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ORIGINAL ARTICLE

Safety and effectiveness of nano-pulse stimulation™ technology to treat acne vulgaris of the back

Bruce E. Katz MD[1] | Mark S. Nestor MD, PhD[2,3,4] | Richard Nuccitelli PhD[5] | Lauren Jauregui Johnston BS[5] | William A. Knape BS[5]

[1]Juva Skin and Laser Center, New York, New York, USA

[2]Center for Clinical and Cosmetic Research, Aventura, Florida, USA

[3]Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, Florida, USA

[4]Department of Surgery, Division of Plastic and Reconstructive Surgery, University of Miami Miller School of Medicine, Miami, Florida, USA

[5]Pulse Biosciences Inc, Hayward, California, USA

Correspondence
Richard Nuccitelli, Pulse Biosciences Inc, Hayward, California, USA.
Email: rnuccitelli@pulsebiosciences.com

Abstract

Background and Objectives: This feasibility study describes the effects of Nano-pulse stimulation™ (NPS™) technology using the CellFX™ System on acne vulgaris of the back with the objectives of demonstrating safety and effectiveness. The CellFX System applies nanosecond pulses of electrical energy to induce highly localized regulated cell death (RCD) in the cellular structures of the targeted zone with no thermal effect on the tissue and negligible effects on surrounding non-cellular components.

Study Design/Materials and Methods: Seventeen subjects were enrolled at two sites with thirteen subjects completing treatment. Three 7X7 cm regions containing at least five bacne lesions each were identified, one region treated with the CellFX across three treatment sessions, the second region treated as a sham using microneedle tip placement without delivering energy, and the third as an untreated control.

Results: CellFX-treated areas showed an average reduction of acne lesions of 82% by 90 days post-last procedure. Acne improvement was observed in 100% of CellFX-treated regions compared to 39% improvement in Sham regions and 31% improvement in the control regions. The most common skin effects were erythema and hyperpigmentation observed in 23% and 92% of the subjects, respectively, at the last timepoint. No serious adverse events were reported.

Conclusions: CellFX is a safe and effective procedure for clearing back acne.

KEYWORDS
acne, bacne, nano-pulse stimulation, nanosecond, pulsed electric fields

1 | INTRODUCTION

Acne vulgaris is a common skin condition typically associated with excess production of sebum by oil-producing glands and often involving the bacterium, *Cutibacterium acnes* (formerly *Propionibacterium acnes*). It commonly occurs on the face, chest, shoulders, and upper back and affects 35% to nearly 100% in teenagers and young adults, depending on the country and specific age group.[1,2] Given the virtually ubiquitous nature of acne in teenagers, there remains an appreciable need for novel therapies. Some new approaches include oxybrasion,[3] microdermabrasion with Pyruvic acid,[4] and cosmetic acids.[5]

The relatively new non-thermal energy modality, Nano-pulse stimulation™ Therapy (NPS™), has been found to target both the sebum secretory glands and the *Cutibacterium acnes* bacterium by inducing regulated cell death[6,7] in dermal secretory glands[8,9] and

killing *C. acnes* in the biofilm condition normally found on the skin.[10] Therefore, it may become a very effective treatment of acne. Here we report on the first clinical trial investigating the use of CellFX™ to treat back acne on thirteen subjects. Previous studies using the CellFX to treat skin lesions demonstrated efficacy clearing seborrheic keratosis,[11] sebaceous hyperplasia,[8] and non-genital warts.[12]

Much is known about the mechanism by which NPS initiates regulated cell death (RCD) in benign skin lesions.[6] The main targets of NPS are the lipid bilayer membranes surrounding cells and intracellular organelles. The electrical pulses are strong enough to force water molecules into those membranes to form thousands of small, transient nanopores with each pulse, allowing small molecules, such as ions and water, to cross the membrane barriers. When a sufficient number of these nanopulses are applied to the target area, the cells are stressed by the subsequent increase in intracellular calcium[13] as well as the disruption of ATP production due to the loss of the mitochondrial membrane potential[14,15] which then initiates a process common to all cells, often called regulated cell death, including apoptosis. There is abundant evidence indicating that CellFX treatments initiates several steps in the RCD pathway including DNA fragmentation,[16] reactive oxygen species generation,[17,18] calreticulin externalization,[19] and mitochondria swelling.[15] This leads to a slow cell death which allows the recruitment of dendritic cells to phagocytize the dead cells and initiate an immune response if any foreign antigens are present.[19–21]

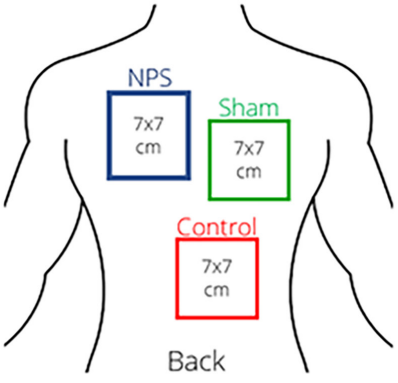
2 | METHODS

2.1 | Study design

This study was designed to determine if the CellFX™ System is safe and effective for the clearance of back acne. This was a multicenter, prospective feasibility study under the supervision of the U.S. Investigational Review Board, Inc. (Protocol #: NP-AF-009). It conforms with the US Federal Policy for the Protection of Human Subjects and was approved as a Non-Significant Risk (NSR) study. Three 7×7 cm areas on the back having a similar number and severity of acne lesions were designated to the three study groups. Each area was divided into 49 1 cm×1 cm squares. One area was treated with CellFX using a 1 cm×1 cm applicator to cover an entire square, one was designated as a sham in which the treatment tip was applied without delivering energy and the third was an untreated control (Figure 1). Baseline assessments of each study area were performed including lesion counts, lesion severity and sebum measurements taken with a calibrated Sebumeter. Active lesions included papules, pustules, and comedones, but were not characterized by the investigators.

