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L. S. Bass
Zucker School of Medicine at Hofstra/Northwell, lbass@prohealthcare.com

M. S. Kaminer

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Insights Into the Pathophysiology of Cellulite: A Review

LAWRENCE S. BASS, MD*† AND MICHAEL S. KAMINER, MD‡§‖

BACKGROUND The etiology of cellulite is unclear. Treatment of cellulite has targeted adipose tissue, dermis, and fibrous septae with varying degrees of success and durability of response.

OBJECTIVE Results from clinical trials that target different anatomical aspects of cellulite can provide insights into the underlying pathophysiology of cellulite.

MATERIALS AND METHODS A search of the PubMed database and ClinicalTrials.gov website was conducted to identify clinical trials that have investigated treatments for cellulite.

RESULTS A lack of trial protocol standardization, objective means for quantification of improvement and reported cellulite severity, and short-term follow-up, as well as variation in assessment methods have made comparisons among efficacy studies challenging. However, the lack of durable efficacy and inconsistency seen in clinical results suggest that dermal or adipose tissue changes are not the primary etiologies of cellulite. Clinical studies targeting the collagen-rich fibrous septae in cellulite dimples through mechanical, surgical, or enzymatic approaches suggest that targeting fibrous septae is the strategy most likely to provide durable improvement of skin topography and the appearance of cellulite.

CONCLUSION The etiology of cellulite has not been completely elucidated. However, there is compelling clinical evidence that fibrous septae play a central role in the pathophysiology of cellulite.

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Cellulite is described as an aesthetic alteration of the skin surface characterized by a padded "orange peel" dimpling of the skin.[1–3] Although robust epidemiologic data are lacking in the scientific literature, cellulite is estimated to occur in 80% to 98% of postpubertal women.[3,4] In healthy men, cellulite is rare, but it can occur because of medical conditions that result in androgen deficiency or require estrogen therapy.[1,4] It has been difficult to achieve durable success with treatments for cellulite, including topical agents, energy-based devices, subcision, and injectable biologic agents, all of which target key

**Bass Plastic Surgery, PLLC, New York, New York; †Plastic & Reconstructive Surgery, Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York; ‡Skincare Physicians, Chestnut Hill, Massachusetts; §Department of Dermatology, Yale School of Medicine, New Haven, Connecticut; ‖Department of Dermatology, Brown Medical School, Providence, Rhode Island*

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tissues (i.e., dermis, adipose, fibrous septae, or a combination of these).[5] However, data from anatomical studies have increased our understanding of the underlying physiology of cellulite.[1,6–8] Integrating this anatomical information with data from clinical studies examining specific tissues involved in cellulite may increase our knowledge of cellulite etiology and lead to improved cellulite treatment strategies. The aim of this review is to provide insights into the pathophysiology of cellulite based on the available data and outcomes from anatomical and interventional clinical studies.

Methods

A search of the PubMed database with no date restriction was conducted in March 2019 using the following search terms: "cellulite" AND ("physiopathology" OR "anatomy" OR "histology" OR "physiology" OR "etiology" OR "causality"). Searches were limited to English-language publications. Reference lists in all relevant publications were examined and used to identify additional articles for inclusion. A search of the ClinicalTrials.gov web site was conducted to identify clinical trials with the intention to target cellulite (search term: "cellulite"). Using this search strategy, 206 articles were identified; of which, 65 articles were included in this review; articles that did not quantify cellulite severity were excluded.

