Original article

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Pilot study: whole body manual subcutaneous adipose tissue (SAT) therapy improved pain and SAT structure in women with lipedema

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Abstract:
Background: Lipedema is a common painful subcutaneous adipose tissue (SAT) disorder in women affecting the limbs. SAT therapy is a manual therapy to improve soft tissue quality.
Objective: Determine if SAT therapy improves pain and structure of lipedema SAT.
Design: Single arm prospective pilot study.
Setting: Academic medical center.
Patients: Seven women, 46 ± 5 years, weight 90 ± 19 kg, with lipedema.
Intervention: Twelve 90-min SAT therapy sessions over 4 weeks.
Outcomes: Dual X-ray absorptiometry (DXA) scans, SAT ultrasound (Vevo 2100), leg volumetrics, skin caliper assessment, tissue exam, weight, resting metabolic rate, pain assessment, lower extremity functional scale (LEFS) and body shape questionnaire (BSQ) at baseline and end of study.
Results: Weight, resting metabolic rate and BSQ did not change significantly. Limb fat over total body fat mass ($p = 0.08$) and trunk fat over total body mass trended down from baseline ($p = 0.08$) by DXA. Leg volume and caliper assessments in eight of nine areas ($p < 0.007$), LEFS ($p = 0.002$) and average pain ($p = 0.007$) significantly decreased from baseline. Fibrosis significantly decreased in the nodules, hips and groin. Ultrasound showed improved SAT structure in some subjects. Side effects included pain, bruising, itching, swelling and gastroesophageal reflux disease. All women said they would recommend SAT therapy to other women with lipedema.
Limitations: Small number of subjects.
Conclusion: SAT therapy in 4 weeks improved tissue structure, perceived leg function, and volume although shape was not affected. While side effects of SAT therapy were common, all women felt the therapy was beneficial.

Keywords: fat, lipedema, pain, subcutaneous adipose tissue, women's health
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Introduction

Lipedema is a painful inherited [1] disorder of excess subcutaneous adipose tissue (SAT) in women that remains poorly recognized by healthcare providers [2], [3]. Lipedema SAT cannot be lost by diet or exercise therefore it can grow to excess resulting in development of lymphedema, venous disease, gait disturbance, loss of mobility and psychological distress [4], [5].

In 'normal' SAT, fat lobules (groupings of adipocytes) slide easily over one another under the skin on fine moist fibers [6] providing a homogeneously smooth feel. Lipedema SAT is sick; it has lost its smooth consistency morphing into pearl-sized (~5 mm) nodules located near lymph nodes but also diffusely on the low back, lower abdomen, hips, buttocks, thighs, medial knee, inferior to the knee, and lateral malleolus, and less often (~30%) on hands and feet [5]. Legs with lipedema SAT can have a stove-pipe configuration forming a cuff of SAT at the ankle where the medial malleolus and the Achilles become surrounded by SAT. Lipedema SAT thickens over time in the absence of treatment forming hardened areas especially on the upper buttocks, hips and groin; dependent areas become heavy with fluid on the breasts, upper arm, hips, thighs and buttocks.

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Dysregulated vascular function is thought to occur in lipedema SAT with dilated venules causing capillary leak [7] resulting in vascular sclerosis, interstitial fluid and fibrotic material [8]. The widened interstitium allows palpation of individual fat lobules as nodules [8]. Slow blood and lymphatic flow occurs in gynoid SAT [9]. With poor flow, SAT becomes inflamed then fibrotic, painful and palpable, akin to a muscle knot that contains inflammatory and pain mediators [10].

Advanced stages of lipedema reflect greater changes in SAT structure. In Stage 1, the skin is smooth with an enlarged and nodular subdermis. In Stage 2, larger masses form, and bands of peri-lobular fascia thicken and contract, pulling the skin down in a mattress pattern. In Stage 3, the skin thins and loses elasticity allowing SAT to grow to excess and fold over inhibiting flow further [2]. Lymphedema develops in Stage 3, more than Stage 2 or Stage 1 [5]. Standard care for lipedema includes compression garments, complete decongestive therapy including manual lymphatic drainage, movement (muscle contraction) to improve flow through the tissue, and food plans to prevent or reduce accumulation of obese SAT which can exacerbate lipedema. Liposuction of lipedema SAT is known to improve quality of life [11], [12], [13], [14] but has considerable cost and side effects including sagging skin and may induce excess SAT growth in non-lipedema areas.

