Biophysical Measurements and Ultrasonographic Findings in Chronic Dermatitis in Comparison with Uninvolved Skin

Taraneh Yazdanparast¹,², Kamran Yazdani³, Philippe Humbert⁴, Alireza Khatami¹, Saman Ahmad Nasrollahi¹, Leila Izadi Firouzabadi¹, Alireza Firooz¹,⁵

Abstract

Background: Nowadays noninvasive techniques are performed to evaluate the biophysical properties of skin in vivo. Aims: The aim of this study was to evaluate the biophysical and ultrasonographic properties of skin in chronic contact or atopic dermatitis to provide better insight into pathogenesis, diagnosis, and treatment response. Materials and Methods: The stratum corneum hydration, transepidermal water loss (TEWL), pH, erythema, melanin, sebum, friction, temperature, elasticity parameters (R0, R2, and R5), the thickness and echo-density of epidermis, dermis, and subepidermal low-echogenic band (SLEB) were measured on lesional, perilesional, and symmetrical skin of 22 chronic dermatitis patients. The average of perilesional and symmetrical skin values (control) was compared with lesional values. Results: Stratum corneum hydration (P<0.001), friction (P=0.02), sebum (P=0.01), and RO (P<0.001) were significantly lower in lesion, TEWL (P=0.03), pH (P=0.001), erythema (P=0.004), and temperature (P=0.04) were significantly higher in lesion. The thickness of epidermis (P=0.002), dermis (P=0.034), and SLEB (P<0.001) were significantly higher in lesion; and the echo-density of dermis (P<0.001) and SLEB (P<0.001) was significantly lower in lesion. Conclusion: Chronic contact and atopic dermatitis are characterized by certain changes in biophysical and biomechanical properties of the skin. The evaluation of these parameters might be useful in the early diagnosis and assessment of treatment response.

Key Words: Biomechanical properties, biophysical properties, chronic dermatitis, ultrasonography

Introduction

Chronic dermatitis is a common inflammatory skin disease that clinically characterized by itching, scratching, ulceration, and lichenification of skin. Its histopathology includes acanthosis, hyperkeratosis, spongiosis, lymphocytic exocytosis, superficial dermal fibrosis, and perivascular lymphocytic infiltration. This disease is an important cause of morbidity. A recent study in the USA showed the prevalence of eczema in adults was 10.2%. Nowdays, there are various noninvasive techniques for measuring the skin physical properties in vivo and cutaneous biometry has also been used to evaluate physical properties of the skin in systemic diseases such as diabetes, thyroid dysfunction, and Ehlers–Danlos syndrome. In general, the quantification of parameters such as skin surface pH, TEWL, and stratum corneum (SC) hydration is necessary for the complete evaluation of the epidermal barrier status.
The other feature of chronic dermatitis that can be evaluated by skin biometlogy is inflammation. Many studies have been done to measure the erythema and temperature of the skin as the main markers of inflammation. Most of them have compared these parameters before and after the treatment.\(^6,^9\)

Furthermore, it is shown that there is a strong association between pathological and ultrasound findings in atopic dermatitis.\(^10\) Evaluation of biophysical parameters of the skin is also useful for assessment of disease severity\(^11,^12\) and has shown that even seemingly healthy skin shows some biophysical changes\(^13\) and defect of skin barrier function precedes clinical atopic dermatitis.\(^14\)

Most of the previous studies have focused on the abnormalities of TEWL and SC hydration as indicators of barrier function in chronic dermatitis but there are few studies that have assessed other skin biophysical parameters such as pH in dermatitis.

We aimed to evaluate several skin biophysical properties of the skin in patients suffering from chronic contact or atopic dermatitis and make comparison between involved and uninvolved skin to provide more insight into the pathogenesis of dermatitis, earlier and more convenient diagnosis, and response to treatment.

**Materials and Methods**

Any patient suffering from chronic dermatitis (atopic or contact dermatitis) with a minimum age of 18 years referred to our clinic from September 2014 to March 2016 was recruited in the study as a convenient sampling method.

The diagnosis was made by a dermatologist and confirmed with histological findings. The exclusion criteria included any systemic diseases that can affect skin conditions, recent history of any other skin diseases or operations in the previous 3 months, use of any systemic or topical or other interventions for their skin disease in the past 2 weeks, and pregnancy.

This study was approved by our institutional review board and the university ethics committee. Informed consents were provided by all the participants. The data of patients were kept confidential. All the measurements were noninvasive and free of charge.

Baseline characteristics including age, gender, locations of the lesions, Fitzpatrick’s skin type, and duration of lesions were recorded.