A local injection of 0.3–0.5 ml of 0.5%–1% lidocaine containing epinephrine and bicarbonate was applied to each treatment area in the CellFX-treated and sham areas of up to 49 treatment areas per box. The total amount ranged from 4.5–32 ml with an average of 14 ml. Each subject initially received a titration treatment with the CellFX System using the 10 mm×10 mm×2 mm treatment tip to 1–3 spot(s) at the corners of the CellFX-treated area to guide selection of the energy to be used for the remainder of the treatment areas. The titration consisted of three energy levels (high, medium, and low). No intervention was applied to the control study area. Each subject returned 7 days later for evaluation of the three CellFX energy levels by the investigator and one of the three levels was selected for completing CellFX cycles to the remaining CellFX 7×7 cm area. Considerations that factored into the appropriate energy level were the subject's Fitzpatrick Skin type and tissue response to the three energy levels. The first half of the CellFX-area was treated with the selected energy level at Visit two in approximately 23 of the 49 10×10 mm treatment spots (Figure 2) and the second half of the treatment area was treated with the same selected energy level at Visit five, approximately 2 weeks after the first treatment. Visit three and Visit six were usually a 3-day follow-up telephone call and Visit four and Visit seven were a 1-week post treatment checkup by the physician post-procedure.

Each subject was evaluated at all study visits and investigator assessment for lesion count, severity, and sebum measurement occurred at 30-, 60-, and 90-days post complete CellFX Procedure



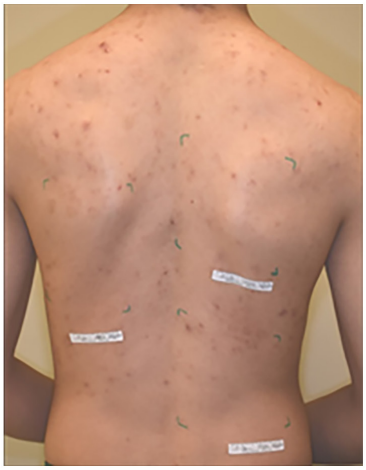


FIGURE 1 Typical example of how the three treatment regions were indicated.

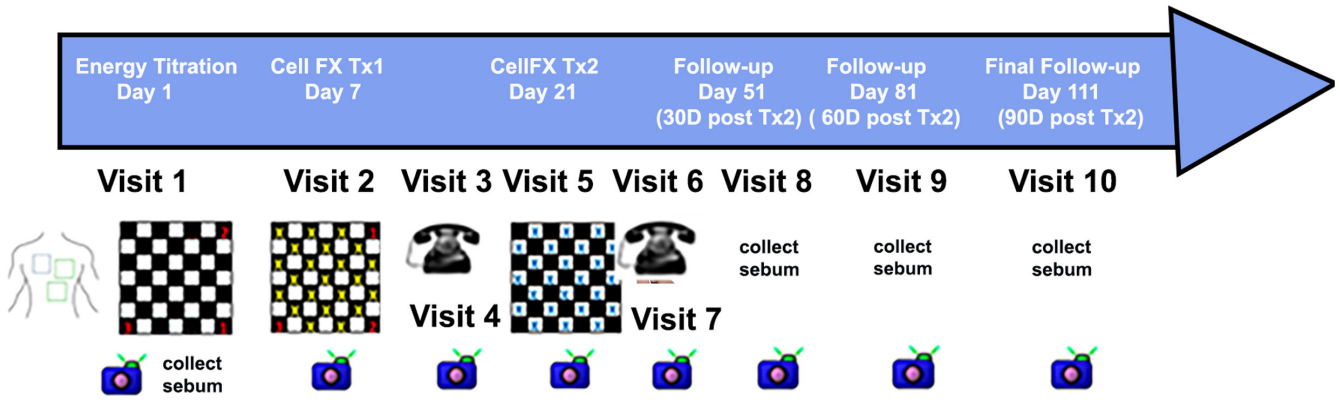


FIGURE 2 Study design.

(90-days post T×2). A photograph of each study area was captured at each in-office follow-up visit.

2.2 | Subjects

Of the 17 subjects enrolled in the study, 59% were male and 41% were female with a mean age of 31 years (18–62 years) with active back acne with a minimum of five acne lesions in each of three 7×7 cm areas. Exclusion criteria included any use of oral Accutane within 6-months of the study beginning, the use of acne topical in the treated area within the last 30 days prior to the study beginning, and antibiotic use within the prior 3 months. The average lesion count at baseline was 14 lesions per 7×7 cm area. Thirteen of the seventeen subjects completed the treatment. Four withdrew due to scheduling commitments or COVID-19-generated clinic closures. However, none withdrew due to the treatment exceeding their tolerance level.

