Quantification of skin lesions with a 3D stereovision camera system: validation and clinical applications

Hans Skvara¹, Patrick Burnett², Julie Jones³, Nikolaus Duschek⁴, Peter Plassmann⁵ and Jean-Philippe Thirion⁶

¹Department of Dermatology, Division of Immunology, Allergy and Infectious Diseases, Medical University of Vienna, Vienna, Austria, ²Translational Medicine, Novartis Institutes for BioMedical Research Inc, Basel, Switzerland, ³Novartis Pharma AG, Basel, Switzerland, ⁴Department of Vascular and Endovascular Surgery, Wilhelminenspital, Vienna, Austria, ⁵University of Glamorgan, Pontypridd, United Kingdom and ⁶QuantifiCare S.A., Valbonne, France

Background/purpose: Three-dimensional (3D) imaging of the skin is a challenging technique. A new 3D digital camera system has been developed that enables 3D reconstruction of the skin and subsequently allows volumetric quantification. Herein we present validation data on calibrated phantoms and the clinical application of this technology.

Methods: Absolute and relative geometric 3D measurements were validated with a static imaging phantom manufactured by a metrology institution and a dynamic imaging phantom adjustable for different volume quantities, respectively. Consequently, in a clinical study, 3D baseline and follow up images from 27 basal cell carcinomas under topical therapy were captured for volumetric analysis.

Results: Validation experiments have demonstrated an average accuracy for surface position of 55 μm and a precision of 8 μm, as well as excellent correlation (0.999) between injected and measured volumes. The geometric baseline analysis of 27 basal cell carcinomas exhibited a high correlation and agreement between 2D and 3D surface measurements. Under topical therapy, it was possible to gain statistically significant differences between verum- and vehicle-treated basal cell carcinomas when analyzing geometric measurements of 3D volume (P = 0.01) and 3D surface (P = 0.001).

Conclusion: In our study we were able to demonstrate that this newly developed 3D camera system offers a precise objective dimensional representation of the skin. This technique is easily applicable and sensitive enough to measure small differences in area and volume before and after intervention.

Key words: 3D – 3D volume – imaging – profilometry – skin texture – basal cell carcinoma

© 2012 John Wiley & Sons A/S
Accepted for publication 26 April 2012

A NUMBER of non-invasive imaging techniques have been developed over the years to provide an objective evaluation of healthy and diseased human skin (1–4), but the design of quantitative technologies to measure the surface and volume of the skin remains an ongoing challenge. In order to monitor skin changes over time, or before and after intervention, the dermatologist traditionally has had only his eyes, his memory and at best a two dimensional (2D) digital camera. Whereas 2D photography is able to overcome the limitation of memory recall, the problem of perspective projecting a 3D object onto a 2D plane makes accurate quantitative measurements from single 2D views impossible.

Three-dimensional (3D) imaging, on the other hand, allows a precise and objective assessment of geometric and volumetric variations of the skin (5, 6). The 3D systems that have been developed within the last years are mainly based on ‘active’ vision. Active vision is the projection of light patterns on surfaces that are imaged with a video camera (7). These light patterns may be created with a laser beam or with a video projector. The advantages of the active vision technology are that it can be applied on surfaces without any color textures (e.g. ceramic, steel) and that it is relatively insensitive to specular reflection (8). However, both, strip projections and video cameras need to be controlled by a computer, which can make

© 2012 John Wiley & Sons A/S
Accepted for publication 26 April 2012

Skin Research and Technology 2012; 0: 1–9
Printed in Singapore: All rights reserved
doi: 10.1111/j.1600-0846.2012.00625.x
the system cumbersome to operate or move. Another drawback is that image texture is acquired independently from the surface which leads to a potential shift between geometry and color texture (8). Because these tools require a time sequence of images to be recorded, any skin movement while recording is further limiting the accuracy of such systems.

