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ORIGINAL ARTICLE

An Alternative Approach Based on Skin Electrical Impedance to Determine Transepidermal Water Loss for Skin Barrier Function Assessments

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Abstract

Purpose The transepidermal water loss (TEWL) has long been measured as an indicator to assess the skin barrier function in dermatological research and clinical practice. However, practical limitations such as time requirement, environmental sensitivity, and measurement complexity hinder the widespread uptake of conventional TEWL measurements in clinical settings and routine monitoring. Consequently, there is a growing need for rapid, robust, and clinically applicable alternatives to conventional TEWL measurements. Here, we present a simple, non-invasive, and time-efficient method based on the skin electrical impedance for skin barrier function assessments.

Methods The skin electrical impedance, TEWL, stratum corneum (SC) thickness, and SC surface water content of 25 healthy adult participants with no history of dermatological diseases were measured at two adjacent forearm sites: intact site with a normal skin barrier and tape-stripped site with an impaired skin barrier. The measured impedance was used to calculate the SC thickness and surface water content, from which the TEWL was estimated and then compared against the TEWL measured using a Tewameter. The estimation accuracy was evaluated by determining the correlation coefficient (R) and root mean square error (RMSE) between estimated and measured TEWL.

Results A strong correlation ($R = 0.891$) was observed between estimated and measured TEWL, with an RMSE of 6.05 g/m²/h, indicating high accuracy of the proposed method.

Conclusion This impedance-based method provides accurate estimations of the TEWL, indicating its potential as a practical alternative to conventional TEWL measurements for skin barrier function assessments, particularly in clinical or high-throughput settings.

Keywords Transepidermal water loss · Electrical impedance · Stratum corneum · Skin barrier

1 Introduction

The transepidermal water loss (TEWL) is widely evaluated as an indicator of the skin barrier function [1, 2] in dermatology, with extensive evidence supporting its validity [3]. However, direct TEWL measurements are subject to numerous constraints, including strict control of the measurement environment and maintenance of the subject at rest prior to the measurements [3]. Additionally, operational and real-time limitations arise from factors such as airflow obstruction, reduction of residual moisture within the probe, and the need to apply a consistent light pressure while maintaining the probe in a vertical position. These issues hinder the widespread application of direct TEWL measurements for clinical diagnosis or routine monitoring of the skin barrier

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function. Therefore, there has been a growing need for the development of rapid, stable methods to replace direct TEWL measurements, enabling simple, rapid evaluations of the skin barrier function.

The electrical impedance method (hereinafter referred to as the IM method) has been developed to determine the water content and composition of biological tissues simply and non-invasively [4–6]. In particular, the frequency-dependent IM method has been applied to determine the water content of the stratum corneum (SC) and to evaluate internal biological structures [6, 7].

The aim of this study is to develop a simple, rapid method in which the IM method is used to determine the SC thickness and surface water content, from which the TEWL is calculated, enabling quantitative evaluation of the skin barrier function. This study is focused on the SC, which plays a crucial role in skin barrier function [8–10]. Using the IM method, we non-invasively determined the thickness and surface water content of the SC of intact skin and skin with a barrier function impaired by tape stripping [11]. The TEWL was subsequently calculated using a theoretical framework based on the thickness and surface water content of the SC, and the feasibility of this approach as an alternative to direct TEWL measurements was evaluated by comparing the calculated values with the directly measured data.

2 Theory

The theory for calculating the TEWL from the skin electrical impedance is presented here.

2.1 TEWL Estimation with Two Frequencies Using IM

The impedance Z of the SC can be represented equivalently by a resistor–capacitor (RC) parallel circuit [12]. Equations (1) and (2) show the relationship between parallel resistance R_P [Ω] and its resistivity ρ as well as parallel capacitance C_P [F] and its dielectric constant ε in this circuit.

$$R_P = \rho \frac{T}{S} \tag{1}$$

$$C_P = \epsilon \frac{S}{T} \tag{2}$$

where S [m^2] is the cross-sectional area of the SC.

When alternating current (AC) is applied to the skin at two frequencies, i.e., an AC signal in the low-frequency range and another AC signal in the high-frequency range, Eqs. (1) and (2) are then related to the SC thickness T and SC water content WC, as shown in Eqs. (3) and (4) [13].

$$R_{PH} = \alpha_{RH} \cdot T^{\gamma_{RH}} \cdot e^{-\beta_{RH} WC} \tag{3}$$

$$C_{PL} = \frac{\alpha_{CL}}{T^{\gamma_{CL}}} e^{\beta_{CL} WC} \tag{4}$$

At low AC frequencies, the parallel capacitance is C_{PL} [F] and the associated constant coefficients are α_{RL}, α_{CL}, β_{RL}, β_{CL}, γ_{RL}, and γ_{CL}. At high AC frequencies, the parallel resistance is R_{PH} [Ω] and the associated constant coefficients are α_{RH}, α_{CH}, β_{RH}, β_{CH}, γ_{RH}, and γ_{CH}.

