




## Article

# Biophysical and Subject-Based Assessment of the Effects of Topical Moisturizer Usage on Xerotic Skin—Part II: Visioscan<sup>®</sup> VC 20plus Imaging

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**Abstract:** As new biophysical methods become available to the skin researcher it is important to understand the type of information that they are capable of measuring, and how it relates to consumer perception of topical moisturizing products. The aim of the work presented here was to understand what dry skin imaging can reveal about the skin and subject feedback from the use of a topical moisturizing product and how it relates to the consumer usage experience of a topical product. Images from a dry skin camera—the Visioscan<sup>®</sup> VC 20plus—during 3 weeks in vivo usage of a topical moisturizing product were analyzed. Subject feedback regarding their skin condition was also collected. Strong statistical improvements ( $p < 0.05$ ) were observed for a wide range of skin parameters derived from the Visioscan<sup>®</sup> VC 20plus. Skin scaliness and smoothness and parameters associated with skin health and appearance (surface, energy, contrast, homogeneity) improved as a result of topical product usage. Subjects reported their skin to feel less dry, to be smoother, and more supple and to look and feel healthier after product usage. The length of time until they felt the need to re-apply the product increased during the study.

**Keywords:** bioengineering; claim substantiation; formulation; dry skin; skin hydration



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## 1. Introduction

As discussed in Part I of this article, dry, sensitive, xerotic skin is the most common dermatological disorder impacting up to around 50% of the world's population [1,2]. Performance assessment of products formulated to address dry skin development is an important aspect of characterizing their behavior as this enables their benefits to be communicated to the consumer.

As the number and type of non-invasive biophysical methods capable of measuring a wide variety of skin parameters have expanded over the last 35 years, their use has become a vital part of research into topical skin products and clinical testing for both the consumer and pharmaceutical markets [3,4]. In addition to new devices, manufacturers are also continuing to develop and refine the devices used to measure the skin. With the development of new and updated measurement techniques, there comes a need to understand what aspects of the skin they can assess, how they compare with earlier versions of the same devices, and how the information they provide relates to actual consumer feedback about topical product usage.

Although visual grading of dry skin is still widely used during clinical assessment, it does require the use of grading scales and a trained assessor which is not always possible [5,6]. In addition to the electrical measures of skin hydration which were mentioned in

Part I of this article, skin dryness can also be captured photographically as dryness impacts its optical properties [7,8]. The Visioscan<sup>®</sup> dry skin camera (Courage and Khazaka GmbH, Cologne, Germany) uses an ultraviolet A (UVA) light source to illuminate skin and captures light that is reflected and emitted due to fluorescence. The device has been reported for a wide variety of uses including imaging of psoriasis, sunscreen remanence on the skin, imaging of mosaic melanoderm patterns, in addition to dry skin assessment [9–13].

In previous work, the authors reported the initial results from a 3-week in vivo study looking at the effects of multi-functional topical moisturizing formulation on a wide range of parameters associated with dry skin [14,15]. In Part I of this article, the authors reported an in-depth analysis of data from the Epsilon<sup>™</sup> E100 2D hydration measurement device collected during the study. In this second part, the authors perform a similar detailed assessment of the data from the Visioscan<sup>®</sup> VC 20plus dry skin camera and compare it with feedback given by the subjects during the study regarding the effects of product usage on their skin. Originally produced around 20 years ago, a new version of the Visioscan<sup>®</sup> has recently been released—the VC 20plus—which has a number of significant changes to its design when compared to the previous model. No direct head-to-head comparisons of the two versions of the device have been published. New insights into how these types of measurement devices can be used to monitor skin properties are discussed. This research is aimed at providing guidance into the use of biophysical skin measurement and subject feedback to understand consumer feedback from the use of topical moisturizing products.

## 2. Materials and Methods

Subjects for the in vivo testing were recruited by proDERM GmbH, Schenefeld, Germany, and the study complied with the World Medical Association's Declaration of Helsinki (2000) concerning biomedical research involving human subjects. The study protocol was approved by an Institutional Review Board of proDERM GmbH (Schenefeld, Germany, approval number 2020/005). The full study design and test product details have been reported previously [14,15]. The results from analysis of the Visioscan<sup>®</sup> VC 20plus images and subject questionnaire data collected across the 3 weeks of the study are discussed here.