Anatomy of Cellulite

The high prevalence of cellulite in women is associated with sex-specific differences in the anatomy of the skin and subcutaneous tissue (e.g., fat and connective tissue)[1,8] and may be hormonally driven by estrogen.[2] These sex-specific differences can help to increase our understanding of cellulite pathophysiology. A 2019 anatomical study[8] demonstrated that dermal thickness is reduced with age in both men and women, suggesting that age-related changes in the dermis are not the primary pathology in cellulite. After analyzing thigh and buttock biopsies of 150 cadavers and 30 living women, Nürnberger and Müller[1] reported that the topographic characteristics of skin with cellulite were caused by adipose protruding into weakened dermal tissue. Microimaging magnetic resonance imaging (MRI) studies and histopathologic analysis (n = 10, posterolateral thigh) have shown no correlation between cellulite severity and adipose layer thickness,[7] and no anatomical differences (n = 60, buttocks, abdomen, upper thigh; n = 30 buttocks) between subcutaneous adipose tissue when comparing the morphology of control skin with subcutaneous fat from cellulite.[7,9–11] However, MRI and anatomical studies have demonstrated that adipose cell chambers in women are larger in height and width compared with men, which may allow adipose cells to protrude into the overlying skin.[1,7,8]

Differences in the number, thickness, orientation, and interrelatedness of septae in cellulite skin have been identified.[1,6–9] Based on pathology studies, the septae of men are oriented at 45° angles to the skin in a crisscrossing pattern, whereas women have septae that are oriented perpendicularly to the skin.[1,6–9] A biopsy study of cellulite reported in 2000 that there was uneven thickness of the septae across samples and that the septae were fibrosclerotic.[12] Authors concluded that fat protrusion into the dermis was a secondary event—the result of continuous and progressive tension placed on the septae, creating dimples and depressions characteristic of cellulite.[12] Additionally, an MRI study in 30 women reported a significant increase in the mean (SD) thickness of septae in skin with cellulite (2.2 [0.9]) versus noncellulite skin (0.3 [0.6]; $p < .001$) of the buttocks; however, there was no relationship between septae thickness and cellulite severity.[9] A 2019 anatomical study of the buttocks from cadavers of 10 men and 10 women demonstrated that the number and type of septae play a key role in the development of cellulite, and the force needed to break the septae in men was significantly greater than in women ($p = .02$).[8]

Treatment of Cellulite

Topical Creams

Methylxanthines (e.g., caffeine) penetrate the skin to act directly on adipose cells, promoting lipolysis,[13] and retinol can prevent in vitro human preadipocyte differentiation.[14] Small clinical studies (6 studies; n = 212 women)[15–20] of topical caffeine (0.1%–13.0%), retinol, or a combination of both, using varying regimens, reported significant improvement in cellulite severity (See **Supplemental Digital Content 1**, Table S1, http://links.lww.com/DSS/A299).[15–45] One study assessing durability noted that cellulite severity improvements were short term (<2 weeks).[17] A sugar derivative, sulfocarrabiose, reduced lipogenesis and increased lipolysis in vitro, and a randomized trial of 25 women applying a 3% sulfocarrabiose cream twice per day on the thigh for 8 weeks noted improvement in cellulite severity using a numeric scale (range: 0, no cellulite to 10, maximum cellulite; $p < .05$).[21]

Massage

LPG Endermologie (Endo-Systems, LLC, Fort Lauderdale, FL) is a US Food and Drug Administration–approved mechanical massage system for cellulite treatment that uses positive pressure from 2 rollers and negative pressure from aspiration to the skin and subcutaneous tissue.[22,23] In 2 observational studies of whole-body endermologie (15 sessions; 35–40 minutes per session; twice weekly), significant improvements from baseline ($p \leq .02$) using the Nürnberger-Müller scale were observed in both studies (See **Supplemental Digital Content 1**, Table S1, http://links.lww.com/DSS/A299).[22,23] However, it is unclear from published data how durable these effects are long term. In clinical practice, improvements in the appearance of cellulite from massage are thought to be short lived.

