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Quantification of cutaneous allergic reactions using 3D optical imaging: A feasibility study

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Abstract

Background: User-independent quantitative measures of cutaneous allergic reactions can help the physicians manage and evaluate the treatment of cutaneous allergic reactions. In this paper, we present and validate a method to quantify the elevation, volume and area of cutaneous allergic reactions to red tattoos.

Methods: The skin surface of allergic tattoo reactions was imaged using an optical 3D scanner. The in-house developed analysis tool measured the elevation, volume and area of the lesions, compared to a reference surface. This reference surface was created by 3D interpolation of the skin after manual removal of the lesions. The error of the interpolation tool was validated using a digital arm model. The error of our optical scanner was determined using a 3D printed lesion phantom. The clinical feasibility of the method was tested in 83 lesions in 17 patients.

Results: The method showed clear potential to assess skin elevation, volume change and area of an allergic reaction. The validation measurements revealed that the error due to interpolation increases for larger interpolation areas and largely determined the error in the clinical measurements. Lesions with a width ≥4 mm and an elevation ≥0.4 mm could be measured with an error below 26%. Patient measurements showed that lesions up to 600 mm^2 could be measured accurately, and elevation and volume changes could be assessed at follow-up.

Conclusion: Quantification of cutaneous allergic reactions to red tattoos using 3D optical scanning is feasible and may objectify skin elevation and improve management of the allergic reaction.

KEYWORDS

3D scanner, allergic reaction, elevation, lichenoid, optical scanner, phantom, red, skin, tattoo ink, volume

1 | INTRODUCTION

The measurement and quantification of cutaneous allergic reactions are important for treatment management and evaluation, since it provides an objective measure free off inter-observer variation and enables the medical specialist to compare the cutaneous allergic reactions before and after treatment. In current clinical practice, the evaluation of the skin is generally performed in a qualitative manner, such as a description of visible signs of inflammation and structure evaluation by touching the skin.[1] Quantitative measurements such as measuring tape or a caliper are used less frequently. Medical photography might be used as a reference in follow-up; however, medical photography only provides a relative quantification. These measurements are user-dependent, and therefore, the reliability and reproducibility are subject to the skill of the investigator. A frequently used semi-invasive method is a skin patch test,[2] a diagnostic tool to determine sensitization or an allergic reaction. However, this test only provides a subjective measure for the severity of the allergic reaction. A user-independent quantitative method to evaluate allergic lesions can be an improvement. Ultrasound[3] is a user-independent quantitative method; however, this method is not commonly used in the clinic for the assessment of allergic reactions.

Since handheld 3-dimensional (3D) scanners can produce high-resolution 3D surfaces and have become portable, inexpensive and require little training, and they are increasingly used in clinical setting. These scanners typically use structured light to measure surfaces.[4] They have been applied to measure body volumes,[5] to compare BMI with 3D,[6] to study growth defects, to design patient-specific prosthetics,[7] as well as measuring wounds [8] and scar height.[9] But up to now, they have not been applied to quantify cutaneous allergic reactions. 3D optical scanning techniques may offer an user-independent, non-invasive, quantitative method for the management or evaluation of skin treatment.

Allergic tattoo reactions are suitable to study the feasibility of 3D optical scanning as the allergic area is chronic, well defined and frequently causing a plaque elevation.[10] Chronic allergic tattoo reactions are predominantly caused by red tattoo ink, and the number of allergic tattoo reactions correlates with the increasing number of aesthetic tattoos.[11]

The purpose of this study is to show the feasibility of 3D optical scanning as a tool to quantify allergic reactions of the skin. Therefore, we developed an analysis tool of the 3D images and tested the method for accuracy and in patients with one or more allergic tattoo reactions.

2 | METHODS

2.1 | Handheld optical 3D scanner

For this study, a handheld optical 3D scanner (Artec Spider, Artec 3D, Luxembourg), henceforth called optical scanner, was used, see Figure 1. The optical scanner has a 3D resolution of 0.1 mm and 3D point accuracy of 0.05 mm, which is smaller than the smallest visible allergic reactions. Furthermore, the optical scanner has a linear field of view ranging from 90 × 70 mm (at 0.17 m) to 180 × 140 mm (at 0.35 m), so even allergic reactions with a diameter up to 100 mm can be assessed. The frame rate of the optical scanner is 7.5 frames per second, while the exposure time of one frame is 0.5 ms[12] Thus, the typical scan time to obtain a scan of one side of the forearm is about 60 seconds, generating 92-338 images. The optical scanner was operated using a regular laptop (HP ZBook 15, Intel Core i7-4700 MQ CPU @ 2.40 GHz, 24 GB RAM, 64-bit OS) running 3D image acquisition software (Artec Studio v.12 professional, Artec 3D).