The participants were instructed not to use any topical products from the night before the assessment. Before measurement, the participants were asked to rest in supine position for 20 min in the standard atmosphere (20–25° centigrade temperature; 25–30% humidity). Measurements were done on lesional, perilesional uninvolved, and symmetrical uninvolved skin. In general, the active border of a lesion was selected as lesional skin and the normal appearing skin on the same location on the other side of the body (if it was not involved) was selected as symmetrical uninvolved, and the normal appearing skin at least 3 cm away from the border of active disease was selected as perilesional uninvolved skin.

The measurements were done by the Multi Probe Adapter system® (MPA) manufactured by Courage + Khazaka electronic GmbH and included the hydration of the SC (using Corneometer® CM 825), TEWL (using Tewameter® TM 300), pH (using Skin-pH-Meter® PH 905), erythema and melanin index (using Mexameter® MX 18), sebum (using Sebumeter® SM 815), friction value (using Frictiometer FR 700), elasticity parameters including R0, R2, and R5 (using Cutometer® 580), and skin temperature (using Skin-Thermometer ST 500, CK GmbH, Cologne, Germany).

Frictiometer measures the torque as friction index and is related to skin elasticity and plasticity. R0 total deformation of skin (Uf) shows total elastic and plastic deformation and R0 is reciprocal of firmness. R2 shows gross elasticity and R2=Ua/UF, where Ua-viscoelastic/plastic recovery and UF=total deformation of skin. R5 shows net elasticity and R5=Ur/Ue, where Ur=immediate elastic recovery and Ue=immediate extensibility or elastic deformation.\(^15\)

Furthermore high-frequency ultrasonography was done by 22 MHz (for dermis) and 50 MHz (for epidermis) probes of DUB skin scanner (TPM: Taberna Pro Medicum Company, Lüneburg, Germany) to assess the thickness and echo-density of epidermis and dermis, and also subepidermal low-echogenic band (SLEB) on lesional, perilesional uninvolved, and symmetrical uninvolved skin. The SLEB was defined as a clearly visual low-echogenic band in the upper dermis directly underneath the epidermal entrance echo, and SLEB thickness was evaluated in micrometers by measuring the vertical distance between the lower margin of the epidermal entrance echo and the lower margin of the echo-poor band.

The SPSS software version 18 (SPSS Inc., Chicago, IL, USA) was used. Mean and standard deviation (SD) were used for description of quantitative data and comparison of quantitative data between two groups was performed by t-test. The Pearson correlations between hydration and TEWL in lesion, perilesional, and symmetrical skin were determined too. Statistical significance level was P<0.05.

**Results**

Twenty-two patients with chronic contact or atopic dermatitis was included in this study, 12 patients were male and 10 were female. The age of the participants...
was between 19 and 69 years (34.73±12.61). The Fitzpatrick skin types were three in 10 and four in 12 participants. The duration of lesions was from 2 to 204 months (46.05±48.92) and the lesions were located on hands in 15, feet in 6, and face in 1 patients.

Measurements of skin biophysical parameters of three skin areas including lesional, perilesional uninvolved skin, and symmetrical uninvolved skin are described in Figure 1.

There was no statistical significant difference in hydration of the SC (P=0.58), TEWL (P=0.64), pH (P=0.10), erythema (P=0.28), melanin content (P=0.51), sebum (P=0.36), friction value (P=0.53), R0 (P=0.09), R2 (P=0.45), R5 (P=0.31), skin temperature (P=0.04), thickness of epidermis (P=0.719), density of epidermis (P=0.810), thickness of dermis (P=0.422), density of dermis (P=0.884), thickness of SLEB (P=0.252), and density of SLEB (P=0.111) between perilesional uninvolved and symmetrical uninvolved skin using paired t-test. So the average of these parameters was used as control and was compared with lesional skin [Tables 1 and 2].

According to the Table 1, SC hydration (P<0.001), friction index (P=0.02), sebum content (P=0.01), and R0 (P<0.001) were significantly lower in lesional skin, whereas TEWL (P=0.03), pH (P=0.001), erythema (P=0.004), and temperature (P=0.04) were significantly higher in lesional skin compared with control. No significant differences were found in melanin content (P=0.06), R2 (P=0.35), and R5 (P=0.46) between lesional skin and control.

The correlations between hydration and TEWL in lesion, perilesional uninvolved skin, and symmetrical uninvolved skin are shown in Figure 2. The correlations between hydration and TEWL were negative in lesion (r=−0.329, P=0.13), perilesional uninvolved skin (r=−0.367, P=0.09), and symmetrical uninvolved skin (r=−0.187, P=0.43), although these correlations were not statistically significant.