Deeper treatments into lipedema SAT have been avoided for fear of damaging the lymphatic system. Larger lymphatics appear normal in earlier stages [15] and weak and leaky only in later stages [16]. These data suggest the need for early intervention to improve sick SAT structure and reduce progression to leaky lymphatics and subsequent lymphedema.

As muscle manipulation treats muscle knots, the aim of deep SAT therapy is to improve the nodules and masses in lipedema towards normal, while waiting for a better understanding of lipedema pathophysiology to improve treatment protocols.

Data was needed to determine if deep SAT therapy improved lipedema SAT structure and if pain decreased concurrently. A therapist from the Netherlands adept in SAT therapy over 13 years was recruited to the US for data collection over 4 weeks. The therapist worked 4.5–6 h per day, 6 days a week so that lipedema subjects could have three treatments per week for the 4-week project. Subject number was therefore limited to seven by time in this initial pilot study.

SAT therapy is a manual therapy that treats SAT tissue on the entire body from the head to the dorsal foot, both back and front of the body for each session. The manual movements are mainly done with flat thumb over thumb pressure, scraping techniques with flat fingers, scissor movements on the first digit side of the palm and deep pressure sweeps into the tissue. The manual techniques optimize smoothing of the tissue and pressure deepens over time as the SAT softens with a goal of also treating fascia and muscle close to the bone. Areas with SAT nodules and masses contain blood vessels and receive a focus during the SAT therapy which can result in bruising in these areas; the bruises reduce with ongoing therapy.

Changes in pain and other subjective signs and symptoms, lower extremity functional scale (LEFS), Body Shape Questionnaire (BSQ)-34, a physical exam including assessment of nodules in the SAT, leg volume, and fat by dual X-ray absorptiometry (DXA) and ultrasound were assessed at baseline and end of study.

Materials and methods

This study was approved by the University of Arizona Human Subjects Protection Program and all women were consented prior to participation to comply with the World Medical Association Declaration of Helsinki regarding ethical conduct of research involving human subjects. The study design was single arm, non-blinded prospective for seven women with lipedema (Table 1) who underwent baseline studies, 12 90-min SAT therapy sessions over 4 weeks followed by repeat studies (Figure 1). Each SAT treatment consisted of treatments in areas and time as follows: neck and upper back (10 min), lower back (10 min), upper legs back side (10 min), lower legs back side (10 min), feet (5 min), lower legs front side (10 min), upper legs front side (10 min), abdomen (10 min), arms and chest (10 min), head and face (5 min). Participant number was limited by time due to a single therapist conducting sessions. The therapist did not participate in data collection or analyses. The participants paid a reduced fee per session. The ClinicalTrials.gov identifier for this study is NCT02907411.

Table 1: Participant baseline demographics.

Demographic	Values
Number	7
Age, years	46 ± 5
Sex	Female
Race	Caucasian – 7; Native American – 3
Ethnicity	7 Non-Hispanic

Average weight, kg	90 ± 19
Number with children	4
Average BMI, kg/m^2	33 ± 8
Average small waist, cm	86 ± 9
Average hips, cm	124 ± 15
Average small waist hip ratio	0.7 ± 0.05
Lipedema Stage 1	0
Lipedema Stage 2	6
Lipedema Stage 3	1
Lymphedema	0
Dercum disease diffuse type	3
Number with lipomas	4
Age first symptoms	21 ± 11
Number with pain	6

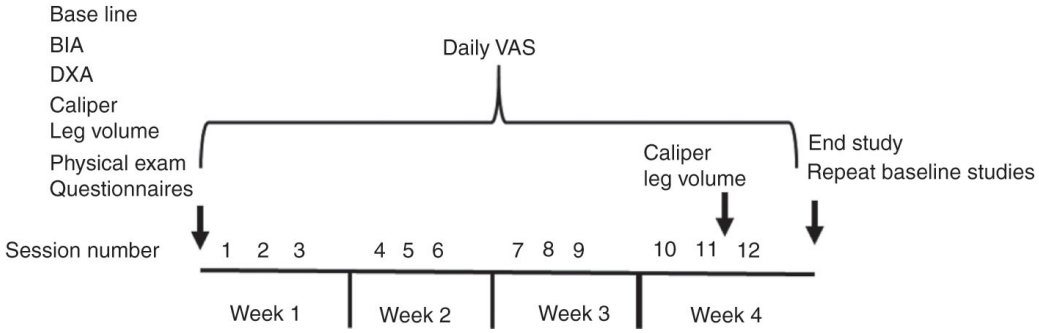

Figure 1: Timeline for SAT therapy sessions and study assessments.
Caliper and leg volume assessments were completed at baseline and before and after the last therapy session. VAS, visual analog scale; BIA, bioimpedance; DXA, dual X-ray absorptiometry.