Estimating the surface water content of the SC is more suitable than estimating the total water content of the SC [13]. Therefore, Eqs. (3) and (4) can be expressed in terms of Eqs. (5) and (6), which defines the estimated SC thickness T_E [μm] and estimated SC surface water content WC_{SE} [mass-%].

$$T_E = \left(\frac{R_{PH}}{\alpha_{RH}}\right)^{\frac{\beta_{CL}}{\gamma_{RH}\beta_{CL} - \gamma_{CL}\beta_{RH}}} \left(\frac{C_{PL}}{\alpha_{CL}}\right)^{\frac{\beta_{RH}}{\gamma_{RH}\beta_{CL} - \gamma_{CL}\beta_{RH}}} \tag{5}$$

$$WC_{SE} = \frac{1}{\gamma_{RH}\beta_{CL} - \gamma_{CL}\beta_{RH}} \ln\left\{\left(\frac{C_{PL}}{\alpha_{CL}}\right)^{\gamma_{RH}} \left(\frac{R_{PH}}{\alpha_{RH}}\right)^{\gamma_{CL}}\right\} \tag{6}$$

The TEWL is related to the ratio of free water on the SC surface and the maximum water supply from the granular layer to the SC surface [14], as expressed in Eq. (7).

$$\text{TEWL} = (WC_{SM} - WC_{bound}) \times D/T^{\gamma} \tag{7}$$

Here, WC_{bound} [mass-%] is the proportion of bound water on the SC surface, γ is a constant, and D [g/m$^{2-\gamma}$/h/mass-%] is a coefficient. WC_{SM} is the measured surface water content of the SC.

T and WC_{SM} in Eq. (7) can be estimated using Eqs. (5) and (6), yielding Eq. (8), which derives the TEWL from the skin electrical impedance.

$$\text{TEWL} = A \times \left(\frac{1}{\gamma_{RH}\beta_{CL} - \gamma_{CL}\beta_{RH}} \ln\left\{\left(\frac{C_{PL}}{\alpha_{CL}}\right)^{\gamma_{RH}} \left(\frac{R_{PH}}{\alpha_{RH}}\right)^{\gamma_{CL}}\right\} - WC_{bound}\right) \times D/\left\{\left(\frac{R_{PH}}{\alpha_{RH}}\right)^{\frac{\beta_{CL}}{\gamma_{RH}\beta_{CL} - \gamma_{CL}\beta_{RH}}} \left(\frac{C_{PL}}{\alpha_{CL}}\right)^{\frac{\beta_{RH}}{\gamma_{RH}\beta_{CL} - \gamma_{CL}\beta_{RH}}}\right\}^{r} \tag{8}$$

3 Methods

3.1 Participants and Measurement Settings

This study included 25 adult men and women (22 males and 3 females) aged 28 to 63 years (mean = 40.8 years) with no history of skin disease. The test sites were two areas adjacent to the center of the inner forearm. One site was intact skin (25 cases), and the other was tape-stripped skin (25 cases) with a reduced skin barrier function [11], which was created by applying and then removing a 3 cm-diameter circular tape.

At the designated measurement sites, the skin electrical impedance, SC thickness, SC surface water content, and TEWL were measured using the methods described below. In total, 50 datasets were obtained for each parameter. To determine the constant coefficients in Eqs. (5), (6), and (7), all datasets were sorted in ascending order of the TEWL. The 25 datasets with odd-numbered ranks were assigned to the pilot dataset, and the remaining 25 even-ranked datasets were assigned to the primary dataset. The constant coefficients were derived using numerical computation based on the KH method applied to the pilot dataset [15]. These coefficients were then applied to the primary dataset to estimate the TEWL from the skin electrical impedance, SC thickness, and SC surface water content. The estimated TEWL values were subsequently compared with the corresponding measured TEWL values in the primary dataset to evaluate estimation accuracy.

All measurements were conducted to minimize the influence of environmental conditions and individual differences. Participants were acclimatized in a temperature-controlled room maintained at 21 °C and 50% relative humidity. Participants were instructed to refrain from applying topical medications to the measurement sites for at least 12 h prior to the measurements. Additionally, the measurement sites were first washed with water and then air-dried for at least 15 min prior to the measurements.

The study was approved by the Ethical Review Committee of ALCARE Corporation (DP04-48-20210909) and Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences and Okayama University Hospital (2210-046), and experiments were conducted in accordance with the Declaration of Helsinki. All participants provided written consent prior to the experiments.

3.2 Measurement of the Skin Electrical Impedance

The device developed in-house to measure the skin electrical impedance is shown in Fig. 1. It comprises several functional units: a main body (Fig. 1(a)), electrode head located at the tip (Fig. 1(b)), display on the side of the main body, and power switch positioned opposite the electrode. After the electrode is placed in contact with the skin (Fig. 1(c)), AC voltages of 500 Hz and 100 kHz are applied to the skin to start the measurement, which is completed in approximately 5 s. The resulting signal is detected by the electrode head, which transmits the detected signal to the arithmetic unit built in the main body. The arithmetic unit of the device processes the signal and calculates the electrical impedance to estimate the TEWL, SC thickness, and SC surface water content, which are displayed in real time on the display. Each test site is measured three times, and the average of the three measured values is recorded as the electrical impedance of the SC.

