Immediate Changes to Skin and Subcutaneous Tissue Strains Following Manual Lymph Drainage in Legs with Lymphedema

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Objectives: To study the immediate impact of manual lymph drainage (MLD) on skin and subcutaneous tissue strains in legs with lymphedema using free-hand real-time tissue elastography (RTE).

Methods: Skin and subcutaneous tissue strain measurements were taken at the middle of the inner thigh and calf by RTE in 20 legs with lymphedema of 18 patients (stage II: 11, late stage II: 7, stage III: 2) and in 70 legs of 35 normal subjects. In patients with lymphedema, the same measurements were repeated immediately following MLD.

Results: Significant negative correlations were found between pre-MLD strains and the MLD-induced changes in thigh and calf skin strains (thigh skin: \( p < 0.01 \), calf skin: \( p = 0.05 \)), but not in subcutaneous tissue strains. Pre-MLD intercepts of these regression lines were closer to normal values as compared to mean pre-MLD values (normal thigh skin: \( 0.54\% \pm 0.30\% \), calf skin: \( 0.25\% \pm 0.18\% \), Pre-MLD thigh skin: \( 0.39\% \pm 0.20\% \), calf skin: \( 0.17\% \pm 0.12\% \), Pre-MLD intercept of thigh skin: \( 0.48\% \), Pre-MLD intercept of calf skin: \( 0.31\% \)).

Conclusions: It appears that MLD did not simply soften the skin, but rather normalized it in terms of strain. However, this was not confirmed in the subcutaneous tissue.

Keywords: ultrasonography, elastography, lymphedema, manual lymph drainage

Introduction

Manual lymph drainage (MLD) is one of the major components of the combined physical therapy (CPT) that is used in the treatment of lymphedema.11 MLD maneuvers are considered to exert force on the interstitial fluids and proteins inside the initial lymphatics, thereby shifting them towards collaterals and/or normally functioning lymphatic vessels.21 These manipulations therefore not only soften tissues directly, but possibly also remove excess local fluid. It is therefore speculated that MLD maneuvers should alter the mechanical properties, such as strain, of the skin and subcutaneous tissue. Strain is defined as deformation of a solid due to stress and is considered to be one of the measures representing tissue hardness.3,4 We previously reported a method of measuring skin and subcutaneous tissue strains using free-hand real-time tissue elastography (RTE).5 Free-hand RTE is an ultrasonography technique that can depict relative tissue displacement induced by probe compression by hand instead of a fixed compressor,6 which is the most commonly available mode in commercial units. In the present study, we measured skin and subcutaneous tissue strains before and after MLD to investigate the immediate impact of MLD on these tissues.

Methods

This study was approved by the Institutional Review Board of Yamaguchi University Hospital (Ube, Yamaguchi, Japan). All participants signed an informed consent form before enrollment. We studied 20 legs of 18 patients with secondary lymphedema (age, 37–84 years; median, 65 years) who were in the maintenance phase of CPT at our clinic between April 2013 and March 2014 and agreed to participate in this study. The patients’ characteristics are summarized in Table 1. The clinical stage of lymphedema was determined in accordance with the Consensus Document of the International Society of Lymphology as follows:1) Stage 0 (or Ia): A latent or sub-clinical condition where limb swelling is not yet evident. Stage I: An early accumulation of fluid that subsides with limb elevation.
Stage II: Tissue swelling that is not reduced by limb elevation alone. Pitting is manifest in earlier stage II, but the limb may or may not pit in later stage II as excess fat and fibrosis supervenes.

Stage III: Lymphostatic elephantiasis in which pitting can be absent while trophic skin changes such as acanthosis, further deposition of fat and fibrosis, and watery overgrowths have developed.

The MLD maneuvers including drainage techniques such as stationary circles, pumping, scooping, and rotary techniques as well as tissue softening techniques such as kneading and the skin fold technique as described by Földi et al.7 were performed by single lymphedema therapist (H.K.). Following pretreatments administered to the body trunk, the above maneuvers were performed for 30–60 min per leg. For comparison, we also studied the legs of 35 healthy adult volunteers including 14 men and 21 women (age, 25–55 years; median, 37 years). These subjects underwent a single assessment only and received no MLD.