Extracorporeal Shock Wave Therapy

Extracorporeal shock wave therapy (ESWT) uses electrical energy to create mechanical disruption of targeted tissues without cytolysis, resulting in extracellular healing responses that create tissue regeneration changes such as collagen remodeling and improvement of local blood circulation from neovascularization.[46–49] Shock waves can pass through tissue and confine effects to areas of differing densities, with no substantial effect on the surrounding tissue.[46,47] Radial systems produce energy in a more dispersed form, creating more diffuse and superficial tissue effects that can nonetheless penetrate up to 25 mm, thus reaching subcutaneous fat and connective tissue structures.[50] Focused waves are typically higher energy and penetrate more deeply into tissue.[51] The mechanism of ESWT efficacy has not been completely elucidated, but studies have indicated that potential mechanisms include induction of the formation and remodeling of collagen, neoelastin formation, and skin laxity improvement.[46,51–53] Because of effects on collagen and improvement in skin characteristics, ESWT has been proposed as a treatment for cellulite by targeting the dermis, adipose, and septae (See **Supplemental Digital Content 1**, Table S1, http://links.lww.com/DSS/A299).[24–45,54]

Clinical trials have evaluated the use of acoustic wave therapy (AWT)[26] and ESWT[25,27] to target the dermis. A randomized controlled trial of 53 women treated with focused ESWT on the buttocks and thighs for 6 sessions reported a significant 2.5-point improvement ($p = .001$) in photonumeric Cellulite Severity Scale (CSS) score compared with sham control at 12 weeks post-treatment.[25] Of note, additional assessments of skin improvement, such as change in the number ($p = .01$) and depth ($p = .001$) of depressions in the treatment group, were significantly reduced versus sham control, but skin elasticity was similar between the groups.[25] A second randomized controlled trial of 16 women treated with radial AWT on the thighs and buttocks for 7 sessions demonstrated statistical significance at 1 and 3 months post-treatment in the overall results ($p = .01$) of skin waviness, surface, and volume of depressions and elevations assessed by 3-dimensional (3-D) imaging.[26] Using 2-dimensional (2-D) photographs, 4 investigators reported significant improvement in cellulite severity using the CSS.[26] A third randomized controlled clinical trial of 14 women treated unilaterally with radial ESWT on the posterior thigh and buttock for 8 sessions reported a mean improvement from baseline of 0.82 cellulite grades at 4 weeks.[27]

Extracorporeal shock wave therapy[24] also has been evaluated in clinical trials to target adipose tissue. Combined radial and focused ESWT treatment of the outer thighs of 15 patients assessed by ultrasound demonstrated significant reductions at 12 weeks in mean fat thickness (0.27 ± 0.13 cm; $p < .0001$) versus untreated legs.[24] This study also reported visual improvement of cellulite that was not statistically analyzed, and it did not use a validated scale.[24] Thus, even though significant reductions in adipose tissue were seen at 12 weeks, it is unclear if the improvements had any effect on cellulite severity because the results were not statistically compared.[24]

One clinical trial has evaluated AWT[28] to target the adipose and dermis, with the intention to improve cellulite appearance. A single-center study of 30 women with moderate-to-severe cellulite (based on CSS score) on the thighs and buttocks reported significant improvement in cellulite severity following 12 sessions with combined focused and radial AWT.[28] The mean CSS score decreased from 11.1 at baseline to 9.5 at 12 weeks post-treatment (primary end point, $p < .001$). Significant improvement from baseline at 12 weeks post-treatment was also reported for reduction in mean subcutaneous fat thickness ($p < .001$).[28]