The optical scanner generates data when making a 3D scan. This raw scan data are polygonized and exported as an Surface Tessellation Language (STL) model, using the 3D image acquisition software of the optical scanner, see Figure 2.

2.2 | Analysis algorithm

The analysis algorithm consists of an interpolation tool, which is required to create a reference surface which is used in the analysis tool, which calculates the elevation, volume and area of the lesions on the STL model.

2.2.1 | Interpolation tool

The scanned skin surface, presented by an STL model, is further processed in a software package (GOM Inspect metrology software). The surface model is manually positioned such that the z-axis is set perpendicular to the skin surface at the location of the allergic reaction. This is a requirement for the analysis tool. This model is henceforth called *original surface model*.

A *reference surface model* is required to determine the elevation and volume in the analysis tool, see Figure 3. The reference surface model represents the shape of the skin without the lesions. To create the reference surface model, regions of interest (ROI's) are selected around the lesions in a duplicate of the original surface model and

FIGURE 1 Handheld optical 3D scanner: Artec Spider, Artec 3D, Luxembourg [Colour figure can be viewed at wileyonlinelibrary.com]

removed to create a *hole surface model*, see Figure 4. These ROI's are selected manually closely around the allergic reaction. Subsequently, the surface in the hole surface model is interpolated over the holes using a standard algorithm of the GOM Inspect software (Close Holes Interactively, type Normal, while neighboring polygons were not deleted) to create the reference model. The algorithm interpolates the existing surface-based continuity of the surface normal vectors of the surrounding triangles. Both original and reference surface model were exported as ASCII-files containing space coordinates.

2.2.2 | Analysis tool

The analysis tool calculates the elevation, volume and area of lesions from the original surface model and the reference surface model. This tool is in-house developed software within MATLAB (Release 2015b, The MathWorks, Inc). The Matlab functions meshgrid (resolution of 0.1 mm in *x*- and *y*-direction) and griddata (linear fit) were used to convert the surface models to a measurable grid (of 0.1 × 0.1 mm in *x*- and *y*-direction), with respective interpolated *z*-coordinates.

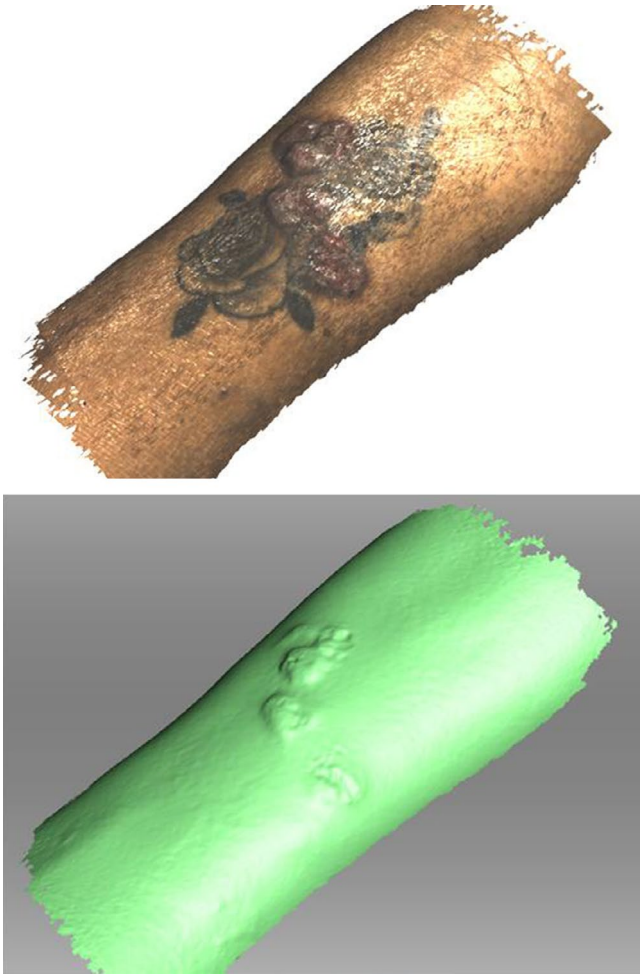

FIGURE 2 The top panel shows raw 3D scan data of an allergic tattoo reaction on a leg in the 3D image acquisition software. The bottom panel shows a polygonized surface of the raw 3D scan data [Colour figure can be viewed at wileyonlinelibrary.com]

The elevation is assessed by calculating the maximum distance between the two surfaces, see Figure 3, based on the normal vector of the reference surface model. The volume is calculated by integrating the volume between the two surfaces. Each gridpoint has a surface area depending on the normal of the surface. The interpolated area is calculated by summation of the areas of all gridpoints in which the original surface model is elevated from the reference surface model. The lesion area is calculated by summation of the areas of all gridpoints in which the elevation (difference between the reference surface model and the original surface model) exceeds a threshold of 0.1 mm.

2.3 | Validation

In this section, the methods are described for assessing the induced errors by the analysis algorithm and the optical scanner.

