

ORIGINAL ARTICLE

Controlled, randomized study evaluating the effects of treating cellulite with AWT[®]/EPAT[®]

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Abstract

Introduction: Cellulite affects 95% of women and can lead to negative consequences. **Objective:** To demonstrate the efficacy and safety of acoustic wave therapy (AWT[®]) using extracorporeal pulse activation technology (EPAT[®]) to manage cellulite. **Methods:** Twenty-five women were included in the study and treated with AWT[®]. Six AWT[®] treatment sessions were performed over the course of 4 weeks. Three thousand pulses were applied to an area measuring approximately 10 × 15 cm on the thigh. The treatment was performed using the D-ACTOR[®] 200 by STORZ MEDICAL AG (Tägerwil, Switzerland). Follow-up visits were performed 1 week and 12 weeks after treatment. Changes in the skin structure were evaluated using the DermaTOP System (Eotech, Paris, France). Skin elasticity measurements were performed using the DermaLab Device (Cortex Technology, Hadsund, Denmark). **Results:** The difference between treated and untreated legs was statistically significant with regard to depressions, elevations, roughness and elasticity after the first follow-up visit. **Conclusion:** The study showed that the AWT/EPAT treatment using the D-ACTOR 200 appears to be a safe and effective treatment alternative for the temporary improvement in the appearance of cellulite.

Key words: Adipose tissue, cellulite, cosmetic application, extracorporeal pulse activation technology

Introduction

Cellulite, although not considered a disease but rather a purely cosmetic problem, affects 95% of women. The cellulite-typical appearance of female skin is caused by the specific structure of the collagen fibre bundles: the fat cell chambers with the surrounding fibre bundles project straight upwards into the corium. The male subcutis, on the other hand, is held together by lattice-shaped tangential fibre bundles. It can sometimes lead to negative consequences, primarily from a psychological point of view (low self-esteem). The pathophysiology of cellulite is complex. Cellulite is a topographical alteration in which the skin acquires an 'orange peel' mattress-like appearance. The pathophysiology involves alterations to the adipose tissue and microcirculation causing fibrosclerosis in the connective tissue. It is a non-inflammatory, degenerative condition, producing alterations to the hypodermis. Anatomically, the cutaneous alterations found in cellulite are largely

due to fibrosis of the connective tissues present in the dermis and/or in subcutaneous fat (1,2). The negatively affected microcirculation may also result in intracellular oedema and reduced lymphatic drainage. Thus, depending on the intensity of these effects, the cellulite can be also classified as fibrotic, oedematous, adipose, or combinatory.

The extracorporeal shock wave technology (ESWT) familiar from lithotripsy fragmentation of kidney or urethral calculi generates high-amplitude acoustic waves of short duration (i.e. 100–1000 bar at ~300 ns). In contrast, extracorporeal pulse activation therapy (EPAT[®]), which is used to relieve muscle aches and pain and temporarily improve localized blood circulation, generates low-amplitude acoustic waves of long duration (i.e. 1–100 bar at 0.2–1.0 ms), or about 1000 times slower than a 'shock wave'. This study applied EPAT for the dermatological/cosmetic application of temporarily reducing the appearance of cellulite. It is known that

metabolism and circulation can be stimulated through the use of acoustic wave therapy (AWT[®]). Neovascularization (the growth of new blood vessels) and increased cell proliferation are proven mechanisms of action of shock and pressure waves. The side effects of acoustic pressure waves tailored to the subcutis are reduced to a minimum; at most, mild pain and a reddening of the skin can be expected during the treatment.

The acoustic wave treatment was evaluated in previous studies demonstrating the beneficial effect on skin appearance and elasticity (3–5). The goal of this study was to demonstrate the efficacy and safety of AWT[®]/EPAT[®] in the management of cellulite. To demonstrate this, we used a clinical evaluation comparing before and after pictures as well as an objective measurement method using a 3D imaging system.

