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Validation of 3D skin imaging for objective repeatable quantification of severity of atrophic acne scarring

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Abstract

Background: One major sequelae of acne is atrophic scarring, yet objective tools to assess scars are lacking. Neither depth nor volume of atrophic scars is readily evaluable clinically and standard 2D photography is significantly affected by lighting and shadows. The aim of our study was to define and evaluate parameters of 3D imaging that can be used to assess severity of atrophic acne scarring.

Methods: Single center study of 31 patients with acne scarring. A target area of 3 × 3 cm was defined on the face. The global severity of atrophic acne scarring in the target area was evaluated by 5 dermatologists and scars were counted and categorized by size (scars < 2 mm, 2-4 mm, and > 4 mm in diameter). Three dimensional images of the target area were acquired with the LifeViz Micro® system and analysis was performed using MountainsMaps® software. An algorithm was developed to quantify the scar volume loss: shape removal step, with an order 5 polynomial, and to calculate the Valley void volume 80% (Vvv 80%) defined in the ISO-25178 standard for 3D surface texture.

Results: Correlation coefficient of the Vvv parameter to mean global severity at the target area rating was 0.77. The volume of scars evaluated with the Vvv parameter was mainly impacted by scars > 2 mm. The evaluations demonstrated good repeatability (with an intra-class correlation coefficient ICC = 0.98).

Conclusions: We demonstrate convergent validation to clinical assessment and repeatability of 3D skin imaging in atrophic acne scarring. Image analysis is straightforward and can be integrated into an automated workflow.

KEYWORDS

acne, assessment, atrophic scarring, skin imaging

1 | INTRODUCTION

Acne scars are an adverse clinical sequela of acne, present to some degree in up to 43% of acne patients. Scarring occurs when acne-associated inflammation, in pre-disposed patients, is prolonged and associated with inadequate wound healing.[1-4] Scars can be not only esthetically displeasing but can also cause psychological distress.[2,5] Acne-related scars can be hypertrophic (increased repairing tissue) or atrophic (decreased repairing tissue); atrophic scars are often further categorized, either by shape (rolling, boxcar, icepick) or, more reliably, by size.[6,7] This study focused on atrophic scars, which are more common in clinical practice.[8]

Objective tools for scars are needed to evaluate the effectiveness of scar treatments at the clinical research level.[9] Various measures are available for scar elasticity and color[10,11] but are not particularly applicable to atrophic acne scars. Objective tools to assess the

depth or volume of atrophic scars are not readily evaluable clinically, in part due to the typically irregular borders and contours of skin scarring.[5] When multiple scars are present, as is typical in acne, the technical problems are magnified.

Several imaging systems are now available to quantitatively measure skin roughness, wrinkles and nodule formation, track changes over time, and for microstructure skin analysis. These systems are

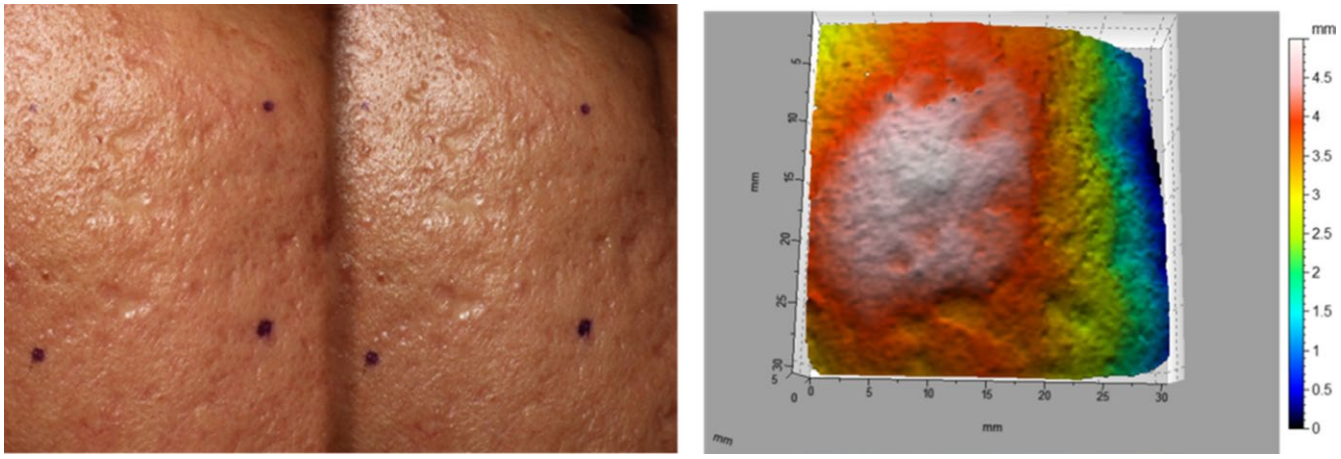

FIGURE 1 LifeViz® Micro: based on 2 pictures the system calculates a 3D representation of the area. Colors code the measured altitude (Z) of each point (blue = 0 to white = 5 mm)