2.3 | NPS treatments

A total of 49 CellFX treatment cycles were applied to each subject's back via microneedle skin surface application to the 7×7 cm area using adjacent placements of the 10 mm×10 mm×2 mm (length×width×depth) treatment tip across three treatment sessions. The initial session applied three titration cycles with energy density levels ranging from 15–120 mJ/mm^3. A single treatment level was subsequently selected and applied to cover the entire CellFX-treated area over two treatment days at 7- and 21-days post-titration evaluation visit (20–85 mJ/mm^3). The average treatment time was 4–30 s per square, averaging 6 min for the first 23 squares and the same for the next treatment. Thirteen subjects completed their scheduled treatment of the entire 7×7 cm area.

2.4 | Sham treatments

A 10.0 mm×10.0 mm×2 mm treatment tip was placed on the skin surface with microneedles being deployed in each designated Sham treatment area during the three treatment sessions, similar to the CellFX-treated area. No NPS energy was delivered.

2.5 | Control study areas

A 7×7 cm area was mapped out to guide the counting and observation of lesions within the study area but there was no contact made with this area.

2.6 | Sebum measurements

Sebum measurements were performed at five locations per study area (four corners and center) to quantitatively measure the sebum level of the skin surface for Baseline, 30-Day, 60-Day, and 90-Day Visits. All sebum measurements were performed with a calibrated Sebumeter (SM 815 MDD), manufactured by Courage & Khazaka. The calibration probe was used before each measurement to provide the highest accuracy.

2.7 | Statistical analysis

Categorical variables are presented using n and the percentage (with the denominator the number with non-missing data). Continuous variables are presented using the mean and standard deviation, unless otherwise specified.

The impact of sebum on % change in lesion count was assessed using Mixed Models for repeated measures including the 30-, 60-, and 90-day changes from baseline. A compound symmetry variance/covariance matrix was used to adjust for within-patient correlation. The dependent variable was % change in lesion count, with visit, area, and the visit-by-area interaction included as fixed effects. Three parameterizations for sebum were evaluated in separate models: mean baseline sebum, mean change in sebum, and an indicator for any increase compared to baseline in sebum measurement. Two-sided p-Values <0.05 were considered statistically significant. Analyses were performed using SAS® version 9.4.

3 | RESULTS

3.1 | Initial response to NPS therapy

The initial response of the skin to CellFX treatment included typical wound-healing effects, such as mild to moderate erythema, edema, eschar, and hyperpigmentation with some crusting and flaking at 7 days (Table 1). Of note, baseline observations of erythema and hyperpigmentation with some cases of crusting, eschar, and edema were reported prior to treatment. By 30 days the edema and other wound effects had subsided and only hyperpigmentation and erythema persisted in about half of the subjects, with eschar reported

TABLE 1 Skin Reactions (CellFX-treated Area).

Skin Effects	Breakdown by Severity (Mild (M)/Moderate (MD)/Moderate–Severe (M-S)/Severe(S))				
	Baseline	7d	30d	60d	90d
	N = 13	*N* = 13[1]	*N* = 13	*N* = 13	*N* = 13
Edema (Swelling)	M: 1 (7.7%)	M: 7 (53.8%)	M: 0 (0%)	M: 0 (0%)	M: 0 (0%)
	MD: 0 (0%)	MD: 3 (23.1%)	MD: 0 (0%)	MD: 0 (0%)	MD: 0 (0%)
	M-S: 0 (0%)	M-S: 0 (0%)	M-S: 0 (0%)	M-S: 0 (0%)	M-S: 0 (0%)
	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)
Erythema	M: 7 (53.8%)	M: 5 (38.5%)	M: 6 (46.2%)	M: 3 (23.1%)	M: 3 (23.1%)
	MD: 4 (30.8%)	MD: 4 (30.8%)	MD: 0 (0%)	MD: 0 (0%)	MD: 0 (0%)
	M-S: 0 (0%)	M-S: 3 (23.1%)	M-S: 0 (0%)	M-S: 0 (0%)	M-S: 0 (0%)
	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)
Bleeding	M: 0 (0%)	M: 1 (7.7%)	M: 0 (0%)	M: 0 (0%)	M: 0 (0%)
	MD: 0 (0%)	MD: 0 (0%)	MD: 0 (0%)	MD: 0 (0%)	MD: 0 (0%)
	M-S: 0 (0%)	M-S: 0 (0%)	M-S: 0 (0%)	M-S: 0 (0%)	M-S: 0 (0%)
	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)
Crusting	M: 2 (15.4%)	M: 0 (0%)	M: 0 (0%)	M: 0 (0%)	M: 0 (0%)
	MD: 0 (0%)	MD: 3 (23.1%)	MD: 0 (0%)	MD: 0 (0%)	MD: 0 (0%)
	M-S: 0 (0%)	M-S: 2 (15.4%)	M-S: 0 (0%)	M-S: 0 (0%)	M-S: 0 (0%)
	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)
Oozing	M: 0 (0%)	M: 1 (7.7%)	M: 0 (0%)	M: 0 (0%)	M: 0 (0%)
	MD: 0 (0%)	MD: 0 (7.7%)	MD: 0 (0%)	MD: 0 (0%)	MD: 0 (0%)
	M-S: 0 (0%)	M-S: 0 (0%)	M-S: 0 (0%)	M-S: 0 (0%)	M-S: 0 (0%)
	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)
eschar	M: 2 (15.4%)	M: 5 (38.5%)	M: 1 (7.7%)	M: 1 (7.7%)	M: 0 (0%)
	MD: 0 (0%)	MD: 6 (46.2%)	MD: 2 (15.4%)	MD: 0 (0%)	MD: 0 (0%)
	M-S: 0 (0%)	M-S: 2 (15.4%)	M-S: 0 (0%)	M-S: 0 (0%)	M-S: 0 (0%)
	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)
Flaking	M: 0 (0%)	M: 4 (30.1%)	M: 0 (0%)	M: 0 (0%)	M: 0 (0%)
	MD: 0 (0%)	MD: 2 (15.4%)	MD: 0 (0%)	MD: 0 (0%)	MD: 0 (0%)
	M-S: 0 (0%)	M-S: 1 (7.7%)	M-S: 0 (0%)	M-S: 0 (0%)	M-S: 0 (0%)
	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)
Hyperpigmentation	M: 7 (53.8%)	M: 3 (23.1%)	M: 3 (23.1%)	M: 4 (30.8%)	M: 5 (38.5%)
	MD: 0 (0%)	MD: 4 (30.8%)	MD: 4 (30.8%)	MD: 4 (30.8%)	MD: 6 (46.2%)
	M-S: 0 (0%)	M-S: 4 (30.8%)	M-S: 4 (30.8%)	M-S: 2 (15.4%)	M-S: 1 (7.7%)
	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)
Hypopigmentation	M: 0 (0%)	M: 1 (7.7%)	M: 0 (0%)	M: 0 (0%)	M: 0 (0%)
	MD: 0 (0%)	MD: 0 (0%)	MD: 0 (0%)	MD: 0 (0%)	MD: 0 (0%)
	M-S: 0 (0%)	M-S: 0 (0%)	M-S: 0 (0%)	M-S: 0 (0%)	M-S: 0 (0%)
	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)	S: 0 (0%)