Materials and methods

In this study, treatment was performed using the D-ACTOR[®] 200 by STORZ MEDICAL AG (Tägerwil, Switzerland) (Figures 1 and 2). The D-ACTOR 200 is a vibrating massage system that operates via compressed air to perform pulse activation therapy on targeted muscles and tissues. The system consists of a control unit, a pneumatically driven handpiece with multiple sizes of applicator heads, and a pressurized air source. The pulses are generated ballistically by accelerating a projectile within the applicator, using pressurized air, which strikes a stationary surface (vibration transmitter). The vibration is most efficiently transmitted directly to the targeted tissue using a coupling ultrasound gel. The maximum energy range is 1.4–5.0 bar.

The treatment was performed according to the following protocol.

Six AWT treatment sessions were performed over a period of 4 weeks (approximately two sessions per week). The initial follow-up visit was 1 week after the last AWT session; the second follow-up visit took place 12 weeks after the last AWT session.



Figure 1. The D-ACTOR[®] 200.



Figure 2. The D-ACTOR[®] applicator.

Three thousand pulses were applied to an area of approximately 10×15 cm on the thigh lateral to medial. The maximum well-tolerated energy level of 2.6–3.6 bar at a repetition frequency of 15 Hz was used. No anaesthesia was needed as the procedure is almost painless. Patients only feel a vibrating sensation. A redness of the skin in the treated area is typically observed for 1–2 hours after the session.

3D images of the skin structure were documented as the primary criterion in the study. The secondary criterion was skin elasticity. The DermaTOP System (Eotech, Paris France) (6,7) was used to create the 3D images; skin elasticity was measured using the DermaLab Device (8,9) (Cortex Technology, Hadsund, Denmark).

The 3D skin texture measurements were performed with the DermaTOP system (Eotech), which is based on an optical triangulation and fringe projection technique. The DermaTOP uses multiple gray-code patterns for the optical triangulation technique and four phase-shifted fringe patterns to improve resolution. Gray-code and fringe patterns are deformed by the object to be measured and are analyzed by the camera to compute the X, Y, and Z coordinates for each pixel of the object. Data from the camera image can be analyzed for 3D morphology or 3D surface changes. Profile or surface roughness and wave statistics as well as surface and object volume changes (depressions and elevations) can be computed.

The elasticity measurements were performed using the DermaLab system (Cortex Technology), which is designed to determine the modulus of elasticity. It works on the basis of the stress/strain ratio created under vacuum conditions (0–65 kPa). The measured values are in MPa. With the probe in place, negative pressure will elevate the skin, and the differential negative pressure needed to lift the skin a predetermined distance is used as input to calculate Young's modulus. Two additional parameters are presented to describe the skin elasticity: retraction time (R), elasticity (E) and viscoelasticity (VE), a

parameter combining both the elevation and retraction phase in one number.

Results

Demographic data

Twenty-five female patients were treated on one side of one leg. Their average age was 42.6 years (range 27–63, SD 8.963); their average BMI was 24 (range 17–31, SD 3.436) (Figures 3 and 4). The assignment of the treated leg was randomized with a block size of 5.

Parameters evaluated

The following 3D image parameters were evaluated:

- SPtm: skin roughness parameter from the topography
- NegVol: volume of depressions
- PosVol: volume of elevations.

Figure 5 shows a typical 3D image enhanced with false color for better contrast.

Figures 6 and 7 show examples of typical clinical improvement of the skin texture after the acoustic wave treatment.

Skin elasticity was also measured in the treated area.

Statistical evaluation

As expected for data of cellulite patients, the raw values of the various measurements show large variations, including outliers. In this case, parametric analyses tend to be biased, especially when patient numbers are relatively low, as is the case in this study.

