Lasers in Medical Science (2024) 39:120
https://doi.org/10.1007/s10103-024-04068-1

REVIEW ARTICLE

Does electrophysical agents work for cellulite treatment? a systematic review of clinical trials

Cláudia Longano[1] · Carly de Faria Coelho[2] · Sandra Alencar Buslik[1] · Cicelina Foguel[1] · Camila Katsuragi[1] · Patrícia Sardinha Leonardo[3] · Rodrigo Álvaro Brandão Lopes-Martins[1,2]

Received: 31 May 2023 / Accepted: 24 April 2024

Abstract
Cellulite, a perceived alteration in skin topography, is predominantly found in adipose tissue-rich body regions such as the hips, buttocks, thighs, and abdomen. Contrary to common belief, the etiology and pathophysiology of cellulite are not well-established or universally agreed upon. This lack of understanding about the actual etiology of cellulite directly influences the selection of suitable treatments that can address both the aesthetic and inflammatory aspects of the condition. Various treatment methods, including electrophysical agents like electric currents, radiofrequency, ultrasound, and photobiomodulation, have been tested. However, the questionable methodological quality of many studies complicates the determination of effective treatments for cellulite. In this study, we conducted a systematic review of clinical studies that utilized electrophysical agents in cellulite treatment. Methods: We employed the PICO (population, intervention, control, and outcome) process to develop our search strategy and establish inclusion/exclusion criteria. We searched five databases: Medline, Central, Scopus, Lilacs, and PEDro, for studies conducted between 2001 and July 2021 that involved cellulite treatment with electrophysical agents. To ensure systematicity and guide study selection, we adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. Results: Our initial search yielded 556 articles: 379 from Medline, 159 from Central, and 18 from Lilacs. After applying our inclusion criteria, only 32 studies remained. Of these, only two (6.2%) were evaluated as having strong and good methodology via the QualSyst tool. Conclusions: Our findings indicate that the quality of evidence from clinical studies on the use of electrophysical agents for cellulite treatment remains subpar. Further studies with robust experimental designs and more precise assessment techniques are necessary. While our study does not refute the effectiveness of the techniques used for cellulite treatment, it underscores the need for additional well-designed trials.

Keywords electrophysical agentes · cellulite · esthetics · laser therapy · radiofrequency · ultrasound

Introduction

The preoccupation with physical appearance and the relentless pursuit of body image satisfaction have emerged as significant areas of interest in contemporary society. This is largely due to the beauty standards propagated by the media. However, various skin disorders, including gynoid lipodystrophy, commonly referred to as cellulite, can lead to body dissatisfaction. Cellulite is a perceived change in skin topography, predominantly found in areas abundant in adipose tissue such as the hips, buttocks, thighs, and abdomen [1].

Contrary to popular belief, the etiology and pathophysiology of cellulite remain far from consensus or well-established understanding. Despite the extensive array of scientific articles exploring various treatment

✉ Rodrigo Álvaro Brandão Lopes-Martins
ralopesmartins@gmail.com

1 Bioengineering – Universidade Brasil, Rua Carolina Fonseca 235, Itaquera, São Paulo, SP, Brasil

2 Laboratory of Biophotonics and Experimental Therapeutics, Universidade Evangélica de Goiás, Unievangélica. Av. Universitária Km 3,5, Anápolis, Goiás, Brasil

3 Laboratório de Tecnologias Em Saúde, LATES, Universidade Evangélica de Goiás, Unievangélica. Av. Universitária Km 3,5, Anápolis, Goiás, Brasil

types, our knowledge about the actual causes and pathophysiology of cellulite remains limited.

The classification of this condition, which remains widely used today, primarily depends on its mattress phenomenon [2], colloquially referred to as an orange peel [1, 3] or cottage cheese-like appearance [4]. This is characterized by dimples in the skin. In grade 1, there are no signs of the orange peel appearance when the person is either standing or lying down. The orange peel aspect only becomes apparent after a pinch test. In Degree 2, the orange peel aspect spontaneously appears only when the woman is standing, but not when lying down. In Degree 3, the orange peel phenomenon is evident even when the woman is in a resting position [2].

While many authors regard cellulite as merely an aesthetic, gender-related disorder due to the orientation of fibrous septa [2, 5, 6], affecting 80 to 90% of post-pubescent women worldwide [7], we propose a different perspective. Given that the pathophysiology of cellulite is not well-established [8], we posit that it is, in fact, a gender-related inflammatory disease. This view aligns with the findings of other researchers. The classification of cellulite as an inflammatory disease is supported [4, 9–11] due to the signs and symptoms it induces, such as edema, pain, fibrosis, and temperature enhancement. These symptoms are particularly pronounced in severe cases of cellulite, as evidenced by infrared thermography [12].

Understanding the pathophysiology of the "orange peel" phenomenon is crucial for advancing scientific knowledge in both invasive and non-invasive treatments for cellulite. These treatments, which are currently being explored, include anti-cellulite cosmetics containing active ingredients that break down fat, surgical procedures, and electrophysical agents [1]. The latter is the primary focus of this study.

Although cellulite is a characteristic found in most women, it can have both physical and emotional effects, particularly on young women, thereby impacting their quality of life [13]. Despite the expansion of the aesthetic industry and concerted efforts to align treatments with scientific advancements, Auh et al. (2018) [14] highlighted a concern in their systematic review. They noted a lack of consistent methodology for quantifying non-invasive fat reduction across all the studies analyzed.

The objective of this systematic review is to evaluate the methodological quality of various types of studies conducted over the past 20 years. These studies have assessed the appearance of cellulite following treatment with one or more electrophysical agents.

Methods

Design

Cellulite is a prevalent topic in the field of aesthetics, primarily because it is viewed as a significant cosmetic concern among women [1]. This perception has led to the use of various electrophysical agents aimed at treating this condition, thereby enhancing beauty and, consequently, boosting self-confidence and self-esteem. Numerous studies have been conducted to evaluate the effects of these electrophysical agents on cellulite treatment. However, the question arises: are the methodologies employed in these studies sufficiently well-designed to provide evidence-based healthcare in routine clinical practice?

To address this query, we conducted a systematic review to evaluate the methodological quality of studies published over a span of 20 years.

Search strategy

Four databases, namely Medline/Pubmed and BVS, Central/Cochrane Library, Lilacs/BVS, and PEDro, were utilized to source studies conducted between 2001 and July 2021. These studies focused on the treatment of cellulite using electrophysical agents.

The PICO process, which stands for population, intervention, control, and outcome, was utilized to formulate the search strategy and establish the inclusion/exclusion criteria [15].

