next morning, after ultrasound examination of the ankle skin, a compressive stocking was applied for 12 h and then the measurements of echogenicity were repeated. At any time of the day, ankle and calf skin was less echogenic in lipodermatosclerosis than in the control. The low echogenic area was confined to the subepidermal region. During the day the low echogenic area expanded in patients with lipodermatosclerosis. This phenomenon was reversed by leg compression. These results indicate that in lipodermatosclerosis oedema is located mainly in the papillary skin. An upright position causes aggravation of oedema, whereas application of compression protects against accumulation of water in the skin during the day. *Key words: leg ulcer; echogenicity; skin oedema.*

(Accepted October 20, 1994.)

Acta Derm Venereol (Stockh) 1995; 75: 120–124.

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The major skin-related sequel of venous insufficiency is cutaneous fibrosis and hyperpigmentation referred to as lipodermatosclerosis (1, 2). Lipodermatosclerosis is a main risk factor for the development of venous leg ulcers (2). Although the exact mechanisms responsible for the transition from lipodermatosclerosis to ulceration are not known, most authors agree that skin oedema promotes ulcer development (1, 3–5). Formation of oedema is enhanced in the upright posture, as hydrostatic pressure in the veins in the lower extremities is transmitted to the microcirculation, where – according to the Starling law – plasma ultrafiltration to the extracellular space increases (1, 6). Therefore, patients with chronic venous insufficiency are advised to avoid the upright position and to wear supportive stockings, the beneficial effect of which is believed to result from the eradication of oedema. However, despite the importance of skin oedema, no method has been available until recently to study

selectively dermal water distribution. Previous studies and investigations from this laboratory indicate that changes of tissue echogenicity reflect alterations of dermal water content (7–13). In this study we compared skin echogenicity, measured *in vivo* by high-frequency ultrasound and digital image analysis, between patients with lipodermatosclerosis and healthy controls. We document that in lipodermatosclerosis oedema is mainly confined to the papillary skin and is exacerbated in the upright posture. The postural aggravation of oedema may be prevented by the application of a compressive stocking.

## PATIENTS AND METHODS

### Subjects

Twenty healthy volunteers (15 women, 5 men; age 75–92, median 85) and 20 patients with lipodermatosclerosis (brownish discoloration and induration) over the medial malleolus (16 women, 4 men; age 75–90, median 82) entered the study after giving their informed consent. Two patients had previously suffered from leg ulcers which had healed subsequently, and two had leg ulcers on the other leg. Ethical approval of the study was given by the Ethic Committee of Copenhagen.