Figure 2 shows a circuit block diagram of the device. The 500 Hz and 100 kHz oscillation circuits apply an alternating voltage to the skin through the electrodes. The high frequency of 100 kHz is relatively unaffected by external noise, making it stable and easy to handle. The skin impedance increases as the AC frequency decreases, and the low frequency of 500 Hz represents the practical limit of current detection. The signal passing through the skin is detected by the detection electrodes, amplified in the detection unit, and then sent to the arithmetic unit. The filter in the detection unit cuts out high-frequency noise in the signal passing through the skin. The cutoff frequencies are 5.82 kHz for the 500 Hz signal and 234 kHz for the 100 kHz signal. The arithmetic unit contains an AD converter that digitizes the amplified electrical signal.

The skin electrical impedance is calculated using the phase difference calculated from the peak value of the current detected by the arithmetic unit and the time difference between the applied voltage and the detected current signal. The arithmetic unit further subtracts the electrical impedance of layers deeper than the SC, such as the granular layer, to derive impedance Z and phase angle θ of the SC only. These values are then used to calculate resistance R_{PH} and capacitance C_{PL} of the SC.

The measurement accuracy was evaluated by comparing the calculated values with those obtained using an LCR meter (IM3523, HIOKI, Ueda, Nagano, Japan), which also models the skin as an RC parallel circuit, to calculate the skin electrical impedance. The electrical impedance was within ± 5%, and the phase angle θ was within ± 1°. From these measurement errors, a correction factor was calculated to calibrate the device.

3.3 Measurement of TEWL, SC Thickness, and SC Surface Water Content

The TEWL was measured using a Tewameter (TM Hex, Courage + Khazaka, Köln, Germany). The skin was cleansed and allowed to acclimatize for 15 min. Then, measurements were taken at intervals of 1 s until the standard deviation (SD) of the readout reached 0.15 g/m²/h or less. The TEWL was measured three times, and the average value was taken as *m-TEWL*. The SC thickness was determined using cross-sectional images of the skin surface acquired with a confocal laser microscope (VivaScope1500 Multi; Caliber I.D.,