[1]Indicated number represents the maximum severity observed across all three 7-days post CellFX procedural sessions (titration, Tx1, Tx2).

in a couple of subjects. By 90 days, mild erythema could be detected in only 23% of the cases, markedly decreased from the baseline observation of 85% erythema, however 100% of subjects showed improvement in acne severity over baseline with an average reduction in lesion count of 82%. Hyperpigmentation faded for most subjects and was expected to resolve over time based on the results of our previous sebaceous hyperplasia study,[8] with the first subject of Fitzpatrick skin type V being the most severe (Figure 4).

There were no serious adverse events reported. Mild muscle discomfort was reported for one subject but resolved quickly without intervention.

3.2 | Lesion clearance

An overview of the three skin areas on two subjects can be seen in Figure 3. Photographs of four subjects enrolled in the study with four different Fitzpatrick skin types are provided in Figure 4. Bacne evaluations were rated better for all subjects in the CellFX-treated area with an average reduction in lesion counts in the CellFX-treated area of 82% by 90-days post second treatment (Figure 5). A complete clearance of all bacne lesions (100% reduction in acne lesions) was observed in 31% of subjects across energy levels. The highest treatment level of 85 mJ/mm^3 exhibited an efficacy of 100% reduction (n = 1 subject) with the lowest level of 20 mJ/mm^3 showing an average efficacy of 86% reduction, ranging from 61% to 100% reduction (n = 5 subjects). This compares to a 67% and 62% reduction in sham and control regions, respectively (Figure 5 and Table 2).

3.3 | Sebum levels

Since increased levels of sebum excretion are often observed with acne, the sebum level was measured at 30–60- and 90-days in the CellFX-treated area (Figure 6). The sebum levels declined at 30-days post-last treatment for the higher treatment energies but recovered to higher concentrations by 90-days. This response was larger for mid-range energies than for lower or higher energies. The sebum levels decreased compared to baseline for about half of the subjects; however, no significant relationship was detected between percent change in lesion count and baseline mean sebum measurement (p = 0.923), change in mean sebum (0.864) or any increase in sebum compared to baseline (p = 0.640) as continuous covariates and percent change in lesion count.

3.4 | Condition and skin improvement

The improvement of acne condition was assessed and rated as better, worse or no change, as compared to baseline. The investigator rated the acne condition in the CellFX procedural square as "Better" in 100% of the subjects 90-Days post treatment. The Sham and Control study squares were rated as "Better" in 39% and 31%, respectively (Sham: n = 5 subjects; Control: n = 6 subjects). Most subjects were rated as "No Change" for the Sham and Control treatment squares (Sham & Control: 74%, n = 7 subjects) at the last study visit (Table 2).