The following keywords and MeSH terms were utilized, combined using Boolean operators as follows: ("cellulite" OR "gynoid lipodystrophy" AND "treatments" AND NOT ("medication" OR "Drugs" OR "pharmaceuticals") AND NOT "surgery"); ("cellulite" OR "gynoid lipodystrophy" AND "low-level light therapy"); ("cellulite" OR "gynoid lipodystrophy" AND "intense pulsed light therapy"); ("cellulite" OR "gynoid lipodystrophy" AND "phototherapy"); ("cellulite" OR "gynoid lipodystrophy" AND "infrared rays"); ("cellulite" OR "gynoid lipodystrophy" AND "electrical stimulation therapy"); ("cellulite" OR "gynoid lipodystrophy" AND ("ultrasound" OR "ultrasonic waves" OR "low-intensity pulsed ultrasound")); ("cellulite" OR "gynoid lipodystrophy" AND ("high-energy shock waves" OR "radio waves")); ("cellulite" OR "gynoid lipodystrophy" AND "radiofrequency").

In order to maintain systematic integrity and guide the selection of studies, we adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines [16].

Selection criteria

Inclusion criteria

This systematic review included all types of peer-reviewed studies, specifically white literature, that presented results of cellulite treatment:

in women aged between 15 and 59 years,
with any electrophysical agent such as, laser, LED, ultrasound, radiofrequency, Infrared light and pulsed magnetic field device and mechanical tissue manipulation device, and.
articles written in English, Portuguese, Spanish, or French.

Exclusion criteria

This review excluded articles:

involving animals experimentation,
involving men,
involving treatments with medications, cosmetics, or other active principles,
involving elderly women, i.e., ≥ 60 years,
studies written in different languages from the ones mentioned above,
studies before 2001, and
secondary studies, comments, and grey literature.

Study identification

The articles were independently screened by two investigators (CL and CC) based on their titles, abstracts, and full texts. The inclusion of a study was determined through consensus between the two investigators. The final selection was subsequently reviewed by a third, experienced researcher.

Data extraction, primary and secondary outcomes

The data was extracted in the following manner: author(s), year of publication, study period, study design, sample size, inclusion and exclusion criteria, electrophysical agents used in cellulite treatment, description of the intervention, and primary and secondary outcomes.

Methodological quality appraisal

In order to evaluate the methodological quality across a wide array of study designs, we employed the QualSyst tool [17]. This tool was chosen due to its provision of scoring systems for both quantitative and qualitative studies. Two investigators independently assessed and categorized the studies. Studies were deemed to be of strong quality if the QualSyst score exceeded 80%, of good quality if the score ranged from 70 to 80%, of adequate quality if the score fell between 50 and 69%, and of limited methodological quality if the score was below 50% [18].

The methodological quality of the studies was appraised by two researchers (CL and CC). Any conflicts that arose during the evaluation were then reviewed and mediated by a third researcher until a consensus was reached.

Results

Search output and flow

Initially, a total of 556 articles were identified: 379 from Medline, 159 from Central, and 18 from Lilacs. However, after applying the inclusion criteria, only 32 articles remained, as depicted in Fig. 1 below.

Of the 556 studies initially identified, duplicate articles were excluded, and the remaining titles and abstracts were analyzed. This process resulted in 74 studies being deemed eligible for comprehensive assessment. However, only 54 of these articles were available in their entirety for review.

Upon thorough analysis of the complete texts, six were excluded due to the inclusion of male participants in their samples. Four studies were disregarded as they incorporated women aged 60 or older. One article focused on lipedema, while another was centered around animal experimentation. Five studies were omitted as they utilized an active principle in conjunction with an electrophysical therapy or pertained to a non-electrophysical therapy. One text was a letter to the editor, and another was a non-experimental study. Two studies were excluded due to the inclusion of a surgical procedure. Lastly, one duplicate article was discovered that had initially slipped through our preliminary analyses.

Main characteristics of the included studies

A total of 726 women underwent cellulite evaluations, primarily utilizing grade rating scales. These scales were often used in conjunction with one or more additional cellulite measurement tools, including photography, ultrasonography, thermography, biopsies, and magnetic resonance imaging (MRI; refer to Table 1).

The most commonly used tool to evaluate the severity of cellulite, among all the studies included in this review, was Nürnberger and Müller, compounding to 34.4%. However, many studies (37.5%) did not use any grade rating scales to evaluate cellulite. They relied only on photographs and/or other resources. Other cellulite grade rating scales, such as the Cellulite Severity Scale (CSS; 12.5%), Ulrich classification (6.2%), Curri's classification (6.2%),

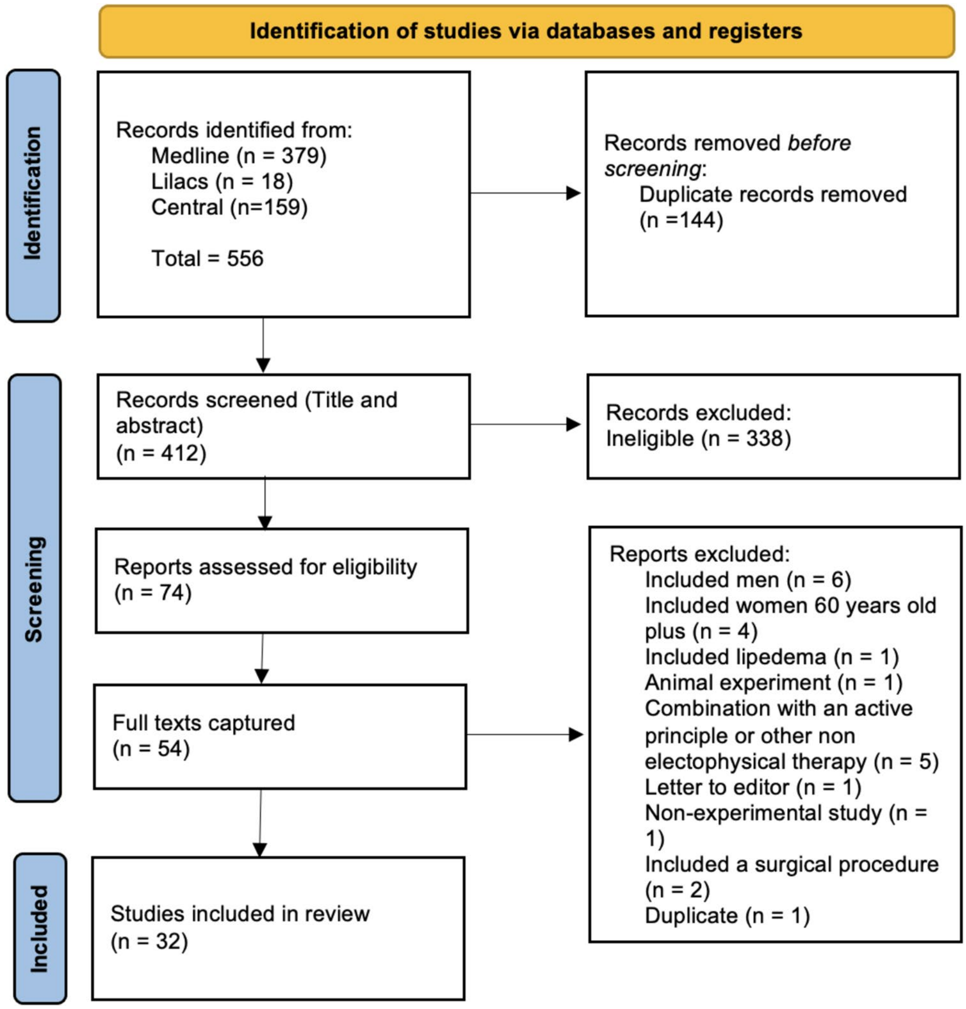

Fig. 1 Overview of screening and selection process for the systematic review according to PRISMA

and Comprehensive cellulite grading scale (3.1%) were used in some of the studies as well (Table 1).