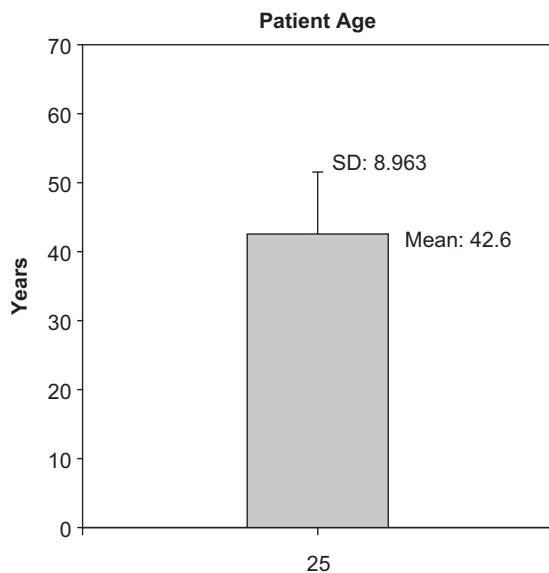


Figure 3. Demographic data: patient age.

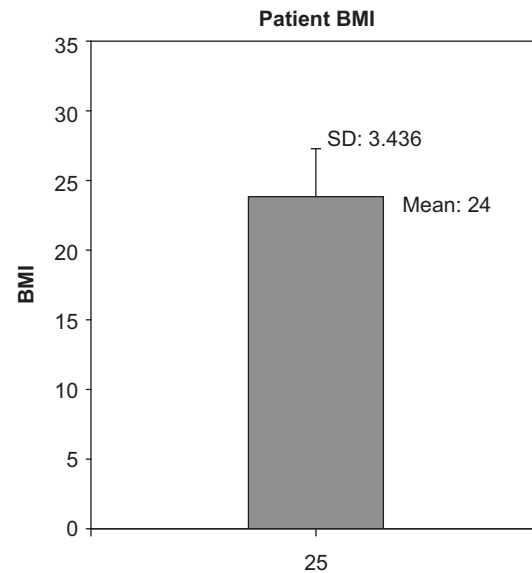


Figure 4. Demographic data: patient BMI.

Thus, a non-parametric approach is preferred in this situation.

As shown in Figure 8, the groups are well comparable at baseline with regard to the full raw scale of the outcome variables, and the effect sizes are near the benchmark of equality. The effect sizes (Mann–Whitney) vary between 0.4718 and 0.4967, indicating only marginal baseline differences between the treated and untreated leg (benchmark for small inferiority = 0.44, equality = 0.5, small superiority = 0.56). In addition, the subgroup of complete pairs has been analyzed for baseline comparability using the Wilcoxon–Pratt test (exact test, gold standard). The results of the paired tests give no indication for baseline group differences (all $p > 0.1$).

In order to reduce the variation and the impact of random factors, various in-depth analyses were performed, including receiver operating characteristics and multivariate cut-off procedures with shifting benchmarks, resulting in the development of robust derivations of the outcome measures of interest.

The most consistent result was achieved by defining a consistent binary response criterion across all outcome variables. Various benchmarks were analyzed for responsivity. A negative change of 20% was found to be the optimal benchmark for dichotomization.

This approach for the cellulite outcome reflects the well-known standardized response measurement in rheumatoid arthritis (RA) trials, defining clinical response in the treatment of rheumatoid arthritis by the application of the 20% improvement benchmark across several relevant outcome criteria, ‘ACR20’ (10).

Since only the results of the first follow-up visit show noteworthy treatment differences (1 week after completion of treatment), the results of the second follow-up (3 months after the last treatment) were not included as part of this analysis.

