

# Can cellulite be treated with low-energy extracorporeal shock wave therapy?

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**Abstract:** The present study investigates the effects of low-energy defocused extracorporeal generated shock waves on collagen structure of cellulite afflicted skin. Cellulite measurement using high-resolution ultrasound technology was performed before and after low-energy defocused extracorporeal shock wave therapy (ESWT) in 21 female subjects. ESWT was applied onto the skin at the lateral thigh twice a week for a period of six weeks. Results provide evidence that low-energy defocused ESWT caused remodeling of the collagen within the dermis of the tested region. Improving device-parameters and therapy regimes will be essential for future development of a scientific based approach to cellulite treatment.

**Keywords:** cellulite (gynoid lipodystrophy), collagen structure of dermis, collagenometry high-resolution ultrasound of skin, low-energy defocused extracorporeal shock wave therapy (ESWT), septa of subcutaneous connective tissue

## Introduction

### Extracorporeal shock wave therapy (ESWT)

Shock waves appear in the atmosphere when explosive events such as lightning strikes occur. These are audibly perceived as loud “bangs”. They transmit energy from the place of generation to distant areas which may cause window panes to shatter. Shock waves are presented by a single, mainly positive pressure pulse of large amplitude that is followed by comparatively small tensile wave components (Wess 2006). When using shock waves for therapy, effects that make the pressure pulse even steeper due to nonlinearities in the propagation medium as well as phenomena such as refraction and diffraction at acoustic interfaces have to be taken into consideration. Besides mechanical effects such as fragmentation of brittle material on acoustic interfaces (ie, glass/air or kidney stone/surrounding tissue), cavitation bubbles (Wolfrum et al 2003) are generated in the propagation medium (ie, water or elastic body tissue), which in turn causes needle-like punctures (ie, leading to stimulating effects such as the generation of action potentials of nerve cells).

High-energy extracorporeal generated shock waves in which mechanical energy is transformed from electrical energy by the piezo-effect were first used therapeutically for kidney stone fragmentation (Haeussler and Kiefer 1971; Hoff and Behrend 1973). Extracorporeal shock wave therapy (ESWT) is now well established and is used more than 90% world wide, as the principal method for treating kidney and urethral stones. Extracorporeal generated shock waves are a means of bringing therapeutically effective energies to locally limited places in the body in a non-invasive way. The fact that shock waves selectively effect acoustical interfaces (connecting two media, each with a different density, eg, oil/water or stone/tissue) and pass through homogenous elastic tissue without damage to the most part is medically important. The damage outside of the treatment zone is almost completely avoided due to the possibility of concentrating energy through focusing.

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The stimulating effect of low-energy defocused extracorporeal generated shock waves on biological processes within the tissues reached has increasingly become the centre of interest in the last few years. The biological mechanism of action after a shock-wave (ie, after the ultra-short physical stress and strain) is still unknown to large extent. It appears that the principle of action is so universal that a multitude of very different indications like musculoskeletal diseases (calcaneal spur, tennis-elbow, golf-arm, lime-shoulder) (Wang et al 2006), orthopedics (pseudarthrosis) (Siebert and Buch 1997), chronic skin lesions (ulcus cruris) and burnings (Sparsa et al 2005; Schaden et al 2006) respond positively to shock wave therapy. Biological reactions of liberation of different agents (measured by immunohistochemistry) such as VEGF (vascular endothelial growth factor), eNOS (endothelial nitric oxide synthase) and PCNA (proliferating cell nuclear antigen) are reported (Wang et al 2006). Shock waves are also effective as a means to increase local blood circulation and metabolism. These effects are considered responsible for final healing. Additionally ESWT seems to have a high anti-bacterial effect. Because of these diverse effects we tested low-energy defocused ESWT for treatment of cellulite.