Differences between baseline and end of study values were performed using 2-tailed paired t-tests. All values are ± standard deviation (SD). Alpha of less than 0.05 was considered significant.

Baseline and end study measures

Tape measurements

Waist was measured at the smallest area between breasts and umbilicus (small waist) and at the umbilicus (umbilical waist) at the end of an expiration. Hip was measured at the largest protrusion of the buttocks so the tape measure was parallel to the floor after confirmation by two study staff. Leg volume was measured with the back of the leg against a measuring grid; measurements began around the malleoli and continued every 4 cm to the upper thigh with 14 total measurements. Neck, largest upper arm, largest lower arm, breast, and infra-mammary fold were also measured.

Bioimpedance

Weight, body mass index (BMI), percent body fat and muscle mass were obtained on a Tanita Ironman dual frequency body composition monitor (Tokyo, Japan).

Calipers

Skinfold thickness measurements were performed in triplicate by one author (KLH), and averaged (TrimCal 4000 caliper; Sequoia Fitness Products, Denver, CO, USA).

Dielectric constant

Tissue fluid in the skin was measured by dielectric constant (Moisture Meter D Compact; Delfin Technologies Limited, Kuoplo, Finland) by one author (KLH). Dielectric constant expresses the ratio of permittivity of a substance to that of free space or a vacuum and does not have units or dimensions.

Temperature

Body temperature in 28 locations was measured by one author (KLH) using a CEN-TECH infrared thermometer (Kansas City, MO, USA).

Physical exam

One author (KLH) examined all participants at baseline and end of study. Lipedema nodules were documented in 11 areas: chest, upper outer arm, cubit area, forearm, upper abdomen, lower abdomen, hips, anterior thighs, medial knee, under the knee and posterior leg. Tissue fibrosis (localized or diffusely firm tissue) was measured subjectively in four areas (nodules, buttocks, hips, groin). Tissue heaviness was assessed at the upper arms, breasts, panniculus, hips, buttocks, thighs.

Hypermobility

Assessed by the Beighton criteria at baseline [17].

DXA scan

Measures of whole-body and regional adiposity were obtained by DXA at baseline and end of study using a GE/Lunar Radiation Corp iDXA (Madison, WI, USA) following standard subject positioning and data acquisition protocols by a certified technician. The iDXA was calibrated daily per manufacturer guidelines. Four women had complete scans; two women had partial scans of the left arm and leg due to size; positioning was similar at baseline and end of study.

Resting metabolic rate (RMR)

RMR was determined at baseline and end of study using MedGem (Microlife, Clearwater, FL, USA), an FDA 510K-cleared Class II handheld medical device measuring oxygen consumption (VO_2) per kg lean body mass from DXA. Participants rested at least 5 min prior to measuring RMR. RMR calculated from DXA data as part of the Mifflin St. Joer equation [18] was compared to MedGem RMR.

Ultrasound

Ultrasound was assessed before and after SAT therapy with 20-, 50-, and 70-MHz probes on a Vevo 2100 (FUJIFILM VisualSonics, Bothell, WA, USA).

BSQ 34

The BSQ has 34 subjective questions about body shape yielding a possible score between 34 and 204. Proposed classification: < 80 no concern, 80–110 mild concern, 111–140 moderate concern and >140 marked concern with shape [19].

LEFS

Twenty questions about a person's ability to perform everyday tasks especially related to leg function [20].

Lifestyle

Subjects were asked to not change diet or exercise during the study, which was validated by questionnaire (data not shown).

Results

Participants

Past medical history

All seven women in this study had lipedema confirmed on exam and three had a diagnosis of Dercum's disease, a more widespread painful SAT disorder [21] (Table 1). Venous disease included spider veins (n = 6), varicose veins (n = 2) and venous insufficiency (n = 4). Five women had a diagnosis of myofascial disease.

Beighton hypermobility criteria

All women had a Beighton hypermobility score of 5 or above with an average score of 7 ± 2 (major criteria), and all had two or more minor criteria; therefore all women met criteria for joint hypermobility [17].

Physical exam

Stemmer sign

All seven participants had negative Stemmer signs on the hands and feet at baseline and end of study indicating an absence of lymphedema in these areas.

Nodules

The average number of nodular areas at baseline was 9.3 ± 2.6, reducing after SAT therapy to 5.9 ± 3.6, which just missed significance ($p = 0.05$).