The thickness of epidermis (P=0.002), dermis (P=0.034), and SLEB (P<0.001) lesion were significantly higher; and the echo-density of dermis (P<0.001) and SLEB (P<0.001) in lesional skin were significantly lower than control areas [Table 2]. No significant difference was found in density of epidermis between lesional skin and control (P=0.898).

SLEB was found in all lesions, 76.2% of perilesional uninvolved areas, and 57.9% of symmetrical uninvolved areas. The thickness of SLEB in lesional skin was significantly higher than control (P=0.001), and the density of SLEB in lesional skin was significantly lower than control (P=0.001).

**Discussion**

The results show that skin suffering from chronic contact or atopic dermatitis is characterized by certain changes in biophysical and biomechanical factors. The properties of perilesional and symmetrical uninvolved skin were not so different and the average amount of them, as control, varied from lesional skin.

![Figure 1: Biophysical parameters of lesional (1), perilesional (2), and symmetrical uninvolved (3) skin areas in chronic contact or atopic dermatitis patients, error bars: 95% confidence interval](image-url)
The SC hydration of a lesion was significantly lower than control. This parameter is an indicator of skin barrier function and this finding is compatible with pathophysiology of disease, the clinical feature of xerosis in chronic dermatitis and had been shown in previous studies.\[12,16\]

Knor showed that the SC hydration was significantly higher on uninvolved skin versus perilesional skin of atopic dermatitis,\[17\] but this difference was not statistically significant in our study. It could be due to an at least 3 cm distance between the border of lesion and measured perilesional area in our study, which was not considered in Knor's study.

TEWL was significantly higher in lesional skin similar to the previous studies.\[11\] It was found that water exposure increased the TEWL and negatively affected the skin barrier function.\[18\] The damage to barrier function in chronic dermatitis is so important that nowadays in addition to anti-inflammatory drugs which reduce the disease severity, the treatment includes topical emollients which hydrate and improve barrier function.\[3\]

The previous studies had shown a negative correlation between skin hydration and TEWL.\[19\] Our study confirmed this correlation in all three measured areas too, but the correlations were not significant; may be larger sample size was required.

The plasticity (friction index) of lesional skin was lower than that in control. In normal population, the skin friction coefficient varies with age, gender, and body site, and positively correlates with SC hydration on some body sites.\[20\] Friction index does not change in pigmentary diseases such as melasma\[21\] and its decrease in chronic dermatitis reflects the histologic changes of hyperkeratosis and parakeratosis, and correlates with the SC hydration decrease. Friction assessment is simple and fast method which significantly correlates with elasticity evaluation results.\[15\]

Skin elasticity assessments with Cutometer showed statistically significant increased stiffness of lesion and the results were compatible with friction coefficient value. It is shown that skin elasticity evaluation using the Cutometer is a reliable method for objective and quantitative evaluation of skin in dermatitis.\[22\] Baek's study showed R2 value, which showed gross elasticity, was correlated with skin moisture.\[23\] In our study this parameter was lower in lesion, which also had lower hydration rate than uninvolved skin.

### Table 1: The comparison of biophysical parameters between lesion and control skin in chronic contact or atopic dermatitis patients

| Parameter (unit) | Mean±SD | P (paired t-test) |
|------------------|---------|-----------------|
| Hydration (arbitrary) | 15.55±14.99 | 35.24±17.44 | <0.001 |
| TEWL (g/m²/h) | 21.18±15.42 | 12.92±10.38 | 0.03 |
| Friction (arbitrary) | 85.68±34.82 | 154.51±94.15 | 0.02 |
| pH (arbitrary) | 6.12±0.76 | 5.76±0.82 | 0.001 |
| Sebum (µg/cm²) | 10.20±34.82 | 44.25±57.30 | 0.01 |
| Melanin content (arbitrary) | 209.76±106.02 | 182.50±75.29 | 0.06 |
| Erythema index (arbitrary) | 367.18±86.65 | 309.70±73.78 | <0.05 |
| Temperature (centigrade) | 30.81±2.43 | 30.23±2.25 | 0.04 |
| R0 (arbitrary) | 0.08±0.08 | 0.15±0.1 | <0.001 |
| R2 (arbitrary) | 0.65±0.23 | 0.73±0.12 | 0.35 |
| R5 (arbitrary) | 0.73±0.35 | 0.62±0.23 | 0.46 |