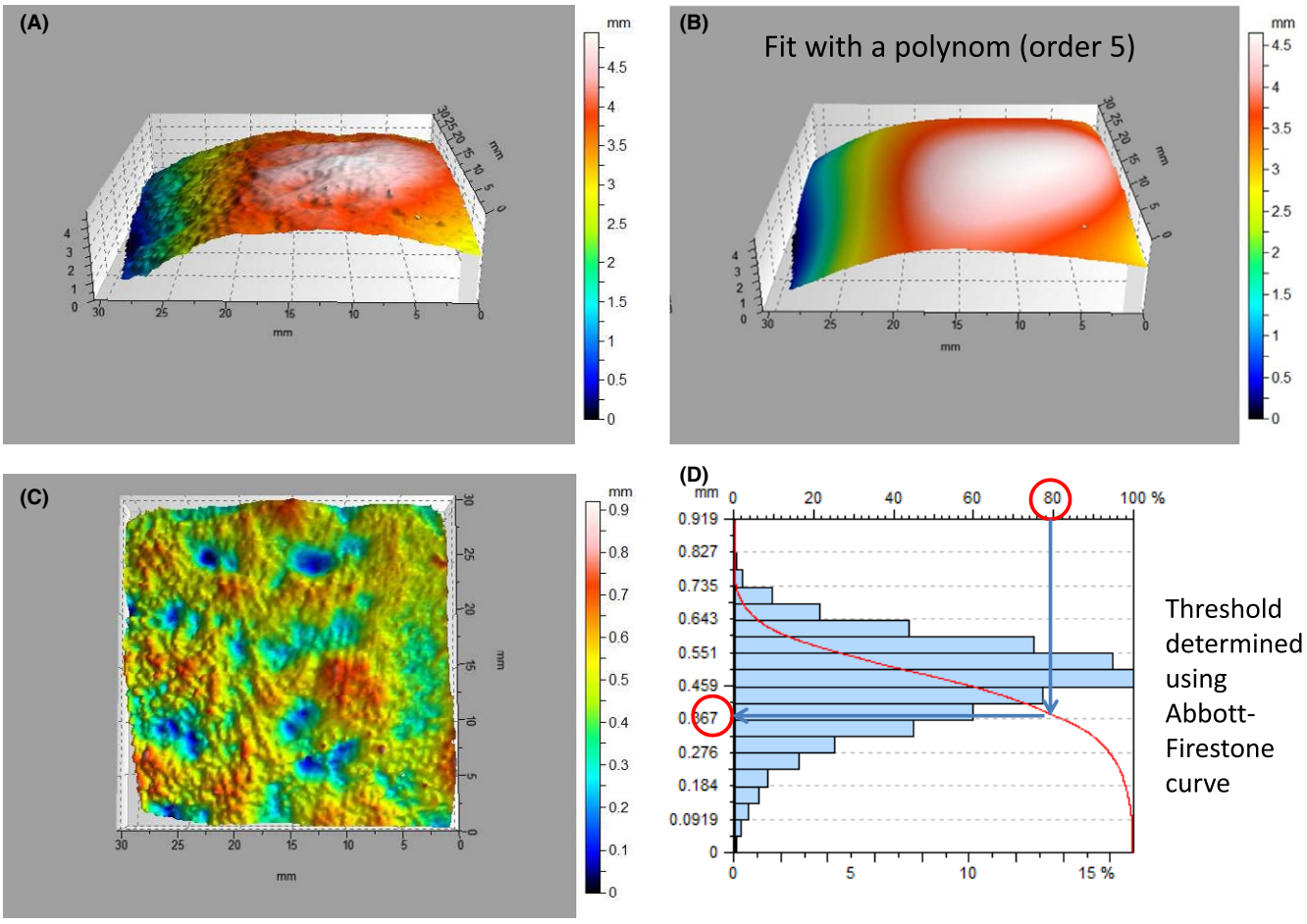

FIGURE 2 Vvv general algorithm used in the study. (A), raw acquired 3D surface of the target area; (B), surface resulting of the fit with a polynom (cheek shape); (C), removing the shape from a: surface a-surface b; (D), Abbott curve and example of the determination of the threshold for 80%