Dry skin images were collected using a Visioscan<sup>®</sup> VC 20plus (Courage & Khazaka GmbH, Cologne, Germany). Exposure time for the images was 50 ms. Analysis of the different image parameters was carried out using the device software.

The irradiance spectra of the Visioscan<sup>®</sup> light sources (VC98 and VC 20plus) were measured using an Ocean Insight FX spectrometer between 250 nm and 800 nm. The spectrometer was calibrated for absolute irradiance with a cosine corrector attached to a 600 µm diameter fiber. Irradiance spectra were normalized to the height of the highest peak in the spectra between 250 nm and 800 nm.

On days 2, 8, 15, and 22 of the study (one day after product application began and the end of week 1, 2, and 3), the subjects were asked to compare the condition of the skin on both legs with a questionnaire using a Visual Assessment Score (VAS) with a scale between −50 and +50 (−50 = untreated leg much more; 0 = no difference; 50 = treated leg much more). The subjects were also asked to evaluate the length of time between feeling the need to reapply the product during week 1, 2, and 3. A four-point scale was used; 1 = <1 h, 2 = 1–3 h, 3 = 3–5 h, 4 = > 5 h.

A significance level of 0.05 (alpha) was chosen for statistical analysis of the Visioscan<sup>®</sup> VC 20plus data. Comparisons of treatment and untreated sites were performed on differences to baseline scores using multifactorial analysis of variants (ANOVA) with product, subject, and side as factors, and the baseline values as covariates. This was carried out with commercially available statistics software (Statgraphics Centurion 18). Subject self-assessment data analysis was shown as the VAS scores and analyzed using ANOVA. Subject data were analyzed in Microsoft Excel 2016 and JMP v15.

### 3. Results and Discussion

While electrical methods to measure skin hydration state are widely used in clinical testing [16–18], the optical properties of skin can also be used to derive information on skin moisturization and hydration. The Visioscan<sup>®</sup> VC 20plus is a dry skin camera that uses a UVA light source to produce images of the skin under highly controlled lighting conditions. UVA light interacts with the skin in a variety of ways [19]. It can be reflected from the skin surface with the same wavelength, or it can be transmitted deeper into the epidermis where it can be attenuated by the melanin. UVA which has passed into the epidermis and is not attenuated by the melanin can pass deeper into the dermis where it can interact with collagen. Cross-linked collagen fluoresces under UVA, resulting in the emission of visible light. Along with fluorescence from collagen, when UVA strikes the surface of the Stratum Corneum (SC), if the SC is dry, these dry corneocytes fluoresce resulting in the emission of visible light [19]. In addition to its effects on fluorescence, skin hydration state also impacts transmission of the light into and through and reflection from the SC [20]. Hydration of the SC influences transmission and scattering of UV light in two ways; firstly, liquid water acts on the surface of the SC to reduce light reflection and backscatter, and secondly, as a result of the take up of water by the corneocytes and into the intracellular regions, internal scattering is reduced. This decrease in internal scattering is due to the reduction in refractive index variation between the different areas within the SC as a result of hydration [20]. Example images from dry/xerotic and normal, hydrated skin are shown in Figure 1a,b. This combination of reflection and fluorescence increases the brightness of the image in areas where the skin is dry and the image properties can then be analyzed to produce a variety of information on the skin's properties, which are summarized in Table 1.