Radiofrequency

Electrothermal effects of radiofrequency (RF) are generated by the impedance of electricity flow through the tissue, and the depth of penetration for multipolar and bipolar RF is reported as approximately half the distance between the 2 electrodes (often less than 2–4 mm); therefore, depending on the distance between the electrodes, application can result in more superficial and subcutaneous heating.[29,55,56] Monopolar and unipolar RF can achieve ≥2 cm depth of penetration into the skin for subcutaneous heating. Multipolar RF has the potential to achieve depths of penetration ranging from <1 cm to >4 cm.[55] Therapeutic effects of RF include collagen denaturation, which can result in skin tightening (See **Supplemental Digital Content 1**, Table S1, http://links.lww.com/DSS/A299).[29,57] Of note, unipolar RF has been shown to increase the number and thickness of septae.[56] Fifty women with Grade-3 (Rossi classification) cellulite on the buttocks were treated with bipolar RF for 12 weekly sessions and reported improvements in cellulite appearance by visual and photographic assessment; however, no statistical analysis was performed at 2 months.[29] One randomized controlled study of 45 women with Grade-1 to Grade-3 cellulite (Nürnberger-Müller scale) used ultrasound to assess the effects of low-level tripolar RF (regimen of 8 procedures conducted every 7–8 days) for the treatment of the posterior thigh; this study demonstrated significant improvement in cellulite grade ($Z = 4.372$, $p < .001$) and reduction in the thickness of subcutaneous tissue ($Z = 4.541$, $p < .001$) pre/post-treatment versus placebo at 4 weeks.[30] Of note, significant changes were reported for dermal thickness in the RF treatment group ($p = .006$), and increasing echogenicity was consistent with an increasing number of septae.[30]

Laser- and Light-Based Devices

Various in vitro and in vivo studies have suggested the potential of low-level laser therapy (LLLT) to activate a biological cascade that increases the production of collagen.[58,59] In a randomized, double-blind, sham-controlled study, thigh and buttock cellulite (Grade-2 or -3 [Nürnberger-Müller scale]) in 68 women was treated with a 532-nm LLLT device (six 30-minute treatments during a 2-week period) with a multiarray noncontact treatment head (See **Supplemental Digital Content 1**, Table S1, http://links.lww.com/DSS/A299).[32] At 2 weeks post-treatment, 55.9% of participants achieved ≥1 Nürnberger-Müller scale decrease from baseline versus sham control ($p < .0001$); the improvements persisted during an additional 4 weeks of follow-up.[32] Infrared light produced from a light-emitting diode (≥6 h/d for 5 consecutive days each week during a 90-day period) demonstrated no significant cellulite improvement in 1 randomized controlled clinical trial of 25 women with Grade-2 or Grade-3 cellulite (Nürnberger-Müller scale).[31] At higher fluence than the LLLT, the non-ablative, long-pulsed 1064-nm neodymium-doped yttrium-aluminum-garnet (Nd:YAG) laser activated a wound repair response that resulted in the stimulation of fibroblast activity and collagen reformation.[60,61] In a randomized clinical trial, mild-to-moderate improvement in cellulite severity was observed after treatment with a long-pulsed 1064-nm Nd:YAG laser.[33]

A subdermal laser technique using a 1440-nm Nd:YAG laser combined with a side-firing fiber and temperature-sensing cannula can effectively treat cellulite through a combination approach.[34] This approach initiates thermal damage to adipocytes, severing fibrous septae via thermal subcision, and targeting the dermis using the thermal energy of the laser to stimulate an increase in collagen.[34] Four observational studies ($n = 107$) evaluated the efficacy of the minimally invasive 1440-nm Nd:YAG laser