The overall skin quality was also evaluated by the physician for each study area at 30-days, 60-days, and 90-days post complete

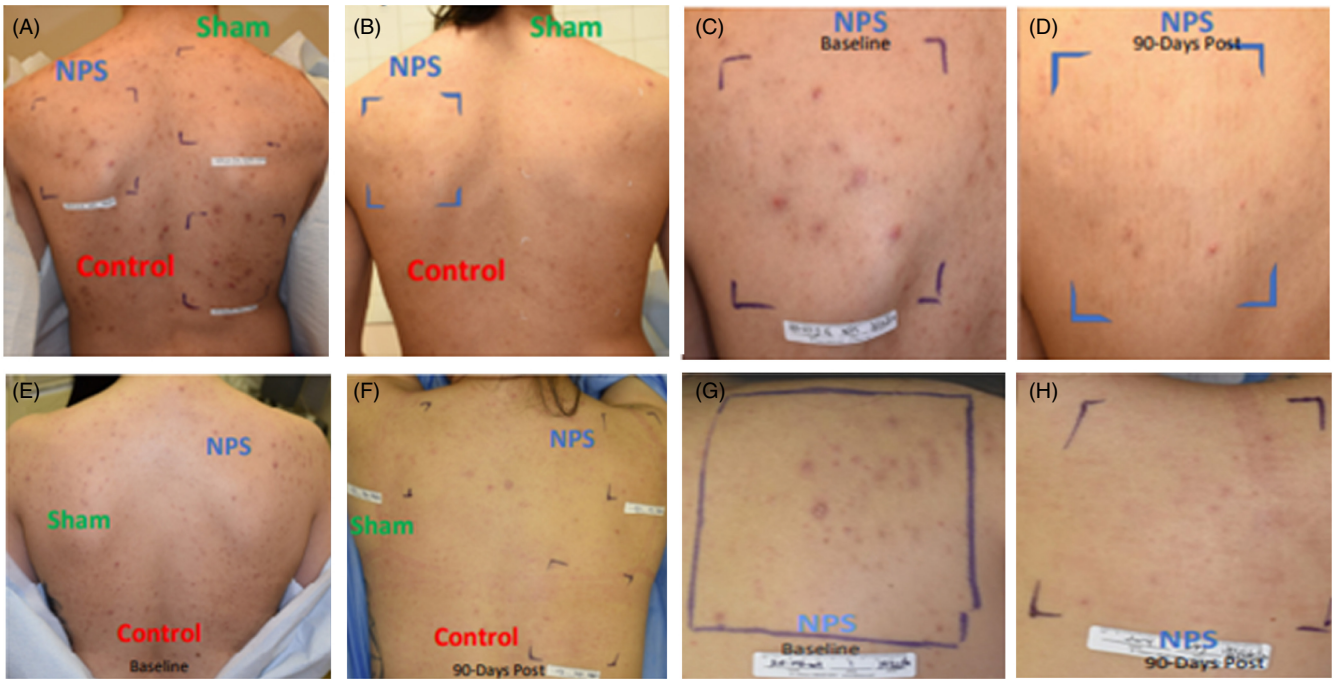


FIGURE 3 Overview of the three skin areas on two subjects. A. Baseline photograph of Fitzpatrick Type IV subject with three skin areas indicated; B. 90-days post treatment; C. Closeup of the CellFX-treated area at baseline; D. Closeup of the CellFX-treated area 90-days post treatment; E. Baseline photograph of Fitzpatrick Type III subject with three skin areas indicated; F. 90-days post treatment; G. Closeup of the CellFX-treated area at baseline; H. Closeup of the CellFX-treated area 90 days post treatment.