Tissue fibrosis

Tissue fibrosis significantly decreased in nodules ($p = 0.04$), hips ($p = 0.04$) and groin ($p = 0.04$) but not buttocks ($p = 0.3$). There was no significant decrease in heaviness of tissue from baseline to end of study for the upper arms ($p = 0.09$), breasts ($p = 0.2$), panniculus ($p = 0.2$), hips ($p = 0.2$), buttocks ($p = 0.09$), or thighs ($p = 0.09$).

Waist-hip ratio

The small- and umbilical-waist-to-hip ratio (WHR) at baseline were less than 1 as expected for a gynoid-shaped female (Table 1). There was no significant change by end of study in the small- (0.7 ± 0.08) or umbilical-WHR (0.8 ± 0.07). All but one woman had a decrease in small-waist measurement; average decrease of −2.9% ± 5% but this did not reach significance. All but one woman had a decrease in hip measurement with an average decrease of −3.3% ± 4% ($p = 0.07$).

Caliper measurements

Caliper measurements were completed at baseline, and before and after the last therapy session. Nine of 12 caliper sites showed a significant decrease from baseline to before the last therapy session (Table 2); the chin (p = 0.1), wrist (p = 0.1), hand (p = 0.1) and foot (p = 0.06) did not significantly change after SAT therapy sessions. When evaluating the change from baseline to after the last SAT therapy session, the only area that did not significantly change from baseline was the hand which trended to decrease (p = 0.05). When determining if a single SAT therapy session resulted in a significant percent change in caliper measurements (before vs. after the last SAT therapy session), the chin (−0.6% ± 37%), triceps (−4.3% ± 12%), biceps (−6% ± 19%), brachioradialis (−3% ± 8%), hands (0.5% ± 47%), umbilicus (−8% ± 17%), flank (4% ± 16%), thigh (−3% ± 6%), calf (−1.3% ± 16%) and foot (−5% ± 22%) did not significantly decrease; the wrist trended to decrease (−19% ± 21%; p = 0.06) and there was a significant decrease in the subscapular area (−17% ± 13%; p = 0.006).

Table 2: Leg volumes and caliper measurements: baseline, before and after final SAT therapy session.

							Leg volume, L
Location	**Baseline**						**End study**
		Before last therapy	**Percent change**	**p-Value[a]**	**After last therapy**	**Percent change**	**p-Value[a]**
Upper left	9.2 ± 3	8 ± 2.5	−14 ± 4	0.001	7.2 ± 2	−20 ± 3	0.004
Upper right	8.9 ± 3	8 ± 2.5	−11 ± 3	0.014	7.7 ± 2	−14 ± 3	0.01
Lower Left	4 ± 0.5	4 ± 0.4	−13 ± 2	0.0003	3 ± 0.4	−16 ± 2	0.0001
Lower right	4 ± 0.7	4 ± 0.5	−11 ± 2	0.002	3 ± 0.4	−14 ± 2	0.001
Full left[b]	13 ± 3	11 ± 2.8	−14 ± 2	0.0006	11 ± 2	−19 ± 3	<0.002
Full right[b]	13 ± 3	12 ± 2.9	−10 ± 2	0.004	11 ± 2.6	−13 ± 3	<0.007
Caliper assessment							
Chin	11 ± 3	10 ± 4	−9 ± 20	NS	9.6 ± 3	−15 ± 12	0.008
Biceps	17 ± 7	12 ± 5	−27 ± 30	0.03	10 ± 4	−34 ± 21	0.01
Triceps	27 ± 10	22 ± 8	−18 ± 14	0.02	20 ± 8	−21 ± 19	0.03
Brachioradialis	14 ± 4	11 ± 3	−19 ± 36	0.02	10 ± 2	−23 ± 13	0.008
Wrist	7 ± 4	5.6 ± 3	−19 ± 25	NS	4.5 ± 1.5	−38 ± 16	0.02
Hand	1.3 ± 0.6	1 ± 0.6	−19 ± 37	NS	0.9 ± 0.5	−24 ± 37	NS
Abdomen	30 ± 7	23 ± 6	−22 ± 11	0.001	21 ± 7	−28 ± 16	0.002
Subscapular	26 ± 6	23 ± 5	−9.7 ± 8	0.02	19 ± 4	−25 ± 11	0.002
Iliac crest	25 ± 14	14 ± 5	−40 ± 11	0.01	14 ± 5	−39 ± 17	0.02
Thigh	56 ± 7	43 ± 5	−22 ± 12	0.002	40 ± 4	−26 ± 10	0.002
Medial calf	39 ± 7	27 ± 3	−31 ± 7	0.0002	26 ± 4	−32 ± 12	0.001
Foot	1.3 ± 0.6	1 ± 0.3	−14 ± 17	NS	0.9 ± 3	−20 ± 19	0.03

[a]p-Value end study vs. baseline volume; [b]upper and lower leg = full leg.
NS, Non-significant.