### Cellulite: the patho-physiology, evaluation and treating-attempts

Cellulite (gynoid lipodystrophy) (Rossi and Vergnanini 2000; Avram 2006; Pavicic et al 2006), the aesthetically disturbing (according to modern taste) dimpling of the skin commonly occurs on the thighs and buttocks affecting most post-adolescent woman of all races. Incipient cellulite is recognized by an “orange peel” aspect while full blown cellulite is characterized by a dimpled skin surface. Cellulite is uncommon in men, the majority of those affected also suffer androgen-deficiency disorders such as Klinefelter-syndrome, hypo-gonadism or cirrhosis (alcoholic liver disease, see ie, *Drunken Bacchus* by Rubens (1577–1640)). While not potentially hazardous to health (Smith 2002) and even considered normal based upon its frequency of occurrence, cellulite remains nonetheless, an issue of cosmetic concern and may induce negative psycho-social side-effects in those suffering its consequences on their appearance.

The patho-physiology of cellulite is understood today as being gender-specific to female skin (Müller and Nürnberger 1972; Nürnberger and Müller 1978; Scherwitz and Braun-Falco 1978; Quatresooz et al 2006). Based upon anatomy and histology of skin Nürnberger and Müller formulated a scheme for development of cellulite (see Figure 1). In skin of men the

septa of subcutaneous connective tissue are thick, parallel to the surface and criss-crossing, causing the polygonal fat-cell chambers to be small. In contrast, in skin of women the septa of the subcutaneous connective tissue are thin, perpendicular to the surface resulting in formation of large standing fat-cell chambers. In subjects with high BMIs, the fat-cell chambers herniate into the corium forming papillae adiposae, which aggravate the dimpling appearance of cellulite, causing protrusions and pits (Pierard et al 2000).

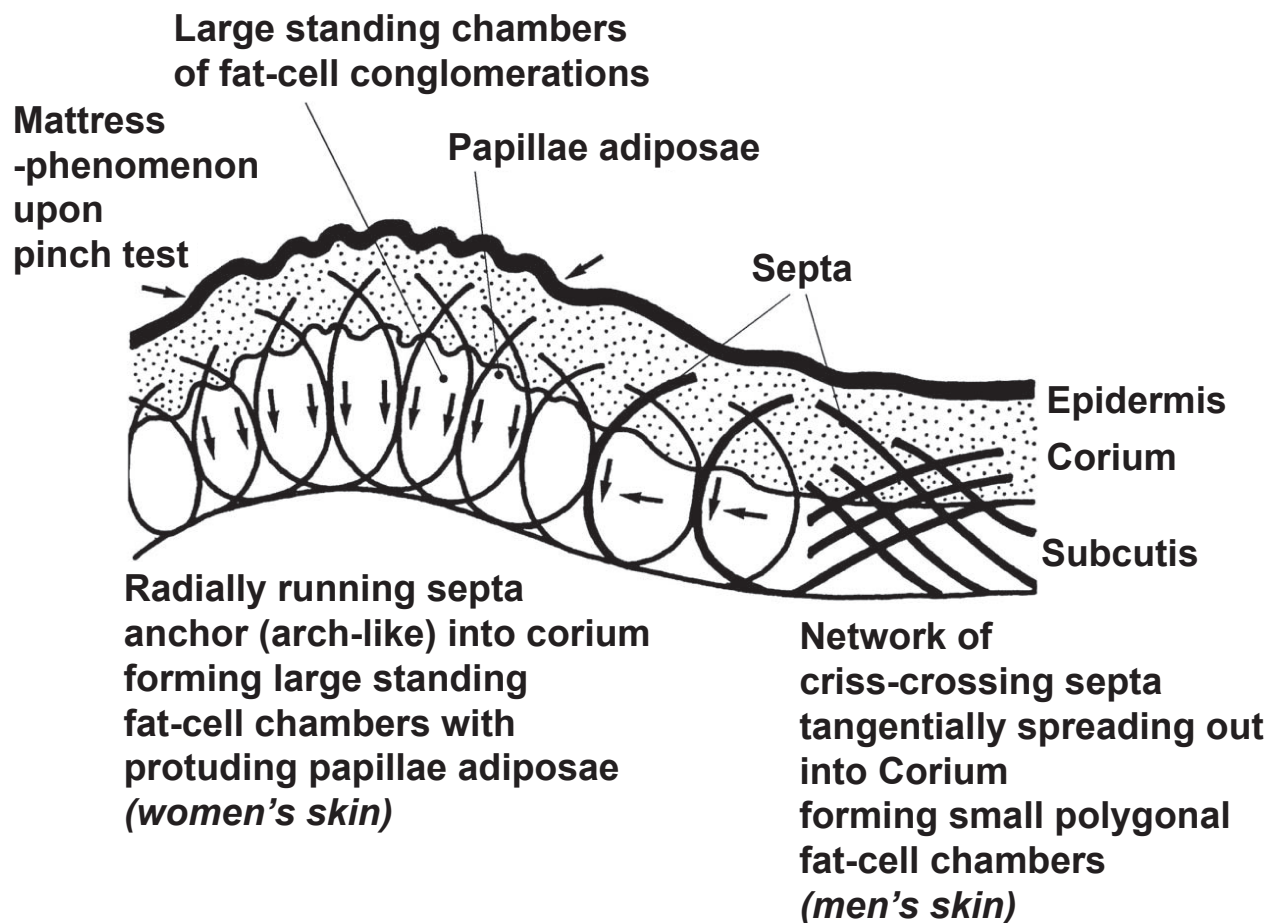
Incipient cellulite recognized by an “orange peel” appearance represents focally enlarged fibro-sclerotic strands partitioning the hypodermis and limiting the out pouching of fat lobules. In contrast, full blown cellulite recognized by a dimpled skin surface represents subjugation of the hyper-trophic response of the hypodermal connective tissue strands when the resistance is overcome by progressive fat accumulation that protrudes into the lower reticular dermis. A simple grading-score of cellulite by inspection (Table 1) was given by Nürnberger and Müller (1978).