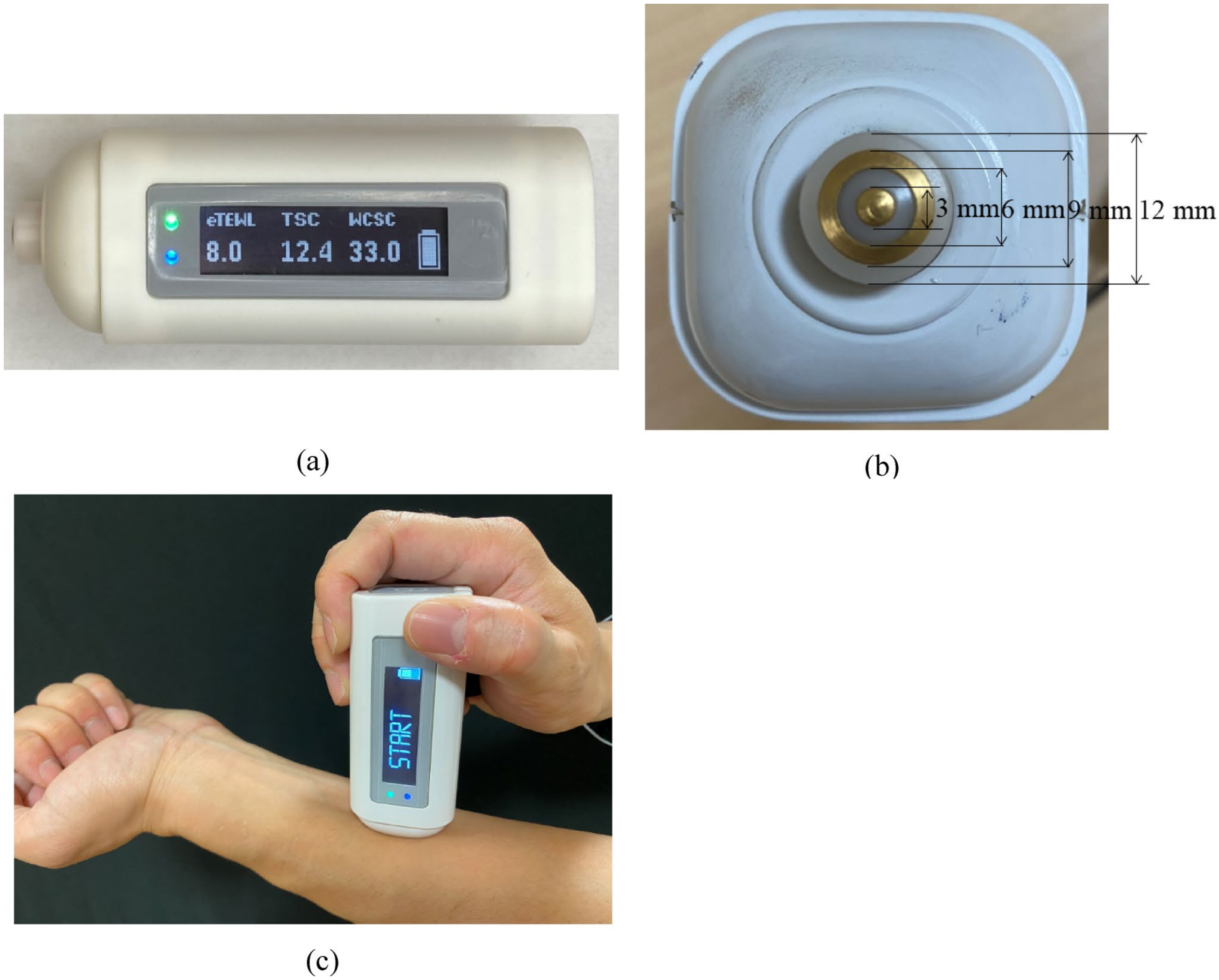

Fig. 1 Photographs of the (**a**) main body and (**b**) electrode of the device. The sensing electrode is the central circular electrode (copper and gold plated, diameter of 3 mm), and the applying electrode is the surrounding concentric ring-shaped electrode. (**c**) Photograph of the device in contact with the skin for electrical impedance measurements

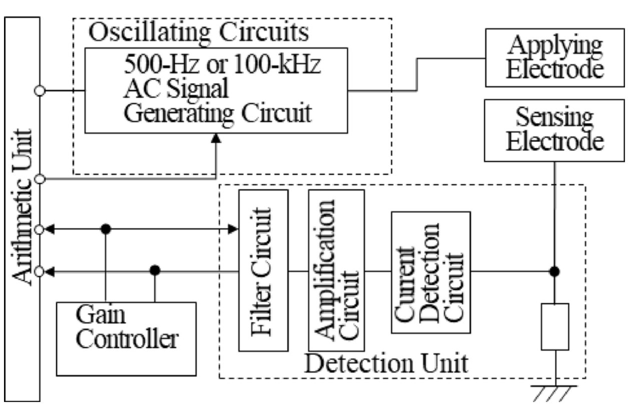

Fig. 2 Block circuit diagram of the device

Andover, MA, USA) [16]. The average value of the three analyzed sites was used as the SC thickness T_M. The SC surface water content was determined using a confocal Raman spectrometer (Model 3510 SCA; River Diagnostics B.V., Rotterdam, Netherlands) to measure the distribution of water from the skin surface to a depth of 20 µm, and the average value was used as the SC water content [17]. The measurement time at each depth was 1 s. The measurement was performed five times, and the average of three points, excluding the maximum and minimum values, was used in subsequent analyses. The average value from the surface layer to 20% of T_M was defined as the SC surface water content WC_{SM}.

3.4 Evaluation of Estimation Accuracy

The measurement accuracy of the device was evaluated using an equivalent circuit of tape-stripped SC, with the TEWL equivalent to 48.44 g/m²/h, SC thickness equivalent to 1.51 µm, and SC surface water content equivalent to 55.64 mass-%. The SC thickness and SC surface water content estimated from the skin electrical impedance were defined as T_E and WC_{SE}, respectively. The TEWL estimated from T_E and WC_{SE} was defined as *e-TEWL*, while the TEWL estimated from T_M and WC_{SM} was defined as *e-TEWLm1*. T_E was compared with T_M, while WC_{SE} was compared with WC_{SM}, and the resulting correlation coefficient (R) and root mean square error (RMSE) were used to evaluate the estimation accuracy. In addition, inverse estimation of $\log(R_{PH})$ and $\log(C_{PL})$ from T_M and WC_{SM} was used to confirm the validity of the comparison between T_E and T_M, as well as the comparison between WC_{SE} and WC_{SM}. Subsequently, *e-TEWLm1* was compared with *m-TEWL* to evaluate its estimation accuracy. Finally, *e-TEWL* was compared with *m-TEWL* to evaluate its estimation accuracy.

4 Results

4.1 Estimation Accuracy

An equivalent circuit simulating tape-stripped SC was used to assess the accuracy of estimating the TEWL. The measurement errors were |Z| ± 5%, θ ± 1.0°, R_{PH} ± 10.1%, and C_{PL} ± 7.7%. Additionally, the estimation accuracies were TEWL ± 1.2 g/m²/h, SC thickness ± 0.1 µm, and SC surface water content ± 0.8 mass-%. Within the ranges of R_{PH} ± 10% and C_{PL} ± 10%, the estimation accuracies were TEWL ± 1.4 g/m²/h, SC thickness ± 0.2 µm, and SC surface water content ± 0.9 mass-%. These errors were approximately one-quarter of the RMSE observed in the TEWL estimation results described below and were not considered to have a significant impact on the estimation performance. These findings confirm that the proposed method provides sufficient accuracy for estimating TEWL.