Tape measurements

There was no significant decrease in tape measure of the neck, largest upper and lower arm, breast, or infra-mammary fold. Average wrist size decreased significantly from baseline (16 ± 1 cm) to end of study (15 ± 0.9 cm; p = 0.001). Largest mid-thigh significantly decreased from 68 ± 7 cm at baseline to 63 ± 8 cm before the last SAT therapy session (p < 0.03).

Leg volume significantly decreased for the left and right thighs, left and right lower legs, and full legs (combined thigh and lower leg) from baseline to before, and after, the last SAT therapy session of the study (Table 2). To understand how an individual SAT therapy session affected leg volume, volume was assessed before and after the last SAT therapy session. Volume decreased but not significantly in the upper left (−7% ± 3%; p = 0.056), lower left (−3% ± 2%; p = 0.07), upper right (−3% ± 2%; p = 0.07), lower right (−3% ± 3%; p = 0.1), full left leg (−6 ± 3; p = 0.05) and full right leg (−3% ± 2%; p = 0.07).

Dielectric constant

All values were in the normal range for dielectric constant. There was no significant change from baseline values to end of study for average dielectric constant for the left (37 ± 3–37 ± 5) or right lower abdomen (39 ± 4–38 ± 4), left medial elbow (27 ± 1–27 ± 3), right medial elbow (28 ± 2–27 ± 3), below left knee (36 ± 4–36 ± 7), below right knee (41 ± 7–37 ± 5), left hand (42 ± 6–42 ± 7), right hand (44 ± 8–40 ± 6), left foot (41 ± 6–39 ± 8), right foot (41 ± 5–39 ± 8), left inferior buttock (40 ± 6–37 ± 6), right inferior buttock (40 ± 5–41 ± 2), left lower thigh (33 ± 4–33 ± 5), and right lower thigh (35 ± 5–32 ± 5).

Body temperature

There was no significant decrease from baseline to end of study in average body temperature in the areas of the forehead, supraclavicular, triceps, biceps, brachioradialis, hips, buttocks, abdomen, flanks, upper thigh, fat pads under knee, or top of the foot. There was a significant increase in the temperature of the upper abdomen (31.4 ± 0.9 °C; $p = 0.003$) and a significant decrease in the left medial knee (30.6 ± 1.2 °C; $p = 0.018$). The right medial knee trended down in temperature from 30.4 ± 0.9 °C; $p = 0.06$).

DXA scan

There was no significant difference from baseline to end of study for total body fat mass (42.8 ± 13 and 42.5 ± 12.5 kg, respectively), trunk fat (19 ± 5.9 and 19.2 ± 5.8 kg, respectively), arm fat (3.9 ± 1.1 and 3.8 ± 1.1 kg, respectively) and leg fat (19 ± 6.5 and 18.6 ± 6.1 kg, respectively). The ratio of limb fat mass over total body fat mass trended down from baseline (1.21 ± 0.2) to end of study (1.18 ± 0.2; $p = 0.08$). The ratio of trunk fat mass trended down from baseline (0.45 ± 0.05) to end of study (0.5 ± 0.05; $p = 0.08$). There was no significant difference in the ratio of gynoid fat/total fat mass at baseline (0.2 ± 0.02) compared to end of study (0.2 ± 0.01).

Resting metabolic rate

There was no significant difference between average calculated RMR at baseline by DXA (1340 ± 157 kcal/day) or assessed by MedGem (1284 ± 158 kcal/day). There was also no significant difference from baseline to end of study for RMR by DXA or MedGem. There also was no significance for RMR/kg lean body mass at baseline for DXA compared to MedGem or at end of study.

Ultrasound

The fat tissue on the lower abdomen and the thigh assessed by ultrasound visually had more fibrotic tissue before than after SAT therapy especially in subjects 1, 2 and 6 (Figure 2).