Other attempts to describe the etiology of cellulite include:

- The deterioration of dermal vasculature (alteration of the pre-capillary arteriolar sphincter) causing edema and tissue hypoxia with thickening and sclerosis of the fibrous septa (Lotti et al 1990; Curri 1993) and
  - The chronic inflammatory processes with diffuse infiltration of macrophages and lymphocytes into the fibrous septa (Draelos and Marenus 1997; Kligman 1997).
- Evaluation of therapeutic interventions for cellulite is made difficult by secondary confounding factors such as change of diet and exercise. Also, standard criteria for assessment treatment responses are lacking from the literature. Some practitioners utilize thigh measurement and photography to assess improvement, but these methods are not precise (Gherardini et al 1997). Currently, the best objective standardized methods for accurately assessing cellulite treatment outcomes are:
- Three dimensional skin surface topography (3-D-SST) by Laser (Smalls et al 2005),

**Table 1** Grading of cellulite

Definition	Grade
• Smooth surface of skin while lying down and standing.	0
• Wrinkles upon pinch-test.	
• Smooth surface of skin while lying down and standing.	1
• Mattress-phenomenon upon pinch-test.	
• Smooth surface of skin while lying down.	
• Mattress-phenomenon spontaneously while standing.	2
• Mattress-phenomenon spontaneously while standing and lying down.	3



**Figure 1** Schema representing the gender difference of the inner structure of skin and subcutaneous tissue. Modified from Müller and Nürnberger (1972).

- Collagenometry with HF-ultrasound at skin (Tikjob et al 1984; Rosenbaum et al 1998; Mole et al 2004),
- MRI imaging of the subcutaneous adipose tissue (Querleux et al 2002; Mirrashed et al 2004) and
- Histology.

In addition to “exercise and weight loss” which require determined personal commitment there are currently no scientifically proven treatments for cellulite, except perhaps for two active substances, caffeine and retinol, applied topically and endermology, a motorized, rhythmic folding-unfolding and suction technique of the panniculus adiposus that make the skin more smooth (Draelos and Marenus 1997; Pierard-Franchimont et al 2000; Bertin et al 2001; Rao et al 2004; Alster and Tanzi 2005; Alster and Tehrani 2006; Smalls et al 2006). Most of the putative evidence for efficacy of the many claimed treatments is anecdotal, subjective or non-existent (Lis-Balchin 1999; Hexsel and Mazzuco 2000; Sainio et al 2000; Sadick and Mulholland 2004; Rotunda et al 2005).