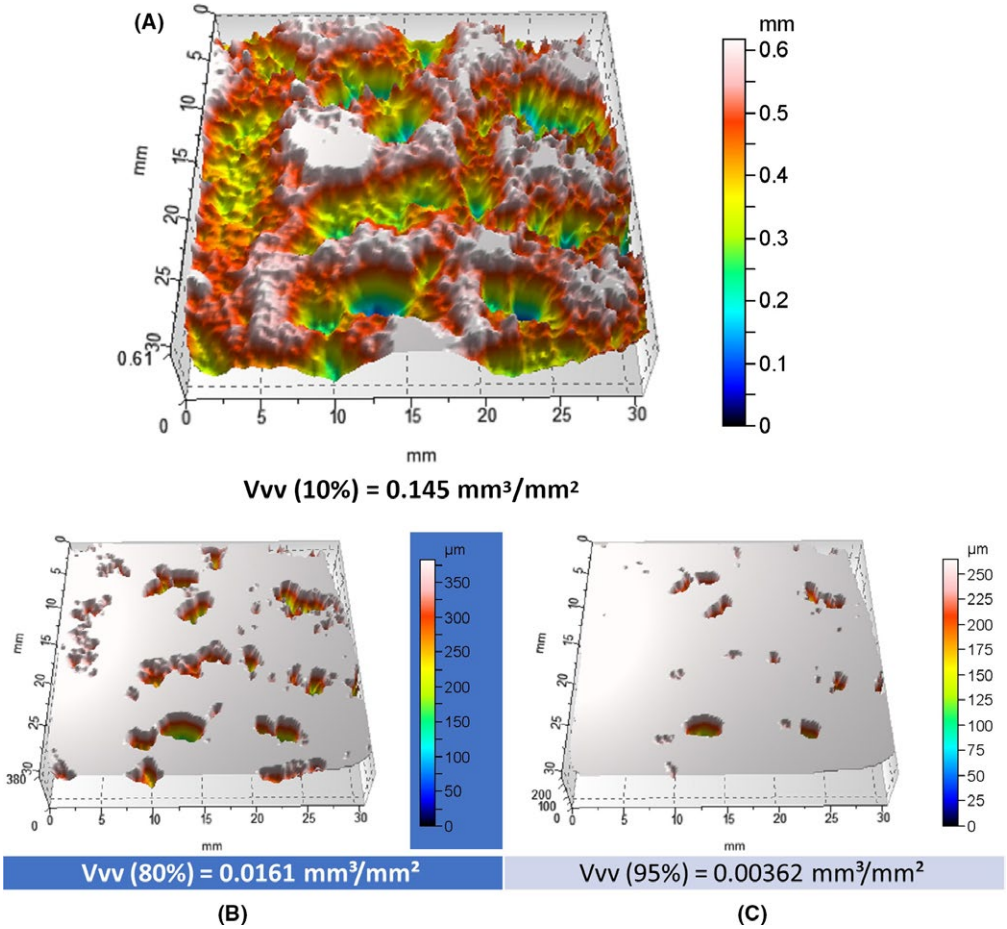

FIGURE 3 Example for thresholding at (A), Vvv (10%) = 0.145 mm³/mm²; (B), Vvv (80%); and (C), Vvv (95%) computation

based on different imaging technologies such stereovision, fringe interference, and advanced optical technologies.

The device used for this study was the 3D LifeViz® Micro (Quantificare SA, France). This is an easy to use, fast, and portable system designed to obtain close-up images of any area of the body, including the face. Standard photography is combined with stereovision technology to produce 3D images. It utilizes a fixed-distance calibration between the camera and integrated dual beam pointers, resulting in improved image reproducibility and consistency in results. The system includes an analysis module to quantify a variety of skin parameters, including volume, height, depth, surface, perimeter, and roughness.

We utilized this device in measuring atrophic acne scarring in a 3 × 3 cm target area of facial skin. It was paired with MountainsMaps® software surface imaging and metrology software (Digital Surf Surface Intelligence, Besançon, France) for image analysis.

2 | METHODS

2.1 | Design

This prospective, non-interventional, single-center trial included subjects aged 18-65 years with facial atrophic acne scars (mild, moderate, or severe), willingness, and ability to complete study procedures, and completion of an informed consent form as well as consent to use images obtained during the study. Patients with significant facial hair or other conditions that would significantly impair evaluation of scars were excluded. Ethics approval was obtained from the Poliambulatorio Agresti Port Authority SRL (Bolognia, Italy).