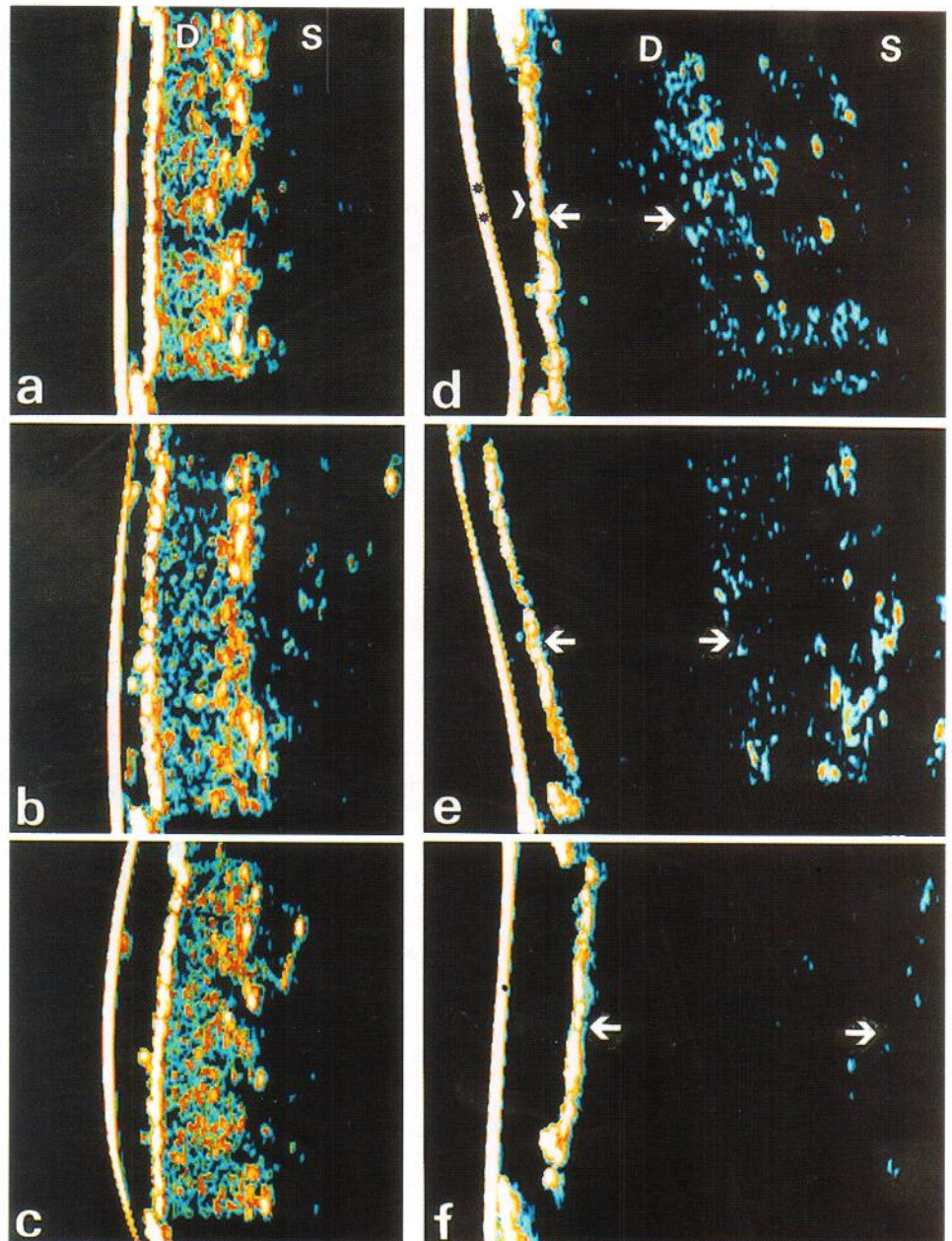
### Skin ultrasonography

A 20 MHz ultrasonograph (Dermascan C, Cortex Technology, Denmark) (7–10) was used to obtain cross-sectional images of the skin (B-mode). The instrument consists of three main parts: the C probe with the transducer mounted on an adjustable balanced supporting arm, the elaboration and visualisation system, and the data storing system. The probe is housed in a water bath and sealed at the point of contact with a plastic diaphragm. The ultrasonic wave is partially reflected at the boundary between adjacent structures and generates echoes of a defined amplitude. The intensity of the reflection echoes is evaluated by the microprocessor and visualised as a coloured two-dimensional image. The gain compensation curve was adjusted in the horizontal position at 22 dB. This gain had been previously found to give the maximal A-scan peaks on the rubber phantom provided by the manufacturer. The velocity of ultrasound in the skin was 1 580 m/s. To obtain a uniform image size and to ensure that images are obtained from the same site, we marked the examined place with an adhesive ring (Beiersdorf) and additionally with a waterproof pen. Ultrasonic coupling gel was applied to the aperture of the ring, and the excess of gel was removed. This enabled standardisation of the volume and thickness of the gel. The probe was placed on the adhesive ring with a transducer over the aperture of the ring, so that the transducer was at the same distance from the skin and its axis was perpendicular to the skin surface. This position was assured by checking the parallel orientation between the ultrasound images of the membrane of the probe and the epidermal entrance echo.