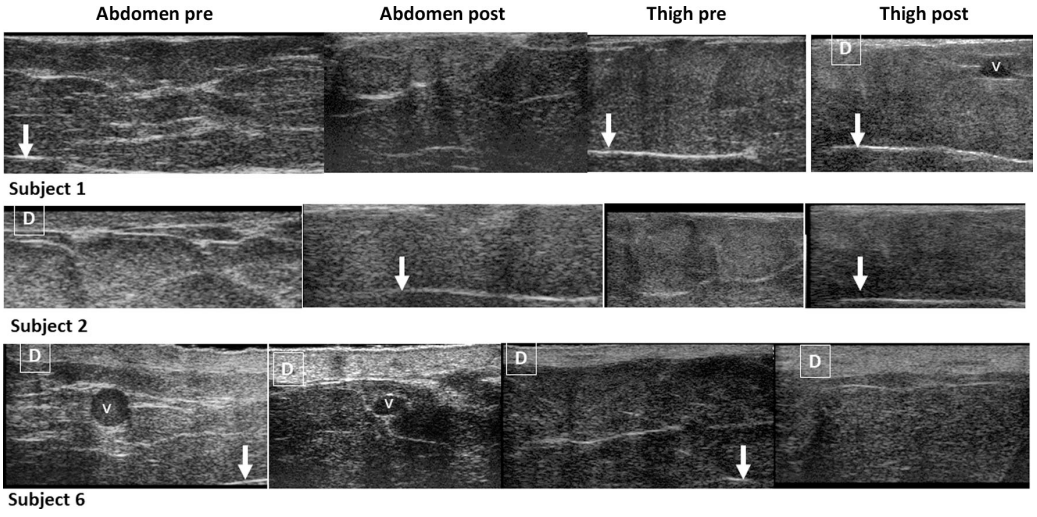

Figure 2: Pre-and post-ultrasound pictures of the abdomen below the umbilicus and anterior thigh for three women. The dermis is marked with a "D" when present; the remainder of the tissue is SAT or vessels (v). Arrows point to fascia. Additional hyperechogenic lines are indicative of thickened connective or fibrotic tissue around nodules or in the tissue.

Pain

At baseline, women described their pain as "like a bruise", and four described their pain as aching. Five of the women had low back pain at baseline; this pain resolved in three by end of the study. At baseline six women had joint pain, five had muscle pain, and five complained of fascia pain. Highest daily pain and average daily pain scores significantly decreased from baseline to end of study (Figure 3). Lowest daily pain trended to decrease from baseline (1.3 ± 0.9) to end of study (0.7 ± 1; p = 0.05). All women experienced pain during each therapy session except one for which the pain was no longer present after the 5th session.

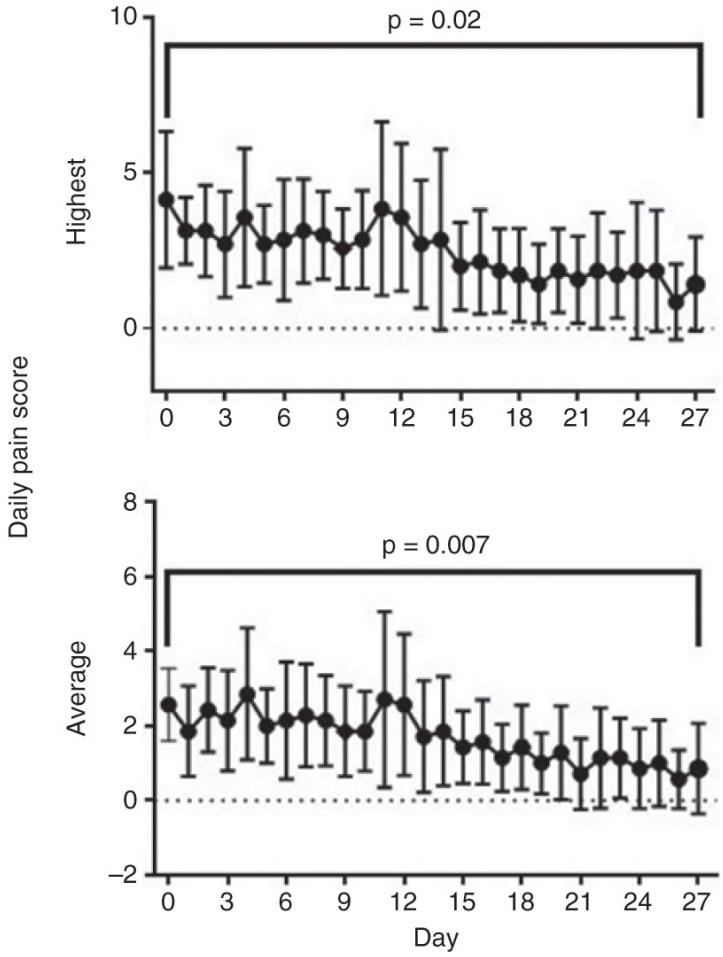

Figure 3: Average daily highest and average pain scores throughout the study for seven women. p-Value compares baseline to end of study.

