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INTRODUCTION

The stratum corneum (SC) plays an important role in skin surface management by protecting the human body against microorganisms and guaranteeing skin barrier function by regulation of moisture grade and temperature. SC imbalance can lead to various inflammatory skin diseases, for instance constitutional eczema. The structure and barrier function of the SC can be studied noninvasively with different measurement tools; water content and transepidermal water loss (TEWL) are two commonly evaluated skin variables. A corneometer measures the water content by measuring electrical capacitance of the skin surface. Until today, single sensor corneometers have been extensively used to assess the skin barrier function and the condition of the SC. However, the same method was not standardized yet.

Methods: The hydration status of SC was measured in 15 healthy Caucasian volunteers with the Epsilon at five body sites (cheek, lower forearm, mid-calf, lower back and abdomen). Transepidermal water loss (TEWL) was measured with the Aquaflex to get more insight into the condition of the skin barrier. A literature search was performed to compare Epsilon values with conventional single sensor corneometers.

Results: The tested anatomical locations showed significant differences in water content (P < 0.001) with large interindividual variations; highest values were found in the cheek (11.64 ε) and lowest values in the mid-calf (4.43 ε). No correlation between water content and TEWL was found. In general, Epsilon values were lower compared to values of conventional corneometers, with a similar trend.

Conclusion: This pilot study showed significant variations in water content at different skin locations measured by the Epsilon. Moreover, the Epsilon measured consistent lower values compared to single sensor corneometers. Further validation of the device is recommended.

KEYWORDS
corneometer, Epsilon, skin barrier, skin capacitance, water content
Corneometers are used, showing significant differences in water content between various skin locations. Recently, the Epsilon, a multi-sensor corneometer with 76 800 sensors at one probe was introduced. Due to this increase in sensors, multiple measurements take place at once. In addition, options for analysis are integrated in this device and water content based images can be obtained.

To the best of our knowledge, this is the first study to investigate the anatomical site variation of water content in human skin with the Epsilon. Also, measured water content values of the Epsilon were compared to values measured by conventional single sensor corneometers by performing a literature search.

# MATERIALS AND METHODS

## 2.1 Participants

Fifteen healthy Caucasian volunteers (nine women and six men; median age 26 years; range 21-62 years) participated in this explorative study. Informed consent was obtained. The study was approved by the local medical ethics committee and conducted according to the principles of the Declaration of Helsinki. Exclusion criteria were as follows: age <18 years, signs of skin diseases or open wounds at the measurements sites, use of immunosuppressive medication, diagnosed with inflammatory dermatoses. Participants were asked not to use cream or body lotion at the day of measurements.

## 2.2 Technical device specifications

Water content of the SC was measured with the Epsilon (Epsilon E100, Biox, UK). This corneometer measures calibrated dielectric permittivity (dielectric constant, $\varepsilon$) through the SC and consists of a probe of 76 800 sensors with a sensing area of $12.8 \times 15$ mm, depth resolution of 20 $\mu$m and spacial resolution of 50 $\mu$m.8,9 The hardware and the probe of the Epsilon are shown in Figure 1A-D. Due to the multiple sensors, skin surface hydration can be mapped, taking skin relief and variable distribution of sweat glands into account (Figure 1E,F). This allows measurement of more average values and exclusion of regions with poor physical contact between sensor and skin. Moreover, the Epsilon is the only corneometer with a linearized and calibrated response, allowing consistent quantitative image evaluation.9

In this study, the standardized Burst mode option was used with a 5 seconds delay after first skin contact (to rule out initial variations in occlusion), a frame interval of 1-second, and a total measurement frame of 30 seconds.

To investigate the overall SC barrier function, TEWL was measured with the Aquaflux (AquafluxAF200, Biox, UK). The closed measurement chamber of the Aquaflux contains sensors for relative humidity and temperature.8,11 After calibration, measurements were performed with standard settings and a maximum measurement time of 80 seconds. The mean TEWL value was based on ten measure points, within a humidity degree of maximum 50%.