2.2 | Scar definitions

Atrophic acne scars were defined as loss of tissue (greater than normal pore diameter) following an acne lesion. Only facial atrophic acne scars were evaluated; post-inflammatory erythema, post-inflammatory hyperpigmentation, traumatic and varicella (chicken pox) scars, and perifollicular elastolysis were not assessed.

2.3 | Study procedures

Subjects attended two study visits (V1 and V2) on sequential days. Prior to any evaluations, an independent dermatologist selected a 3 × 3 cm target area on each subjects' face, which had to include at least 2 icepick (<2 mm) scars and 2 small atrophic scars (2-4 mm). If the subjects had large (> 4 mm) scars, the target area included at least one of them as long as the other criteria were also met. Full face

TABLE 1 Baseline characteristics of the study population

	N subjects (%)
Gender	
Female	14 (45.2%)
Male	17 (54.8%)
Total	31 (100.0%)
Ethnic background	
Asian	3 (9.7%)
Caucasian	23 (74.2%)
Mestizo	1 (3.2%)
Negroid/Black	3 (9.7%)
Other	1 (3.2%)
Fitzpatrick skin type	
II	9 (29.3%)
III	16 (51.6%)
IV	2 (6.5%)
V	2 (6.5%)
VI	2 (6.5%)
Active acne	10 (32.4%)
Atrophic acne scars	31 (100%)
Almost clear	4 (13%)
Mild	14 (45%)
Moderate	6 (19%)
Severe	7 (23%)
PIH	17 (56.3%)

pictures were obtained with Visia (Canfield) and 3D photography of the target area was performed with LifeViz® Micro at the start of both study visits. Figure 1 represents an example of LifeViz® Micro and the corresponding 3D representation.

2.4 | Clinical assessments for validation

The global severity of atrophic acne scarring in the target area was evaluated by 5 dermatologists on a 0-4 scale (clear, almost clear, mild, moderate, and severe).[12] Definitions for global severity provided to investigators were: clear = none, no visible atrophic scars from acne; almost clear = few small scattered atrophic scars visible at 50 cm; mild = easily recognizable at 50 cm, less than ½ the face is involved, some small atrophic scars; moderate = many small atrophic scars with ≤ 3 large scars (>4 mm), up to 75% of the face involved; and severe = multiple small and large (>4 mm) atrophic scars, > 75% of face involved. The dermatologists were asked to count acne scars. The size of each scar clinically identified was evaluated using 2- and 4-mm biopsy tools as guides, and each scar was classified by size into 1 of 3 categories: <2 mm, 2-4 mm, and > 4 mm in diameter.

2.5 | 3D analysis

Based on the 3D data of the target area, a quantification approach was established to evaluate several parameters and to establish skin surface topography (depth, surface, roughness, and volume). As the study was conducted with acne patients, the main goal was to find quantitative parameters that are less influenced by positive volume (due to papules/pustules or other primary acne lesions) to ensure the methodology could be used in patients with both scarring and active acne. 3D volume parameters tested were based on ISO 21758 standard for 3D surface texture as described by Blateyron[7] and included: Valley void volumes Vvv (80%), Vvv (95%), void volume Vvv (10%), with pre- or post-morphology filtering. These parameters correspond to the volumes of the negative valley (ie, scars) below a given threshold on the Abbott curve (curve obtained by cumulating the values of the depths distribution from the highest peak (0%) to the deepest valley (100%) of the surface to be evaluated). The Vvv general algorithm is illustrated in Figure 2.

The normative Valley void volume Vvv (80%) was selected for two reasons: (1) it correlated best with clinical severity and (2) from the whole set of 3D volume parameters of the ISO 21758 standard, it is the least sensitive to the presence of active acne lesions. To quantify scarring in the target area, the following algorithm was developed: a shape removal step with an order 5 polynomial and calculation of the Vvv (Valley void volume 80%) defined in the ISO-25178 norm. The void