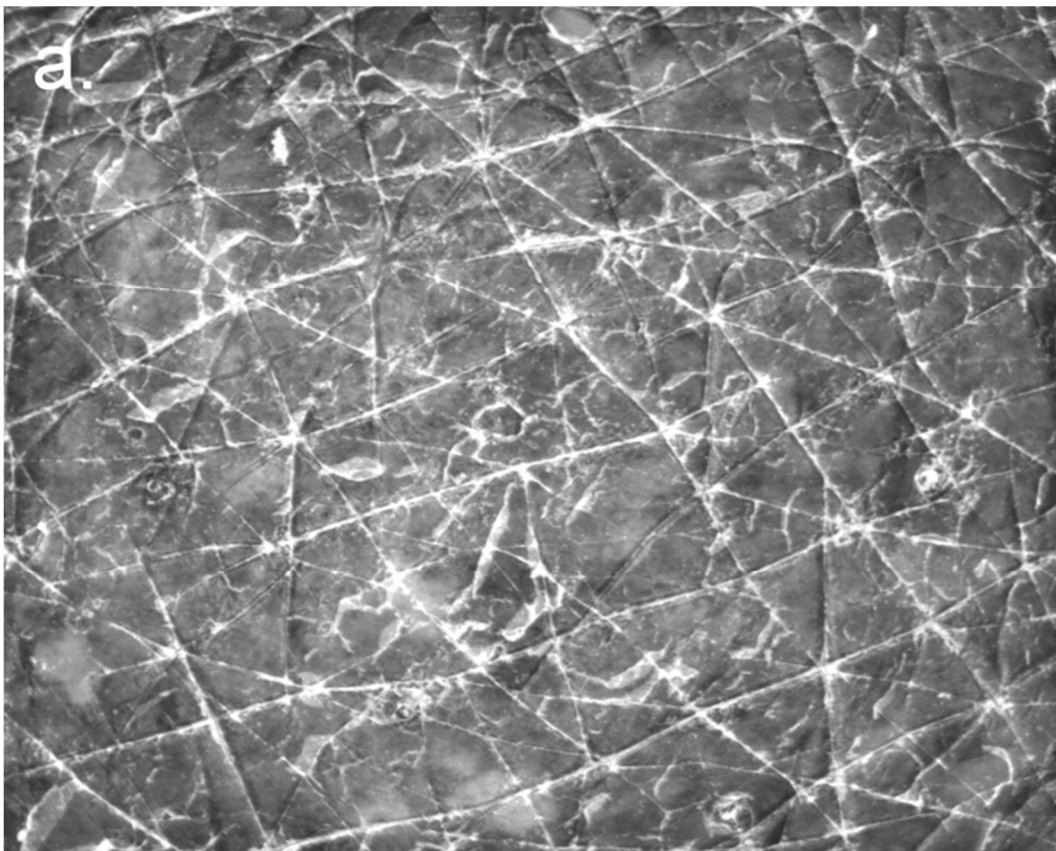


Figure 1. Cont.



**Figure 1.** Example Visioscan® VC 20plus images for (a) dry/xerotic skin and (b) normal/hydrated skin.

Analysis of the data from the study after 1, 2, and 3 weeks of product usage are given in Table 2 and shown as changes from baseline for the treated and untreated sites on the skin. The SELS (surface evaluation of living skin) parameters—scaliness (SEsc), roughness (SEr), smoothness (SEsm), and wrinkles (SEw)—did show differences between the treated and untreated sites across the 3 weeks of the study. SELS parameters have been compared with roughness scores derived from the direct optical assessment of the skin surface, and although the readings from both devices were not directly related, both provided information on the roughness of the skin [22]. In the data presented here, typically, the treated site was less scaly (smaller SEsc score), and smoother (smaller SEsm score) than the untreated site. However, the roughness score (SEr) did not vary between the treated and untreated sites across the study and the wrinkle score (SEw) was greater for the treated site at week 2 and 3 which was not expected. The reason for the increase in the wrinkle score is not clear, especially as skin smoothness was shown to improve at the same time. One potential explanation is that reduced scaliness and the corresponding decrease in the number of white pixels in the image, making the texture of the skin more visible therefore emphasizing the presence of any features such as wrinkles, although the authors acknowledge that at the moment this is a hypothesis. It should also be noted that the analysis of the Scaliness results given here resulted in a slightly stronger statistical break than was observed in the initial assessment of the data [15]. The analysis carried out here used ANOVA with the baseline as a covariate while previous data analysis was carried out using a paired *t*-test which could account for the observed differences in significance [15].

Mean greyscale is one of the simplest approaches to image analysis for these images. As can be seen in Figure 1, as the skin becomes drier, the image becomes brighter due to increased fluorescence. The mean greyscale score of the image would therefore be expected to decrease as the skin becomes more hydrated. While the reduction in mean greyscale scores was greater for the treated site than for the untreated, the difference between the

two was only significant at the 2-week time point. Mean greyscale is not included in the Visioscan<sup>®</sup> user manual [21] as a recommended method of analyzing the images but it is mentioned here for completeness as it is a very simple approach to analyze the images. However, it fails to take into account the aspects of the image beyond the simple average greyness and as such is not as discriminatory as other approaches. The surface score, which takes into account the waviness of the skin derived from the image was more discriminatory than the roughness (SEr) score, showing significantly reduced surface scores for the treated site at all time points throughout the study. This behavior was not observed for the volume score, which only became statistically significant at the end of week 3 of the study.