SD: Standard deviation, TEWL: Transepidermal water loss

### Table 2: The comparison of sonographic findings between lesion and control skin in chronic contact or atopic dermatitis patients

| Parameter (unit) | Mean±SD | P (paired t-test) |
|------------------|---------|-----------------|
| Thickness of epidermis (µm) | 153.20±32.56 | 134.60±29.73 | <0.05 |
| Density of epidermis | 68.15±29.05 | 68.90±24.13 | 0.89 |
| Thickness of dermis (µm) | 1785.21±419.85 | 1567.28±317.66 | 0.03 |
| Density of dermis | 12.00±10.41 | 25.50±15.00 | <0.001 |
| Thickness of SLEB (µm) | 347.42±128.49 | 112.08±40.27 | <0.001 |
| Density of SLEB | 3.09±1.72 | 10.94±7.77 | <0.001 |

SD: Standard deviation, SLEB: Subepidermal low echogenic band
Skin pH was significantly higher in lesion. This finding has been previously reported and attributed to several factors such as reduced free amino acids and urocanic acids, deficient filaggrin, and reduced sweat secretions. So Schmid–Wendtner believed that the application of synthetic detergents with a pH of about 5.5 might be a way of prevention and treatment of dermatitis and some other skin diseases.

We found less sebum in lesion than in control. Davoudi et al. showed that sebum of palms of hands was higher and sebum of forehead was lower in mustard-induced dermatitis patients in comparison with control. Xie’s study showed lower SC hydration and sebum level and higher pH and TEWL of the face in chronic dermatitis patients. This correlates with our findings on differences between the lesional skin and control skin of dermatitis patients.

Mexameter is a sensitive and precise equipment for the analysis of skin color and erythema. Both the erythema index and temperature of the lesion were higher than of the control in this study. These findings reflect the inflammatory response and correlates with the increased vascularity in chronic dermatitis. It was shown that erythema of skin suffering from radiodermatitis was significantly higher than its symmetrical area, the skin surface temperature was also higher but the difference was not statistically significant.

Ultrasonographic findings showed that the thickness of epidermis, dermis, and SLEB in lesions were significantly higher and the echo-density of dermis and SLEB were significantly lower than that of control. Increased epidermal thickness due to epidermal hyperproliferation has already been shown histologically in chronic dermatitis and our study showed that high-frequency ultrasonography was also able to detect this finding.

The thickness of dermis was higher and its echo-density was lower than control. This finding can be justified by the existence of SLEB in dermis. SLEB represents infiltration of inflammatory cells and papillary edema.

We found that the thickness of SLEB was higher and the density of SLEB was lower in chronic contact or atopic dermatitis skin compared with control. In Polanska study, SLEB was present in uninvolved skin of 12.7% patients and similar to our study; its average thickness was lower than average thickness of SLEB in lesions. This finding is compatible with the fact that the more inflammation leads to more SLEB thickness and less SLEB density. Holm’s study showed that SLEB of involved skin was wider than uninvolved skin in patients with chronic dermatitis.

SLEB in nonlesional skin of dermatitis patients might reflect the subclinical eczematous reaction and the susceptibility for the development of typical lesions. In our study, SLEB was found in about 3/4 of perilesional areas and about half of symmetrical areas, so it seems that the farther the distance from the lesion, the less likelihood of development of chronic dermatitis.
Uninvolved skin of the patient needs to serve as the control in the evaluation of skin biophysical characteristics,[12] as these parameters change with age, sex, and season.[32,33] The previous studies have compared some skin biophysical properties such as SC hydration, TEWL, sebum, and skin roughness in clinically unaffected skin of patients with atopic dermatitis and skin of healthy persons.[13,34,35] But there are few researches similar to our study which have made this complete comparison between affected and unaffected skin of chronic contact or atopic dermatitis patients and evaluated both perilesional and symmetrical uninvolved skin as unaffected area. Polańska has shown the significant differences in ultrasonographic findings, TEWL, capacitance, and erythema between normal and lesional skin of chronic dermatitis patients.[14] The present study confirmed their findings and in addition showed that lesional skin in chronic contact or atopic dermatitis had significantly lower sebum, plasticity and elasticity, and higher pH and temperature than normal skin of patients, and also SLEB was more common in uninvolved skin around lesion compared with healthy skin, which was a novel finding.

**Conclusion**

Skin biometrology and high-frequency ultrasonography are precise, noninvasive and quantitative measuring tools in dermatology which can be used to give valuable information. Skin suffering from chronic contact or atopic dermatitis is characterized by certain changes in biophysical and biomechanical factors. These findings might help in the development of new drugs, with the aim of correction of altered skin properties. Similar studies for other skin diseases are recommended to find the abnormalities in the lesional skin, which may also help to differentiate chronic inflammatory skin disorders.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

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