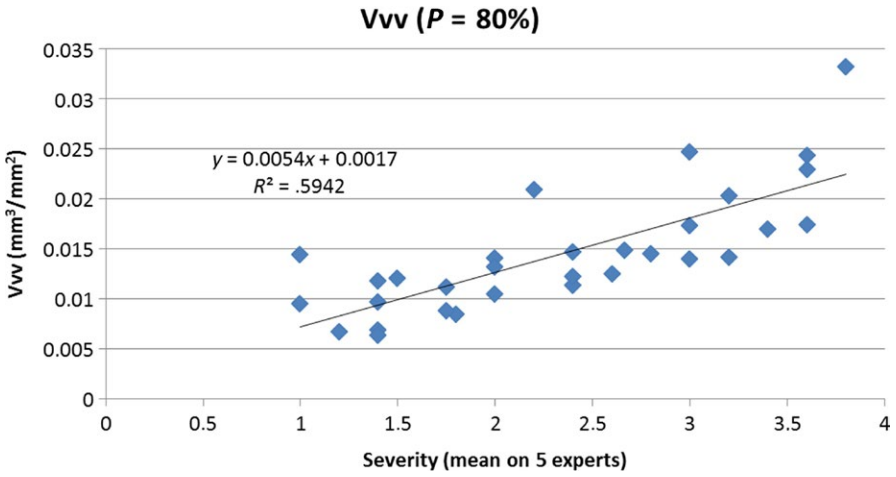

FIGURE 4 Comparison of dermatologists' mean severity of atrophic acne scars assessment and Vvv

TABLE 2 Estimated parameters related to the multiple regression model

Parameter description Scar size	Estimated values	Standard error of estimate	Pr > |t|
Intercept (b_0)	0.00663	0.00158	0.0003
Target area scar count (b_1) Scars < 2 mm	0.00005622	0.00017560	0.7514
Target area scar count (b_2) Scars 2 mm-4 mm	0.00163	0.00050351	0.0033*
Target area scar count (b_3) Scars > 4 mm	0.00128	0.00110	0.2552

*$P \leq .01$.

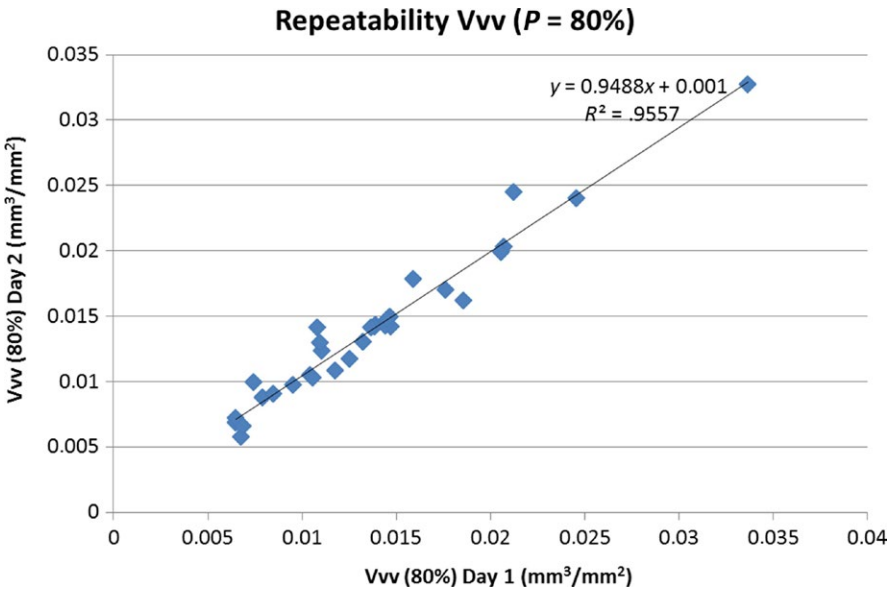

FIGURE 5 Repeatability of Vvv: comparison Day 2 vs Day 1

volume Vvv is defined as the volume of the voids at a material ratio p (in %):

$$Vvv(p) = \frac{K}{100} \int_{p}^{100\%} \left[Smc(p) - Smc(q) \right] dq$$

where *Smc (p)* is the height at which a given area material ratio p is satisfied, and ***K*** a constant to convert to mm^3/mm^2. Figure 3 illustrates the computation of Vvv (10%) from the surface given as example in Figure 2.

The Valley void volume Vvv is defined as the volume of void in the valleys, defined below the material ratio p (in %). Figure 3 also illustrates the computation of Vvv (80%) and Vvv (95%) from the surface given as example in Figure 2.

2.6 | Statistical analysis

The correlation between Valley void volume Vvv (80%) and clinical rating (ie, the mean of global severity of each target area assessed by 5 dermatologists) was performed. The output is the Pearson correlation coefficient. A multiple regression model was used to examine how the mean of counted acne scars by 5 experts (< 2 mm, 2-4 mm, > 4 mm) defined as independent explanatory variables (Xk) were related to the Valley void volume Vvv defined as the dependent variable (Y). The model was expressed as:

$$y_i = b_0 + b_1 x_{i1} + b_2 x_{i2} + b_3 x_{i3} + e$$

Where $i = 1$. n are the index of observed area, y_i the corresponding computed Vvv, x_{ik} The mean of the number of counted scars for the i-th observed area and the k-th stratified class b_0, b_1, b_2, b_3 are the parameters to estimate (ie,: scar size < 2 mm, 2-4 mm, > 4 mm), and e is the error term. Index k is related to the class (< 2 mm, 2-4 mm, and > 4 mm; x_{ik} is the mean of the observers' counts). The outputs were estimated values of parameters b_0, b_1, b_2, b_3, standard error of estimate; F test of the analysis of variance.