In addition to cellulite grade rating scales, photography emerged as a prevalent tool, utilized in 87.5% of the studies. Ultrasonography, which provides visualization of the epidermis and dermal thickness, was employed in 34.4% of the studies reviewed. Thermography, a method that measures skin temperature to grade cellulite severity, was used in 12.5% of the studies. Biopsies, conducted to investigate potential histological changes, were featured in 12.5% of the studies. MRI, a tool used to visualize skin architecture, was only present in one study, accounting for 3.1% of all the studies included in this review (Table 1).

Table 1 illustrates the disparity in theories regarding cellulite etiology among the studies included in this review. In 18.7% of the studies, cellulite was characterized as an inflammatory condition, while 12.5% described it as non-inflammatory. Notably, the remaining 68.7% of the studies did not express any particular stance on the pathophysiology of cellulite.

The methods of cellulite evaluation, as well as the electrophysical agents used for cellulite treatment, varied significantly across the studies. As depicted in Fig. 2, 35% of the studies employed a combined therapy approach to treat cellulite. This approach is defined as the application of two or more different technologies within the same therapy session. Radiofrequency was used as a treatment method in 28% of the studies, while 16% utilized shock wave therapy for cellulite treatment. In 9% of the studies, the outcomes of two different electrophysical agents were compared within the same study. Laser treatment was used in another 9% of the studies, and a mere 3% employed electrolipolysis as a treatment method for cellulite.

Overall, electrophysical agents, despite their varying mechanisms of action, have demonstrated an improvement in the appearance of cellulite and have proven to be safe for treating this condition (Table 2).

Table 1 Numbers of participants, methods of cellulite evaluation, and theories of cellulite pathophysiology mentioned in each study included in this systematic review

Included Studies	Number of Volunteers	Cellulite Evaluation	Theories of cellulite pathophysiology
Alster; Tanzi (2005) [19]	20	Photography	Inflammatory
Kulick et al. (2006) [20]	16	Photography	Not mentioned
Nootheti et al. (2006) [21]	20	Nürnberger-Müller + photography	Inflammatory
Wanitphakdeedecha; Manuskiatti (2006) [22]	12	Digital photography	Inflammatory
Goldberg; Fazeli; Berlin (2007) [23]	30	Nürnberger-Müller + photography + biopsies + MRI	Not mentioned
Sadick; Magro (2007) [24]	16	Photography	Not mentioned
Alexiades-Armenakas; Dover; Arndt (2008) [25]	10	Comprehensive cellulite grading scale + photography	Not mentioned
Kuhn et al. (2008) [26]	1	Nürnberger-Müller + ultrasonography + contact thermography + biopsies	Not mentioned
Romero et al. (2008) [27]	10	Optical skin analysis + photography + skin biopsies	Not mentioned
Bousquet-Rouaud et al. (2009) [28]	12	Nürnberger-Müller + ultrasonography + photography	Inflammatory
van der Lugt et al. (2009) [29]	50	Curri's classification + biopsies + 3D photography	Not mentioned
Manuskiatti et al. (2009) [30]	37	Nürnberger-Müller + ultrasonography + photography	Not mentioned
Gold et al. (2011) [31]	83	Photography	Not mentioned
Hexsel et al. (2011) b [32]	9	CSS + photography	Non-inflammatory
Machado et al. (2011) [33]	22	Photography	Not mentioned
Mlosek et al. (2011) [34]	45	Nürnberger-Müller + ultrasonography + photography	Not mentioned
Chu; Calegari (2012) [35]	28	Ulrich classification + computerized biophotogrammetry	Non-inflammatory
Filippo; Salomão Jr. (2012) [36]	21	Photography	Not mentioned
Truitt et al. (2012) [37]	19	Nürnberger-Müller + photography + thermography	Not mentioned
Valls et al. (2012) [38]	1	Ulrich classification + computerized biophotogrammetry	Non-inflammatory
Bravo et al. (2013) [39]	8	Nürnberger-Müller + ultrasonography + photography	Inflammatory
Hexsel et al. (2013) [40]	15	CSS + photography	Not mentioned
Jackson; Roche; Shanks (2013) [41]	64	Nürnberger-Müller	Not mentioned
Russe-Wilflingseder et al. (2013) [42]	17	3D photography SkinSCAN	Non-inflammatory
Valentim da Silva et al. (2013) [43]	8	Curri's classification + ultrasonography	Not mentioned
De La Casa Almeida et al. (2014) [44]	27	CSS + photography	Not mentioned
Schlaudraff et al. (2014) [45]	14	Digital photography + contact thermography	Inflammatory
Albornoz-Cabello; Ibánez-Vera; Cruz-Torres (2017) [46]	9	Nürnberger-Müller + ultrasonography	Not mentioned
Wanitphakdeedecha et al. (2017) [47]	25	Nürnberger-Müller + ultrasonography + photography	Not mentioned
Fritz; Salavastru; Gyurova (2018) [48]	30	Photography + ultrasonography + thermography	Not mentioned
Modena et al. (2019) [49]	27	CSS + photography + ultrasonography	Not mentioned
Maia et al. (2020) [50]	20	Photography + ultrasonography	Not mentioned

Methodological appraisal by QualSyst

Table 2 illustrates that out of the 32 studies included in this review, only two (6.2%) were evaluated as having strong and good methodology through the QualSyst tool. These were the study by Maia et al. (2020) [50], which utilized shock wave therapy for cellulite treatment, and the study by Jackson; Roche; Shanks (2013) [41], which employed photobiomodulation (laser) as a cellulite treatment method. It is noteworthy that both studies were randomized controlled trials, wherein participants were randomly assigned to either the treatment or control groups.