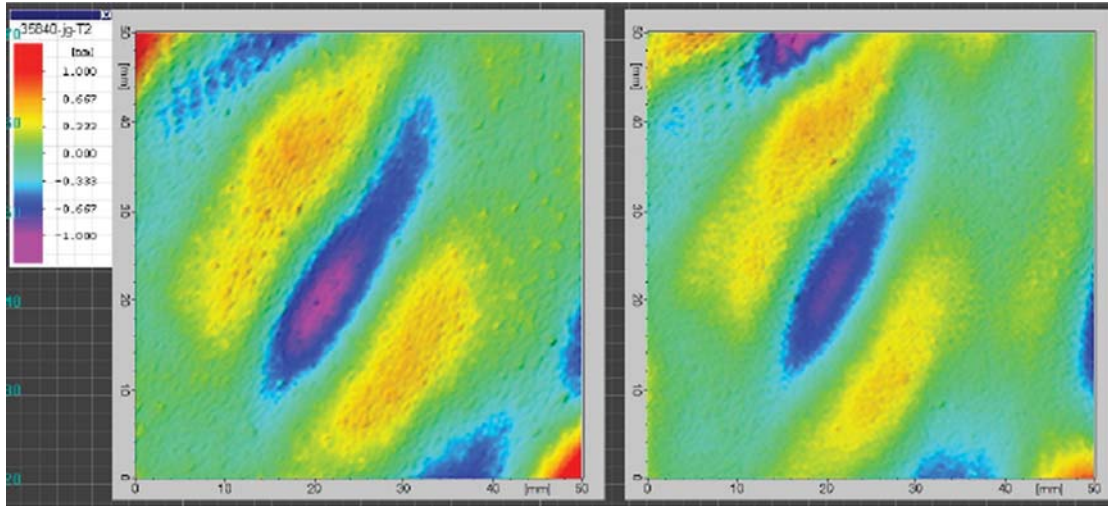


Figure 5. 3D image of the skin structure prior to treatment and at the first follow-up, 1 week after the last treatment session.

Figure 9 shows the percentage of patients who responded in the five relevant outcome variables of interest, as defined below:

- volume of depressions (volume below the negative threshold)
- volume of elevations (volume above the positive threshold)
- roughness parameter from the topography (average peak-to-peak height)
- Young's elasticity (E) modulus
- viscoelasticity (VE) (dividing the elasticity modulus by the retraction time provides a parameter in which both the elevation phase and the retraction phase are taken into account).

Response was defined using the benchmark for success/failure as described above (20% improvement). Each result is based on the available measurement pairs of treated leg ('Treatment') and untreated leg ('Control') at the first follow-up (1 week).

As shown in Figure 10, there are relevant differences between the outcomes of the treated and untreated legs 1 week after baseline (follow-up 1). The percentage of responders and the corresponding p -values of the tests for marginal homogeneity are summarized below.

Response rates (treated vs untreated leg):

- Depressions response 50.0%, treated leg vs 20.0%, untreated leg, $p = 0.0160^a$
- Elevations response 55.0%, treated leg vs 15.0%, untreated leg, $p = 0.0021^a$
- Roughness response 30.0%, treated leg vs 5.0%, untreated leg, $p = 0.0371^a$
- Elasticity response 33.3%, treated leg vs 5.6%, untreated leg, $p = 0.0348^a$
- Viscoelasticity response 16.7%, treated leg vs 11.1%, untreated leg, $p = 0.6529$.

(^astatistically significant)

Superiority is observed for the group of treated legs with regard to all analyzed outcome criteria.



Figure 6. AWT treatment. Clinical picture: (A) pretreatment and (B) 1 month after the last treatment.



Figure 7. AWT treatment. Clinical picture: (A) pretreatment and (B) 1 month after the last treatment.

With regard to depressions, elevations, roughness and elasticity, the difference between treated and untreated legs is statistically significant (2×2 contingency table, two-sided test for marginal homogeneity, $\alpha = 0.05$). With regard to viscoelasticity, the result is not statistically significant.

In addition to the single response variables, an overall responder index was calculated combining the five single results to a composite index (0 = no response in any outcome, 5 = response in all five outcome variables, response definition as described above). This procedure is recommended by the ICH E9 Guideline and usually leads to less variance and higher responsiveness.

Figure 10 shows the result of the cumulative analysis of the composite index for overall response (complete pairs only, values for both legs available).

Response in at least one cellulite outcome criterion was achieved in 75.0% of the treated legs as compared to only 25.0% of the untreated legs (corresponding to a difference in response rates of

50.0% in favour of the test treatment). Response in at least two out of five cellulite outcome criteria was achieved in 62.5% of the treated legs as compared to 12.5% of the untreated legs (corresponding to a difference in response rates of 50.0% in favour of the test treatment).

The difference between the two treatments with regard to the ordinal scale of overall success is statistically significant ($p = 0.0002$, contingency table with ordered categories, two-sided test for marginal homogeneity, $\alpha = 0.05$).