4.2 SC Thickness and Surface Water Content

Figure 3(a) shows the relationship between the measured T_M and estimated T_E of the pilot dataset, which was characterized by R of 0.810 and RMSE of 2.01 µm. Figure 3(b) shows the relationship between measured WC_{SM} and estimated WC_{SE}, which was characterized by R of 0.841 and RMSE of 4.45 mass-%. These R values indicated high correlation between measured and estimated values.

4.3 R_{PH} and C_{PL}

To validate the results for estimating the SC thickness and surface water content, the values of $\log(R_{PH})$ and $\log(C_{PL})$ were determined by substituting T_M and WC_{SM} of the pilot dataset into Eqs. (3) and (4). Figure 4(a) shows the relationship between measured $\log(R_{PHM})$ and estimated $\log(R_{PHE})$, while Fig. 4(b) shows the relationship between measured

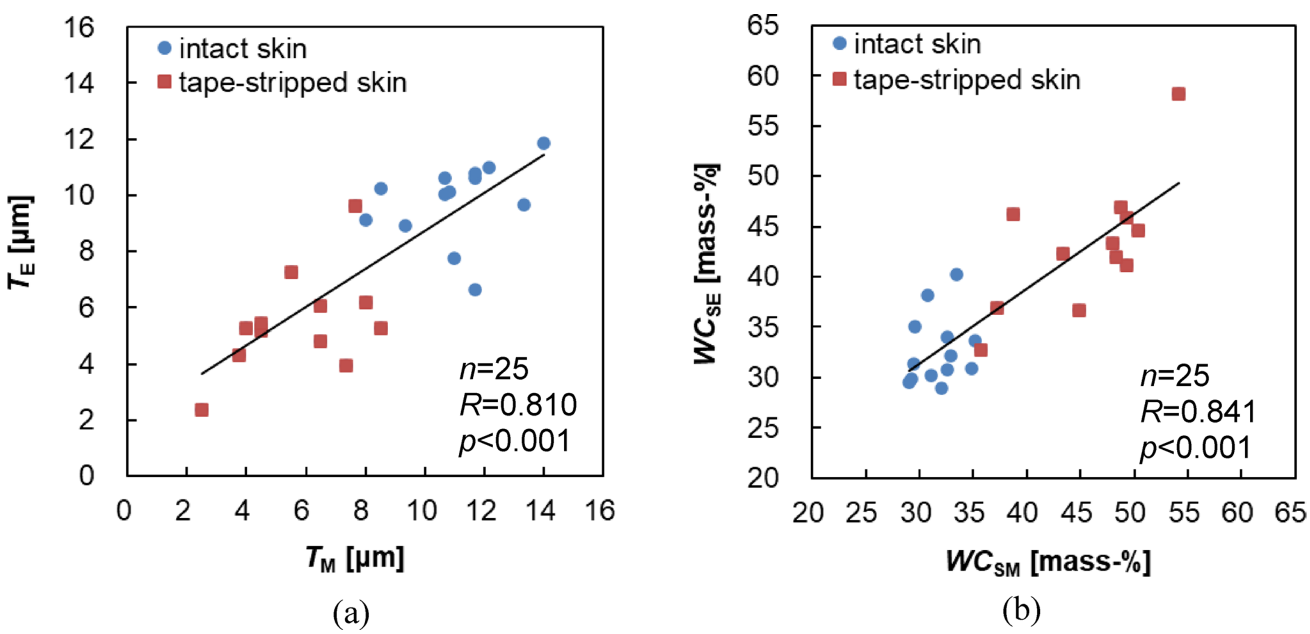

Fig. 3 (**a**) Estimation of the SC thickness using the pilot dataset. Average T_E = 7.7 µm (SD = 2.7 µm); average T_M = 8.5 µm (SD = 3.2 µm). (**b**) Estimation of the SC surface water content using the pilot dataset. Average WC_{SE} = 37.7 mass-% (SD = 7.3 mass-%); average WC_{SM} = 38.4 mass-% (SD = 8.2 mass-%)