In contrast to ‘active’ vision, ‘passive’ vision or ‘stereovision’ makes use of multiple simultaneous views and image correlation to reconstruct 3D surfaces (9). The basic principle is similar to the human visual perception. ‘Stereovision’ systems are attractive as they permit direct visualization of the subject in 3D with stereo glasses. Whereas image acquisition occurs within 1/200 s, the main drawbacks are that these instruments need textured surfaces to operate and may be sensitive to specular reflection. ‘Auto-calibration’ can be used when only stereovision is of interest, but it is mandatory to rely upon absolute calibration in order to obtain useful geometric measurements (10).

A new 3D camera technology (LifeViz™ – QuantifiCare, Valbonne, France) has been developed that is based on stereovision with absolute calibration to be used for accurate 3D reconstruction and quantification of skin structures and their evolution. Herein we present the working principle and its clinical application.

Materials and Methods

The 3D LifeViz™ system (Fig. 1) is a compact and easy to use stereovision system with absolute calibration. The optical system consists of a dual-lens beam splitter manufactured and calibrated with an accuracy of better than 1/100th of a millimeter, which enables a very accurate reconstruction of the skin surface. A dual beam pointer is used to ensure reproducibility for image acquisition in terms of distance and centering. This fixed distance has no influence on geometrical accuracy, but is needed to ensure that the images are well focused. The system is therefore designed for a fixed distance that can be set in a range between 20 cm (‘Micro’ system) to 80 cm. It also makes use of a unique dual flash system (patent pending) that employs so called ‘inverse cross polarisation’ in order to largely avoid the problems caused by specular reflections which are common in other stereo-photogrammetric systems. This setup produces stereo image pairs with sufficient textural information for the cross-correlation algorithms to work efficiently. The camera itself can therefore be operated independently from a computer, which facilitates transportation and makes 3D image acquisition more amenable to a clinical environment. 3D surface reconstruction and analysis can then be performed offline, either at the clinical site or on a central server. Figure 2(a) shows a 2D macroscopic image of a nodular basal cell carcinoma. In Fig. 2(b) and 2(c) the reconstructed surface image is presented.

The 3D LifeViz™ software consists of three parts: image management, 3D surface reconstruction/visualization and 3D surface analysis. Two types of quantification can be performed with this technology: absolute and relative measurements. Absolute measurement is using a single acquisition (time point), enabling direct measurement of 3D perimeter and 3D surface via skin structure segmentation (which can be manual or semi-automated). Defining 3D volumes from a single time point is challenging as it means to define a ‘floor’ for the lesion. A lesion can be an elevation in case of a tumor or a psoriatic plaque but can also appear as a hole in case of wounds, scars or wrinkles. The lesion floor is defined as the lowest surface based upon the 3D contour of the lesion (Fig. 3). When two time points are available, for example a baseline and a follow-up image, then relative volume variation can be computed within a segmented Region of Interest (ROI) once 3D surfaces are matched. In that case semi-auto-
mated methods are used to perform such sur-
face matching, based on corresponding points
measured from cross-correlation.

Validation phantoms
To validate absolute 3D measurements, we have
used an imaging phantom manufactured by a
metrology institute (National Physical Labora-
tory, Teddington, UK) referenced to as the
NPL-A-11B artifact [Fig. 4(a)]. The settings of
the milling machine used to manufacture this
device was a sphere of 12.5 mm of radius
carved in the planar surface and with a maxi-
mal depth of 5 mm, leading to a diameter of
the hole of 20 mm.

To calibrate the manufactured object, 50 sur-
face points were measured with a 3 axis
machine in 3 dimensions. An ideal sphere was
then fitted to the measured points using the
least mean square method. The 4 degrees of
freedom (center position in 3D + radius) of the
sphere minimizing the square difference
between the sphere surface and the 50 3D
points were calculated, as well as the standard
error relative to this interpolation (square root
of residual mean square between minimizing
sphere and the 50 measured points).

To validate relative 3D measurements we
have used a fixed volume system (closed box)
with a deformable membrane [Fig. 4(b)]. It is
filled with boiled water in order to remove the
formation of bubbles as far as possible in the liquid which would compromise the measurement. Filling is performed with a syringe, with large graduation every 100 mm$^3$ and fine graduation every 10 mm$^3$ (0.01 cc$^3$). Accuracy of this physical simulation is mainly limited by the elasticity of the syringe piston, which creates errors of ±5 mm$^3$. Larger errors with larger quantities due to additional elasticity constraints (such as the box itself or residual bubbles) may be expected.