2.3.1 | Interpolation induced errors

The interpolation tool creates a reference surface. The accuracy of this algorithm together with the shape of the original surface determines the accuracy of the elevation and volume measurements. The errors induced by the interpolation tool are estimated by applying the analysis tool to a surface model of a lower arm without any lesions, see Figure 5. The lower arm of a volunteer was scanned with the optical scanner. From these data, a digital 3D model, henceforth called arm model, was created. The volunteer had no visible lesions on the arm, only a few small naevi.

Duplicates of the arm model were created. In each duplicate, an ROI was selected to be removed from the model, in order to create hole surface models. The holes were interpolated to create reference surface models, as described by the interpolation tool. Since the original surface model of the arm had no lesions, the reference surface models intents to be similar to the original surface model. Any deviations between the two surfaces are due to induced errors

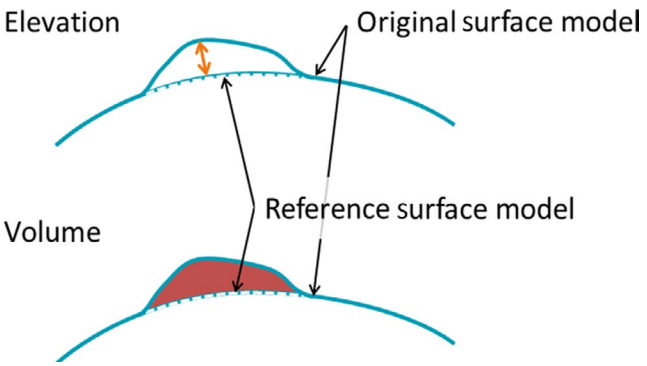

FIGURE 3 The analysis tool calculates the elevation and the volume of the lesions from the original surface model and the reference surface model. The elevation is given as the maximum distance between the surfaces, whereas the 3D volume is the integrated volume between the surfaces [Colour figure can be viewed at wileyonlinelibrary.com]

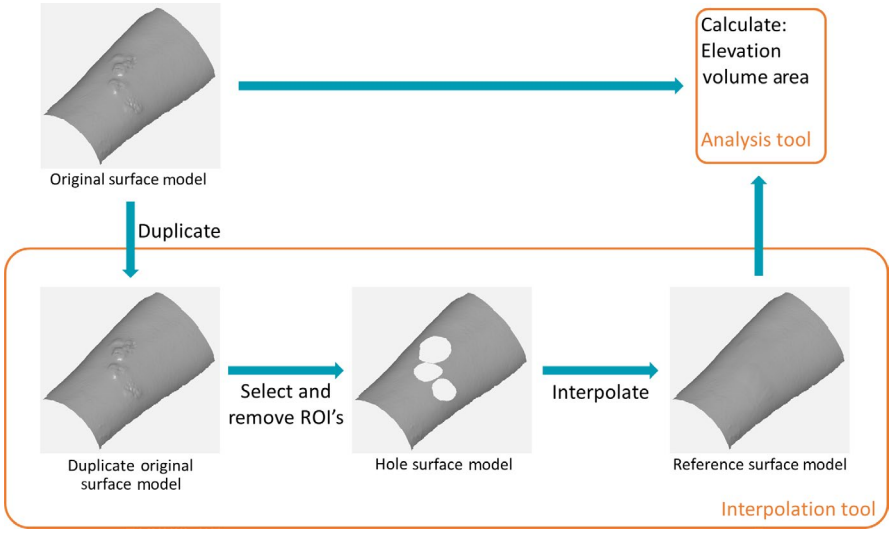

FIGURE 4 Flow scheme of the interpolation tool. The tool duplicates the original surface model. ROI's are manually selected around the lesions on the duplicate original surface model, which are subsequently removed to create a hole surface model. The surface is interpolated over the holes to create the reference surface model. The original surface model and the reference surface model are then used to calculate the elevation, volume and area in the analysis tool [Colour figure can be viewed at wileyonlinelibrary.com]

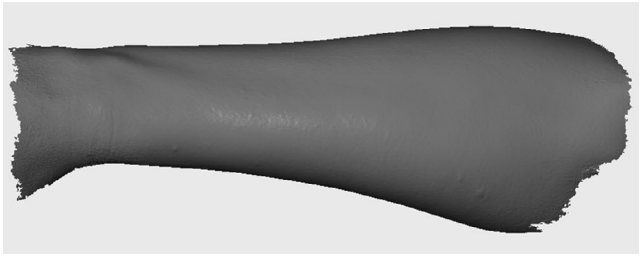

FIGURE 5 Arm model without any lesions, as applied to quantify the errors induced by the interpolation tool

by the interpolation tool. Using the analysis tool, these errors in the elevation and volume were determined.