(Cellulaze; Cynosure, Westford, MA) for the treatment of cellulite.[34–37] In a study of 10 women with moderate-to-severe cellulite who received a single treatment, significant improvement in skin thickness (ultrasound) and elasticity was demonstrated at 1, 3, 6, and 12 months post-treatment (1, 3, and 6 months, $p < .001$; 12 months, $p \leq .02$) in the treated thigh versus the untreated thigh; however, no significant improvement was seen in cellulite severity.[34] In a subsequent multicenter study of a larger participant population ($n = 57$), single treatment of bilateral thighs and/or buttocks with the 1440-nm Nd:YAG laser resulted in significant mean improvement from baseline in both dimples and contour scores (5-point scales), as observed via digital photography, at 2 months (dimple: 1.4, $p < .001$; contour: 1.0, $p < .001$), 3 months (dimple: 1.4, $p < .001$; contour: 0.9, $p < .001$), and 6 months (dimple: 1.5, $p < .001$; contour: 1.1, $p < .001$) versus the untreated area.[35] The ≥1-point improvement recorded at 6 months was maintained at 12 months in 90% of the treatment sites (46 of 51 treatment areas in 30 patients).[62] A study of 15 women with Grade-2 or Grade-3 cellulite in the thighs and buttocks reported significant improvement after a single treatment in both mean dimple appearance (0–5 scale; baseline, 2.2; 6 months, 1.2; $p < .005$) and mean contour irregularities (0–5 scale; baseline, 1.9; 6 months, 1.0; $p < .005$) with the use of 1440-nm Nd:YAG laser, as observed by blinded investigators reviewing 2-D photography.[36] Furthermore, 3-D photography demonstrated that overall mean dimple depth improved by 42% ($p = .0002$) and 49% ($p = .0003$) at 3 and 6 months, respectively.[36] Using DermaLab Elasticity Module (Cortex Technology, Hadsund, Denmark), 25 women with Grade-2 or Grade-3 posterior or lateral thigh cellulite (Nürnberger-Müller scale) identified significant improvements from baseline in skin elasticity after a single treatment ($p < .01$) at 2, 3, 6, and 24 months post-treatment with the 1440-nm Nd:YAG laser.[37] Improvements in cellulite severity and dermal thickness were also reported but were not quantified.[37]

Liposuction

Since the 1970s, liposuction has been the standard treatment for body contouring by removal of subcutaneous adipose tissue.[63] However, clinical studies evaluating the efficacy of liposuction for the treatment of cellulite are extremely limited. In addition, several studies that did not quantify cellulite severity as an end point did not meet the criteria to be included in this review. A prospective study with 72 women treated with 20 sessions of endermologie or ultrasound-assisted liposuction reported that the liposuction treatment group had no improvement in the reduction of cellulite (endermologie, 50% ± 16.9; liposuction, 0%; $p = .001$).[63] It has been suggested that subcutaneous fibrosis and lipoatrophy from liposuction may cause secondary cellulite or aggravate existing cellulite.[64] In most cases, tumescent liposuction neither improves nor worsens cellulite.[65]

Subcision

One of the first studies of manual subcision was a retrospective study of 232 women with Grade-2 or Grade-3 cellulite of the buttocks and thighs, with improvement assessed by photographs.[66] After 1 treatment session, 183 (78.9%) participants reported being satisfied with the improvement, and 47 (20.3%) participants had "reasonable results." The improvement in cellulite appearance was reported to be persistent (>2 years) in 9.9% ($n = 23$) of participants.[66] However, the size of the cohort available for evaluation at that post-treatment interval (≥2 years) and the percentage of patients available for long-term follow-up who had persistent improvement were unclear.[66] If there was evidence of durable improvement in 9.9% of patients at >2 years,[66] then these results are consistent with historical anecdotal experience indicating that manual subcision often has late recurrence. Also, improvements were not quantified according to the cellulite grading scale used to score pretreatment cellulite severity.[66] In a multicenter study of 200 women who underwent 1 procedure with a manual subcision device for cellulite, mean improvement of 8.1 (range, 7.3–9.4) on a 10-point scale was reported at 6 months postprocedure, based on photographic evidence (See **Supplemental Digital Content 1**, Table S1, http://links.lww.com/DSS/A299).[38] A study of manual subcision in 2 women evaluated anatomical changes with MRI imaging in addition to quantifying cellulite severity using the CSS for up to 7 months post-treatment; MRI imaging demonstrated that baseline dimple location correlated with the presence of thick fibrous septae located beneath the dimple. Following manual subcision, MRI imaging confirmed the septae were no longer present beneath the dimple at 7 months post-treatment, and more importantly, cellulite severity was improved.[54]