Echographic images were recorded on floppy discs and further processed by a dedicated computer software (GIPS, Cortex Technology, Hadsund, Denmark). In this system the amplitudes of the echoes of single image elements (pixels) are ascribed to a numerical scale (0–255). The low echogenic area extends from 0–30 (7, 8, 11–13). The number of low echogenic pixels (LEPs) was counted in the dermal region between epidermis and the interface to the subcutaneous fat layer (Fig. 1). It has been previously postulated that the number of LEPs is proportional to the degree of skin oedema (7, 8, 11–13).



Fig. 1. Diurnal changes of skin echogenicity. Ultrasound images were recorded from the skin over the medial malleolus of a healthy individual (*a–c*) and a patient with lipodermatosclerosis (*d–f*). *a, d*: morning, before getting up; *b, e*: 2 h after getting up; *c, f*: 12 h after getting up. Colour scale of echogenicity: white > yellow > red > green > blue > black. In *a* and *d*: dermis is marked with *D*, subcutaneous tissue with *S*. In *d*: the membrane of the ultrasound probe is marked with \*\*, the epidermal entrance echo with >. Note widening of the subepidermal low echogenic band in patients with lipodermatosclerosis (arrows).



#### Design of the study

Images were taken in duplicate three times a day: in the morning before getting up (baseline), 2 h after the first measurement, and in the evening (12 h after the first measurement) from the following regions: 5 cm over the medial malleolus, lateral side of the calf 10 cm below knee, anterior thigh 10 cm over knee, middle volar forearm, middle anterior arm. Next morning, a compressive stocking was applied to the leg, which has been previously examined, and ultrasound scanning was performed in the morning and 12 h later, as described above. We used Sigvaris® (Ganzoni, St. Gallen, Switzerland) under-knee compressive stockings, compression class 2, which exert a pressure of 30–40 mm Hg. The size of the stockings was chosen individually. During the day of the experiment all the volunteers were normally active.

#### Statistical analysis

The principle of statistical analysis of diurnal changes of skin echogenicity was described in detail in ref. 8. Briefly, after logarithmic transformation of data the baseline (morning) value of LEPs was subtracted from the mean values obtained from the second and third measurement,

the average diurnal changes were calculated (14). A one-sample *t*-test vs. 0 was used to estimate the significance of average LEP changes. In other cases a one- and two-sample *t*-test was used, as indicated.

## RESULTS

### Baseline echogenicity of the skin in controls and patients with lipodermatosclerosis

In normal individuals the distribution of low echogenic pixels (LEPs) in dermis was random over the medial malleolus (Fig. 1a) and in other examined sites, apart from sunexposed forearm skin, where LEPs were concentrated in the subepidermal region. In lipodermatosclerosis LEPs were present mainly in the subepidermal area, forming a low echogenic band (Fig. 1d). This band was constantly present at the level of the ankle, and in 17 patients it was also visible on the calf. Skin in other areas did not