Free-hand RTE was performed with an ultrasound machine (HI VISION Preirus, Hitachi Aloka Medical, Ltd., Tokyo, Japan) by single examiner (K.N.) as previously reported by our group.6 Briefly, with the patients lying in the supine position in the room conditioned at temperature of 25°C, a coupling medium, i.e. Phantom, (Sonar Pad®, Nippon BXI Inc., Tokyo, Japan), each trimmed into 60 × 60 mm squares, were placed on the skin at the middle of the inner thigh and the middle of the inner calf. Repeated rhythmical compression was applied using an ultrasound probe at a controlled peak force intended to maintain these phantom strains at 0.23%–0.47%, levels at which normal leg skin and subcutaneous tissue can be optimally assessed. For measurement of the skin strain, the region of interest (ROI) was set between the inferior margin of the entry echo and the dermo-hypodermal junction. For the subcutaneous tissue, the ROI was set between the dermo-hypodermal junction and the superior margin of the deep muscular fascia. When the subcutaneous tissue was very thick, the lower margin was set as the lower limit of the elastography window. The measurements were performed immediately before and after MLD (Fig. 1).

**Statistical analysis**

Results are expressed as means ± standard deviation or as counts, unless otherwise indicated. Strains were measured twice each time and the average values were used. To compare strains between normal legs and legs with lymphedema, we used the Mann-Whitney U-test. The Wilcoxon signed-rank sum test was used to calculate the significance of changes in tissue strains before and after MLD. The correlations between pre-MLD tissue strains and the amount of strain change induced by MLD were tested using simple linear regression analysis. Statistical analyses were performed using JMP 11.0 (SAS Institute, Cary, NC, USA). A p-value of less than 0.05 was considered significant.

**Results**

The skin and subcutaneous tissue strains in normal legs and in legs with lymphedema prior to MLD are depicted
The overall changes to skin and subcutaneous tissue strains in the thigh and calf are shown in Fig. 3. Mean pre- and post-MLD strains in the thigh skin and subcutaneous tissue showed no significant differences (skin: pre, 0.39% ± 0.20% vs. post, 0.46% ± 0.21%; subcutaneous tissue: pre, 0.90% ± 0.35% vs. post, 0.92% ± 0.42%). In the calf, however, both skin and subcutaneous tissue strains were significantly increased by MLD (skin: pre, 0.17% ± 0.12% vs. post, 0.24% ± 0.12%; subcutaneous tissue: pre, 0.67% ± 0.25% vs. post, 0.75% ± 0.27%).

The correlations between pre-MLD strains and the strain changes induced by MLD are shown in Fig. 4A. No such correlations were detected for thigh and calf subcutaneous tissues. However, both the thigh and calf skin showed linear correlations (thigh: $p < 0.01$, calf: $p = 0.05$). When these regression lines were observed closely, the pre-MLD strain intercept was at 1.16% in the thigh skin and 0.31% in the calf skin. These were each closer to normal values than to mean pre-MLD values (Fig. 4B).