**Table 1.** Summary of Visioscan<sup>®</sup> VC 20plus measurement parameters [21].

| Parameter              | Description  |
|------------------------|--|
| SELS—Scaliness (SEsc)  | Number of pixels where the grey level is higher than the threshold of SEsc. SEsc is determined by the loop (inflection point) of the second part of the greyscale histogram. This is the point at which virtual tangents would change their direction. The smaller the SEsc, the less is the desquamation of the stratum corneum and the less scaly the skin.                        |
| SELS—Roughness (SEr)   | The grey levels beyond the threshold in comparison to the roughness of the whole image (number of wrinkles on the calculatory lines). The smaller SEr, the rougher the skin.   |
| SELS—Smoothness (SEsm) | This takes the average width of the histogram and the average width of the wrinkles in x and y direction into account. Smooth, even skin shows a lower variety of different grey levels, thus the histogram over the grey level distribution is smaller (more narrow). The smaller the SEsm the smoother the image (the less different the pixels thus the less wide the histogram). |
| SELS—Wrinkles (SEw)    | The average number and average width of horizontal and vertical wrinkles (calculatory lines). The more visible wrinkles (broad, deep wrinkles) the higher this value.  |
| Mean grey scale        | Mean grey scale value of the pixels in the image. The higher the value the whiter the pixels and the drier the skin.   |
| Surface                | Here, the size of the “wavy” surface of the skin is compared to a fully stretched flat (“ironed”) surface (x:1). The smoother the area was before stretching, the closer the two values are together. E.g., 113 = the stretched area is 13 % larger than the original surface). After topical treatment of the skin, the Surface parameter should decrease.                          |
| Volume                 | Volume calculates the virtual amount of liquid needed in the calculation area to fill the image until the average height of all mountains. The smoother an area before filling up, the less virtual liquid is needed. The result is expressed in mm <sup>3</sup> . After topical treatment of the skin, the Volume parameter should decrease.  |
| Energy                 | Energy is the rate of changes in the color/brightness/magnitude of the pixels over local areas. A homogeneous combination of medium grey values (high energy) should indicate a young, smooth skin. When moisture or anti-aging treatments are applied to the skin, the energy value should go up.   |
| Variance               | Variance is the average of a local variance over an amount of pixels. The actual value of the pixel is compared to the average. High roughness will lead to increased variance values.   |
| Contrast               | Contrast indicates the difference between grey levels of the two neighboring pixels. If the contrast is higher, the higher the different values of two neighbors. A good skin condition will show lower contrast values.   |
| Entropy                | Entropy indicates the “mess/disorder” of an image. Smooth, even skin should show a lower entropy then rough skin.  |
| Homogeneity            | Homogeneity indicates the uniformity of an image. The larger the difference between the grey levels in the picture the lower the homogeneity value. A highly hydrated skin has a higher homogeneity value than a very dry one.   |

The energy, variance, contrast, entropy, and homogeneity behaved very consistently throughout the study, all showing statistically significant differences between the treated and untreated sites at all time-points except for energy at end of week 3. However, while a statistical difference between the treated and untreated sites was observed throughout the study for these parameters, entropy did not behave in the expected way. Based on

the description of this parameter in the user manual for the device, smooth, even skin should show reduced entropy compared to rough skin [21]. However, the opposite was seen here with the treated site having higher entropy than the untreated site. The entropy score indicates the “mess/disorder” of an image and when it is higher, more combinations of different grey levels appear in the image. If the skin is very dry, then more pixels in the image will be very bright. This could actually reduce the variability of the pixel brightness in the case of dry skin, i.e., reduce the entropy, which would explain the observed behavior, although further work would need to be carried out to confirm this.

**Table 2.** Visioscan® VC 20plus data change from baseline at the end of Week 1, 2, and 3. Statistical differences between the Treated and Untreated sites (multifactorial ANOVA) with >95% significance ( $p < 0.05$ ) are shown in bold and underlined. Data for the SEsc, SEr, SEsm, SEw, mean grey scale, surface and volume scores is given to two decimal places, while the Energy, Variance, Contrast, Entropy and Homogeneity scores are shown to four decimal places.