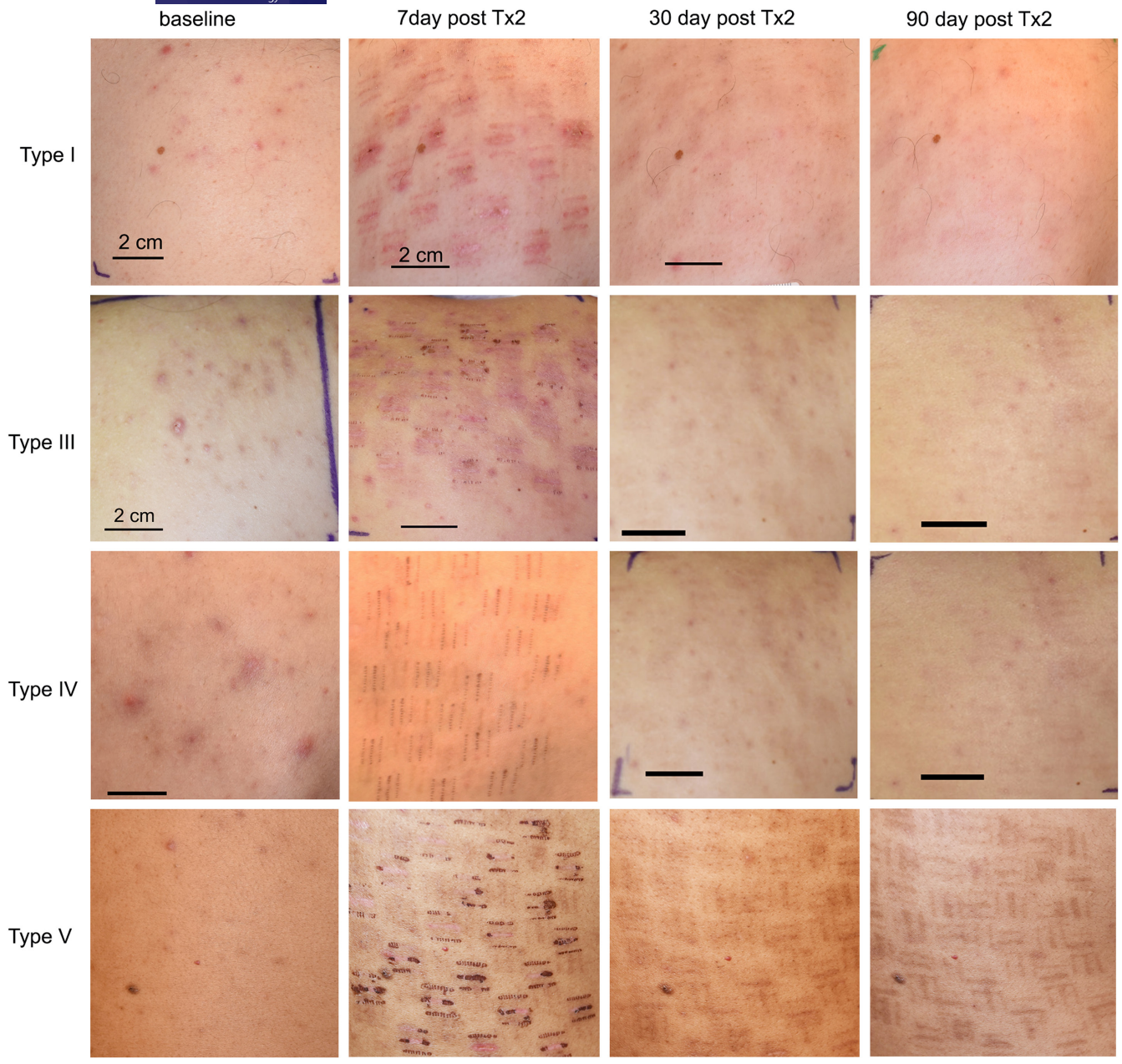


FIGURE 4 Typical responses in the CellFX-treated area over time for four different Fitzpatrick skin types.

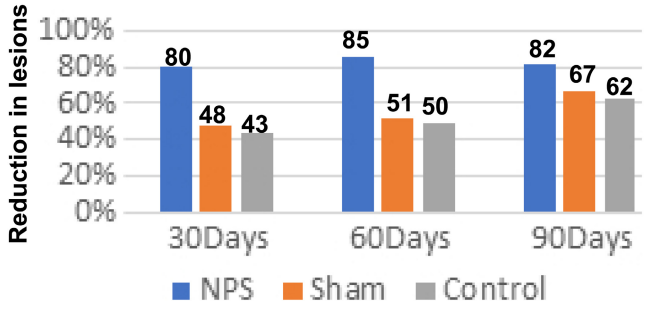


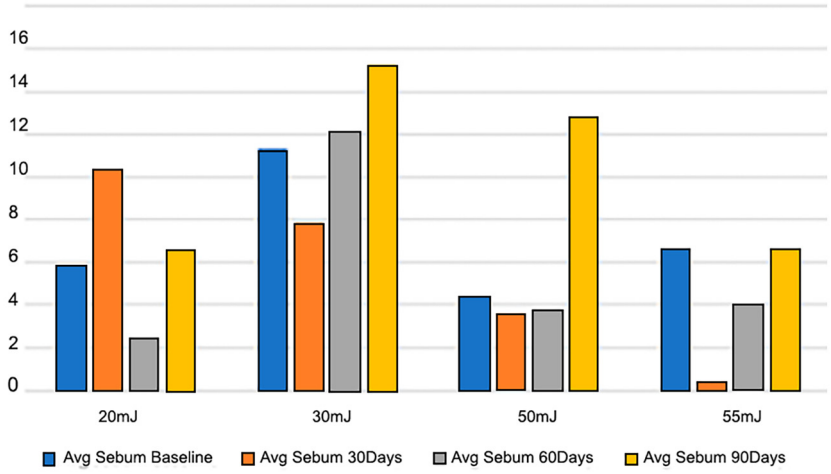
FIGURE 5 Reduction in total lesion counts in the three treatment areas over time.

CellFX procedure. The assessment rating of better, worse or no change was recorded, as compared to baseline. The investigator rated the skin quality improvement in the CellFX procedural square as "Better" in most of the subjects 90-Days post treatment (54% $n = 7$ subjects). The Sham and Control study squares were rated as "Better" in 8% and 15%, respectively (Sham: $n = 1$ subjects; Control: $n = 2$ subjects). Most subjects were rated as "No Change" for the Sham and Control treatment squares (Sham: 85%; $n = 11$ subjects & Control: 69%, $n = 9$ subjects) at the last study visit. Table 1 summarizes the percent reduction of acne lesions along with acne and skin quality improvement.

TABLE 2 Change in acne at last study Visit.