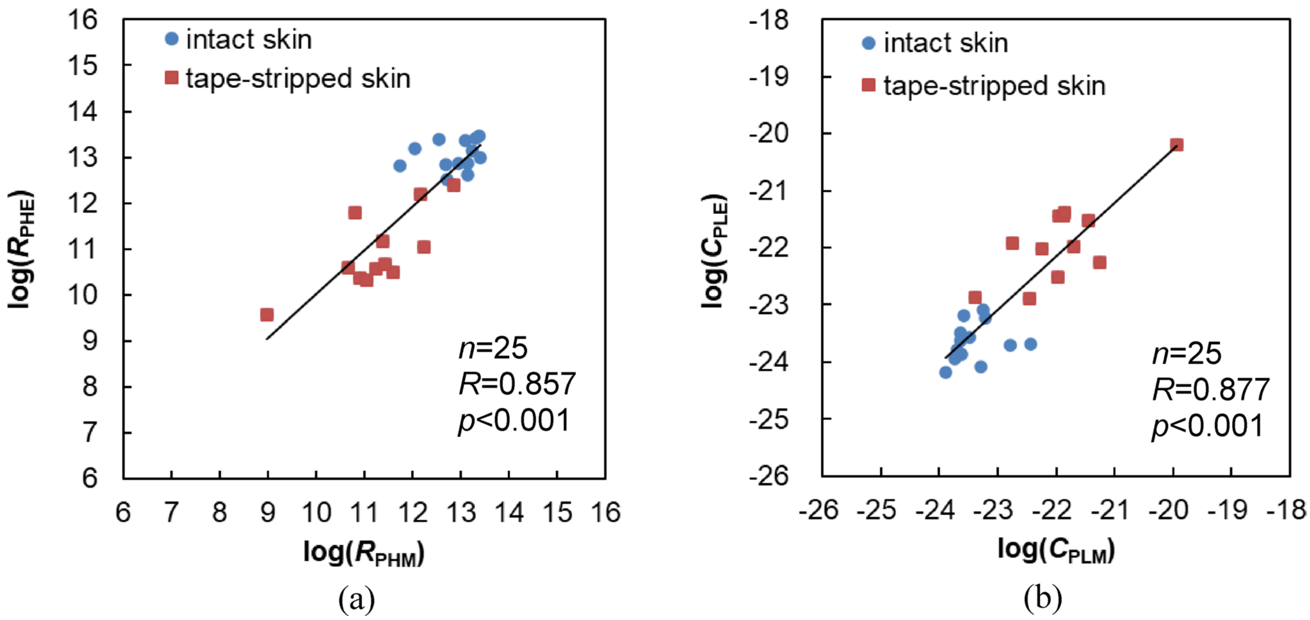

Fig. 4 Estimation of (**a**) $\log(R_{PH})$ and (**b**) $\log(C_{PL})$ using the pilot dataset

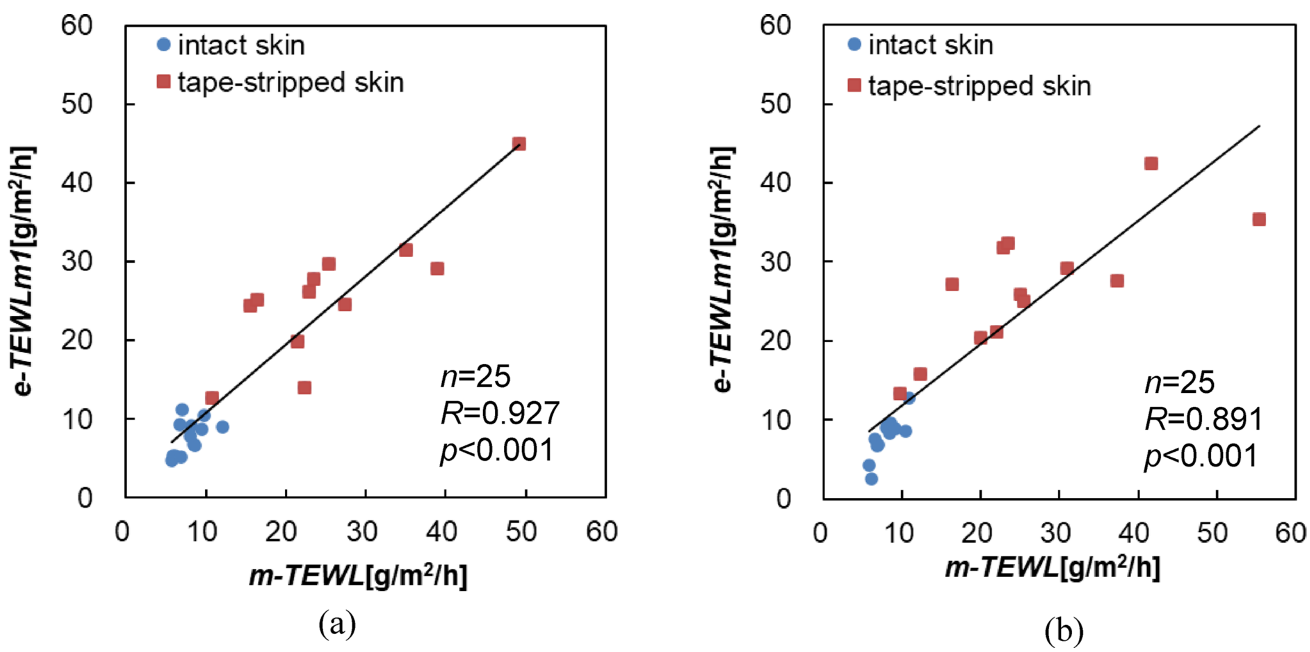

Fig. 5 Estimation of the TEWL from the measured SC thickness and surface water content. (**a**) Estimation using the pilot dataset. Average *e-TEWLm1* = 16.4 g/m^2/h (SD = 11.0 g/m^2/h); average *m-TEWL* = 16.5 g/m^2/h (SD = 11.7 g/m^2/h). (**b**) Estimation using the primary dataset. Average *e-TEWLm1* = 17.7 g/m^2/h (SD = 11.3 g/m^2/h); average *m-TEWL* = 17.5 g/m^2/h (SD = 12.9 g/m^2/h)

$\log(C_{PLM})$ and estimated $\log(C_{PLE})$. The R values of these two relationships were 0.857 and 0.877, respectively, indicating strong correlation. These R values validated the proposed method for estimating the SC thickness and SC surface water content from the skin electrical impedance.