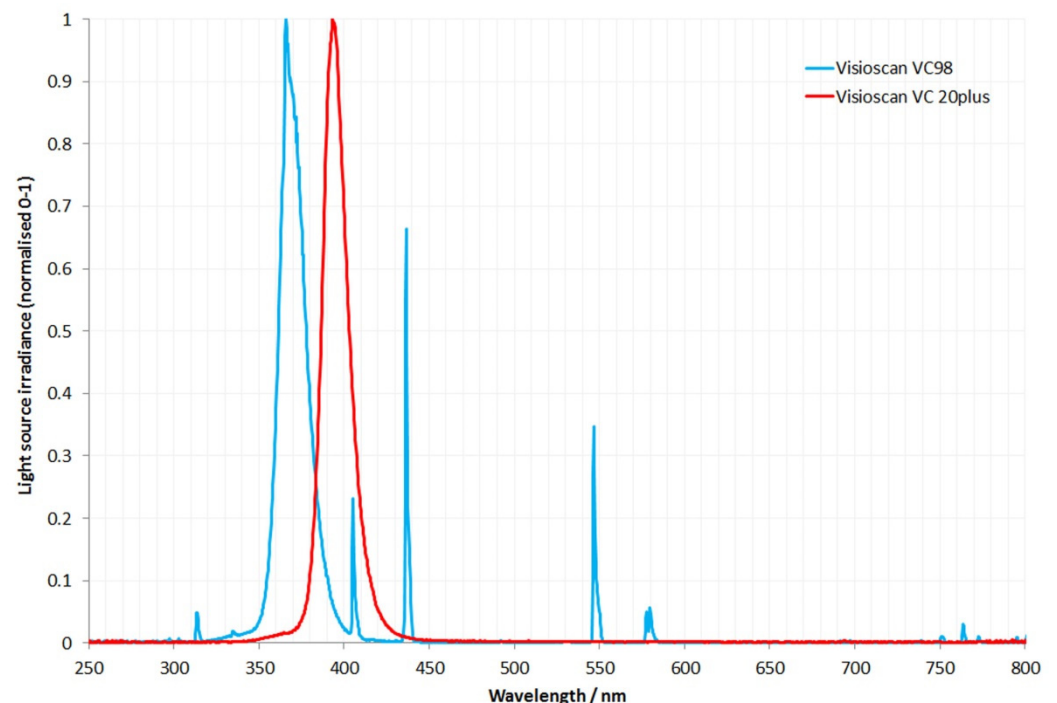
| Parameter              | Week 1                           |                                  | Week 2                           |                                  | Week 3                           |                                  |
|------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
|                        | Treated                          | Untreated                        | Treated                          | Untreated                        | Treated                          | Untreated                        |
| SELS—Scaliness (SEsc)  | <b><u>−1.45</u> +/- 0.19</b>     | <b><u>−0.57</u> +/- 0.19</b>     | <b><u>−1.02</u> +/- 0.34</b>     | <b><u>0.36</u> +/- 0.37</b>      | −0.94 +/- 0.43                   | 0.83 +/- 0.43                    |
| SELS—Roughness (SEr)   | 5.13 +/- 2.61                    | 4.47 +/- 2.82                    | 6.83 +/- 2.09                    | 0.65 +/- 2.29                    | 4.01 +/- 3.30                    | 7.57 +/- 3.37                    |
| SELS—Smoothness (SEsm) | <b><u>−64.78</u> +/- 18.15</b>   | <b><u>−1.92</u> +/- 19.84</b>    | −33.34 +/- 15.33                 | −11.14 +/- 16.77                 | −29.61 +/- 23.55                 | −18.00 +/- 24.85                 |
| SELS—Wrinkles (SEw)    | 15.26 +/- 7.97                   | 10.89 +/- 8.11                   | <b><u>22.99</u> +/- 4.86</b>     | <b><u>3.21</u> +/- 5.11</b>      | <b><u>23.13</u> +/- 6.18</b>     | <b><u>−0.41</u> +/- 6.17</b>     |
| Mean grey scale        | −12.71 +/- 2.92                  | −7.43 +/- 3.44                   | <b><u>−10.47</u> +/- 2.00</b>    | <b><u>0.26</u> +/- 2.24</b>      | −8.48 +/- 1.89                   | −4.09 +/- 2.07                   |
| Surface                | <b><u>−154.48</u> +/- 20.27</b>  | <b><u>−62.62</u> +/- 21.76</b>   | <b><u>−163.66</u> +/- 23.95</b>  | <b><u>−30.51</u> +/- 26.07</b>   | <b><u>−169.75</u> +/- 24.97</b>  | <b><u>−52.66</u> +/- 25.58</b>   |
| Volume                 | −6.75 +/- 6.64                   | −4.10 +/- 7.89                   | −22.77 +/- 5.79                  | −6.42 +/- 6.51                   | <b><u>−24.14</u> +/- 3.40</b>    | <b><u>−4.51</u> +/- 3.80</b>     |
| Energy                 | <b><u>0.0084</u> +/- 0.0012</b>  | <b><u>0.0030</u> +/- 0.0012</b>  | <b><u>0.0067</u> +/- 0.0015</b>  | <b><u>−0.0003</u> +/- 0.0016</b> | 0.0077 +/- 0.0021                | 0.0016 +/- 0.0021                |
| Variance               | <b><u>−1.3238</u> +/- 0.1691</b> | <b><u>−0.5450</u> +/- 0.1815</b> | <b><u>−1.3293</u> +/- 0.2042</b> | <b><u>−0.2416</u> +/- 0.2224</b> | <b><u>−1.4230</u> +/- 0.2120</b> | <b><u>−0.4198</u> +/- 0.2167</b> |
| Contrast               | <b><u>−0.6486</u> +/- 0.0941</b> | <b><u>−0.2526</u> +/- 0.1009</b> | <b><u>−0.6234</u> +/- 0.1243</b> | <b><u>−0.0779</u> +/- 0.1353</b> | <b><u>−0.6738</u> +/- 0.1035</b> | <b><u>−0.2701</u> +/- 0.1062</b> |
| Entropy                | <b><u>0.0627</u> +/- 0.0086</b>  | <b><u>0.0190</u> +/- 0.0094</b>  | <b><u>0.0554</u> +/- 0.0077</b>  | <b><u>0.0127</u> +/- 0.0084</b>  | <b><u>0.0614</u> +/- 0.0093</b>  | <b><u>0.0174</u> +/- 0.0097</b>  |
| Homogeneity            | <b><u>0.0966</u> +/- 0.0157</b>  | <b><u>0.0371</u> +/- 0.0166</b>  | <b><u>0.0924</u> +/- 0.0157</b>  | <b><u>0.0235</u> +/- 0.0157</b>  | <b><u>0.1021</u> +/- 0.0144</b>  | <b><u>0.0283</u> +/- 0.0146</b>  |