Changes in acne @ 90-Days post procedure	Statistic	CellFX (# Patients, %)	Sham (# Patients, %)	Control (# Patients, %)
Percent reduction in acne lesions (% change in lesion count from baseline to last study visit)	Avg. % Change	82%	67%	62%
Acne Severity/Clearance				
Severity	Clear	4 (30.8%)	0 (0.0%)	0 (0.0%)
	Mild	9 (69.2%)	10 (76.9%)	11 (84.6%)
	Moderate	0 (0.0%)	3 (23.1%)	2 (15.4%)
Treatment response	Overall	13 (100.0%)	9 (76.9%)	8 (84.6%)
Improvement over baseline	3-point	2 (15.4%)	0 (0.0%)	0 (0.0%)
	2-point	3 (23.1%)	2 (15.4%)	1 (7.7%)
	1-point	6 (46.2%)	7 (53.8%)	7 (53.8%)
	No Change	2 (15.4%)	3 (23.1%)	4 (30.8%)
	Worse	0 (0.0%)	1 (7.7%)	1 (7.7%)
Acne improvement	Better	13 (100.0%)	5 (38.5%)	4 (30.8%)
	Worse	0 (0.0%)	1 (7.7%)	2 (15.4%)
	No Change	0 (0.0%)	7 (53.8%)	7 (53.8%)
Skin quality improvement	Better	7 (53.8%)	1 (7.7%)	2 (15.4%)
	Worse	2 (15.4%)	1 (7.7%)	2 (15.4%)
	No Change	4 (30.8%)	11 (84.6%)	9 (69.2%)

FIGURE 6 Average sebum levels by treatment level.



4 | DISCUSSION

This is the first study of tissue lesion effects of CellFX treatment on back acne and the results indicate an impressive effectiveness of CellFX at eliminating acne lesions. A complete clearance of all acne lesions was observed in 31% of subjects at both the highest and lowest energy levels with an average efficacy of an 82% reduction at 90 days post treatment across all energy levels evaluated. This compares to a 67% and 62% reduction in sham and control regions, respectively. This large short-term reduction in the number of acne lesions in these control regions was unexpected and suggests that the CellFX treatment on neighboring skin may somehow reflect a potential loco-regional effect extending beyond the CellFX-treated areas to influence the lesions in untreated regions as well (Figure 7). Areas treated with CellFX showed a fast response and sustained reduction of acne lesions through 90 days post-last treatment, with an average of 80% decrease in acne lesions seen by 30 days post-treatment. When equated to the response levels of the CellFX group, 48% and 43% reduction in acne lesions were seen in the sham and control groups by 30 days, respectively. While no histology of the treated lesions was collected in this study, two previous studies[8,9] included histological sections of NPS-treated skin that indicated the clearance of sebaceous glands within the treatment zone.

High sebum levels have often been associated with acne in teenagers and sebum levels did decline over the first 30 days following CellFX treatment. However, there was no significant relationship found between the sebum levels and the change in lesion count.

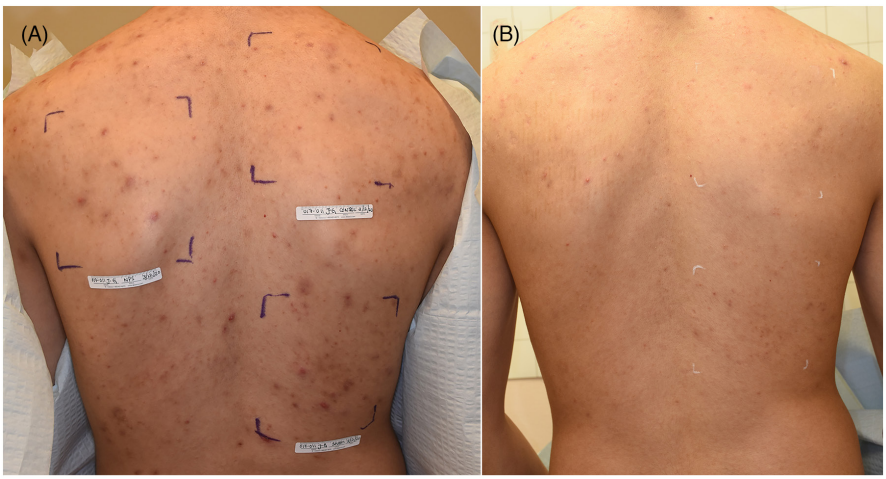


FIGURE 7 Enlarged photos of a subject before (A) and 90 days after (B) the CellFX treatment to illustrate the surprising clearing of lesions in the sham and control regions that suggests a loco-regional effect of the treatment extending beyond the specific treated area.

The overall skin quality was also evaluated by the physician for each study area at 30-, 60-, and 90-days post-last CellFX procedure. For skin treated with CellFX, the skin quality was rated better for more than 50% of the cases compared to only 8% of the sham-treated area (Table 2). This is an added benefit of CellFX treatment because it not only reduces the lesion count but also improves the overall skin quality. Hyperpigmentation was present in most subjects but continued to improve over time and was expected to resolve based on our observations of a similar treatment of sebaceous hyperplasia[8] that was carried out to a full year.

4.1 | Limitations

The main limitation of the CellFX procedure is the requirement for the lidocaine injection prior to each treatment to reduce pain. A secondary limitation is the hyperpigmentation that occurs on Fitzpatrick IV patients.

5 | CONCLUSION

In summary it is concluded that the CellFX Procedure is a safe and effective treatment for back acne and can achieve a short-term improvement in the number of acne lesions on the back. We followed 90 days post last treatment with no increase in lesions. Some patients returned after 6 months with maintenance of clearance. Further studies will be needed to further assess the longevity of the results as well as effectiveness on acne in other regions of the body.

AUTHOR CONTRIBUTIONS

BEK and MSN conducted all of the treatments. LJJ and WAK designed the study and helped write the manuscript. RN wrote the first draft of the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

This was a multicenter, prospective feasibility study under the supervision of the U.S. Investigational Review Board, Inc. (Protocol #: NP-AF-009). It conforms with the US Federal Policy for the Protection of Human Subjects and was approved as a Non-Significant Risk (NSR) study.