Of the ten studies evaluated (31.2%), each demonstrated adequate methodology. Four of these studies [27, 28, 33, 44] were identified as randomized controlled trials. However, the randomization in these studies was limited to the lower limbs, typically using the contralateral side as a control due to its non-treated status. Only in the study by Machado and colleagues (2011) [33] was the contralateral side used to test a different cellulite treatment technology. Furthermore, the

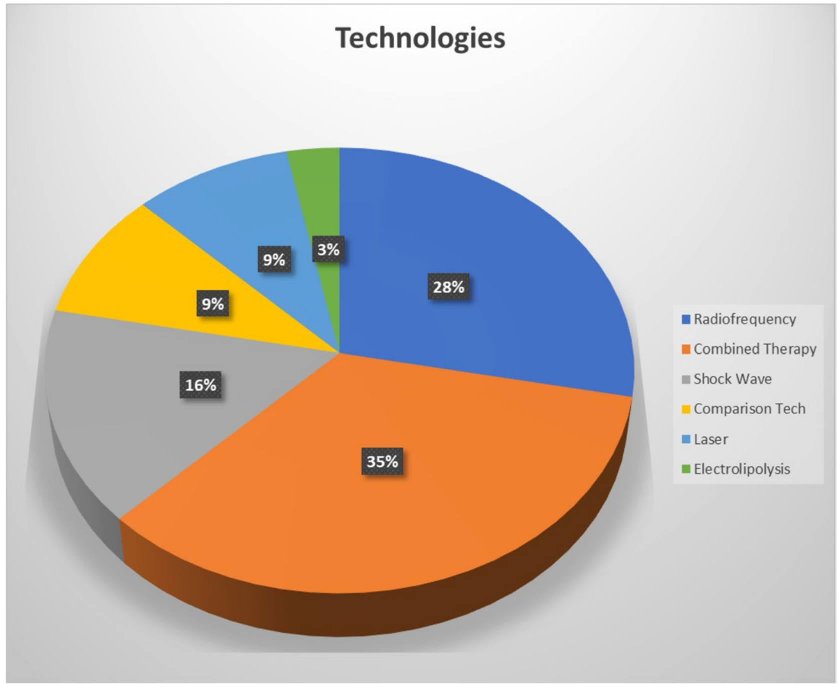

Fig. 2 The graph shows the percentage of electrophysical agents used to treat cellulite in studies between 2011 and 2021

majority of these studies did not specify their randomization method. Two additional studies [34, 42] were also randomized controlled trials. These studies randomly assigned participants to either treatment or control groups, utilizing laser and shock wave technologies, respectively, for cellulite treatment. Another study was a pilot study [30], employing radiofrequency technology for cellulite treatment. A further study was a non-randomized controlled trial [39], which also used radiofrequency for cellulite treatment. Lastly, two studies [29, 43] did not specify their study design, but both employed radiofrequency technology for cellulite treatment (Table 2).

The remaining 20 studies, constituting 62.5% of the total, were evaluated using limited methodologies. Of these, seven studies claimed to be randomized controlled trials, but the randomization was conducted between the lower limbs, as previously mentioned. Furthermore, the method of randomization was not specified in the majority of these studies. Among these seven studies, three [19, 24, 31] utilized combined therapy, one [21] compared the outcomes of two different electrophysical agents, one [45] employed shock wave therapy, one [25] used radiofrequency, and one [37] treated cellulite with photobiomodulation. The remaining studies, classified as having limited methodology, included three pilot studies that used radiofrequency [46] and combined therapy [22, 32] for cellulite treatment; two case studies that employed electrolipolysis [38] and shock wave [26] as cellulite treatments; two non-randomized controlled trials, one of which [35] compared two different technologies for cellulite treatment, and the other one [49] used shock wave therapy for cellulite treatment; two cohort prospective studies [36, 40], that both used combined therapies for cellulite treatment; and four studies that did not specify the study design. Of them three [20, 47, 48] also treated cellulite with combined technologies, and one [23] treated cellulite with radiofrequency (Table 2).

RF- radiofrequency; IR—infrared light; VAC—mechanical suction-based massage device; US – ultrasound; LED – light-emitting diode; PMF – pulsed magnetic fields.

Discussion

A detailed search was conducted in the primary health science databases over a period of 20 years, focusing on cellulite treatment with electrophysical agents. Out of the 556 articles collected, only 32 met our inclusion criteria.

Overall, the outcomes of cellulite treatments were highly promising, despite the vast array of electrophysical agents used and their varying mechanisms of action.

However, were these studies robust enough to guide clinical routines based on evidence? In other words, can we rely on the quality of these studies to incorporate these various electrophysical agents into the daily treatment of cellulite in aesthetic clinics? The scientific evidence, in addition to the methodological quality of the clinical trials, was deemed insufficient.

The results of most studies, accounting for 62.5%, were evaluated as limited (with a score below 50%) using the QualSyst tool. In contrast, only 6.2% were assessed as strong

Table 2 This table provides a summary of all 32 studies included in this systematic review. It details the technologies used to treat cellulite in each study, outlines the study designs, and presents a consensus of QualSyst scores along with methodological quality outcomes

Included Studies	Electrophysical Agents	Outcomes	Study Design	Consensus of QualSyst Scores	Methodology Quality
Alster; Tanzi (2005) [19]	Combined therapies (RF + IR + VAC)	Cellulite was significantly, and safely reduced	Randomized controlled trial (Randomization of lower limbs and used the contralateral side as control. Randomization method was not specified)	0.45	Limited
Kulick et al. (2006) [20]	Combined therapies (RF + IR + VAC)	Improvement on cellulite aspect	Not mentioned	0.20	Limited
Nootheti et al. (2006) [21]	Technologies comparison (RF + IR + VAC vs Laser + Cold + VAC)	Improvement on cellulite aspect	Randomized trial (Randomized lower limbs, but each leg was treated with a different technology. Randomization method was not specified)	0.20	Limited
Wanitphakdeedech; Manuskiatti (2006) [22]	Combined therapies (RF + IR + VAC)	Beneficial effects	Pilot study	0.45	Limited
Goldberg; Fazeli; Berlin (2008) [23]	Radiofrequency	Improvement on cellulite aspect	Not mentioned	0.40	Limited
Sadick; Magro (2007) [24]	Combined therapies (RF + IR + VAC)	Positive results	Randomized controlled trial (Randomization of lower limbs and used the contralateral side as control. Randomization method was not specified)	0.35	Limited
Alexiades-Armenakas; Dover; Arndt (2008) [25]	Radiofrequency	Improvement on cellulite aspect	Randomized controlled trial (Randomization of lower limbs and used the contralateral side as control. Randomization method was not specified)	0.45	Limited
Kuhn et al. (2008) [26]	Shock waves	Optimization of critical application parameters	Case study	0.40	Limited
Romero et al. (2008) [27]	Combined therapies (RF + IR + VAC)	Improvement on cellulite aspect	Randomized controlled trial (Randomization of lower limbs and used the contralateral side as control. Randomization method was not specified)	0.50	Adequate
Bousquet-Rouaud et al. (2009) [28]	Laser	Effective and safe	Randomized controlled trial (Randomization of lower limbs and used the contralateral side as control. Randomization method was not specified)	0.65	Adequate
van der Lugt et al. (2009) [29]	Radiofrequency	Improvement on cellulite aspect	Not mentioned	0.65	Adequate
Manuskiatti et al. (2009) [30]	Radiofrequency	Beneficial effects	Pilot study	0.65	Adequate