Clinical application – Basal cell carcinoma

In order to demonstrate clinical applicability we present geometric data (3D volume, 3D surface, 2D surface, height) from a skin tumor (basal cell carcinoma – BCC) under therapy with a topically applied hedgehog inhibitor (LDE225). The study was conducted in Vienna (Department of Dermatology, Division of Immunology, Allergy and Infectious Diseases, Medical University of Vienna, Austria) after approval of the local ethics committee of the Medical University of Vienna and the Austrian health authority (Bundesministerium für Gesundheit, Vienna, Austria). The study was conducted according to the principles embodied in the Declaration of Helsinki, and all patients provided written informed consent before participating. The rational of this study and detailed results have been published recently (11). Herein, we introduce the working principle of the LifeViz™ technology and additionally performed geometric data. Briefly, eight patients with Nevod Basal Cell Carcinoma Syndrome (NBCCS) were included. NBCCS is a genetic disorder which, inter alia, leads to the emergence of multiple basal cell carcinomas (BCCs) owing to overactive signaling of the hedgehog pathway. Twenty seven BCCs were studied under therapy with LDE225 (13 lesions) versus vehicle (14 lesions). Two to four lesions were followed-up for each patient, with a randomized application of LDE225 or of the vehicle only. We present digital photography data from five consecutive visits: day -1 (baseline), 8, 15, 22 and 29. Thereafter, the therapy was stopped and the lesions were excised. Two independent camera systems were used for the measurements: The stereovision camera and a 2D photo-dermatoscope tool-kit (LiteScope™) based on Heine's Delta 20 dermatoscope. The photo-dermatoscope produces calibrated pictures enabling 2D surface measurements, while the stereovision system was used to measure 3D surface (meaning the surface area of a 3D object that you would get if you laid the total surface of a 3D object out flat), 3D volume and lesion height over time.

Statistical analysis of the clinical data

Patients may have been treated for one or two lesions with each of LDE225 and the vehicle cream. In the comparison of LDE225 to vehicle, the measurements were summed for each patient and treatment to give the total volume, surface and height for LDE225- and vehicle-treated BCCs for each patient. The percentage change from baseline was calculated and compared on day 29 between LDE225 and vehicle using a within-patient two-sided t-test. No adjustment was made for multiple testing. Statistical analysis was performed using SAS version 9.2.

The amount of agreement between the different methods was calculated as the mean of the difference between each pair of values, using

Fig. 4. Validation phantoms: (a) NPL-A-11B artifact (b) variable volume simulator.
data at the lesion level and including all time points. The limits of agreement are presented as the mean of these differences ± 1.96 standard deviations.

**Results**

**Validation of absolute measurements**

The geometric features of the NPL-A-11B are the following (± = standard error):

<table>
<thead>
<tr>
<th>Phantom</th>
<th>3D Volume: 850.53 mm³ ± 4.25 mm³</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3D Area: 392.70 mm² ± 1.96 mm²</td>
</tr>
<tr>
<td></td>
<td>3D Circumference: 62.83 mm ± 0.31 mm</td>
</tr>
</tbody>
</table>

These parameters were then measured using the 'Micro' version of the stereovision system. The lesion floor was defined as the minimal surface based on the segmentation of the half-sphere, which is the only part being observer-dependent:

<table>
<thead>
<tr>
<th>Precision</th>
<th>3D Volume: 863.18 mm³ ± 1.3 mm³ (standard deviation)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3D Area: 368.85 mm² ± 1.1 mm²</td>
</tr>
<tr>
<td></td>
<td>3D Circumference: 62.38 mm ± 0.08 mm</td>
</tr>
</tbody>
</table>

To assess accuracy, the error of each measurement was calculated as the difference between the real value and the measured value and is summarized as the standard error (square root of the residual mean square between measured and theoretical sphere parameters for five independent measurements). In addition, the standard error expressed as a percentage of the total value measured is provided.