4.4 Estimation of TEWL from SC Thickness and Surface Water Content

The relationship between measured *m-TEWL* and *e-TEWLm1* estimated using the pilot dataset is shown in Fig. 5(a). R of this relationship was 0.927, which indicated high correlation. Additionally, RMSE was 4.30 g/m²/h. The constant coefficients were determined using the pilot dataset and then

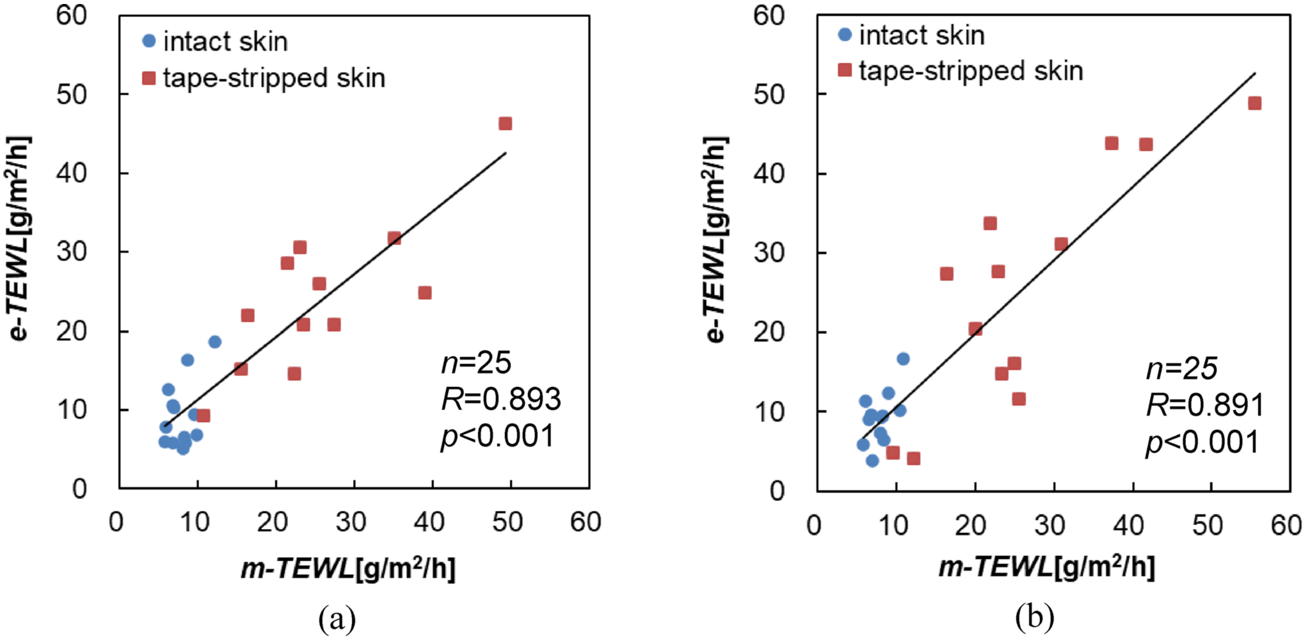

Fig. 6 Estimation of the TEWL from the skin electrical impedance. (**a**) Estimation using the pilot dataset. Average *e-TEWL* = 16.5 g/m^2/h (SD = 10.5 g/m^2/h); average *m-TEWL* = 16.5 g/m^2/h (SD = 11.7 g/m^2/h). (**b**) Estimation using the primary dataset. Average *e-TEWL* = 17.6 g/m^2/h (SD = 13.5 g/m^2/h); average *m-TEWL* = 17.5 g/m^2/h (SD = 12.9 g/m^2/h)

applied to the results of the primary dataset (Fig. 5(b)). *R* of the resulting relationship between *m-TEWL* and *e-TEWLm1* was 0.891, indicating high correlation. Additionally, RMSE was 5.76 g/m²/h.

4.5 Estimation of TEWL from the Skin Electrical Impedance

We estimated the TEWL using the SC thickness and SC surface water content estimated from the skin electrical impedance. The relationship between measured *m-TEWL* and *e-TEWL* estimated using the pilot dataset is shown in Fig. 6(a). *R* was 0.893, which indicated high correlation. The constant coefficients were determined using the pilot dataset and applied to the results of the primary dataset (Fig. 6(b)). *R* of the resulting relationship between *m-TEWL* and *e-TEWL* was 0.891, indicating high correlation. Additionally, RMSE was 6.05 g/m²/h.