The device used for the work presented here was the Visioscan® VC 20plus and at this stage, the key differences between this and the previous version of the device, the Visioscan® VC98 which had remained fundamentally unchanged for around 20 years, will be summarized. The main differences between the Visioscan® VC98 and the Visioscan® VC 20plus are:

1. Different light source. The VC 20plus has a light-emitting diode (LED) source with a reflector compared to the fluorescent light tube of the VC98.
2. Image resolution is higher with the VC 20plus (1280 × 1024 pixels compared to 640 × 480 pixels for the VC98).
3. Better focusing with the VC 20plus due to a moveable lens that can adapt to the skin surface position.
4. The VC 20plus automatically adapts the light for the first image of a subject’s skin site in a trial then has the same brightness for comparison of follow-up images of the same subject in the same trial at the same skin site.

One of the key differences between the two versions of the device is the spectral distribution of the light source used to illuminate the skin as shown in Figure 2. The Visioscan® VC 20plus uses an LED illumination source with a peak emission between 390 nm and 400 nm, while the previous VC98 used a fluorescent light tube with peak emission at around 365 nm with a number of sharp emission bands also present at longer wavelengths in the visible and infrared parts of the spectrum. Fluorescence of the dry skin is initiated after exposure to UVA, however, the degree of fluorescence is likely to be influenced by the wavelength of light that is used to illuminate the skin [19]. In addition, the transmission of the SC is slightly reduced at 365 nm compared to 390–400 nm which will also impact how it appears under these illumination wavelengths [20]. The authors