To improve the reproducibility of the manual procedure, a vacuum-assisted system was introduced to provide precise control of the procedure area and user-selected treatment depth.[3] In a randomized clinical trial, 55 women with moderate-to-severe cellulite (CSS score) underwent a single procedure and reported a significant reduction in mean (SD) CSS score of 2.1 (0.7, $p < .0001$) and 2.0 (0.8, $p < .0001$) at the 3- and 12-month follow-up, respectively, via blinded investigator-assessment of photographs (See **Supplemental Digital Content 1**, Table S1, http://links.lww.com/DSS/A299).[39] At 3 and 12 months post-procedure, 92.7% (51/55) and 94.0% (47/50) of participants achieved ≥1-point improvement in CSS score, respectively.[39] At 3 years postprocedure, the mean (SD) reduction in CSS score from baseline remained significant (2.0 [1.0]; $p < .0001$) for 45 participants from the original study, and 91.1% (41/45) had achieved ≥1-point improvement in CSS score.[40] At 5 years postprocedure, the mean reduction in CSS score was maintained (1.8; $p < .0001$) by 37 participants from the original study, and 87% had achieved ≥1-point improvement in CSS score.[41] In a separate study of 16 women, in addition to cellulite improvement (CSS score), a mean improvement of 67.4% in negative volume and 58.4% in minimum dimple height, determined by 3-D imaging 6 months postprocedure, was reported following vacuum-assisted subcision.[42] In a subsequent retrospective study of vacuum-assisted subcision, 23 women with mild-to-moderate cellulite severity reported mean improvement from baseline of 2.9 (buttocks) and 2.8 (thighs), based on photographic assessment (score range, 0–4), using a limited release technique.[43] Overall mean cellulite improvement from baseline was reported as 3.1.[43] Both manual and vacuum-assisted subcision have been efficacious in smoothing the skin topography through the release of the collagen-rich subdermal septae, although durability of this effect has been demonstrated only for vacuum-assisted subcision.

Collagenase Clostridium histolyticum

In a Phase 2a, randomized, double-blind, placebo-controlled study ($n = 150$), women treated with collagenase *Clostridium histolyticum* (CCH) 0.48 mg or 0.84 mg had significant improvement from baseline in investigator-performed mean Global Aesthetic Improvement Scale scores at Day 73 versus placebo (0.9 [0.48-mg dose] and 1.1 [0.84-mg dose] vs 0.5 [placebo]; $p < .05$ vs placebo for both; See **Supplemental Digital Content 1**, Table S1, http://links.lww.com/DSS/A299).[44] A Phase 2b, randomized, double-blind study evaluated the efficacy of subcutaneous CCH 0.84 mg in 375 adult women with moderate-to-severe cellulite of the buttocks or posterolateral thighs.[45] At Day 71, 10.6% and 44.6% of patients in the CCH group were 2-level and 1-level composite responders (improvement in both Clinician Reported Photonumeric CSS and Patient Reported Photonumeric CSS), respectively, versus 1.6% and 17.9%, respectively, for placebo ($p < .001$ vs placebo for both).[45]

Effectiveness of Cellulite Treatments by Target Tissue

The main premise of this review is that our understanding of cellulite pathophysiology may increase by reviewing clinical studies that target tissues associated with cellulite. Studies failing to show the efficacy (e.g., inconsistent results between studies, limited, or no results) or studies with inadequate follow-up or only short-term durability post-treatment do not provide data in support of applicable target tissue(s) as the etiology of cellulite. Two studies that targeted the dermis using focused and radial ESWT devices demonstrated statistically significant improvements in skin characteristics and cellulite severity.[25,26] These studies are suggestive that surface skin changes can, to some degree, mask or improve the appearance of cellulite at the intervals evaluated. A 532-nm LLLT device, theorized to target skin, also demonstrated significant improvements in cellulite severity, but only with follow-up of a few weeks and in combination with weight loss compared with the control group.[32] To date, no clinical studies targeting adipose alone have demonstrated improvement in cellulite severity. In contrast, clinical studies selectively releasing septae through vacuum-assisted subcision or through an enzymatic agent have demonstrated significant improvements in cellulite severity that appear to be potentially durable.[38–40,42,44,45,54,66]