Bioimpedance

There was no change in weight from baseline (Table 1) to end of study (90.7 ± 18). Muscle mass increased significantly from baseline (47.6 ± 4.6 kg) to end of study (50.7 ± 7.6 kg; p = 0.03). Fat mass trended to decrease from baseline (19.7 ± 3.8 kg) to end of study (17.8 ± 3.4 kg; p = 0.056).

LEFS

Average LEFS score significantly improved from 62 ± 10 at baseline to 73 ± 10 at end of the study (p = 0.002).

BSQ34

The average BSQ34 score did not significantly change from 121 ± 37 at baseline to 127 ± 33 at the end of study.

Questions during SAT therapy

All seven women developed bruising from the SAT therapy, which decreased over the sessions (Figure 4). The bruising was in the neck (n = 1), upper chest (n = 1), upper arms (n = 7), wrist (n = 1), upper abdomen (n = 3), lower abdomen (n = 3), flanks (n = 3), hips (n = 1), front of thighs (n = 5), inner thighs (n = 3), lateral thighs (n = 4), back of thighs (n = 2), above knee (n = 1), under knee (n = 2), front of lower legs (n = 4), back of lower leg (n = 3), inner ankle (n = 3) and outer ankle bone (n = 1). Six women felt ill and four women had itching after the SAT therapy. Three women stated their gastroesophageal reflux worsened, three women felt dizzy, one had diarrhea and one woman had skin tearing requiring zinc oxide use after two initial sessions. Three women had swelling after 75% of SAT therapy sessions (Table 3); the swelling was in the upper arms, front, back and lateral aspect of the thighs and above and below the knee and on the front and back of the lower leg. Six women qualitatively experienced a decrease in their SAT (Table 3). All women stated that the therapist treated deeper into the tissue as sessions continued.

Figure 4: Bruising on the arms at the end of the SAT therapy sessions, A and B represent different participants.

Table 3: Number of women with signs and symptoms and subjective locations of SAT reduction after SAT Therapy sessions.

	Increased	Decreased	No change	NA
Overall body pain	0	7	0	0
Feelings of being tense	0	4	1	2
Fibrotic tissue	0	7	0	0

Skin color (blood flow)	7	0	0	0
Ability to move the skin	6	0	0	1
Loose skin	2	1	3	1
Loose SAT	3	2	1	1
SAT pain	0	5	0	2
Skin smoothness	6	0	1	0
Numb areas of tissue	0	5	0	2
Energy level	5	0	2	0
Leg or arm heaviness	0	5	2	0
Ability to walk easily	5	0	1	1
Muscle pain	0	5	0	2
Joint pain	0	5	1	1
Pain in the veins	0	7	0	0
Back pain	0	4	0	3
Loose clothing	5	0	2	0

Number of women stating SAT reduced or not in areas of the body

	SAT reduced	**SAT not reduced**
Face	5	2
Upper chest	4	3
Front ribs	3	4
Back ribs	2	5
Lower arms	3	4
Wrist	2	5
Upper abdomen	3	4
Lower abdomen	3	4
Flanks	2	5
Hips	2	5
Thighs	3	4
Around knees	5	2
Lower legs	3	4
Ankle	3	4
Feet	1	6

[a]No subcutaneous adipose tissue (SAT) reduction noted by the women for neck, hands, upper arms, fingers, chest under the neck, breasts, or toes.
NA, Not applicable.

Benefits after SAT therapy

After the 12 SAT therapy sessions, four women noted they could feel the shower water temperature in areas that had been numb previous, six noted they were warmer overall or in hands or feet, two experienced horripilation, a reaction that had been absent for some time, and six felt they could move better. Six of seven women stated they had greater range of motion and six felt less like hiding their bodies. Five of the women stated their clothes fit looser after SAT therapy. All seven women stated they could see or feel more of their bones; the bones were on the upper arms (n = 2), lower arms (n = 5), wrist (n = 3), hands (n = 2), fingers (n = 2), chest under neck (n = 3), ribs in front (n = 4), ribs in back (n = 1), hips (n = 3), around the knee (n = 5), back of thighs (n = 1), anterior lower legs (n = 3), posterior back legs (n = 1) and ankle bone (n = 4). None of the women noted increased visibility of bones on the front, lateral or inner thighs, feet or toes. Two women with restless leg syndrome noted improvement after SAT therapy sessions. Six women felt their limbs were lighter after SAT therapy and the same six had greater range of motion. All women stated they would recommend SAT therapy to other women with lipedema.