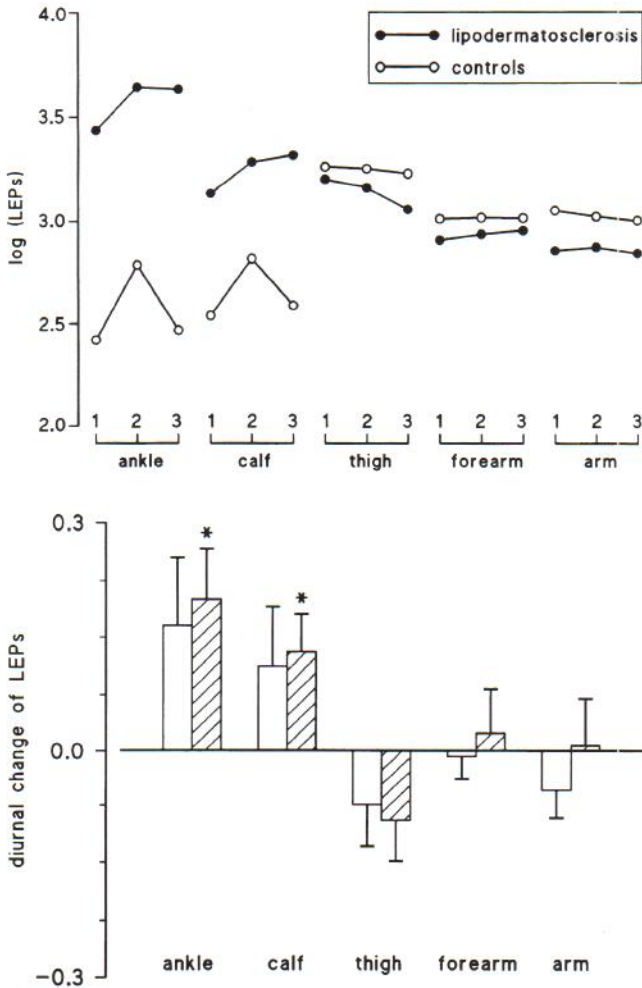


Fig. 2. (a) Diurnal changes of LEPs in skin in the healthy group (open circles) and patients with lipodermatosclerosis (closed circles). The LEP number in the ultrasound skin images was quantified as described in *Material and Methods*. Abscissa: 1: morning, before getting up; 2: 2 h after getting up; 3: 12 h after getting up. (b) Average changes of LEPs during the day in skin of control persons (open bars) and patients with lipodermatosclerosis (hatched bars). Average values were calculated and statistical analysis was performed as described in *Material and Methods* and ref. 14. Bars represent 2 SE of the mean; \*significant,  $p < 0.05$ , against baseline (one-sample *t*-test vs 0).

differ from the control group. LEP values of the ankle and calf skin were significantly higher in patients with lipodermatosclerosis than in the controls (*t*-test for independent samples,  $p < 0.001$ ) (Fig. 2a). In other examined regions the echogenicity of the skin did not differ between the groups.

*Diurnal changes of skin echogenicity*

A biphasic change of skin echogenicity during the day was observed in ankle skin. Two hours after getting up, the LEP number increased both in the control group and in the patients with lipodermatosclerosis (Fig. 2a). In the ankle, 12 h after getting up the amount of LEP returned to the baseline values in the controls (one-sample *t*-test,  $p = 0.58$  vs. 0), but in the patients with lipodermatosclerosis it was still elevated ( $p = 0.05$ ) (Fig. 2a). In average, the LEP number increased significantly in the ankle and calf skin in patients with lipodermatosclerosis (Fig.

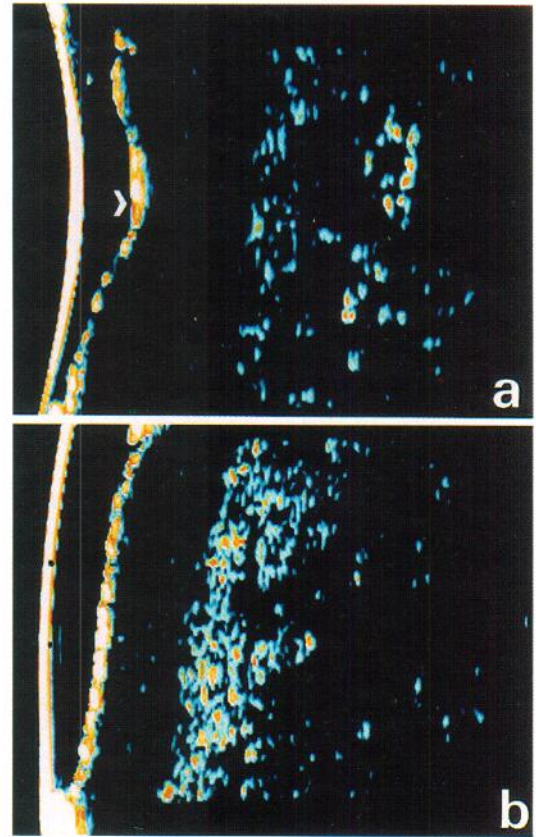


Fig. 3. Ultrasound images of ankle skin from a patient with lipodermatosclerosis in the morning (a) before and (b) 12 h after the administration of compression. The epidermal entrance echo is marked with > in a. Note decrease of thickness of the subepidermal low echogenic band after compression therapy.