In addition to the test of marginal homogeneity, the precise Wilcoxon–Pratt test (gold standard) was performed for the overall response scale (composite index), resulting in $p = 0.0127$ (two-sided). Again, the overall response shows a statistically significant group treatment difference.

We did not see any complications, except immediate redness following the session, as already mentioned. The pain is minimal, except if treatment is performed on bony areas, which should be avoided.

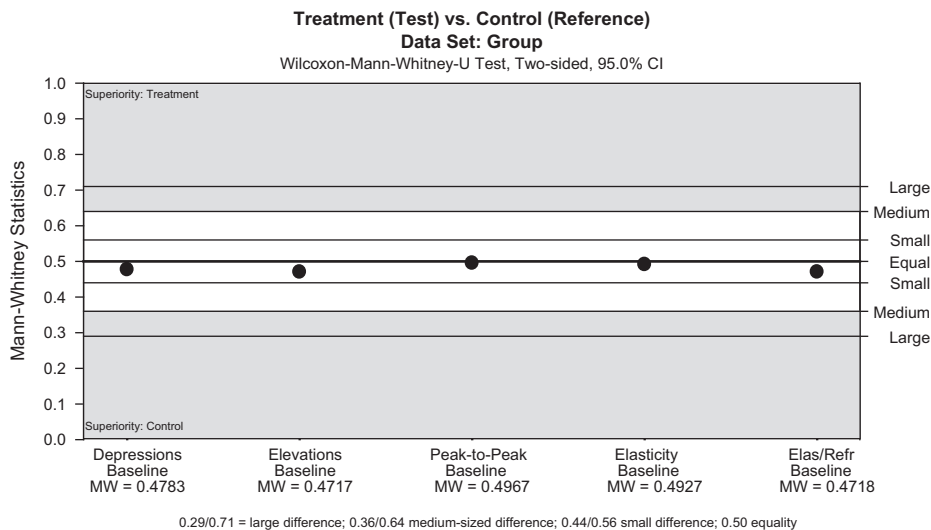


Figure 8. Baseline for treatment group versus control group.

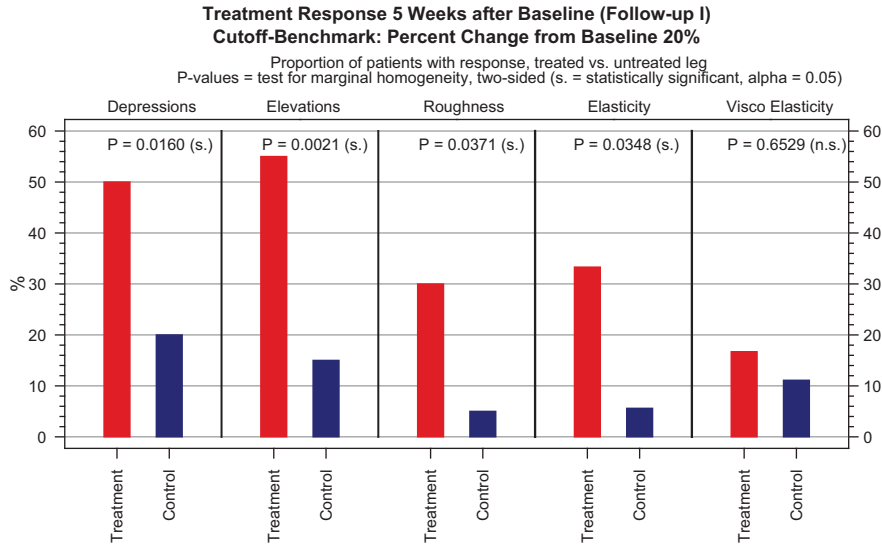


Figure 9. Treatment response 1 week after last treatment (follow-up 1).