Table 2 (continued)

Included Studies	Electrophysical Agents	Outcomes	Study Design	Consensus of QualSyst Scores	Methodology Quality
Gold et al. (2011) [31]	Combined therapies (Laser + VAC)	Improvement on cellulite aspect	Randomized controlled trial (Randomization of lower limbs and used the contralateral side as control. Poor randomization method)	0.45	Limited
Hexsel et al. (2011) b [32]	Combined therapies (RF + IR + VAC)	Effective and safe	Pilot study	0.45	Limited
Machado et al. (2011) [33]	Technologies comparison (US vs Electrolipolysis)	Improvement on cellulite aspect	Randomized trial (Volunteers were randomized in 2 different treatment groups. Randomization method was not specified)	0.55	Adequate
Mlosek et al. (2011) [34]	Radiofrequency	Cellulite reduction	Randomized controlled trial (Poor randomization method)	0.55	Adequate
Chu; Calegari (2012) [35]	Technologies comparison (Electrolipolysis vs Endermology)	Beneficial effects with both technologies	Non-randomized clinical trial	0.40	Limited
Filippo; Salomão Jr. (2012) [36]	Combined therapies (RF + LED + Endermology + US)	Effective and safe	Cohort prospective study	0.20	Limited
Truitt et al. (2012) [37]	Laser	Mild or moderate improvement on cellulite aspect	Randomized controlled trial (Randomization of lower limbs and used the contralateral side as control. Randomization method was not specified)	0.45	Limited
Valls et al. (2012) [38]	Electrolipolysis	Effective	Case study	0.35	Limited
Bravo et al. (2013) [39]	Radiofrequency	Effective and safe	Non-randomized clinical trial	0.55	Adequate
Hexsel et al. (2013) [40]	Combine therapies (Laser + IR + VAC)	Effective and safe	Cohort prospective study	0.45	Limited
Jackson; Roche; Shanks (2013) [41]	Laser	Effective and safe	Randomized controlled trial	0.75	Good
Russe-Wilflingseder et al. (2013) [42]	Shock wave	Effective and safe	Randomized controlled trial	0.60	Adequate
Valentim da Silva et al. (2013) [43]	Radiofrequency	Improvement on cellulite aspect	Not mentioned	0.50	Adequate
De La Casa Almeida et al. (2014) [44]	Radiofrequency	Effective	Randomized controlled trial (Randomization of lower limbs and used the contralateral side as control)	0.50	Adequate
Schlaudraff et al. (2014) [45]	Shock wave	Effective and safe	Randomized controlled trial (Randomization of lower limbs and used the contralateral side as control. Randomization method was not specified)	0.45	Limited

Table 2 (continued)

Included Studies	Electrophysical Agents	Outcomes	Study Design	Consensus of QualSyst Scores	Methodology Quality
Albornoz-Cabello; Ibánez-Vera; Cruz-Torres (2017) [46]	Radiofrequency	Effective	Pilot study	0.40	Limited
Wanitphakdeedecha et al. (2017) [47]	Combined therapies (RF + PMF)	Effective and safe	Not mentioned	0.35	Limited
Fritz; Salavastru; Gyurova (2018) [48]	Combined therapies (RF + pressure)	Effective and safe	Not mentioned	0.40	Limited
Modena et al. (2019) [49]	Shock wave	Improvement on cellulite aspect	Non-randomized clinical trial	0.45	Limited
Maia et al. (2020) [50]	Shock waves	Effective	Randomized controlled trial	0.90	Strong

or good (with a score above 80% and ranging from 70 to 80%, respectively). This suggests a dearth of high-quality studies in the literature to guide aesthetic clinicians in their routine treatment of cellulite with electrophysical agents. There could be several reasons for this outcome. Firstly, despite the extensive search conducted, it was challenging to find a clear definition of cellulite pathophysiology. This difficulty extended to finding an accurate method to evaluate this dysfunction. Consequently, without an ideal method to measure the study's target, it becomes problematic to assess subsequent results with products that affect this target.

Luebberding, Krueger, and Sadick (2015) [1] argue that the current methods for measuring cellulite grades lack sufficient reproducibility and precision. Consequently, this makes the evaluation of anti-cellulite products and procedures challenging.

A recent review [51] has concluded that the scales currently in use possess limitations due to their qualitative assessment of cellulite or their inability to capture clinically relevant features of cellulite. However, the review recommends the combined application of the Clinician Reported Photonumeric Cellulite Severity Scale (CR-PCSS) and the Patient Reported Photonumeric Cellulite Severity Scale (PR-PCSS). These are validated tools that offer both clinician and patient perspectives on cellulite. It is crucial to note that none of the studies examined in this review utilized either of these tools.

Additionally, they advocated for the use of reliable imaging techniques to characterize cellulite and assess treatment efficacy51 more effectively. It was only recently that we demonstrated the potential of infrared thermography as a valuable tool for the diagnosis and evaluation of cellulite treatments [52].

The second reason for the poor methodological quality appraisal pertains to the inadequate randomization methods employed in most studies included in this review. Despite claiming to be randomized controlled trials, many studies either failed to use a robust method of randomization, neglected to mention the randomization method used, or improperly randomized the lower limbs of volunteers, using the contralateral side as a control. This is in contrast to the proper procedure of random distribution and, crucially, concealed allocation of volunteers into treatment and control groups, as advocated by a "true" randomized controlled trial [53]. Furthermore, the other types of studies included in this review were generally poorly designed, thereby limiting the accuracy of their conclusions.

The methodology and subsequent results could be influenced by the randomization of lower limbs and the use of the contralateral side, which is the non-treated side, as a control. This is due to the potential systemic effects that electrophysical agents can produce. This phenomenon was observed by Adatto et al. (2010) [54] and Russe-Wilflingseder; Russe

(2010) [55], who noted that the control side was impacted by the acoustic wave treatment administered to the treated side.

The ideal study design for interventional studies, i.e., studies that analyze the effects of a treatment in humans, is a randomized controlled trial. This design is considered the gold standard in evidence-based research due to its high quality of evidence, as explained by Hariton and Locascio (2018) [53]. However, the development of such studies often encounter challenges such as ethical considerations, practicality, sample size, and cost. In light of these drawbacks, well-developed observational studies can provide valuable insights, even in the absence of randomization, by effectively limiting bias and confounding factors [56]. Nevertheless, randomization remains a crucial tool for reducing bias and examining the relationship between an intervention and its outcomes [53].