ROI´s with variable size and position were applied, on 32 positions (8 positions transversally, four positions axially) and sizes ranging from 25 to 1200 mm^2. The ROI´s were rectangular for practical reasons. To calculate the standard deviation of the induced error, the results were grouped based on the intended size of the ROI's. The actual size of the ROI's increased somewhat due to the 3D nature of the surfaces, while the selection of the ROI's was performed in a 2D view. The intended sizes of the ROI's were 5 × 5 mm (25 mm^2), 10 × 10 mm (100 mm^2), 15 × 15 mm (225 mm^2), 20 × 20 mm (400 mm^2), 20 × 40 mm (800 mm^2) and 30 × 30 mm (900 mm^2).

The elevation error was measured as the largest distance between the original surface model of the arm and a reference surface per ROI. A positive value was given if the original surface was above the reference surface, and vise versa for a negative value. The same holds for the measurements of the volume error.

2.3.2 | Scanning induced errors

Secondly, the accuracy of the optical scanner in combination with the analysis tool was tested. The measurement errors were quantified using a 3D printed lesion phantom, see Figure 6, which was created using MATLAB. The phantom consists of a flat surface with Gaussian-shaped lesions. Due to the flat surface, interpolation

FIGURE 6 Photography of the 3D printed lesion phantom to quantify the errors induced by using the optical scanner and the analysis tool. The lesion phantom contains Gaussian-shaped lesions ranging from 0.1 to 5 mm in elevation and 0.5 to 16 mm in diameter [Colour figure can be viewed at wileyonlinelibrary.com]

errors do not contribute. The lesions vary in diameter and in elevation; elevation ranges from 0.1 to 5 mm, and the base diameter of the lesion ranges from 0.5 to 16 mm. The standard deviations (SD) defining the Gaussian-shaped lesions were chosen such that the height of the Gaussian at the edge of the base area equals the print resolution of the 3D printer (0.1 mm), resulting in a SD ranging from 0.08 to 2.64 mm. The subsequent Gaussian-shaped lesions had volumes ranging from 0.004 to 217 mm^3.

The 3D printed lesion phantom was scanned with the optical scanner, and the analysis algorithm (interpolation tool and analysis tool) was applied to measure the elevation, volume and area of each lesion

separately. The 3D printed lesion phantom was scanned six times, and the resulting elevation and volume were averaged for each original lesion.

To estimate a total error of a lesion measurement with a specific lesion size, elevation and hole area, the variances (the square of SD's) of the two errors (induced by interpolation and scanning) are added to calculate the combined SD. This total error is shown as the error in the in vivo results for elevation and volume. The error in the area measurements due to the interpolation tool is not determined in this study.

2.3.3 | In vivo feasibility evaluation

The feasibility of quantification of allergic reactions using the optical 3D scanning method was evaluated in patients with allergic tattoo reactions. Patients were included at The Academic Tattoo Clinic Amsterdam in the period of September 2017 until July 2018. Patients with a constant, chronic cutaneous tattoo reaction, confined to the red area, were included.

After diagnosis was made by the dermatologist, informed consent of the patient was obtained to participate in the study to collaborate voluntarily in the study. If complied, a 3D scan was obtained by moving the optical scanner around the lesion at a skin distance in the range of 17 to 35 cm. Patients with follow-up appointments in the inclusion period were scanned multiple times, typically 2-6 months later.

Patients with allergic tattoo reactions were treated with super-potent topical corticosteroids for several weeks.

The Medical Ethics Review committee of the VU University Medical Center judged that the Medical Research Involving Human Subjects Act did not apply for this study, this is registered at "Centraal Meldpunt Gegevensverwerking": VUmc_2017-2434. All patients and the volunteer gave informed consent.

The described analysis algorithm was used to assess elevation, volume and area of lesions caused by allergic tattoo reactions, before and after treatment. In case of multiple distinguishable lesions in a patient, each was measured separately. To evaluate whether individual lesions could be measured accurately, the elevation and volume of each individual lesion are plotted against the lesion area. To evaluate whether changes in elevation and volume of lesions during treatment could be measured significantly, the elevation and volume of individual lesions were plotted for each visit to the outpatient department.