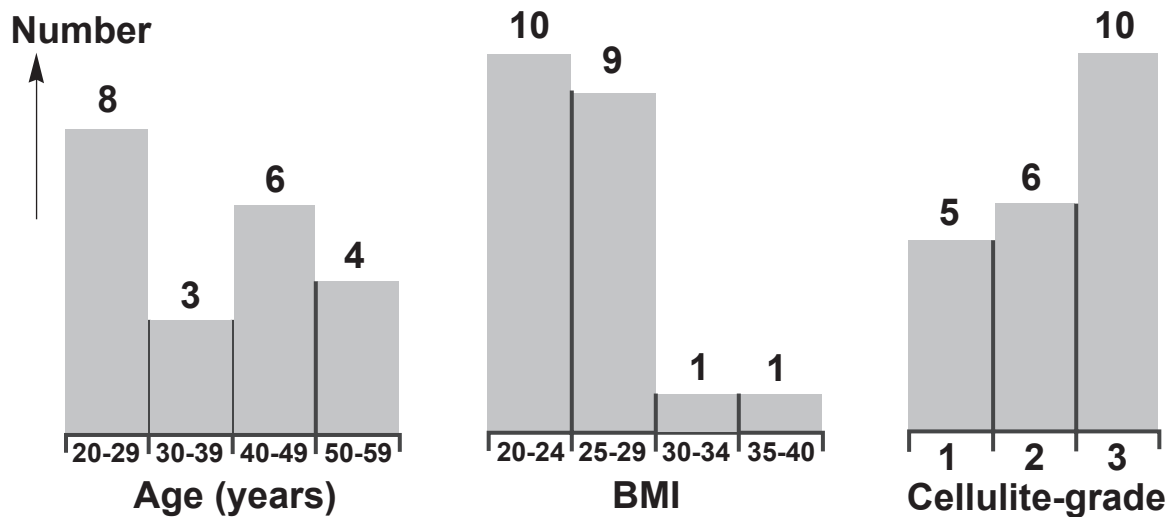
Low-energy defocused ESWT is a new approach for cellulite treatment. It represents an easy to handle, non-invasive,

side effect free, local therapy type with short application periods. Siems et al (2005) found increased concentrations of serum malondialdehyde (MDA) and plasma protein carbonyls in cellulite patients with edematous and lipid enriched dermis resulting from oxidative stress. Concentrations of both these substances decreased after application of ESWT with or without complex physical decongestive therapy (CPDT). Also lipid peroxidation products were released demonstrating the sclerosis-preventing effect of ESWT and/or CPDT (smoothing of dermis and hypodermis). Expression of factors stimulating angiogenesis and lymphangiogenesis was not induced by ESWT and/or CPDT (Siems et al 2005).

## Methods and human resources

### Criteria for inclusion and exclusion of subjects

21 female, non-pregnant, healthy test persons of age between 20 and 60 years with cellulite parameters were selected to participate in the study (Figure 2). Exclusion criteria related to health status were:



**Figure 2** Human resources: distributions of 21 female test persons. Left: histogram for age, middle: histogram for body mass index (BMI), right: histogram for grading of cellulite according to Table 1.

- Disease of the skin,
- Thrombosis or post-thrombosis syndrome,
- Known malignoma or chemotherapy,
- Anti-coagulation therapy,
- Cortisone-therapy,
- Known metabolic disorder (ie, diabetes-mellitus, hypercholesterinemia etc.),
- Inflammation within treatment area and
- Other simultaneous treatment of cellulite.

The giving of informed consent was required of subjects undergoing treatment.

### High-resolution ultrasound of the skin

The high-resolution ultrasound of the skin represents an imaging-producing and non-invasive diagnostic tool, which is able to give an exact representation of the skin and its adnexa. The ultrasound system (Collagenoson<sup>®</sup>) used in this study included a probe of 22 MHz (yielding a high-resolution axial of 50  $\mu$ m, lateral of 200  $\mu$ m and a depth of 6 mm) that was placed upon wet skin. It measured the micro-structure of the mesenchymal connective tissue and the collagen structures within the extracellular matrix of the dermis (collagenometry), showing both the epidermis and the boundary between dermis and sub-cutis. With this device the structure and the quality of the collagen and thus the result of therapy could be exactly evaluated.