Clark et al. (2013) [57] highlighted the issue of inadequate reporting in trials, attributing this to a lack of training in trial methodology. They recommended several measures to address this problem. Firstly, authors should adhere to the Consolidated Standards of Reporting Trials (CONSORT). Secondly, randomized controlled trials should be reviewed by a trained methodologist. Lastly, they emphasized the importance of allocation concealment post-randomization, suggesting that this should be a mandatory requirement when registering a trial on the International Clinical Trial Registry.

Regrettably, our findings continue to align with the conclusions drawn by Clark et al. (2013) [57]. Of the four studies that were classified as "true" randomized controlled trials, only one [50] was evaluated using a robust methodology. Another study [41] was assessed using a sound methodology, while the remaining two studies [34, 42] were evaluated using an adequate methodology, as determined by the QualSyst tool.

It is worth noting that adequate methodology is defined as studies that fall within a quality assessment score range of 50–70% (or 0.50 to 0.70). In our interpretation, studies with methodological scores of 0.55 and 0.6, such as the two methodologically adequate randomized controlled trials previously mentioned, possess significantly lower methodological quality compared to a study scored at 0.7.

In discussing randomized controlled trials, it is crucial to note that despite Jackson, Roche, and Shanks (2013) [41] declaring no conflicts of interest, Steven Shanks is the owner of Erchonia Corporation. This company manufactures the low-level laser device utilized in this study. Consequently, this connection could have unintentionally influenced the final outcomes.

The third factor contributing to the classification of studies with limited methodological quality was the focus on combined therapies. These therapies, which comprised 35% of the studies included in this review, involve the use of two or more different electrophysical agents to treat cellulite in a single session. Of these studies on combined therapies, only one [27] were classified as having adequate methodology. However, they scored low at 0.50, while the remaining studies were all classified as having limited methodological quality.

Each electrophysical agent operates via a distinct mechanism of action. Therefore, how can we confidently attribute the results to the combined effect of all these resources? How can we ascertain whether one resource is not counteracting the effect of another, thereby allowing the third one to treat cellulite independently? It is noteworthy that nearly all studies involving combined therapies were assessed with limited methodological quality, which was not a mere coincidence.

The validity of these inquiries is further compromised when we examine studies that compare two different technologies or two combined therapies applied to each lower limb. The majority of these studies were evaluated with limited methodological quality. For instance, the study by Machado et al. (2011) [33] was assessed with adequate methodology, but still received a low score (0.55). As previously mentioned, we are already aware that some electrophysical agents can produce a systemic effect. However, how can we accurately compare two different technologies with distinct mechanisms of action? Undoubtedly, the conclusion drawn from such a comparison will not be precise enough to guide clinicians in selecting the most effective technology for treating cellulite.

The studies, as organized in ascending order of publication year in Table 2, suggest a shift in scientific focus over time. It appears that the questions raised may have influenced the direction of research, as there has been a noticeable decrease in the number of studies on combined therapies and comparison technologies in recent years compared to earlier periods.

A limitation of this review lies in the difficulty of categorizing the studies as either qualitative or quantitative in order to adhere to the QualSyst checklist. Kemt, Lee, and Cook (2004) [17] posited that the QualSyst tool may not accurately assess the methodological quality of the studies due to the subjectivity inherent in the questions on both the quantitative and qualitative studies' checklists. This issue is further compounded by the lack of standard operational definitions of internal validity in the literature, as well as the absence of a universally accepted "gold standard" against which to compare their tool.

A further limitation of this review is the diversity of study designs analyzed. Although the QualSyst tool may not provide precise measurements of the methodological quality of these studies, it enables researchers to seek answers that may not be obtainable solely through randomized controlled trials. This tool facilitates a comprehensive search across a wide range of documents, from peer-reviewed articles to gray literature [17].

Conversely, a significant strength of this study lies in its comprehensive examination of the methodological quality of research conducted over the past two decades. This research has tested electrophysical agents for cellulite treatment and can guide clinicians in the aesthetic field in their daily practices. Furthermore, this systematic review serves as a gateway for scientists interested in conducting research in this area, which is currently lacking in studies with a high quality of evidence.

Conclusion

In summary, our findings indicate that the methodological quality derived from clinical studies concerning the use of electrophysical agents for treatment remains subpar.

Further research, utilizing robust experimental designs and more precise assessment techniques, is required to ascertain the most effective treatment strategies.

While this study does not dispute the efficacy of current cellulite treatment techniques, it underscores the necessity for further research of superior methodological quality.

Authors Contribution Claudia Longano – Writing and scientific search; Carly de Faria Coelho – Search strategy and design. Sandra Alencar Buslik, Cicelina Voguel, Camila Katsuragi, Patrícia Sardinha Leonardo – Analysis and selection of studies. Rodrigo Alvaro B. Lopes Martins – General supervision and coordenation of the study.

Funding Prof. Rodrigo Lopes-Martins was supported by the—CNPq.

Declarations

Competing Interest The authors declare no conflit of interest for this publication.

Informed Consent Not applicable.