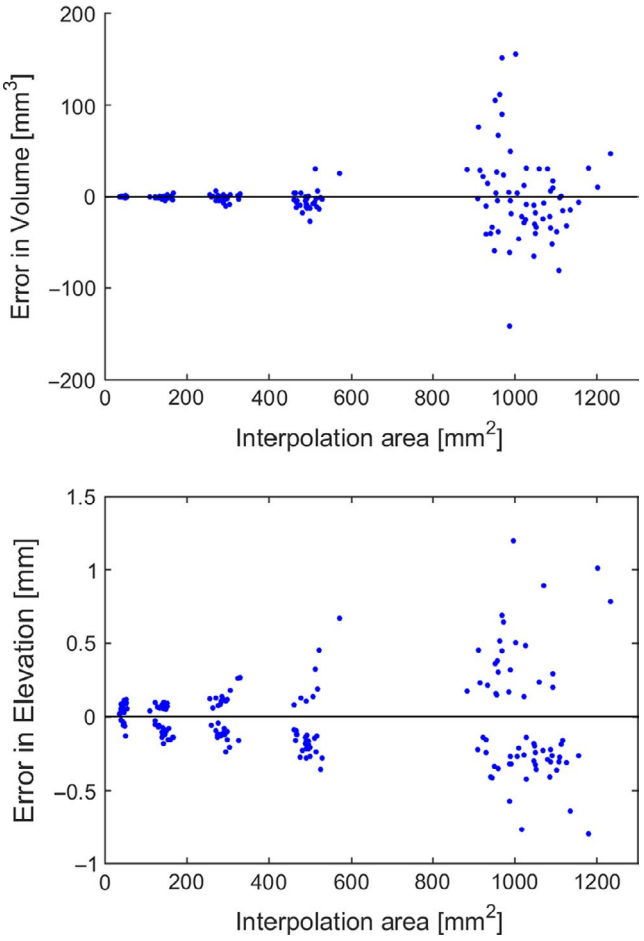

FIGURE 7 The error in elevation (bottom panel) and the volume (top panel) due to the interpolation tool, plotted against the interpolation area, as assessed in the arm model [Colour figure can be viewed at wileyonlinelibrary.com]

3 | RESULTS

3.1 | Interpolation induced errors

Figure 7 shows the determined error in elevation and volume due to interpolation algorithm in the arm model. The mean error in both elevation and volume enlarges with increasing interpolation area, as also presented in Table 1. At large holes, especially rectangular shapes, the interpolation induces large errors.

TABLE 1 Mean error and standard deviations in elevation and volume due to interpolation errors for different size ranges of the interpolation area, as determined from the data of Figure 7

Interpolation area (mm^2)	Elevation		Volume	
	Mean (mm)	SD (mm)	Mean (mm^3)	SD (mm^3)
25-100	0.03	0.06	0.02	0.4
100-225	−0.03	0.10	−0.5	1.5
225-400	−0.02	0.14	−1	3
400-800	−0.1	0.2	−4	11
>800 (rectangle)	0.1	0.5	27	83
>800 (square)	−0.1	0.4	−14	29