<table>
<thead>
<tr>
<th>Accuracy</th>
<th>3D Volume: 12.7 mm³ (1.49%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3D Area: 23.9 mm² (6.08%)</td>
</tr>
<tr>
<td></td>
<td>3D Circumference: 0.45 mm³  (0.73%)</td>
</tr>
</tbody>
</table>

The 3D volume is measured over a 2D surface area of 314 mm², which means an average error of 0.040 mm (40 μm) in the absolute position of the surface.

**Validation of relative measurements**

Figure 5 represents the measured volume variation quantities (in mm³) when compared with the injected quantities. It shows a substantial linear correspondence between injected and measured volumes. A slight over-estimation of the volume variation can be observed for larger volumes, demonstrating a linearly-related error that may be due to the acquisition system but could be well related to the linear elasticity of the physical system. In short, it cannot be established if this bias is due to the method or to the phantom. The correlation between measurements and injected quantities is:

\[ \text{Correlation} : 0.999 \]

Precision is provided as the standard error relative to the linear interpolation and is important in order to discriminate different populations for fine discrepancies.

\[ \text{Precision (standard error relative to linear regression)} : 1.46 \text{mm}^3 \]

For a surface measurement of 178 mm², this leads to an average precision in surface positioning of 0.008 mm (8 μm). Average precision does not mean that all details of 8 μm in depth can be detected, as image resolution itself is limited to 20 × 20 μm, but a larger structure with 8 μm depth variation can still be detected.

Accuracy measured as the residual mean square differences between measurements and injected quantities for the whole set of measures is:

\[ \text{Accuracy (standard error relative to injected values)} : 9.8 \text{mm}^3 \]

![Validation of relative volume variation](image)
The measurement surface being 178 mm$^2$ means an average error in surface position estimation of 0.055 mm (55 $\mu$m). This is the maximal error of the measurement system as part of the measurement error is due to the elasticity of the physical system. It is coherent with the accuracy measured with the NPL-A-11B artifact.

Photographic assessments of BCC measurements under topical therapy

In this study 13 lesions were treated with the topical hedgehog inhibitor (LDE225) whereas 14 lesions received the vehicle during four weeks.

In Fig. 6 the distribution of lesions height relative to their 2D surfaces at baseline is demonstrated. Table 1 presents the average, maxima and minima of the geometric parameters at baseline. The flattest lesion is 90 $\mu$m in height, which is far above the average height variations that can be detected with the 3D system (8 $\mu$m). Moreover it must be noted that the average volume of the lesions is very small: 4.15 mm$^3$ on an average, with 0.52 mm$^3$ for the smallest lesion.

Table 2 shows the correlation between the different absolute measurements. Lack of high correlations between measurements should be interpreted as reflecting the differences in the underlying characteristics of the lesions (for example, large flat lesions compared to small higher lesions). The highest correlation is, as expected, between the 2D and 3D surface measurements. On average the 2D and 3D surface areas were within 4 mm$^2$ of each other (limits of agreement –18 to 24 mm$^2$). The high correlation (0.88) between 2D and 3D surfaces measurements is notable as these measurements were obtained via two very different devices, a 2D photo-dermatoscope and the 3D stereovision camera. The 2D and 3D measurements are coherent, with an average of 28 mm$^2$ for 2D surface versus 31 mm$^2$ for 3D surface as shown in Fig. 7.

During treatment, lesion volumes have been reduced from 6.88 mm$^3$ to 3.43 mm$^3$ at Day 29 in LDE225-treated BCCs, which was highly significant compared with vehicle-treated BCCs in which we observed a volume change from 7.14 mm$^3$ to 6.40 mm$^3$ [P = 0.01 (within-patient two-sided t-test)] [Fig. 8(a)]. Figure 9 shows the 3D reconstruction of a nodular basal cell carcinoma before (a, b) and 4 weeks after treatment with LDE225 (c, d), showing a 91% volume reduction compared with baseline.