**FIGURE 1** The Epsilon is a novel instrument for measuring near-surface dielectric permittivity ($\varepsilon$) and contact imaging of the skin. Its proprietary electronics and signal processing algorithms map the sensor’s nonlinear signals onto a calibrated scale for measuring properties such as stratum corneum hydration. A, The Epsilon instrument on the parking stand. B, A measurement performed on the inner arm. C, Close-up of the Epsilon measurement head with the metal bezel. D, The sensor surface embedded in an epoxy frame. E, Typical contact image of the inner forearm skin. F, A contact image of the skin in the face with visible sweat gland activity.
2.3 | Study procedure

In each participant, water content and TEWL were investigated at five anatomical locations: cheek, first 1/3 of the flexor surface of the lower forearm, mid-calf, lower back and abdomen (Figure 2). For water content, one Burst mode measurement per body site was performed; for TEWL, the average of three measurements per body site was obtained. Standardized environmental circumstances were created; room temperature was kept constant at 20°C and exposed skin was air-acclimatized for at least 5 minutes prior to measurements.

2.4 | Statistics

Burst mode results from the Epsilon from all body sites were used to create regression functions and y-axis intersections were calculated. Statistical analysis was done with SPSS Statistics 22 (IBM Corporation, Armonk, New York). A Kruskal-Wallis test with Dunn-Bonferroni post hoc method was performed to demonstrate possible differences between the water content among the body sites. A relationship between water content and TEWL was investigated using Pearson correlation analysis. Tests were performed at 0.05 significance level.

2.5 | Comparison with conventional corneometers

To compare the Epsilon results with conventional corneometer values, a PubMed search was performed. Study inclusion criteria were as follows: in vivo setting, healthy/normal human skin, non-experimental setting OR use of a baseline control area in case of an intervention with topical therapies. Studied body sites preferably corresponded to the body sites chosen in this pilot study.