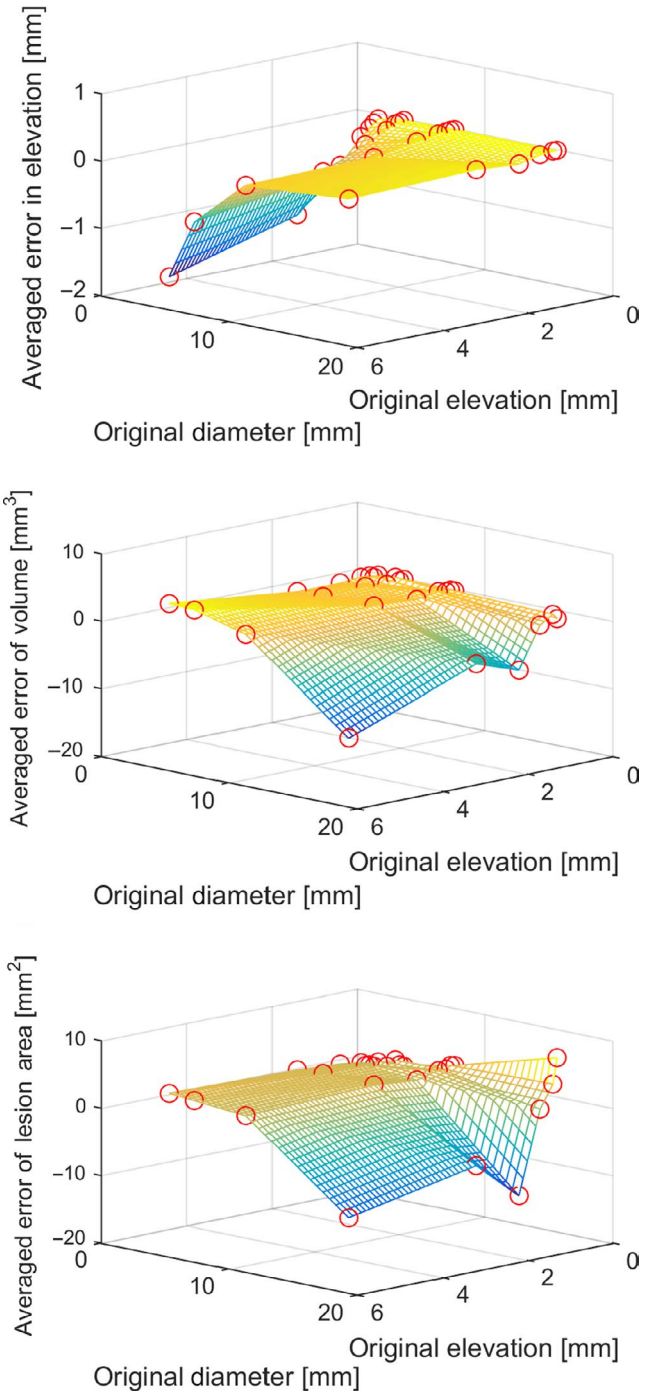

FIGURE 8 The averaged error over six measurements in elevation (top panel), volume (middle panel) and area (bottom panel) due to the optical scanner and analysis tool, plotted against the width and elevation of the 3D printed model [Colour figure can be viewed at wileyonlinelibrary.com]

3.2 | Scanning induced errors

The 3D printed lesion phantom was used to quantify the measurement error induced by the scanning method. Figure 8 shows the average error over 6 measurements of elevation, volume and area for each lesion on the phantom, against the original lesion elevation and diameter. Lesions with a diameter of 4.0 mm and larger, and an elevation 0.2 mm and larger, have a mean error in elevation of ≤26% (SD ≤ ±12%). Lesions with a diameter of 4.0 mm and larger, and an elevation of 0.5 mm and larger, have a mean error in volume of ≤ 22% (SD ≤ ±17%).

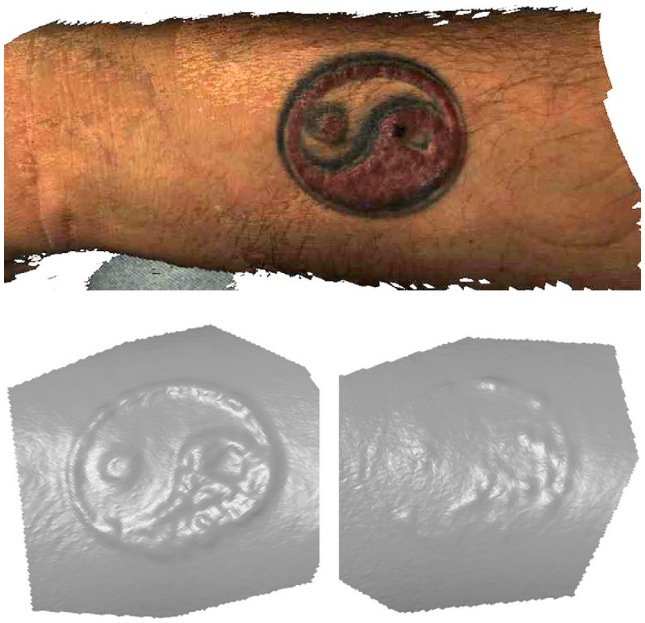

FIGURE 9 The images show an allergic tattoo reaction on the lower arm skin of a patient. Shown are the raw 3D scan data the original allergic tattoo reaction (top panel), the 3D surface model prior to treatment (left panel) and the 3D surface at follow-up, after treatment (right panel). Our analysis showed an elevation of 1.2 mm, volume of 390 mm^3 and area of 1100 mm^2 for this lesion prior to treatment, and an elevation of 0.7 mm, volume of 30 mm^3 and an area of 380 mm^2 after on follow-up [Colour figure can be viewed at wileyonlinelibrary.com]

3.3 | In vivo feasibility evaluation

Seventeen patients were scanned with the optical scanner. In total, 83 lesions were assessed and analyzed. Scanning and analysis were successful in all cases. Making a 3D scan of a lesion using the optical scanner took approximately 60 seconds. The majority of the lesions were on arms (33) and legs (34), and others were on the back (10) or elsewhere (6). Six patients (18 lesions: 7 on arms, 10 on legs, 1 on the back) were scanned during follow-up, and two patients (8 lesions: 7 on legs, 1 on the back) were scanned during a second follow-up.

The 3D optical scanning method is capable of visualizing the skin elevation effectively as shown in a typical example of a tattoo allergy in Figure 9. Especially by removal of the skin and tattoo colors in the 3D surface (in the middle panel), the elevations become clear, as well as the treatment effect in the right panel.