Discussion

Application of RTE to the assessment of peripheral lymphedema

MLD maneuvers are considered to move local fluids into the initial lymphatics, accelerate the lymphatic contraction rate, and advance lymph towards deeper drainage trunks.\(^8\) Since MLD is not a technique capable of moving a large amount of fluid at once,\(^9\) the measurement of extremity volumes or circumferences may not properly reflect the immediate outcome of MLD. Improved lymphatic pumping and the resultant increase in lymph flow following MLD in lymphedema patients were already elucidated using lymphangioscintigraphy\(^10\) or near-infrared fluorescence imaging.\(^11\) Softening the hard, fibrotic lesion is another aim of MLD, not only to ease patient discomfort but also to create new tissue channels for fluid drainage.\(^12\) However, the change in tissue hardness induced by MLD has not been investigated in a precise manner. A tonometry test has been used for the assessment of tissue hardness.\(^13\) Strictly speaking, however, this test objectively determines the depth of pitting but not the tissue hardness itself.\(^14\) For this purpose, we previously reported the use of free-hand RTE.\(^4\) Tissue strain as measured by RTE is still affected by the surrounding tissue, and therefore RTE cannot measure the true mechanical property.\(^15\) Moreover, the idea of strain is basically applied to solid matter, but the skin and subcutaneous tissues contain various components including free water that easily shift horizontally in legs with lymphedema, potentially affecting measurements. Nevertheless, the strains measured by RTE could possibly represent purer mechanical properties than tonometry. Moreover, this method can assess skin and subcutaneous
We previously reported that the mean skin and subcutaneous tissue strains in legs with lymphedema of varying severity were not significantly different from those in asymptomatic legs. In the current study, however, pre-MLD skin and subcutaneous tissue strains were significantly lower, or tended to be lower, than those in normal legs. This could be because the current study included more advanced stage lymphedema patients as well as relatively younger normal volunteers. Consistent with the previous report, the order of tissues from highest to lowest strain was the same in normal legs and legs with lymphedema in the present study, namely, subcutaneous tissue of the thigh > subcutaneous tissue of that in the calf > skin of the thigh > skin of the calf.

**Immediate impact of MLD on skin and subcutaneous tissue strains**

Skin and subcutaneous tissue strains in the thigh were unaffected by MLD, whereas MLD increased skin and subcutaneous tissue strains in the calf. Upon closer examination, however, these changes were quite variable. Therefore, we correlated these MLD-induced changes in strain with pre-MLD strains. Significant linear correlations between these parameters were found for skin, but not for subcutaneous tissue. Namely, the lower the pre-MLD skin strains, the more the strains were increased. Interestingly, when pre-MLD strains were large, they decreased again according to the pre-MLD value. When the pre-MLD strain intercepts of these regression lines (i.e., the theoretical strain reaching points induced by MLD) were compared with mean pre-MLD strains, they were closer to the mean normal values. It was thus assumed that MLD was not simply softening the skin, but was rather “normalizing” it in terms of strain. The increase in strains in harder tissue could be attributed to a direct effect of massage, which possibly breaks excess collagen bundles and releases the confined fluid they contain. On the other hand, the decrease in strains in softer tissue is possibly caused by the temporary removal of excess fluid that can be observed in other types of massage as well.

We could not demonstrate any significant impact on strains of subcutaneous tissues by MLD. One possible explanation was that RTE was not suitable to assess strains in deeper tissue, which might have been affected by MLD. At present, there are no proper devices to assess strains of the subcutaneous tissue, and therefore our future challenge is to develop a proper measuring equipment for this purpose.

**Limitations**

The current study has some limitations. First, the study involved a limited number of patients from a single center, making it difficult to reach a definitive conclusion. Second, the currently employed technique of free-hand RTE using a phantom is still developing. The data may deviate due to the nature of the free-hand technique. Future validations of intra- and inter-observer differences, impacts of conditions that affect the result are needed. Moreover, skin and...
subcutaneous tissue strains can be affected by other factors such as age. For instance, this could be related to unexplainable difference of skin and subcutaneous tissue strains in the thigh between normal and lymphedema legs, which were not confirmed in the calves. Although the compression force applied by the probe was controlled using a phantom, some technical skill is still required to obtain stable results. Thus, at present, it is uncertain whether tissue strain measured by free-hand RTE is a proper parameter for assessing skin and subcutaneous tissue hardness in extremities with lymphedema. Third, there is a wide variety of MLD modifications, and it is therefore unclear whether the current results hold true for a variety of MLDs. The impact of previous MLDs on the following MLD in terms of strains has not yet been tested, which is another issue requiring validations.

Conclusions

We assessed the immediate impact of MLD on skin and subcutaneous tissue in legs with lymphedema using RTE. We concluded that MLD did not simply increase skin strains, but seemed to “normalize” them.

Disclosure Statement

All authors have no conflict of interest.

Author Contributions

Study conception: KS
Data collection: KS, HK, KN, TH, KU, MS, YT
Analysis: KS, OY
Investigation: Not applicable
Writing: KS
Funding acquisition: Not applicable
Critical review and revision: all authors
Final approval of the article: all authors
Accountability for all aspects of the work: all authors

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