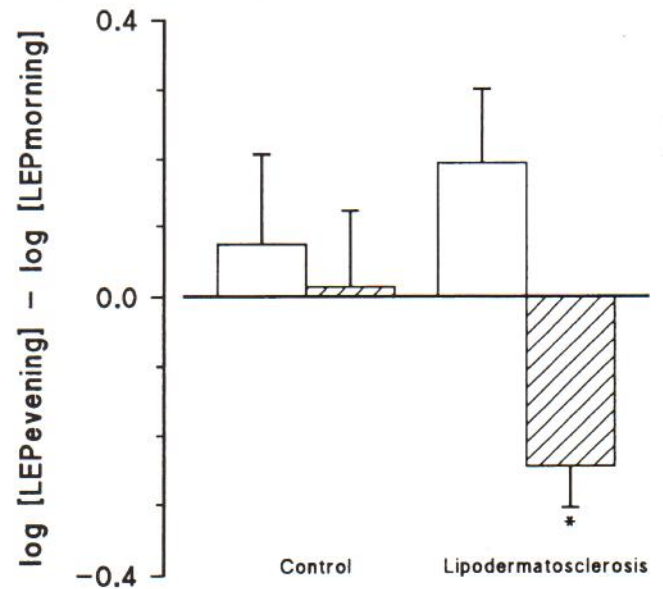


Fig. 4. Influence of compression on diurnal changes of dermal LEPs in the healthy group and patients with lipodermatosclerosis. The LEP number was quantified in the ultrasound skin images recorded in the morning before getting up and 12 h later; then after logarithmic transformation the difference ( $\log[\text{LEP}_{\text{morning}}] - \log[\text{LEP}_{\text{evening}}]$ ) was computed. \*significant ( $p = 0.001$ ) vs. 0 (one-sample *t*-test). Open bars - without compression; hatched bars - with compression.



2b). This increase of LEPs was almost entirely confined to the subepidermal region (Fig. 1e, f). Skin echogenicity in other regions was not significantly changed in either group (Fig. 2b).

#### *The influence of compression on diurnal changes of skin echogenicity*

Twelve hours after getting up, skin echogenicity was not affected by compression in the control group. In contrast, compressed ankle skin in the patients with lipodermatosclerosis contained significantly fewer LEPs than uncompressed skin ( $p = 0.001$ , paired *t*-test) (Figs. 3, 4). However, despite this decrease of the LEP number, lipodermatosclerotic skin was still less echogenic of the end of the day than in the controls ( $p < 0.001$ ).

## DISCUSSION

This study showed that in lipodermatosclerosis, skin echogenicity in the ankle region was markedly lowered, indicating increased water content and hence skin oedema. During the day the amount of dermal water further increased, whereas compression prevented oedema formation.

A number of studies indicate that echogenicity of the tissues, including dermis, is inversely related to the amount of fluid contained (7–13, 15). This notion has been reinforced by the results of nuclear magnetic resonance imaging of the skin, as the relative proton density representing water is increased in areas which are also known to be echolucent (16, 17).

To quantify the echogenicity of dermis we obtained trans-sectional ultrasound images of the skin, in which the LEP number was counted. In patients with lipodermatosclerosis, high hydrostatic pressure in dependent parts of the body, caused by the change of body position from supine to upright, significantly affected skin echogenicity. The LEP number increased in ankle and calf skin in this group, while in other areas, where the hydrostatic pressure was considerably lower, no major changes of skin echogenicity were detected. Because upright posture is a well-known factor promoting oedema formation in dependent tissues (1, 7, 8), it is likely that our findings are explained by the redistribution of dermal fluid. Thus, during the day, in patients with lipodermatosclerosis but not in healthy subjects, the amount of dermal water increased in the ankle region and to a lesser degree in the calf skin. It is conceivable that mechanisms that protect against oedema formation in the upright posture are impaired in lipodermatosclerosis. The injury of the venous valves and venous hypertension (1), defective venoarteriolar-arteriolar reflex (18, 19) and damaged lymphatic drainage (20) may account for the poor compensation for gravitational stress in patients with lipodermatosclerosis.