The elevation and volume of all measured lesions against the lesion area are presented in Figure 10. The lesions had an elevation between 0.2 and 4.9 mm, a volume between 0.6 and 1600 mm^3 and an area between 7 and 2600 mm^2. In this figure, the total error due

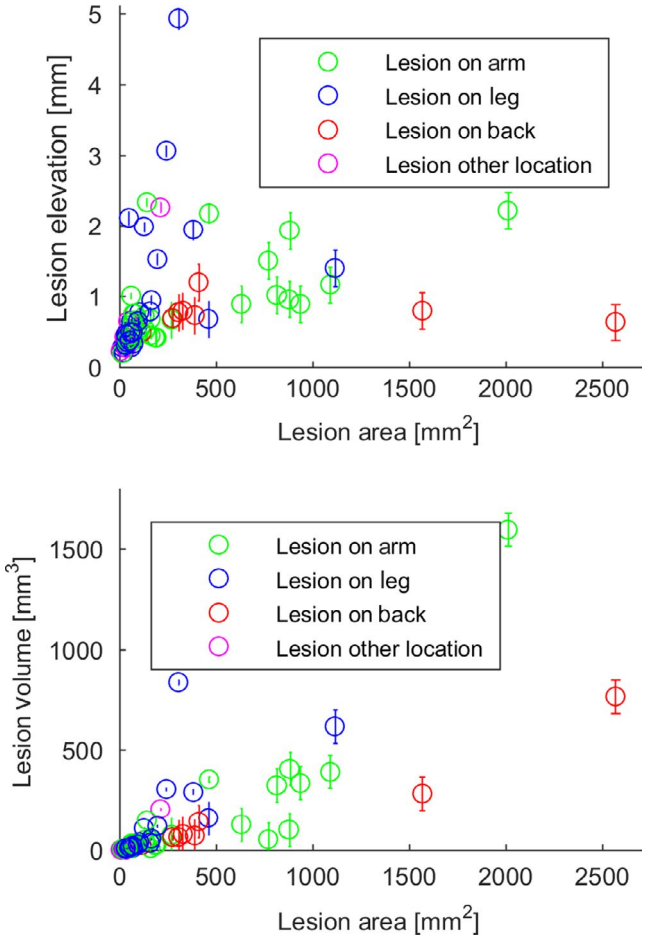

FIGURE 10 The measured elevation (top panel) and volume (bottom panel) are plotted against the lesion area for all measured in vivo lesions. The error bars show the total error due to the interpolation tool and the optical scanning method [Colour figure can be viewed at wileyonlinelibrary.com]

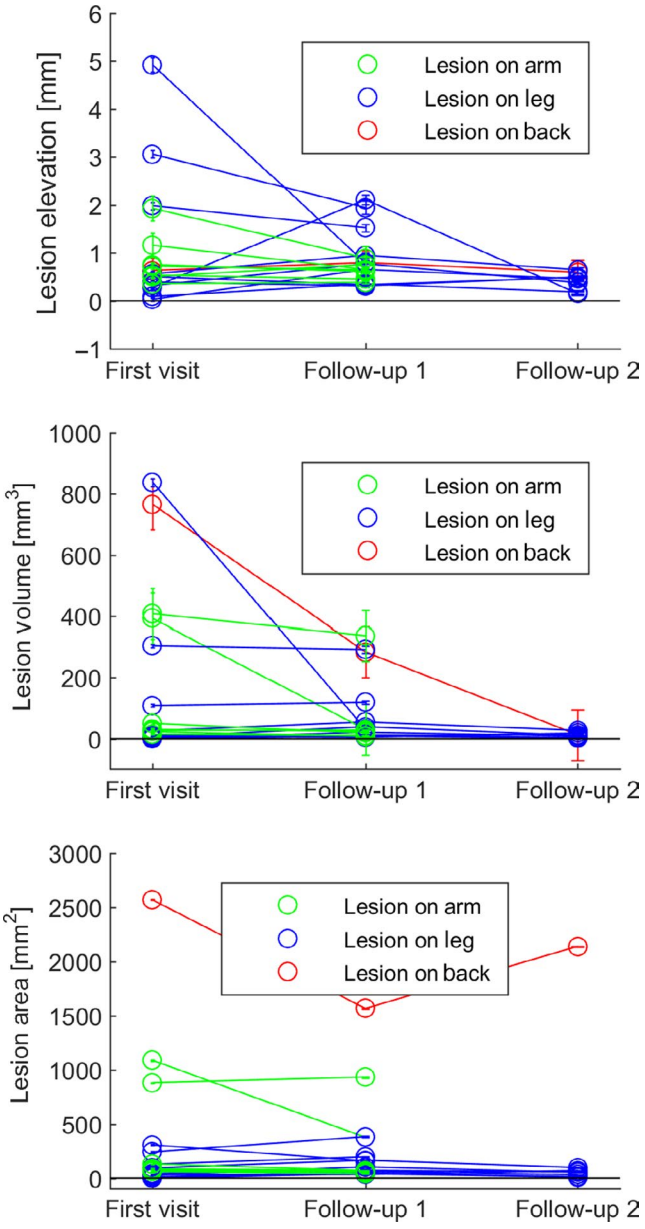

FIGURE 11 The measured elevation (top panel), volume (middle panel) and area (bottom panel) for lesions of patients with follow-up 3D scans. The error bars show the total error due to the interpolation tool and the optical scanning method [Colour figure can be viewed at wileyonlinelibrary.com]

to interpolation and scanning method, as assessed by the validation described above, is shown. Clear is that lesions on arms and legs with an area up to 600 mm^2 can be measured accurately. The total error for in vivo lesions is dominated by the interpolation induced error.