3 | RESULTS

3.1 | Anatomical variation in water content

The water content differed significantly between the five body sites ($P < 0.001$). As Figure 3 shows, the cheek had the highest water content.
| Study                     | Device                | Population     | Skin location | Forehead (a.u.) | Cheek (a.u.) | Forearm (a.u.) | Calf (a.u.) |
|--------------------------|-----------------------|----------------|---------------|-----------------|--------------|----------------|-------------|
| O’goshi et al\(^5\)      | Corneometer CM820    | 53 healthy volunteers |               | 74 (38-122)\(^a\) | 75 (37-100) | 65 (43-115) | 50 (28-90) |
|                          | Corneometer CM82      |                |               | 72 (29-113)\(^a\) | 74 (24-96)  | 65 (50-100) | 49 (29-90) |
|                          | Corneometer CM810     |                |               | 78 (41-131)\(^a\) | 81 (33-104) | 71 (52-113) | 50 (27-95) |
| Egawa et al\(^17\)       | Corneometer CM825     | 45 healthy volunteers | Winter:       | 36 ± 11\(^b\)       | 37 ± 9       | 37 ± 6        |            |
|                          |                       |                | Spring:        | 37 ± 11\(^b\)       | 36 ± 7       |               |            |
|                          |                       |                | Autumn:        | 48 ± 9\(^b\)        | 38 ± 10      |               |            |
|                          |                       |                | Summer:        | 50 ± 11\(^b\)       | 47 ± 8       |               |            |
| O’goshi et al\(^6\)      | Skicon-100\(^c\)     | 26 healthy volunteers |               | 73 ± 52\(^b\)       | 80 ± 56\(^b\) | 50 ± 27\(^b\) | 26.5 ± 31\(^b\) |
|                          | Skicon-200EX         |                |               | (16-369)\(^a\)      | (27-272)     | (11-123)      | (9-125)    |
| Algiet-Zielińska et al\(^22\) | Corneometer CM825   | 10 healthy volunteers | Left side:    | 46.67 ± 10\(^b\)  | 39.77 ± 13.78| 32.57 ± 13.82|            |
|                          |                       |                | (28.1-65.35)\(^b\) |   | (19.60-59.52)|            |            |
|                          |                       |                | Right side:   | 51.04 ± 12.50\(^b\) | 44.2 ± 12.65| 36.0 ± 12.71 |            |
|                          |                       |                | (30-64.64)\(^b\) |   | (27.18-66.72)|            |            |
| Kleesz et al\(^12\)      | Corneometer CM825    | 125 healthy volunteers |               | 75 ± 13\(^b\)       | 72 ± 16      | 62 ± 13       | 58 ± 10    |
| de Farias Pires et al\(^23\) | Corneometer CM820   | 1339 healthy volunteers | Female:      | 37 (9-78)\(^a\)     | 32 (10-56)  |               |            |
|                          |                       |                | Male:         | 28 (5-66)\(^a\)     | 27 (2-56)   |               |            |
| Young et al\(^24\)       | Corneometer CM825    | 21 healthy volunteers |               | 25 (24.5-25.5)\(^b\) |            |               |            |
| Marrakchi et al\(^25\)   | Corneometer CM-420   | 20 healthy volunteers | 24-34 y:     | 89.33 ± 12.7\(^b\)  | 87.40 ± 12.4| 81.70 ± 11.1 |            |
|                          |                       |                | 66-83 y:     | 76.90 ± 18.2\(^b\)  | 76.83 ± 16.9| 66-83 y:     |            |
| Fluhr et al\(^26\)       | Corneometer CM825    | Seven healthy volunteers |               | 46.4 ± 6.5\(^b\)    |            |               |            |
| Lodén et al\(^27\)       | Corneometer CM820    | 17 healthy volunteers |               | 70 (69-82)\(^a\)    |            |               |            |
| Esposito et al\(^28\)    | Corneometer CM820    | 10 healthy volunteers |               | 22 (20-24)\(^b\)    |            |               |            |
| Cheng et al\(^29\)       | Corneometer CM825    | 30 healthy volunteers | 55 ± 9\(^b\)  |               | 55 ± 8       |               |            |
| Hillebrand et al\(^30\)  | Corneometer 820PC    | 602 healthy females | 5-15 y:      | 59.90 ± 11.7\(^b\)  | 51.5 ± 4.30 |              |            |
|                          |                       |                | 25-35 y:     | 76.87 ± 10.0\(^b\)  | 48.4 ± 4.30 |              |            |
|                          |                       |                | 45-54 y:     | 78.74 ± 10.8\(^b\)  | 54.82 ± 6.0 |              |            |
|                          |                       |                | 55-65 y:     | 77.48 ± 11.9\(^b\)  | 55.65 ± 6.5 |              |            |
| Agache et al\(^31\)      | Corneometer CM820    | 20 healthy volunteers |               | 55.45 ± 2\(^b\)     |            |               |            |
content (median 11.64ε), followed by the forearm (9.35ε), abdomen (7.45ε), lower back (7.07ε) and mid-calf (4.43ε). Post hoc analysis revealed that the water content of the mid-calf was significantly lower than the water content of the cheek ($P < 0.001$) and the forearm ($P < 0.001$). Additionally, a large interindividual variation in water content among the various skin locations was seen. There was no significant correlation between water content (measured by Epsilon) and TEWL ($r = 0.194$, $n = 75$, $P = 0.095$).

### 3.2 | Comparison with conventional corneometers

Table 1 shows literature-based reference values of the water content with single sensor corneometers. In general, single sensor corneometers showed higher water content values than the Epsilon. In line with the Epsilon, also conventional corneometers measured lower values of the calf compared to the cheek and forearm.