### Table 1. Geometric parameters of all 27 basal cell carcinomas at baseline.

<table>
<thead>
<tr>
<th></th>
<th>3D volume (mm$^3$)</th>
<th>3D surface (mm$^2$)</th>
<th>2D surface (mm$^2$)</th>
<th>Height (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>4.15</td>
<td>31.41</td>
<td>28.29</td>
<td>0.45</td>
</tr>
<tr>
<td>Maximum</td>
<td>12.92</td>
<td>107.41</td>
<td>66.06</td>
<td>1.16</td>
</tr>
<tr>
<td>Minimum</td>
<td>0.52</td>
<td>11.54</td>
<td>7.58</td>
<td>0.09</td>
</tr>
</tbody>
</table>

### Table 2. Correlation between different geometric parameters for all time points (absolute measurements).

<table>
<thead>
<tr>
<th></th>
<th>3D volume</th>
<th>3D surface</th>
<th>2D surface</th>
<th>Height</th>
</tr>
</thead>
<tbody>
<tr>
<td>3D volume</td>
<td>1.00</td>
<td>0.42</td>
<td>0.37</td>
<td>0.72</td>
</tr>
<tr>
<td>3D surface</td>
<td>1.00</td>
<td>0.88</td>
<td>–0.18</td>
<td></td>
</tr>
<tr>
<td>2D surface</td>
<td>1.00</td>
<td>1.00</td>
<td>–0.19</td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 7. Comparison of 2D surface measured with photo-dermoscopy and 3D surface measurements calculated with 3D stereovision.
The 3D surface has been reduced from 45.99 mm$^2$ to 29.37 mm$^2$ at Day 29 in LDE225-treated BCCs whereas an increase in surface was observed in vehicle-treated lesions from 60.02 mm$^2$ to 62.69 mm$^2$ ($P = 0.001$ [within-patient two-sided t-test]) [Fig. 8(b)].

Lesion height was reduced from 0.76 mm to 0.54 mm at Day 29 in the LDE225-treated lesions, and although it was also reduced in the vehicle-treated lesions from 0.76 mm to 0.67 mm, significance was still approached ($P = 0.08$ [within-patient two-sided t-test]) [Fig. 8(c)].

**Discussion**

Within recent years, enormous progress has been made in the ability to document and fol-
low up the profilometry of the skin (12–14). Polarized light-based measurements have been used to enhance visualization of the skin’s surface and subsurface structures (15), to measure the skin texture (13) and to evaluate photoaging (16). Furthermore, cross-polarized imaging has been established as a powerful tool to assess subsurface skin features such as pigmentation and erythema (17, 18), and recently skin texture has also been measured in vivo through 3D imaging (19).

The acquisition of 3D images is a major step towards objective dimensional representation in dermatology. Herein we demonstrated the accuracy and precision of a newly developed 3D system down to 8 μm using calibrated imaging phantoms. In a clinical setting, we demonstrated that this tool is sensitive enough to measure small differences in area and volume after a clinical intervention in a small study population.

One major advantage of a passive stereovision system is its ease of operation. Image acquisition can be performed in a practical and rapid manner which is of great advantage in clinical routine as well as in clinical studies. The data can then be centralized in a data center and processed uniformly throughout trial duration to ensure consistency in the measurements. Unpublished observations have shown that this technology is also ideally suited for the in vivo investigation of the treatment success after filler application into fine wrinkles, wound management as well as treatment of acne scars and keloids.

In conclusion, we describe a simple photographic method to document the skin structure in a micrometer range. The method has been validated with an imaging phantom manufactured by the National Physical Laboratory (Teddington, UK) and a volume simulation model for accuracy and precision. In clinical trials for example, this system can be easily used to objectify changes of lesional skin along with treatment. Therefore we hypothesize that passive stereovision will be a beneficial additive tool in future dermatology.

References
Quantiﬁcation of skin lesions with a 3D stereovision camera system

Address:
Hans Skvara
Division of Immunology, Allergy and Infectious Diseases
Department of Dermatology
Medical University of Vienna
Währinger Gürtel 18-20
1090 Vienna
Austria
Tel: +43 1 40400 7736
Fax: +43 1 40400 7574
e-mail: hans.skvara@meduniwien.ac.at