3 | RESULTS

3.1 | Patient characteristics

Demographic and acne characteristics of the 31 subjects participating in this study are shown in Table 1. Active acne lesions (> 5 superficial inflammatory lesions) were present in 32.4% subjects (16.13% in each male and female). Mean age was 41.5 years; this older age reflects the search for subjects with acne scars but quiescent acne in 2/3 of the patient population.

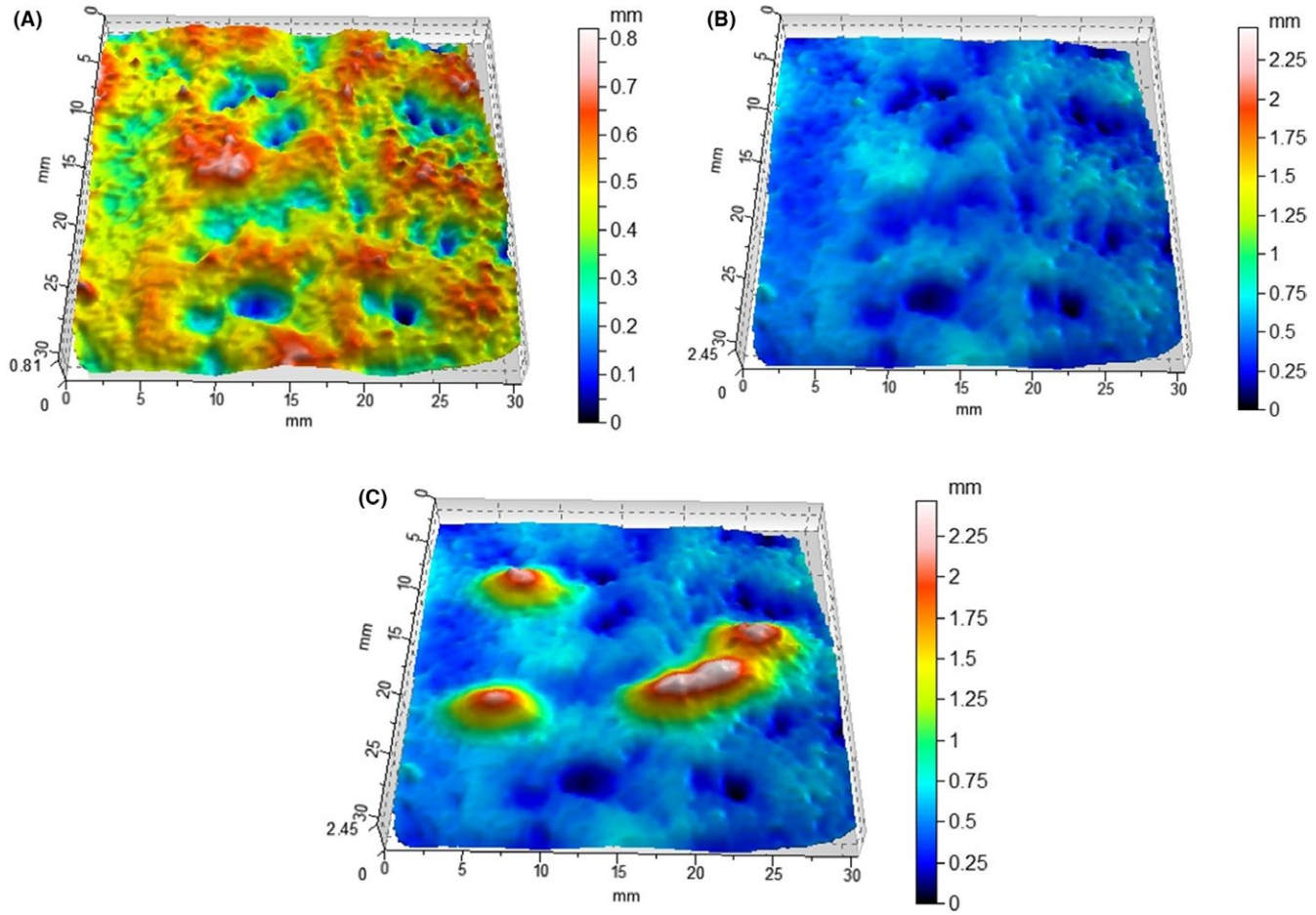

FIGURE 6 Simulated surface with added acne spots. (A), Baseline target area in a depth scale from 0 to 0.8 mm; (B), Baseline target area in a depth scale from 0 to 2.5 mm; (C), Trial with 5 simulated active acne lesions added to the baseline target area

3.2 | Correlation with dermatologist mean severity rating

The correlation coefficient of the Vvv (80%) parameter to the mean clinical rating of scar severity of the target zone by the 5 experts was 0.77 (Figure 4).