Discussion

SAT therapy is a unique manual treatment designed to improve all components of soft tissue. Despite the small number of participants in this study, significant benefits were found after 12 sessions over 4 weeks. It should be noted that by experience, 24 sessions are the minimum number required to improve lipedema SAT in women with Stage 1–2 lipedema; more sessions would be required for a woman with Stage 3 lipedema. In addition, additional sessions yearly would be required to maintain benefit.

In this study, SAT tissue improved as the study progressed and was significantly reduced in volume at the end of the study compared to baseline. The quality of SAT tissue significantly improved in the following measures: 1) SAT nodules, a striking feature of lipedema [2], [21], suggesting reduced lipedema tissue; 2) Size of caliper measurements, suggesting the thickness of the SAT reduced; 3) Palpable fibrosis of the tissue, again suggesting an improvement in structure; 4) Bones were qualitatively more visible on the body per the participants; 5) Volume of the legs assessed by tape measure; 6) Fibrosis in the SAT by ultrasound.

The amount of fat in the legs did not significantly decrease by DXA scan suggesting the quality of the tissue changed more than the total amount of SAT. This conclusion is supported by the women being able to feel the therapist treat deeper into their tissue by the end of the study, improvement in the ability to move the skin, and notable improvements in skin color (skin blood flow). There was no difference in the BSQ from the beginning to end of the study again suggesting a change in SAT quality rather than amount during the treatment.

Volume and caliper size were assessed at baseline and before and after the last SAT therapy session to determine if any significant changes were maintained from the preceding treatment rather than demonstrating reduction only after a session had occurred. There was a significant reduction in leg volume before and after the last therapy session, confirming reduction in volume was maintained from the previous therapy sessions. Similarly, there was a significant reduction in caliper measurements before and after the last SAT therapy session supporting a maintenance of improvement in SAT quality.

Skin fluid measurements by dielectric constants were normal at baseline and end of study, and did not significantly change, suggesting normal amounts of fluid in the skin in our subjects before and after SAT therapy. Women with lipedema anecdotally note cold and warm areas of SAT on their bodies; temperature measurements in the tissue were similar at baseline and end of study except on the abdomen and medial knee, therefore our small study group may not have had skin temperature changes experienced by other women with lipedema.

The LEFS significantly improved by the end of the study suggesting lower leg function had improved; no other measures of function were assessed. We suggest that physical function assessments should be completed for interventional studies on lipedema.

Tissue blood flow was not measured directly in this study but all seven women noted improvements in skin color (blood flow) and all five of the women with numbness in their tissue noted improvement. Skin blood flow or oxygenation measurements should be considered for interventional studies on lipedema.

Side effects in the study were common including pain, bruising, and heartburn; follow-up studies can determine if these side effects were persistent or subsided over time. Despite these side effects, all of the women would recommend SAT therapy to women with lipedema.

This pilot study has limitations. The primary limitation is the small sample size due to one therapist providing all treatments in a short period of time. With more therapists trained in SAT therapy, the study could be repeated to allow for additional participants. Another limitation of this study was the small number of sessions per participant, also attributed to the single therapist. The study was also not randomized to compare to other manual therapies (e.g. manual lymphatic drainage). The treatment time is also 90 min which may be longer than standard treatment times allowed. More research in this area may allow for modulation of treatment times. Finally, to fund the therapist's time, subjects paid for session at a discounted rate. This study model has been used successfully previously [22].

Conclusion

SAT therapy significantly improved pain and quality of lipedema SAT. Larger randomized controlled trials are needed in women with lipedema comparing SAT therapy to other manual therapies including manual lymphatic drainage therapy.

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Conflict of interest: Alyna Eekema owns the Quadrivas Clinic & Academy in the Netherlands where she instructs practitioners in SAT therapy, called Quadrivas Therapy.

Informed consent: Informed consent has been obtained from all individuals included in this study.

Ethical approval: The research related to human use complied with all the relevant national regulations and institutional policies, the study was approved by the University of Arizona Human Subjects Protection Program and all women were consented prior to participation to comply with the World Medical Association Declaration of Helsinki regarding ethical conduct of research involving human subjects.

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