Figure 11 shows the elevation, volume and area for lesions of patients that had one or more follow-up scans. It shows that changes in elevation, volume and lesion area can be measured significantly.

4 | DISCUSSION

This paper presents an analysis method to quantify lesions of allergic tattoo reactions using a 3D optical scanner, in terms of elevation, volume and area of a lesion. The method showed to be feasible in a clinical setting, with changes observed in follow-up above the estimated error range.

The results show the interpolation algorithm works accurately for arms and legs, with an interpolation area smaller than 600 mm^2. The shape of skin is determined by the underlying structures, such as bone, veins, muscle and fat. If these underlying structures express themselves in the ROI, and are smaller or of a similar size of the ROI, the interpolation tool will not be able to take these into account perfectly and therefore introduces larger errors. The interpolation tool is able to reconstruct the skin surface as long as all "information" about the ROI is present in the surrounding skin. Therefore, the analysis algorithm worked well on most lesions of the arms and legs, and it showed more difficulties for lesions of an ankle or back (due to the shoulder blades). Therefore, the location of lesions in allergic reactions should be researched in the future to minimize the errors made by the interpolation tool. The interpolation tool also seemed vulnerable to physiological skin surface anomalies such as underlying veins

and tendons on the edge of the ROI. ROI's were chosen as such to minimize these problems. Patients could be asked to take certain stance to minimize this effect.

The interpolation tool showed a larger SD for rectangular holes compared to square holes, see Table 1. The interpolation tool seems dependent on the shape of the hole. Since tattoos appear in all kind of shapes and sizes, no default shape could be used. Therefore, in the future the dependence of the interpolation tool on shape of the tattoo should be further studied. In the evaluation in patients (Figures 7-10), the SD as assessed with ROI's over the whole forearm is applied, which is an overestimation of the error in case of lesions in less irregular shaped parts of the skin.

As shown by the results, the optical scanner works accurately for lesions with a diameter of 4 mm and larger. We expect the error for lesions smaller than 4 mm to be caused by the combination of the optical scanner and the analysis algorithm. Lesions with a diameter smaller than 4 mm typically have an elevation of 0.1-0.2 mm, and 0.1 mm is the resolution of the applied optical scanner.[12]

Most of the evaluated lesions had a diameter above 3 mm and an interpolation area below 600 mm^2, see Figure 10. This study shows that the method is relevant for most, but not all allergic tattoo reactions.[13]

The 3D optical scan method shows in follow-up significant changes in elevation and volume, as can be seen in Figure 11. These results were not compared to the clinical outcome of the treatment as assessed by the dermatologist, since the clinical outcome is greatly dependent on the subjective parameter itch,[13] and itch is not measured using our method. However, the quantification of lesions could be used as an objective marker in the evaluation of treatment. This should be further studied in a larger patient cohort. This technique could also be promising as a marker in evaluation of new treatments. This 3D optical scanning method will also be useful for the quantification of allergic reactions in skin patch and prick tests, since the size of these lesions are within the limits of the optical scanner and the analysis algorithm.

The acquisition of the 3D data takes approximately 60 seconds. 3D scanning is therefore workable in a clinical setting. However, the post-processing of the data and the analysis algorithm were applied partial manually in this study, taking about 1 to 2 hours per patient. For clinical use, the time for post-processing and the analysis algorithm needs to be reduced to a few minutes. This can be done by combining the analysis in one software environment and further automation.

The optical scanner we applied in this study is an industrial scanner with high specifications. The optical scanner showed potential to quantify measures such as elevation and volume for allergic reactions. Since optical 3D scanners are currently rapidly developing and are becoming more widely available, this technique shows great promise to become a commonly used application.

Follow-up of this work should include a test of reproducibility and inter- or intra-observer variability. Also, the clinical value should be studied in a larger patient cohort. Furthermore, the diagnostic value of 3D scanning can be explored in other dermatological fields. All skin lesions with an altered skin surface such as psoriasis, skin tumors, hemangioma, hypertrophic scars [9] and keloids might be assessed and followed in time by this new technology.

5 | CONCLUSIONS

In this study, we developed a method to quantify lesions of allergic tattoo reactions in terms of elevation, volume and area using a 3D optical scanner. The measurement error was quantified using an arm model and a lesion phantom, showing good measurement for lesion with diameters above 2.5 mm and areas smaller than 600 mm^2. Significant changes in elevation and volume of lesions on arms and legs could be measured over time.

Therefore, we conclude that quantification of lesions of allergic reactions using a 3D optical scanner is feasible. 3D optical scanning is a promising technique for the evaluation and quantification of the effectiveness of (new) therapies.

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