From the multiple regression model, the Vvv parameter was mainly explained by the number of scars with a size from 2 to 4 mm, with an estimated parameter value b_2 as reported in Table 2.

3.3 | Repeatability

Repeatability of Vvv was evaluated by 3D imaging of each patient with the same operator for 2 consecutive days. The criteria used was the single measure intra-class correlation (ICC) described by McGraw & al.[10] The measured (ICC) was equal to 0.98 (with for a 95% CI from 0.95 to 0.99). Figure 5 illustrates the reliability of the Vvv computed on 2 consecutive 3D acquisitions.

3.4 | Void volume as robust parameter for acne scars evaluation

The most important issue when addressing an objective evaluation of acne scars is the presence of active acne lesions that causes local changes on the observed target area.

Simulations were conducted to identify the least sensitive parameter of the ISO 21758 standard from our 3D image acquisitions. The principle followed was to add local elevations (spots) mimicking skin surface deformations due to acne papules. We produced 20 simulated surface trials from a baseline target area, with 5 spots in each trial, modeled with Gaussian kernels, with random positions, elevations, and spreads.

An example of such surface is presented in Figure 6.

We computed several amplitude parameters for each simulated surface, and reported in Table 3 the mean value (trial_mean), standard deviation (trial_std), and standard measure of dispersion (CV) to evaluate the sensitivity of parameters. Figure 7 shows the coefficient of variation for simulated trials.

TABLE 3 Sensitivity of amplitude parameters and void volumes on simulated surfaces

	Sq	Ssk	Sku	Sp	Sv	Sz	Sa	Vv (p = 10%)	Vvv (p = 80%)	Vvv (p = 95%)
	Root mean square height (mm)	Skewness <no unit>	Kurtosis <no unit>	Maximum peak height (mm)	Maximum pit height (mm)	Maximum height (mm)	Arithmetic height (mm)	Void volume (mm^3/mm^2)	Valley void volume (mm^3/mm^2)	Valley void volume (mm^3/mm^2)
Baseline	0,115623876	−0,49387115	3,36022304	0,36041193	0,45957907	0,819991	0,09088401	0,14284646	0,015868401	0,003359562
trials_mean	0,31436998	1,6810573	7,24974684	1,528899563	0,604638227	2,13353779	0,213173115	0,435853363	0,017470651	0,003619656
trials_std	0,105844637	1,04334474	4,82200371	1,005334961	0,036712525	1,023515519	0,047341299	0,09996782	0,000939163	0,000211489
trials_CV	0,336688117	0,620647794	0,66512719	0,657554613	0,060718167	0,479726923	0,222079127	0,229361	0,053756613	0,058427816

4 | DISCUSSION

Creating an objective tool for assessing atrophic acne scars is critical for the sensitive and accurate objective evaluation of treatment effect, particularly in clinical research. Two dimensional scar imaging has inherent limitations due to variability with environmental factors such as lighting. An example is shown (Figure 8) where an image of the same area with different lighting conditions/orientation demonstrates drastically different effects on scar visibility. Standardized 2D photography may be inappropriate due to this sensitivity to incident lighting and camera positioning. In addition, many of the existing full-face digital camera devices do not have adequate resolution to reliably detect and quantify scar volumes. Thus, it is important to identify and evaluate other non-invasive assessment tools, such as 3D imaging.

The current limitation of LifeViz Micro is the small target area due to its limited resolution. As technology evolves, we envision that a clinically useful full-face evaluation technology will be developed in the near future. Improvements in facial imaging and modeling will allow incorporation of objective analyses and high-quality acne scarring research. MountainsMaps software provided an easy to use process that can be adapted for batch modes.