References

1. Luebberding S, Krueger N, Sadick NS (2015) Cellulite: an evidence-based review. Am J Clin Dermatol 16(4):243–256. https://doi.org/10.1007/s40257-015-0129-5
2. Nürnberger F, Müller G (1978) So-called cellulite: an invented disease. J Dermatol Surg Oncol 4(3):221–229. https://doi.org/10.1111/j.1524-4725.1978.tb00416.x
3. Rossi AB, Vergnanini AL (2000) Cellulite: a review. J Eur Acad Dermatol Venereol 14(4):251–262. https://doi.org/10.1046/j.1468-3083.2000.00016.x
4. Emanuele E (2013) Cellulite: advances in treatment: facts and controversies. Clin Dermatol 31(6):725–730. https://doi.org/10.1016/j.clindermatol.2013.05.009
5. Querleux B, Cornillon C, Jolivet O, Bittoun J (2002) Anatomy and physiology of subcutaneous adipose tissue by in vivo magnetic resonance imaging and spectroscopy: relationships with sex and presence of cellulite. Skin Res Technol 8(2):118–24. https://doi.org/10.1034/j.1600-0846.2002.00331.x
6. Rosenbaum M, Prieto V, Hellmer J, Boschmann M, Krueger J, Leibel RL, Ship AG (1998) An exploratory investigation of the morphology and biochemistry of cellulite. Plast Reconstr Surg 101(7):1934–1939. https://doi.org/10.1097/00006534-199806000-00025
7. Avram MM (2004) Cellulite: a review of its physiology and treatment. J Cosmet Laser Ther 6(4):181–185. https://doi.org/10.1080/14764170410003057
8. Sadick N (2018) Treatment for cellulite. Int J Womens Dermatol 5(1):68–72. https://doi.org/10.1016/j.ijwd.2018.09.002
9. Pérez Atamoros FM, Alcalá Pérez D, AszSigall D, Ávila Romay AA, Barba Gastelum JA et al (2018) Evidence-based treatment for gynoid lipodystrophy: A review of the recent literature. J Cosmet Dermatol 17(6):977–983. https://doi.org/10.1111/jocd.12555
10. Draelos ZD, Marenus KD (1997) Cellulite. Etiology and purported treatment Dermatol Surg 23(12):1177–1181
11. Rawlings AV (2006) Cellulite and its treatment. Inter J Cosmet Sci 28(3):175–190. https://doi.org/10.1111/j.1467-2494.2006.00318.x
12. Bauer J, Hoq MN, Mulcahy J, Tofail SAM, Gulshan F, Silien C, Podbielska H, Akbar MM (2020) Implementation of artificial intelligence and non-contact infrared thermography for prediction and personalized automatic identification of different stages of cellulite. EPMA J 7;11(1):17–29. https://doi.org/10.1007/s13167-020-00199-x
13. Hexsel D, Weber MB, Taborda ML, Dal'Forno T, Zechmeister-Prado D (2011) A quality of life measurement for patients with cellulite. Surgic Cosmet Dermatol 3(2):96–10
14. Auh SL, Iyengar S, Weil A, Bolotin D, Cartee TV, Dover JS, Maher IA, Sobanko JF, Cohen JL, Poon E, Alam M (2018) Quantification of noninvasive fat reduction: A systematic review. Lasers Surg Med 50(2):96–110. https://doi.org/10.1002/lsm.22761
15. da Costa Santos CM, de MattosPimenta CA, Nobre MR (2007) The PICO strategy for the research question construction and evidence search. Rev Lat Am Enfermagem 15(3):508–511. https://doi.org/10.1590/s0104-11692007000300023
16. Page MJ et al (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 372:n71. https://doi.org/10.1136/bmj.n71
17. Kmet LM, Lee RC, Cook LS (2004) Standard Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields. Alberta Heritage Foundation for Medical Research. https://doi.org/10.7939/R37M04F16
18. Lee L, Packer TL, Tang SH, Girdler S (2008) Self-management education programs for age-related macular degeneration: a systematic review. Australas J Ageing 27(4):170–176. https://doi.org/10.1111/j.1741-6612.2008.00298.x
19. Alster TS, Tanzi EL (2005) Cellulite treatment using a novel combination radiofrequency, infrared light, and mechanical tissue manipulation device. J Cosmet Laser Ther 7(2):81–85. https://doi.org/10.1080/14764170500190242
20. Kulick M (2006) Evaluation of the combination of radio frequency, infrared energy and mechanical rollers with suction to improve skin surface irregularities (cellulite) in a limited treatment area. J Cosmet Laser Ther 8(4):185–190. https://doi.org/10.1080/14764170601009622
21. Nootheti PK, Magpantay A, Yosowitz G, Calderon S, Goldman MP (2006) A single center, randomized, comparative, prospective clinical study to determine the efficacy of the VelaSmooth system versus the Triactive system for the treatment of cellulite. Lasers Surg Med 38(10):908–912. https://doi.org/10.1002/lsm.20421
22. Wanitphakdeedecha R, Manuskiatti W (2006) Treatment of cellulite with a bipolar radiofrequency, infrared heat, and pulsatile