5 Discussion

The TEWL is an important indicator that has been widely used for many years to evaluate the skin barrier function. An increase in the TEWL indicates that the moisture retention function and structural integrity of the SC are disrupted, which is useful in clinical diagnosis [3]. In this study, we developed a method for estimating the TEWL from the skin electrical impedance, serving as a new method to replace direct TEWL measurements for skin barrier function assessments. Moreover, we evaluated its usefulness and reliability by comparing the results obtained using this method with actual measurement data.

The estimated *e-TEWL* of the primary dataset showed a high correlation ($R = 0.891$, $p < 0.001$) with the measured TEWL, and RMSE was 6.05 g/m²/h. Therefore, the estimation accuracy of *e-TEWL* was comparable to that of *e-TEWLm1*, supporting the validity of the proposed method. Furthermore, because skin electrical impedance measurements can be completed in approximately 5 s, the proposed method can provide rapid and simple estimations of the TEWL, indicating that it may serve as a useful and reliable alternative method for assessing daily skin barrier function.

The measured *m-TEWL* of intact skin was concentrated around 10 g/m^2/h, with minimal variation. In contrast, the *m-TEWL* of tape-stripped skin was evenly distributed over a wide range. A similar trend was observed for *e-TEWL* estimated from the skin electrical impedance, with the *e-TEWL* of intact skin concentrated around 10 g/m^2/h and that of tape-stripped skin distributed over a wide range. These results suggest that *e-TEWL* reflects changes in measured *m-TEWL* and may effectively capture variations in skin conditions, particularly the barrier function.

Olesen et al. [18] used confocal laser microscopy to confirm that the SC of 10 healthy participants was completely removed after 35 consecutive tape strippings. In their study, complete removal of the SC increased the TEWL by 31.8 g/m²/h, from a baseline of 8.5 g/m²/h. In contrast, our study involved 25 healthy adult participants, and in the pilot dataset, the measured minimum SC thickness after tape stripping was 2.5 µm (the average value before tape stripping was 10.0 µm). At this point, the measured TEWL reached a maximum of 49.2 g/m²/h (the average value before tape stripping was 8.0 g/m²/h), indicating that a substantial reduction in the SC thickness leads to a marked increase in the TEWL, consistent with the result reported by Olesen et al. [18].

Tape stripping is a well-established method for reproducibly reducing the skin barrier function. Atopic dermatitis (AD) is a representative dermatological condition characterized by an impaired barrier function. This dysfunction increases the TEWL and percutaneous allergen penetration, leading to a wide range of clinical manifestations including intense pruritus. Therefore, accurate assessment of the skin barrier function plays a critical role in understanding the pathophysiology of AD and evaluating therapeutic efficacy. The non-invasive assessment method proposed in this study has the potential to quantitatively capture structural and functional alterations in the SC. This approach may serve as a novel diagnostic tool in dermatological research and clinical practice. Given its simplicity and immediacy, the method may also serve as a practical alternative in clinical or high-throughput settings where conventional TEWL measurements may prove challenging to implement. Future studies should aim to validate this method across broader populations, including pediatric and older individuals, as well as at different anatomical sites with varying skin characteristics. Moreover, longitudinal clinical investigations are warranted to establish the clinical utility of this technique in patients with atopic dermatitis and other dermatological conditions.

6 Conclusion

The method proposed in this study estimates the TEWL from the skin electrical impedance, and it was evaluated using both intact skin and tape-stripped skin. A strong correlation was observed in the primary dataset, with the estimation accuracy of *e-TEWL* comparable to that of *e-TEWLm1*. By providing simple and accurate estimations of TEWL, the proposed method based on the skin electrical impedance has the potential to serve as a novel and practical alternative for evaluating the skin barrier function.

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Author Contributions All authors contributed to the conception and design of the study. Material preparation and data collection were performed by Osamu Uehara. Data analysis was performed by Osamu Uehara and Takao Nakamura. The first draft of the manuscript was written by Osamu Uehara, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Declarations

Competing Interests Osamu Uehara is an employee of ALCARE Co., Ltd. The measurement device used in this study was developed by ALCARE Co., Ltd., and the experiments were conducted using the company's research facilities and equipment. Study participants were recruited as volunteers from among employees of ALCARE Co., Ltd. who had no involvement in the study design, data acquisition planning, data analysis, or interpretation of the results. As described in the Acknowledgments section, employees of ALCARE Co., Ltd. provided technical and analytical support for this study; however, they were not involved in the study design, data interpretation, or decision-making regarding the conclusions. Takao Nakamura has received one million yen per year in collaborative research funding from ALCARE Co., Ltd. The authors declare that these relationships did not influence the scientific conduct, analysis, or conclusions of this study.

Ethical Approval The study was approved by the Ethical Review Committee of ALCARE Corporation (DP04-48-20210909) and Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences and Okayama University Hospital (2210-046), and experiments were conducted in accordance with the Declaration of Helsinki.

Consent to Participate All participants provided written consent prior to the experiments.

Consent to Publish The authors affirm that human research participants provided informed consent for publication of the images in Fig. 1(c).

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