### Application of ESWT and device-parameters

The low-energy defocused ESWT was applied according to the following parameters:

- ActiVitor-Derma<sup>®</sup> (shock waves are produced by electro-hydraulic means) with ActiVitor Probe D0 corresponding to a depth of entrance of 5 mm and surface focus of 25 mm times 25 mm,
- Energy flow density per shot set at 0.018 mJ/mm<sup>2</sup>,
- Skin of lateral left and right thigh treated with 40000 shots onto surface of 160 cm<sup>2</sup> per side (shots homogenously distributed by partitioning 160 cm<sup>2</sup> into 8 times 5 squares of 4 cm<sup>2</sup> with 100 shots per square).

### Course of study

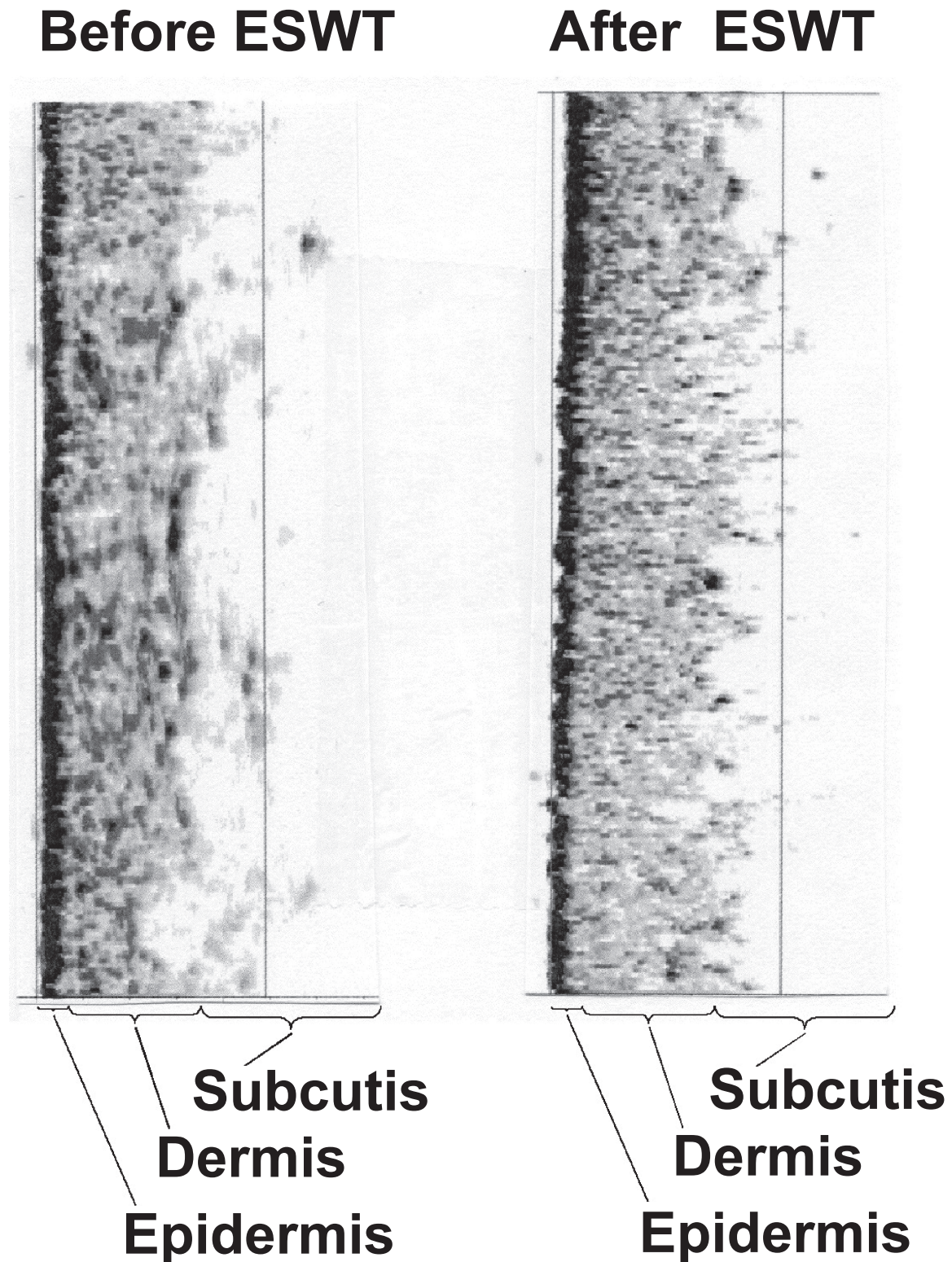
Collagenometry was carried out before and after low energy defocused ESWT to selected areas of the skin of the thighs (latero-posterior) twice a week during a treatment period of 6 weeks. At the end of the treatment period (equivalent to 96000 shots per person) a questionnaire was filled out concerning the tolerance (pain and side effects) and the subjective outcome of cellulite.