suction device: a pilot study. J Cosmet Dermatol 5(4):284–288. https://doi.org/10.1111/j.1473-2165.2006.00271.x
23 Goldberg DJ, Fazeli A, Berlin AL (2008) Clinical, laboratory, and MRI analysis of cellulite treatment with a unipolar radiofrequency device. Dermatol Surg 34(2):204–9. https://doi.org/10.1111/j.1524-4725.2007.34038.x. discussion 209
24. Sadick N, Magro C (2007) A study evaluating the safety and efficacy of the VelaSmooth system in the treatment of cellulite. J Cosmet Laser Ther 9(1):15–20. https://doi.org/10.1080/14764170601134461
25. Alexiades-Armenakas M, Dover JS, Arndt KA (2008) Unipolar radiofrequency treatment to improve the appearance of cellulite. J Cosmet Laser Ther 10(3):148–153. https://doi.org/10.1080/14764170802279651
26. Kuhn C, Angehrn F, Sonnabend O, Voss A (2008) Impact of extracorporeal shock waves on the human skin with cellulite: a case study of an unique instance. Clin Interv Aging 3(1):201–210. https://doi.org/10.2147/cia.s2334
27. Romero C, Caballero N, Herrero M, Ruíz R, Sadick NS, Trelles MA (2008) Effects of cellulite treatment with RF, IR light, mechanical massage and suction treating one buttock with the contralateral as a control. J Cosmet Laser Ther 10(4):193–201. https://doi.org/10.1080/14764170802524403
28. Bousquet-Rouaud R, Bazan M, Chaintreuil J, Echague A (2009) High-frequency ultrasound evaluation of cellulite treated with the 1064 nm Nd:YAG laser. J Cosmet Laser Ther 11(1):34–44. https://doi.org/10.1080/14764170802612968
29. van der Lugt C, Romero C, Ancona D, Al-Zarouni M, Perera J, Trelles MA (2009) A multicenter study of cellulite treatment with a variable emission radio frequency system. Dermatol Ther 22(1):74–84. https://doi.org/10.1111/j.1529-8019.2008.01218.x
30. Manuskiatti W, Wachirakaphan C, Lektrakul N, Varothai S (2009) Circumference reduction and cellulite treatment with a TriPollar radiofrequency device: a pilot study. J Eur Acad Dermatol Venereol 23(7):820–827. https://doi.org/10.1111/j.1468-3083.2009.03254.x
31. Gold MH, Khatri KA, Hails K, Weiss RA, Fournier N (2011) Reduction in thigh circumference and improvement in the appearance of cellulite with dual-wavelength, low-level laser energy and massage. J Cosmet Laser Ther 13(1):13–20. https://doi.org/10.3109/14764172.2011.552608
32. Hexsel DM, Siega C, Schilling-Souza J, Porto MD, Rodrigues TC (2011) A bipolar radiofrequency, infrared, vacuum and mechanical massage device for treatment of cellulite: a pilot study. J Cosmet Laser Ther 13(6):297–302. https://doi.org/10.3109/14764172.2011.630086
33. Machado GC, Vieira RB, de Oliveira NML, Lopes CR (2011) Análise dos efeitos do ultrassom terapêutico e da eletrolipoforese nas alterações decorrentes do fibroedema geloide. Fisioter Mov 24(3):471–479
34. Mlosek RK, Woźniak W, Malinowska S, Lewandowski M, Nowicki A (2012) The effectiveness of anticellulite treatment using tripolar radiofrequency monitored by classic and high-frequency ultrasound. J Eur Acad Dermatol Venereol 26(6):696–703. https://doi.org/10.1111/j.1468-3083.2011.04148.x
35. Chu SB, Calegari A (2012) Comparação dos efeitos da endermologia e da eletrolipoforese no tratemto do fibro edema gelóide. Fisioterapia Brasil 13(5):336–341. https://doi.org/10.33233/fb.v13i5.562
36. Filippo A, Salomão A Jr (2012) Tratamento de gordura localizada e lipodistrofia ginóide com terapia combinada: radiofrequência multipolar, LED vermelho, endermologia pneumática e ultrassom cavitacional. Surg Cosmet Dermatol 4(3):241–246
37. Truitt A, Elkeeb L, Ortiz A, Saedi N, Echague A, Kelly KM (2012) Evaluation of a long pulsed 1064-nm Nd:YAG laser for improvement in appearance of cellulite. J Cosmet Laser Ther 14(3):139–144. https://doi.org/10.3109/14764172.2012.685480
38. Valls MGC et al (2012) Análise dos efeitos da eletrolipólise no tratamento do fibro edema gelóide por meio da biofotogrametria computadorizada. Fisioterapia Brasil 13(1):54–58. https://doi.org/10.33233/fb.v13i1.464
39. Bravo B, Issa M, Muniz RL, Torrado CM (2013) Treatment of gynoid lipodystrophy with unipolar radiofrequency: Clinical, laboratory, and ultrasonographic evaluation. Surg Cosmet Dermatol 5:138–144
40. Hexsel D, Siega C, Schilling-Souza J, De Oliveira DH (2013) Noninvasive treatment of cellulite utilizing an expedited treatment protocol with a dual wavelength laser-suction and massage device. J Cosmet Laser Ther 15(2):65–69. https://doi.org/10.3109/14764172.2012.759237
41. Jackson RF, Roche GC, Shanks SC (2013) A double-blind, placebo-controlled randomized trial evaluating the ability of low-level laser therapy to improve the appearance of cellulite. Lasers Surg Med 45(3):141–147. https://doi.org/10.1002/lsm.22119
42. Russe-Wilflingseder K, Russe E, Vester JC, Haller G, Novak P, Krotz A (2013) Placebo controlled, prospectively randomized, double-blinded study for the investigation of the effectiveness and safety of the acoustic wave therapy (AWT(®)) for cellulite treatment. J Cosmet Laser Ther 15(3):155–162. https://doi.org/10.3109/14764172.2012.759235Erratum.In:JCosmetLaserTher.2013Jun;15(3):162.Russe-Wilfingsleder,Katharina[correctedtoRusse-Wilflingseder,Katharina];Russe,Elisabeth[added]. PMID: 23688206
43. Valentim da Silva RM, Barichello PA, Medeiros ML, de Mendonça WC, Dantas JS, Ronzio OA, Froes PM, Galadari H (2013) Effect of capacitive radiofrequency on the fibrosis of patients with cellulite. Dermatol Res Pract 2013:715829. https://doi.org/10.1155/2013/715829
44. De La Casa AM, Suarez Serrano C, Medrano Sánchez EM, Diaz Mohedo E, Chamorro Moriana G, Rebollo Salas M (2014) The efficacy of capacitive radio-frequency diathermy in reducing buttock and posterior thigh cellulite measured through the cellulite severity scale. J Cosmet Laser Ther 16(5):214–224. https://doi.org/10.3109/14764172.2014.949272
45. Schlaudraff KU, Kiessling MC, Császár NB, Schmitz C (2014) Predictability of the individual clinical outcome of extracorporeal shock wave therapy for cellulite. Clin Cosmet Investig Dermatol 7:171–183. https://doi.org/10.2147/CCID.S59851
46. Albornoz-Cabello M, Ibáñez-Vera AJ, De la Cruz-Torres B (2017) Efficacy of monopolar dielectric transmission radio frequency in panniculus adiposus and cellulite reduction. J Cosmet Laser Ther 19(7):422–426. https://doi.org/10.1080/14764172.2017.1342041
47. Wanitphakdeedecha R, Sathaworawong A, Manuskiatti W, Sadick NS (2017) Efficacy of multipolar radiofrequency with pulsed magnetic field therapy for the treatment of abdominal cellulite. J Cosmet Laser Ther 19(4):205–209. https://doi.org/10.1080/14764172.2017.1279332
48. Fritz K, Salavastru C, Gyurova M (2018) Clinical evaluation of simultaneously applied monopolar radiofrequency and targeted pressure energy as a new method for noninvasive treatment of cellulite in postpubertal women. J Cosmet Dermatol 17(3):361–364. https://doi.org/10.1111/jocd.12525
49. Modena D, Silva CN, Delinocente TCP (2019) Araújo TB (2019) Effectiveness of the Electromagnetic Shock Wave Therapy in the Treatment of Cellulite. Dermatol Res Pract 1:1–6. https://doi.org/10.1155/2019/8246815
50. Maia R, Silva R, Alvarez C, Froes P, Vasconcelos L, Silva J, Ventura A, Carreiro E (2020) Comparison between shock wave therapy and mechanical massage for the treatment of cellulite in women. Physiot Quart 28:36–41. https://doi.org/10.5114/pq.2020.96234

51 Young VL, DiBernardo BE (2021) Comparison of Cellulite Severity Scales and Imaging Methods. Aesthet Surg J 41(6):NP521–NP537. https://doi.org/10.1093/asj/sjaa226
52. Lopes-Martins RAB, Barbaroto DP, Da Silva BE, Leonardo PS, Ruiz-Silva C, Arisawa EALS (2022) Infrared thermography as valuable tool for gynoid lipodystrophy (cellulite) diagnosis. Lasers Med Sci 37(6):2639–2644. https://doi.org/10.1007/s10103-022-03530-2
53. Hariton E, Locascio JJ (2018) Randomised controlled trials - the gold standard for effectiveness research: Study design: randomised controlled trials. BJOG 125(13):1716. https://doi.org/10.1111/1471-0528.15199
54. Adatto M, Adatto-Neilson R, Servant JJ, Vester J, Novak P, Krotz A (2010) Controlled, randomized study evaluating the effects of treating cellulite with AWT/EPAT. J Cosmet Laser Ther 12(4):176–182. https://doi.org/10.3109/14764172.2010.500392
55. Russe-Wilflingseder K, Russe E (2010) Acoustic wave treatment for cellulite - A new approach. AIP Conf Proc 1226(1):25–30. https://doi.org/10.1063/1.3453782
56. Hoppe DJ, Schemitsch EH, Morshed S, Tornetta P 3rd, Bhandari M (2009) Hierarchy of evidence: where observational studies fit in and why we need them. J Bone Joint Surg Am 91(Suppl 3):2–9. https://doi.org/10.2106/JBJS.H.01571
57. Clark L, Schmidt U, Tharmanathan P, Adamson J, Hewitt C, Torgerson D (2013) Poor reporting quality of key Randomization and Allocation Concealment details is still prevalent among published RCTs in 2011: a review. J Eval Clin Pract 19(4):703–707. https://doi.org/10.1111/jep.12031