were unable to find a direct comparison of the results from the VC98 and newer VC 20plus devices. Previously, Visioscan<sup>®</sup> VC98 scores have been reported to correlate with dry skin grades [23]. Similar behavior to the results reported here was observed by Dobrev, although in that work the Wrinkles score increased with skin dryness [23]. It should also be noted that the entropy score reported by Dobrev decreased as the skin became drier [23] which is consistent with the results reported here, but opposite to the expected behavior of the entropy parameter according to the user manual for the device [21]. Moreover, the base size for the study reported by Dobrev [23] was 50 subjects, over three times the number of subjects in the work reported in this study, which is likely contributing to the more definitive changes observed in that work. While not a direct comparison between the two devices in the same type of study design, similar behavior was seen for the Visioscan<sup>®</sup> VC98 and VC 20plus dry skin parameters except for the Wrinkles score. Although this provides strong evidence for the use of the Visioscan<sup>®</sup> VC 20plus as a dry skin imaging method, more work is recommended before any direct comparisons can be drawn between the results obtained by the two versions of the device.

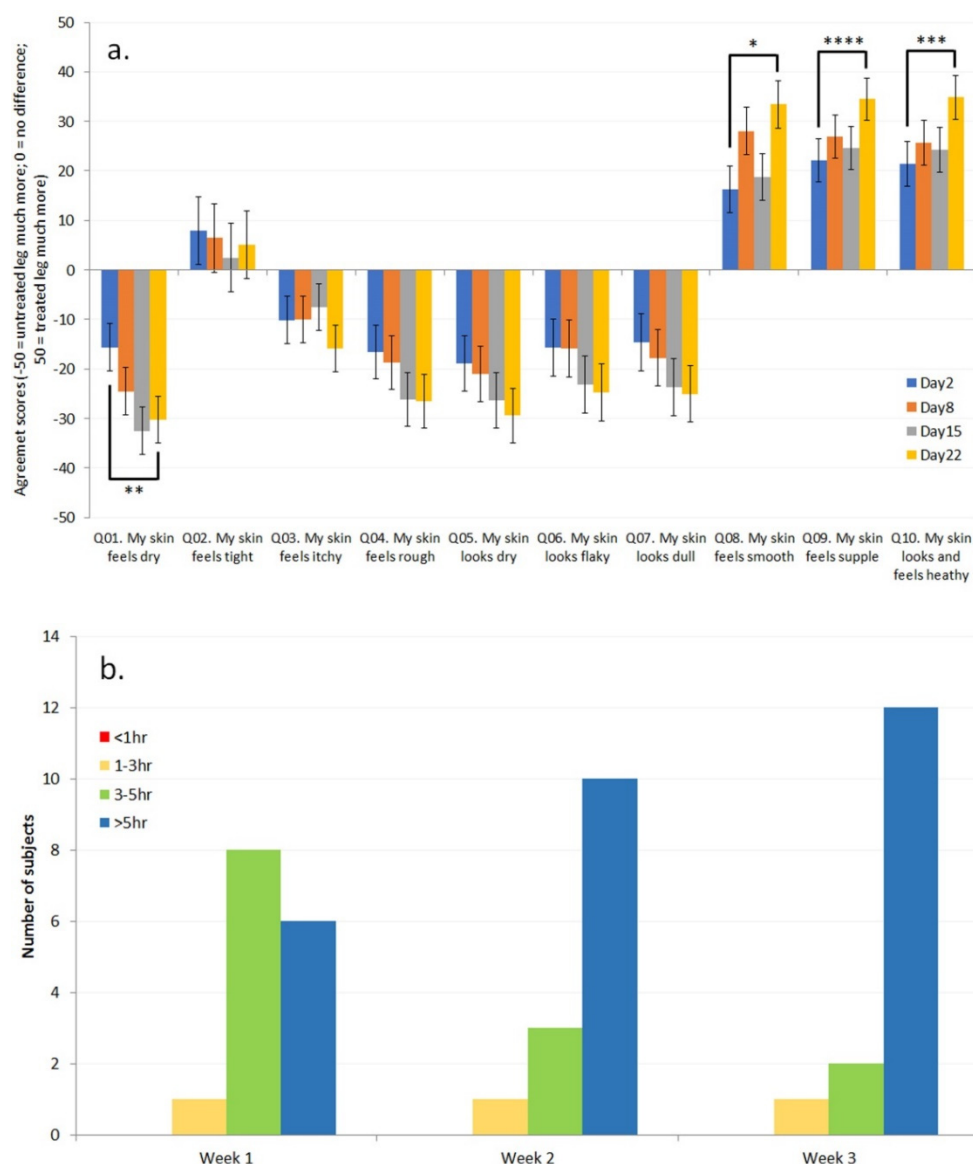


**Figure 2.** Irradiance spectra of the light sources used in the Visioscan<sup>®</sup> VC98 and VC 20plus between 250 nm and 800 nm. Spectral intensity has been normalized to the maximum intensity for each light source.