ORCID

Bruce E. Katz https://orcid.org/0000-0001-8255-6552
Mark S. Nestor https://orcid.org/0000-0002-8978-7932
Richard Nuccitelli https://orcid.org/0000-0002-1089-3194

REFERENCES

1. Habeshian KA, Cohen BA. Current issues in the treatment of acne vulgaris. *Pediatrics*. 2020;145(Suppl 2):S225-s230.
2. Heng AHS, Chew FT. Systematic review of the epidemiology of acne vulgaris. *Sci Rep*. 2020;10(1):5754.
3. Chilicka K, Rogowska AM, Szyguła R, Rusztowicz M, Nowicka D. Efficacy of Oxybrasion in the treatment of acne vulgaris: a preliminary report. *J Clin Med*. 2022;11(13):3824.
4. Rusztowicz M, Chilicka K, Szyguła R, et al. A Split face comparative study to evaluate the efficacy of 40% pyruvic acid vs. microdermabrasion with 40% pyruvic acid on biomechanical skin parameters in the treatment of acne vulgaris. *J Clin Med*. 2022;11:6079.
5. Chilicka K, Rusztowicz M, Rogowska AM, Szyguła R, Asanova B, Nowicka D. Efficacy of hydrogen purification and cosmetic acids in the treatment of acne vulgaris: a preliminary report. *J Clin Med*. 2022;11(21):6269.
6. Nuccitelli R. Nano-pulse stimulation therapy for the treatment of skin lesions. *Bioelectricity*. 2019;1:235-239.
7. Tang L, Yao C, Sun C. Apoptosis induction with electric pulses – a new approach to cancer therapy with drug free. *Biochem Biophys Res Commun*. 2009;390(4):1098-1101.
8. Munavalli GS, Zelickson BD, Selim MM, et al. Safety and efficacy of nanosecond pulsed electric field treatment of sebaceous gland hyperplasia. *Dermatol Surg*. 2019;46:803-809.
9. Newman J, Jauregui L, Knape WA, et al. A dose-response study of nanosecond electric energy pulses on facial skin. *J Cosmet Laser Ther*. 2020;22(4–5):195-199.
10. Poudel A, Oludiran A, Sözer EB, Casciola M, Purcell EB, Muratori C. Growth in a biofilm sensitizes *Cutibacterium acnes* to nanosecond pulsed electric fields. *Bioelectrochemistry*. 2021;140:107797.

11. Hruza GJ, Zelickson BD, Selim MM, et al. Safety and efficacy of nanosecond pulsed electric field treatment of seborrheic keratoses. *Dermatol Surg*. 2019;46:1183-1189.
12. Nuccitelli R, LaTowsky BM, Lain E, et al. Safety and efficacy of Nano-pulse stimulation treatment of non-genital, cutaneous warts (verrucae). *Lasers Surg Med*. 2021;53:1301-1306.
13. Vernier PT, Sun Y, Marcu L, Salemi S, Craft CM, Gundersen MA. Calcium bursts induced by nanosecond electric pulses. *Biochem Biophys Res Commun*. 2003;310(2):286-295.
14. Vernier PT. Mitochondrial membrane permeabilization with nanosecond electric pulses. *Annu Int Conf IEEE Eng Med Biol Soc*. 2011;2011:743-745.
15. Nuccitelli R, McDaniel A, Connolly R, Zelickson B, Hartman H. Nano-pulse stimulation induces changes in the intracellular organelles in rat liver tumors treated In situ. *Lasers Surg Med*. 2020;52(4):882-889.
16. Nuccitelli R, Tran K, Sheikh S, Athos B, Kreis M, Nuccitelli P. Optimized nanosecond pulsed electric field therapy can cause murine malignant melanomas to self-destruct with a single treatment. *Int J Cancer*. 2010;127(7):1727-1736.
17. Nuccitelli R, Lui K, Kreis M, Athos B, Nuccitelli P. Nanosecond pulsed electric field stimulation of reactive oxygen species in human pancreatic cancer cells is Ca^{2+}-dependent. *Biochem Biophys Res Commun*. 2013;435(4):580-585.
18. Pakhomova ON, Khorokhorina VA, Bowman AM, et al. Oxidative effects of nanosecond pulsed electric field exposure in cells and cell-free media. *Arch Biochem Biophys*. 2012;527(1):55-64.
19. Nuccitelli R, Berridge JC, Mallon Z, Kreis M, Athos B, Nuccitelli P. Nanoelectroablation of murine tumors triggers a CD8-dependent inhibition of secondary tumor growth. *PLoS One*. 2015;10(7):e0134364.
20. Chen R, Sain NM, Harlow KT, et al. A protective effect after clearance of orthotopic rat hepatocellular carcinoma by nanosecond pulsed electric fields. *Eur J Cancer*. 2014;50(15):2705-2713.
21. Skeate JG, Da Silva DM, Chavez-Juan E, Anand S, Nuccitelli R, Kast WM. Nano-pulse stimulation induces immunogenic cell death in human papillomavirus-transformed tumors and initiates an adaptive immune response. *PLoS One*. 2018;13(1):e0191311.

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