In contrast to the control skin, the majority of LEPs in lipodermatosclerosis were localised in the subepidermal area and formed an echolucent band. Such a subepidermal low echogenic band has been described previously in the skin surrounding leg ulcers, but its origin remained obscure (7). It has been proposed that the subepidermal low echogenic band could represent oedema ("oedema band"), an area of altered architecture of collagen fibres, or distended blood vessels (7, 8). In view of the dynamic diurnal changes of the subepidermal low echogenic

band revealed in this study, it is conceivable that this band indeed reflects a site of fluid accumulation in the skin.

The subepidermal localisation of oedema in lipodermatosclerosis may have significant pathophysiologic consequences. Oedema impairs skin oxygen consumption (21), most probably by a mechanical interference with oxygen diffusion between capillaries and target tissues. Therefore the presence of oedema in the subepidermal region, where capillary loops are localised, could significantly impair epidermal metabolism and ultimately cause epidermal necrosis and ulcer development. Protein-rich oedema fluid is also believed to promote fibrin cuff formation around capillaries (22) and sequester growth factors necessary for skin growth and repair (23). Epidermis is a rich source of growth factors (24), and therefore oedema in the subepidermal region may prevent their diffusion to deeper dermal layers.

Clinical experience has recognised oedema of the lower extremity as a deleterious factor precipitating leg ulcer development in the area of lipodermatosclerosis and impairing leg ulcer healing (1, 3). However, a relationship between the incidence of leg oedema and leg ulcer has not been established (25). The apparent difficulty was to establish a method for oedema measurement. Clinically detectable pitting in the ankle area and Stemmer's sign are found exclusively in advanced forms of oedema, and these symptoms can be detected only in little over half of the population with leg ulcers (25). Volumetric methods, like plethysmography or foot volume estimation, measure muscle and subcutaneous tissue oedema rather than more clinically relevant dermal oedema. Therefore, determination of skin echostructure may provide a rapid and sensitive method of intradermal oedema assessment, especially in cases of minute oedema not recognised clinically.

Compressive therapy is an effective measure to prevent leg ulcer development. The mechanism(s) of action of compressive stockings have been a matter of extensive debate; however, the most prevalent opinion is that compression eliminates oedema via an increase of tissue pressure (26, 27). Our results support this theory, since application of compressive stockings significantly counteracted posture-related increase of oedema in the ankle skin in patients with lipodermatosclerosis.

Despite the widespread use of compression, the optimal amount of pressure necessary to prevent venous ulcer is not known (3, 26, 27). It is conceivable that monitoring of skin echogenicity in the compressed leg will make it possible to precisely assess the efficacy of compressive treatment in oedema reduction. This should help to establish a proper compressive regimen for an individual patient with lipodermatosclerosis and/or leg ulcer and will facilitate the long term control of the efficacy of therapy.

## ACKNOWLEDGEMENTS

I am grateful to Dr. Jørgen Serup for initiating my interest in skin ultrasonography and for his help during this study and to Professor Jørgen Søndergaard for his constructive comments and encouragement during experiments. The author wishes to thank Ms Inger Blomgren-Hansen and the staff of Kildevæld Sogns Plejehjem, Dr. Niels Horwitz and the staff at the Department of Geriatrics, Bispebjerg Hospital, Copenhagen for their help throughout the study and Dr Signe Birk Jensen from the Statistical Department, Leo Pharmaceutical Products,



for advise on the statistical analysis. The study was supported by grants from The Leo Foundation and The Haensch Foundation.

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