Discussion

The EPAT investigation was designed as a single-centre controlled clinical study. An untreated control area was used in order to evaluate the clinical value of EPAT in cellulite patients. The use of a control made it possible to discriminate between real treatment effects and the improvement of symptoms not caused by EPAT. The patients served as their own controls. Only one leg was treated, the other one served as reference. The treatment was performed using a D-ACTOR 200. In six treatments, an area of approximately 10 × 15 cm was treated with a median energy level of 3.4 bar and 15 Hz. The measurements from 3D topography scans showed that depressions can be reduced when

treated with AWT. There is a statistically significant improvement between the treated and untreated sides for the volume parameters (elevations and depressions), as well as for the roughness parameter after the treatment period (1-week follow-up). At the 3-month follow-up, while the treated legs maintained improvement, the untreated legs matched the improvement of treated legs, suggesting a systemic treatment effect.

The skin elasticity results show an obvious positive improvement after the treatment. The improvement in the skin elasticity value *E* was statistically significant, while the viscoelasticity value *VE* tended toward improvement; the improvement was not statistically significant.

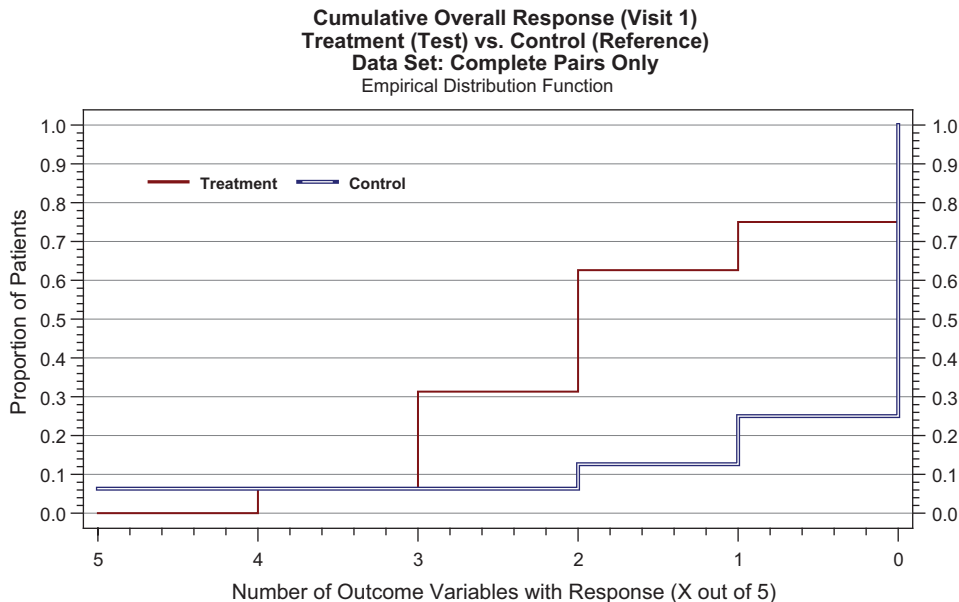


Figure 10. Cumulative overall response: complete pairs only.

In summary, cellulite treatment with EPAT results in statistically significant temporary improvement in skin texture and elasticity. No side effects were observed.

Conclusions

The purpose of this study was to investigate the safety and efficacy of AWT in treating the cosmetic appearance of cellulite under controlled, standardized treatment and follow-up conditions.

Patients clearly benefit from a reduction in the appearance of cellulite using acoustic wave therapy (AWT) 1 week after the last treatment (follow-up 1). The observed differences between treated and untreated legs are considerable with regard to the visual parameters of dimples (elevations and depressions), skin roughness, and skin elasticity.

This study demonstrates that AWT with the D-ACTOR 200 improves the visual appearance of cellulite in the gluteal-femoral region. While this study focused on the cosmetic effects of EPAT, it is theorized that the results achieved by acoustic wave stimulation may have resulted in improved lymph-drainage and microcirculation within the tissue. At follow-up 2 (3 months after the last treatment), the result was not only maintained, but the treated leg showed even further improvement. EPAT treatment with the D-ACTOR 200 appears to be a safe and effective treatment alternative for temporary improvement in the appearance of cellulite.

Declaration of interest: P. Novak and A. Krotz are employees of STORZ Medical.

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