### 4 | DISCUSSION

This pilot study is the first to measure water content of the SC in different body sites with the Epsilon. Our findings showed significant differences among the body sites, in correspondence with previous studies that also showed this trend.\(^5\)\(^-\)\(^7\)\(^,\)\(^12\)\(^,\)\(^13\) Many factors could influence these regional differences, for example, variations in the presence of sebaceous glands and lipids, natural moisturizing factor (NMF), size of corneocytes, exogenous compounds on skin surface and occlusion.\(^4\)\(^,\)\(^12\)\(^,\)\(^14\) Also, SC thickness variation could play a role; the smallest SC cell number is found in genital skin, followed by the face, neck, scalp, trunk, extremities and palmar plantar region.\(^4\)\(^,\)\(^14\)\(^,\)\(^15\) Moreover, skin surface hydration gradually increases in deeper layers of the SC, reaching a certain high level in the fully hydrated epidermis.\(^16\)\(^,\)\(^17\) It is therefore more likely to measure water content in deeper and more hydrated layers of skin with thinner SC (eg, cheek), resulting in higher values.

Another important finding was that water content values of the Epsilon were lower compared to values of conventional corneometers. First, it is important to bear in mind that Epsilon measurement units are displayed using a calibrated dielectric permittivity scale ($\varepsilon$) rather than an arbitrary scale (a.u.) as used in conventional corneometers. As both instrument types use the same capacitance measurement principle, they should correlate well; this was already shown by one-to-one testing of both devices on the volar forearm of healthy volunteers.\(^18\) With the multisensory character of the Epsilon, the sensing depth will probably be more superficial compared to conventional corneometers, which make one big electrical loop through the skin. This increases the chance that Epsilon measurements are confined to the relatively "dry" SC only. Another advantage of the Epsilon is the Burst mode setting, correcting for time-dependent skin occlusion differences, while conventional corneometers perform single time point measurements. Thirdly, due to the "skin mapping" character of the Epsilon, the number of values in one measurement can be averaged. All of the above could potentially lead to more accurate water content values.

The large interindividual variation of water content among the different skin locations could be influenced by individual parameters, for example, age, gender and lifestyle.\(^4\)\(^,\)\(^5\)\(^,\)\(^13\)\(^,\)\(^19\) This was not studied in more detail because of the explorative character of this pilot.

Interestingly, no correlation was found between water content and TEWL. One would expect that TEWL increases in a disrupted skin barrier, resulting in lower water content, and vice versa. However, also previous studies showed no or only weak correlations between these two measurements.\(^20\)\(^,\)\(^21\) As mentioned earlier, other factors besides from TEWL and water content seem to be responsible for alterations of skin barrier function.

Despite the relatively small number of volunteers, these pilot results are promising. Larger populations of healthy volunteers and patients should be investigated for further validation of the Epsilon. This could elucidate the potential of this device for diagnosis and/or therapeutic monitoring of subjects having skin diseases with decreased barrier function, for example, inflammatory dermatoses. It would also be interesting to study possible interactions between water content and other noninvasive skin barrier measurements (eg, NMF and sebum levels)\(^16\)\(^,\)\(^20\) and the possible impact of inter-seasonal fluctuation on skin condition.

In conclusion, we found significant regional differences in water content in human skin measured by the Epsilon. Moreover, the

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**TABLE 1** (Continued)

| Study          | Device          | Population               | Skin location | Forehead (a.u.) | Cheek (a.u.) | Forearm (a.u.) | Calf (a.u.) |
|----------------|-----------------|--------------------------|---------------|----------------|--------------|----------------|-------------|
| Richters et al\(^{20}\) | Corneometer CM825 | 30 volunteers with nonsensitive skin |               |                |              |                |             |

a.u., arbitrary units.
Words in italic describe specific conditions/subgroups studied.
\(^{a}\)Median ± SD (range).
\(^{b}\)Mean ± SD (range).
\(^{c}\)Measures skin conductance; close correlation to skin capacitance.\(^{16}\)

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Epsilon measures lower water content values compared to conventional single sensor corneometers and these values show an equal trend in differences of water content among different body sites. It is recommended to investigate these findings in a larger population for further validation of the Epsilon and to determine if this device can be implemented into the clinical setting.

CONFLICT OF INTEREST
None declared.

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