Subject feedback during a study can be used in addition to biophysical testing to provide further insight into the way that topical product usage impacts the skin condition [24–27]. In the study discussed here, after 1 day and 1, 2, and 3 weeks of product usage the subjects were asked to compare the condition of their skin on the treated and untreated sites, Figure 3a.

As a result of product usage, they reported reduced look and feel of dryness, increased suppleness and smoothness, reduced flakiness, dullness and itch, and reduced roughness throughout the study, and an overall improvement in the healthiness of the look and feel of their skin. These factors generally showed improvement throughout the 3 weeks of the study. The subjects observed improvements in similar aspects of their skin to those measured with the Visioscan<sup>®</sup>; a reduction in scaliness, surface area (surface score) in addition to a range of parameters associated with healthy, hydrated skin (energy, variance, entropy, contrast and homogeneity). In addition to questions about the nature of the skin condition, the subjects were also asked to record the length of time that they were

comfortable waiting before reapplying the product. No subjects reported that they felt the need to reapply the product <1 h after application. This distribution of the time period rankings shifted towards longer time frames throughout the study, indicating that the subjects were less troubled by their dry skin as the study period progressed, Figure 3b. The test product contained a range of ingredients including glycerine, niacinamide, and dexpanthenol which would be expected to positively improve skin hydration over the course of the experiment [28–31], which was observed by both the Visioscan<sup>®</sup> imaging and the subject feedback.



**Figure 3.** Subject feedback data during the study. (a) Comparison of the test (treated) and control (untreated) legs (−50 = untreated leg much more; 0 = no difference; 50 = treated leg much more) on day 2, 8, 15, and 22 (after 1 day and 1, 2 and 3 weeks of product usage). Statistical differences between the data for day 2 and day 22; \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ , \*\*\*\*  $p < 0.0001$ . (b) Length of time before the subjects thought re-application of the product was required in week 1, 2, and 3.

At this stage limitations with the study design and analysis should be discussed. Imaging with the Visioscan<sup>®</sup> only captures a small area of the skin (approximately 1 cm<sup>2</sup>) with each photograph. This is very different to visual dry skin grading where the assessor looks at a wide area of the skin to make their assessment of the skin condition. Analysis of a small area could result in focusing on a specific region rather than assessing the



average condition of the skin in the test area. As discussed previously, the base size of the study reported here was relatively small due to the inclusion of a wide range of different measurements [14,15]. This small base size has no doubt contributed to higher errors for the measures resulting in it being more difficult for some of the measurements to show statistical breaks at the 95% confidence level.

#### 4. Conclusions

As the range of biophysical methods available to the skin researcher increases, it is important to determine what aspects of the skin they can measure and assess, and how relevant they are to consumer experience during the use of topical moisturizing products.

In the second part of this article, analysis of images from a new dry skin camera—the Visioscan<sup>®</sup> VC 20plus—has been presented and discussed. Overall, the latest version of this camera behaved similarly to the previous version (Visioscan<sup>®</sup> VC98) with respect to dry skin imaging. Through the assessment of a wide range of parameters that the device can measure, it has been possible to demonstrate how the use of a topical moisturizing product has resulted in an improvement in skin dryness and overall condition. Subject feedback data have also been analyzed to give further understanding into the results of the biophysical testing. Both subjective feedback and instrumental measurements provide valuable data to understand the use of topical products on the skin and that subjective evaluation can be used to validate how instruments evaluate skin properties.

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**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** The data are not publicly available due to subject confidentiality.

**Conflicts of Interest:** H.S., S.T. and R.d.S. are employees of Bayer Consumer Care AG. P.B. and B.L. are employees of Bayer Healthcare SAS. J.C. and A.B. are consultants who have worked with Bayer Consumer Care AG and Bayer Healthcare SAS. S.B. is an employee of proDERM GmbH where the study was carried out.

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