We found 3D skin imaging to be an objective measure for quantification of severity of atrophic acne scarring. However, for 3D imaging to be relevant in the clinical setting, an analysis method for this technology must be created that provides good repeatability. This study identified a normalized parameter Vvv (volume of scars mm^2) for the observed surface that is: (1) correlated to clinical severity, (2) repeatable, and (3) statistically correlated with clinical observations of scars in the range of 2 mm to 4 mm. Repeatability was excellent, with comparison of data from V1 to V2 yielding an ICC of 0.98. The mean values are significantly far from the reference baseline value, except for valley void volumes Vvv (80%) and Vvv (95%). Moreover, the dispersion coefficient (CV) is acceptable only for maximum pit height and valley void volume Vvv (80%), Vvv (95%) as shown in Figure 8. A CV exceeding approximately 0.2 is often indicative of problems in the data or indicates that the experiment is flawed. These data confirm that valley void volumes are robust parameters for quantifying acne scars.

A prior study on acne scarring also correlated results of dermatologists' subjective scores with a 3D photographic modeling system using 3 angled cameras to create a topographic map with computer-generated quantitative volumetric measurements.[13] This group reported a "statistically significant linear correlation (Spearman rank order correlation 0.76, $P < .05$) suggesting that facial scar imaging may help quantify postacne scarring."

The importance of a reliable, repeatable, and standardized methodology of analyzing 3D images is underscored by the fact that there are a few scattered reports of 3D image assessment of the impact of acne scar treatment. Brauer et al reported that 3D imaging measurements of scar volume showed a 24.3% improvement with pulsed laser in scar volume, but did not detail the methodology for computation of volume.[14] In discussing the use of 3D imaging, these investigators noted that a limitation "was the potential for lack of reproducibility with possible variation in angle or pressure, as well as misalignment

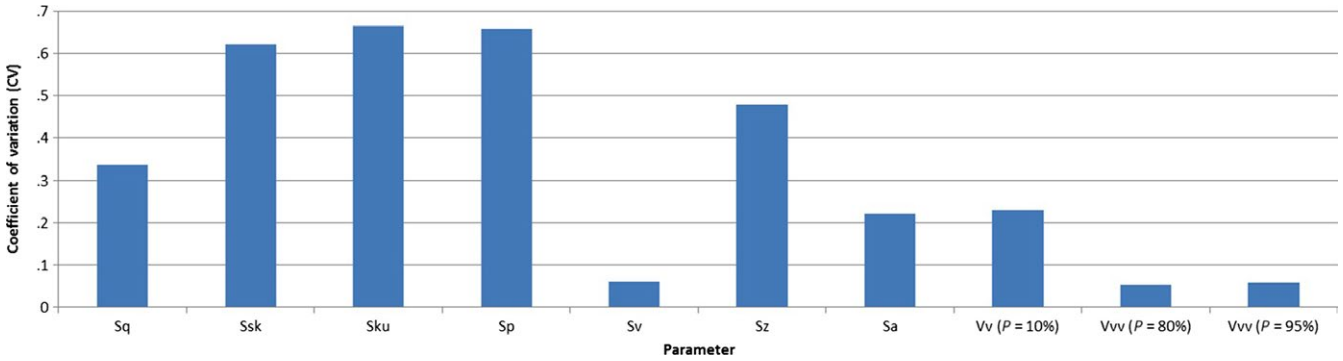

FIGURE 7 Coefficient of variation computed on the simulated trials

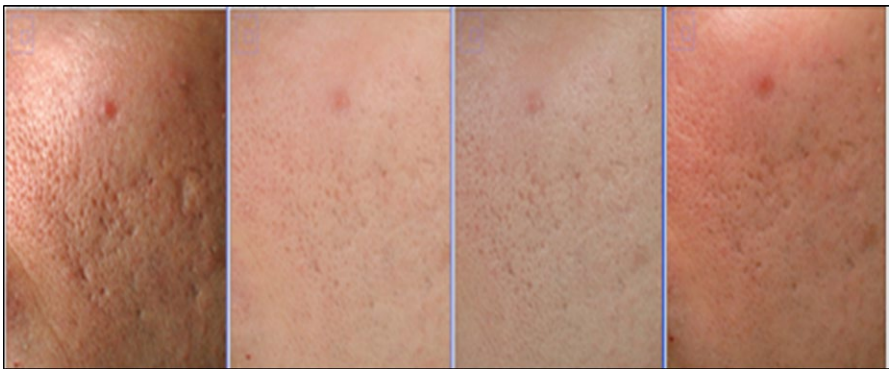

FIGURE 8 Example of limitations of 2D imaging–same area with different lightening condition showing the impact of lighting on scars visibility

of before-and-after images." We did not experience a similar problem about pressure, since LifeViz captures images without any skin contact. However, we had the same issue of alignment variation in before/after images, and are refining a positioning system. In our experience, the presence of active acne did not have a marked impact on reproducibility of scar assessment. The ability to assess scars when acne lesions are present is an advantageous property of this technology.

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