Technologies that target multiple tissues also have been used as an approach for the treatment of cellulite. Topical creams containing various active ingredients that target the dermis and adipose have demonstrated statistically significant improvements in cellulite severity with daily application; however, the durability of these improvements after cessation of treatment was unclear or short term ($\leq$2 weeks).[15–19,21] The durability of statistically significant improvements seen after treatment targeting the dermis and subcutaneous tissue with endermologie is unclear.[22,23] Combined, focused, and radial AWT targeting dermis and adipose tissue demonstrated statistical improvements in cellulite severity and reductions in adipose tissue at 3 months.[28] Low-level RF[30] and subdermal laser-based devices[34–37] have also been used as an alternative approach for the treatment of cellulite to target the adipose, dermis, and septae. Both low-level tripolar RF and the 1440-nm Nd:YAG laser demonstrated significant short-term improvements in cellulite severity, with the laser treatment demonstrating durable efficacy at 12 months.[30,35,62] These approaches also demonstrated improvement in skin characteristics.[30,34,37] It is difficult to determine from these studies if one or another of the target tissues was predominately responsible for the improvements seen, or if a combination of small responses cumulated in a clinically meaningful overall result. Therefore, these combination target studies do little to support or refute the case for a given target tissue as the principle pathophysiological culprit in the appearance of cellulite.

Overall, multiple clinical studies that targeted septae alone or in combination with other tissues have reported significant durable ($\geq$12 months) improvements in cellulite severity.[34,39–41,62,66] The successes seen with this approach are consistent with the anatomical differences in septae between cellulite-affected skin and normal skin that were first documented in 1978[1] and confirmed in subsequent biopsy and imaging studies.[1,7,9,12]

Discussion and Conclusions

The etiology of cellulite still has not been fully elucidated in a single comprehensive, scientifically valid study. Limitations of using efficacy studies (See **Supplemental Digital Content 1**, Table S1, http://links.lww.com/DSS/A299) to elucidate the etiology of cellulite include variations in trial protocol design and duration, evaluation time points, treatment parameters, and end points reported, as well as variation in photography techniques and number and training of graders. The inability to objectively quantify the severity of cellulite at baseline, lack of grading scale standardization among studies, and variability in assessing degrees of cellulite improvement are further limitations.[67]

There are 2 central findings of this review: (1) the presence of visible cellulite is associated with histologic changes in the dermis, adipose tissue, and septae, compared with unaffected skin, and (2) efficacy with a treatment strategy that targets fibrous septae (1 of the 3 primary anatomical features of cellulite) is evidence of a cause and effect relationship for the development of cellulite. The lack of efficacy from strategies that target adipose tissue suggests that alterations in adipose tissue are not the primary etiology of cellulite.[24] Short-term improvements have been demonstrated with specific technologies intended to enhance dermal thickness or promote skin remodeling, or a strategy that targets the dermis and adipose tissue simultaneously. However, the lack of durable efficacy suggests that dermal or dermal/adipose changes are not the primary cause of cellulite. Young adult female skin commonly presents with cellulite, which suggests that aging-related changes in dermal thickness are not the primary cause of cellulite.

Clinical data support that targeting the collagen-rich fibrous septae in cellulite dimples through mechanical, surgical, or enzymatic approaches (with or without concomitant treatment of dermis or adipose) is most likely to improve skin topography and produce durable improvement in the appearance of cellulite. Furthermore, a 2019 anatomical study appears to support the importance of the number and type of septae in the etiology of cellulite.[8] Researchers are pursuing further insights into the anatomy and physiology of cellulite, but additional clinical studies to refine existing etiology hypotheses are also needed and can only lead to a better understanding of this common condition in women.

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Address correspondence and reprint requests to: Lawrence S. Bass, MD, Bass Plastic Surgery, PLLC, 568 Park Avenue, New York, NY 10065, or e-mail: drbass@drbass.net