### Analysis of the image from high-resolution ultrasound

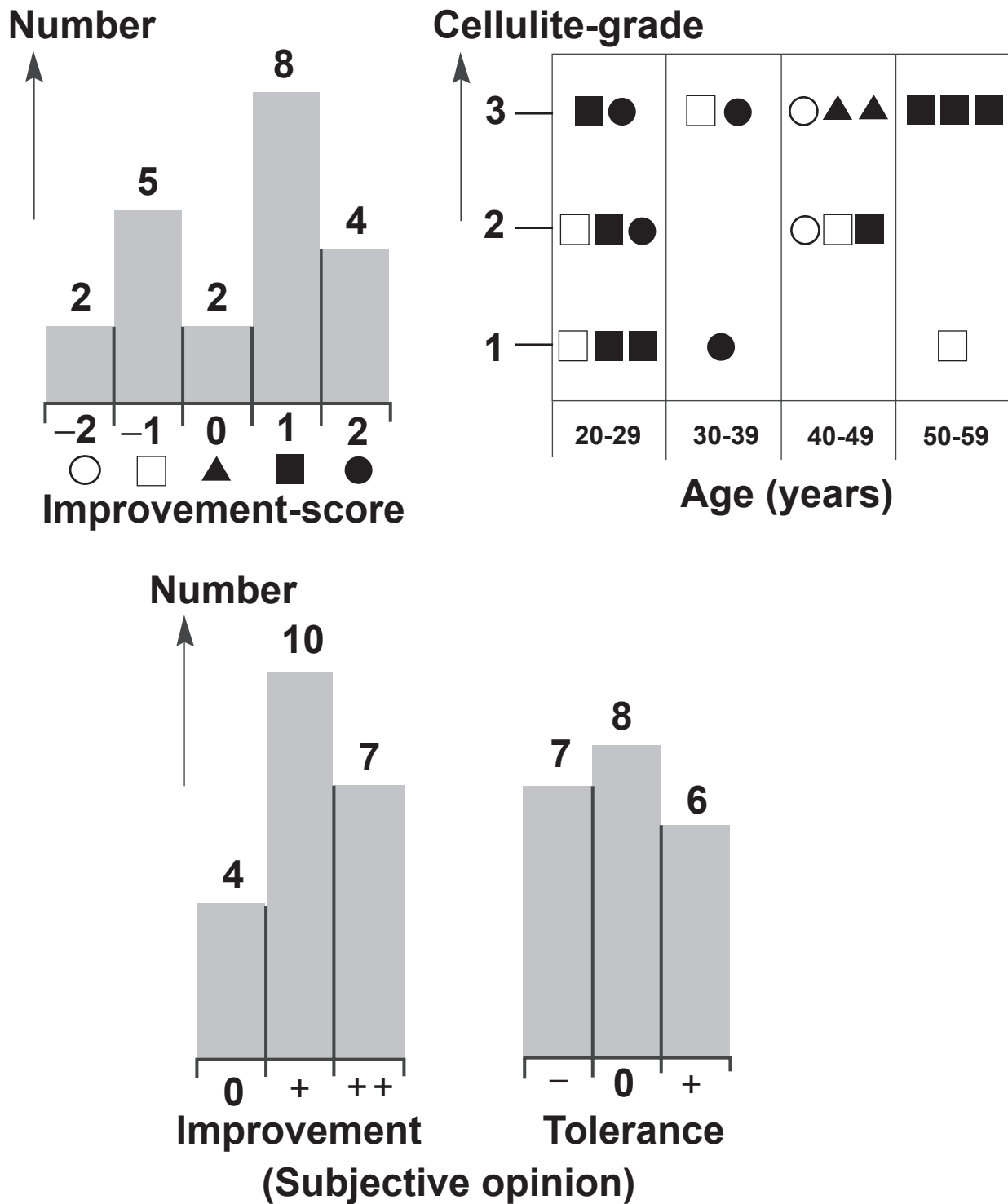
A remodeling of collagen within the dermis can be imaged by collagenometry (Figure 3). Dividing the dermis into the side to the epidermis and into the side to the sub-cutis and analyzing the change in the distributions of each side the following rating scale was used:

- -1: a change to more irregular,
- 0: no change,
- 1: a change to more regular

These scores are summed to determine the outcome (Figure 3, case with a total score of 2).



**Figure 3** Collagenometry (Collagenoson®) taking high-frequency high-resolution ultrasound measurements of the extra-cellular matrix of the skin before and after treatment with low energy defocused extracorporeal shock wave therapy (ESWT). Case of improvement-score of +2 (clear improvement). Both ultrasound samples taken from the treated area. Determination of improvement-score: dividing the dermis into the side to the epidermis and into the side to the sub-cutis and analyzing the change in the distributions of each side (-1: change to more irregular, 0: no change, 1: change to more regular).



**Figure 4** Results: distributions of 21 female test persons. Upper left: histogram for improvement score (see Figure 3, -2 (○): clear worsening, -1 (□): worsening, 0 (▲): no change, +1 (■): improvement, +2 (●): clear improvement) from collagenometry (Figure 3). Upper right: improvement score as function of age and cellulite-grade. Lower left: histogram for subjective opinion 0: no improvement, +: little improvement, ++: good improvement (smoothing of skin and more stretched). Lower right: histogram for low energy defocused ESWT tolerance -: negative tolerance (not suitable, some pain), 0: indifferent, +: tolerance positive tolerance (suitable, no pain).

## Results

The above improvement-scoring procedure analyzing changes in the microstructure of the skin by collagenometry is presented in Figure 4 (upper part). The data indicate that low-energy defocused ESWT may be effective in treating cellulite by remodeling collagen within the skin. From this small sample of test persons we cannot conclude that there are differential effects of treatment based upon age or cellulite stage.

Questionnaire responses are summarized in Figure 4 (lower part). Most subjects reported an improvement of the skin treated. Seven reported a clear improvement (cellulite reduction, skin more tight, finer fabric of skin and underlying tissue). A few subjects reported that treatment was unacceptable because it caused some pain. After two months the subjective evaluation of effects on the locally treated skin was reevaluated. At that time six test persons reported an improvement (cellulite reduction, skin more tight, finer fabric of skin and underlying tissue) after a delay of 2–4 weeks (an effect well known in treatment of calcaneal spurs by ESWT). Ten subjects did not identify any local change since the end of treatment. Five subjects reported a re-occurrence of cellulite. The therapist who applied ESWT complained that the sound associated with treatment was irritating and required ear protection.

## Discussion and conclusion

The results of this study suggest that low-energy defocused ESWT is effective in treating cellulite through the remodeling of skin collagen. This effect can be corroborated by measuring the microstructure of the skin using high frequency ultrasound (Collagenoson®) as well as by the subjective comments of the subjects. The data also suggest that improvement from treatment may have a latent period of from 2 to 6 months. It may also be possible that successful cellulite treatment will result from low-energy defocused ESWT using higher energy flow density, ie, more than 0.018 mJ/mm<sup>2</sup>. Alternative wrapping of the machine to protect patients and therapist from too loud sound exposure is also suggested as well as different techniques for applying the low-energy defocused ESWT to make it more suitable, eg, whole-body skin treatment under water in an ordinary bath tub by low-energy unfocused (plane-wave) ESWT.

Further investigation is needed to determine whether a scientific based therapy concept for cellulite can be developed by optimizing device-parameters such as the applied energy flow density and the shape of focus as well as therapy regimes, age and cellulite grade specific parameters. Depending upon

the outcomes of these investigations, low-energy defocused ESWT may become one of the few evidence-based therapies for future clinical management of cellulite.

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