Original Research

Biophysical and ultrasonographic changes in lichen planus compared with uninvolved skin[☆],[☆☆]

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A B S T R A C T

Background: Lichen planus (LP) is a chronic inflammatory disease of the skin. Currently, noninvasive techniques are used to evaluate biophysical properties of the skin in vivo.
Objective: In this study, we aimed to evaluate skin biophysical properties in patients with LP and make a comparison between involved and uninvolved skin to provide a better understanding of the pathogenesis of LP.
Methods: The stratum corneum hydration, transepidermal water loss, pH, erythema, melanin, sebum, friction, temperature, elasticity parameters (R0, R2, R5), and thickness and echo-density of the epidermis, dermis, and subepidermal low echogenic band were measured on lesions of classic LP in 21 patients and compared with the average of perilesional and symmetrical uninvolved skin (as control) with a paired t test.
Results: Stratum corneum hydration ($p = .002$), sebum ($p = .04$), R0 ($p = .005$), and echo-density of the dermis ($p = .005$) were significantly lower, but pH ($p = .007$), melanin content ($p < .001$), erythema ($p < .001$), temperature ($p = .01$), thickness of dermis ($p = .02$), and subepidermal low echogenic band ($p < .001$) were significantly higher in LP lesions.
Conclusion: An evaluation of its biophysical, biomechanical, and ultrasonographic characteristics showed that the skin is an objective, noninvasive, and quantitative measuring tool that can be used to provide valuable information about skin changes in classic LP.
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Introduction

Lichen planus (LP) is a chronic inflammatory disease that involves both the skin and mucous membranes (Herrero-González et al., 2016). The reported prevalence of LP in general is up to 5% (Wang and van der Waal, 2015); LP occurrence is mostly in patients age >45 years (Manolache et al., 2008). LP has various clinical manifestations and subtypes with a variable configuration and morphology.

The most common type is classic LP (Ireddy and Udbalkar, 2014). Many variants of LP exist, but classic LP typically presents as pruritic, polygonal, violaceous, flat-topped papules and plaques (Weston and Payette, 2015).

Histologically, LP is characterized by band-like, lymphohistiocytic infiltrate at the dermoepidermal junction with vacuolar degeneration of epidermal basal layer (Lehman et al., 2009). Generally, the epidermal layer acts as a barrier to keep skin homeostasis. Impaired barrier function might result in increased transepidermal water loss (TEWL) and cause skin to lose hydration (Lee and Lee, 2014).

The quantification of biophysical parameters, such as TEWL, stratum corneum (SC) hydration, and skin surface pH, is necessary for the complete evaluation of the epidermal barrier status (Darlenski et al., 2009). Skin erythema and temperature measurement have been used as noninvasive ways to investigate inflammation (Curto et al., 2014;

Kwon et al., 2014). Also, a strong association has been shown between ultrasound and pathological findings in other inflammatory skin diseases, such as atopic dermatitis (Polańska et al., 2013a, b). For LP, ultrasound biomicroscopy has been used previously to investigate ultrasound finding correlations with clinical and pathological findings. The results showed that the dermis appeared as a sound shadow (El-Zawahry et al., 2007).

In this study, we aimed to evaluate several skin biophysical and ultrasonographic properties in patients with LP and compare involved and uninvolved skin to better understand the pathogenesis of LP to help earlier and more convenient diagnoses and follow response to treatment.

Patients and methods

All patients age > 18 years with classic LP who were referred to the Center for Research & Training in Skin Diseases & Leprosy between September 2014 and March 2016 and fulfilled the eligibility criteria were recruited by a convenient sampling method until the sample size was met. The diagnosis was made by a dermatologist on the basis of clinical and histologic findings. The exclusion criteria were recent history of any other skin disease, any kind of surgery in the previous 3 months, use of any systemic or topical treatment or any other intervention for the treatment of LP in the previous 2 weeks, any systemic disease that could affect the skin, and pregnancy.

The study was approved by the Center for Research & Training in Skin Diseases & Leprosy institutional review board and the Tehran University of Medical Sciences ethics committee. Oral informed consent was provided by all participants, and all data were kept confidential. Baseline characteristics of the patients including age, sex, location of the lesions, Fitzpatrick's skin type, and duration of the lesions were recorded.

Participants were instructed not to use topical products on their skin as of the night prior to the biophysical assessments. Before measurements, participants were asked to rest and relax in the supine position for 20 minutes in a standard atmosphere (20°C-25°C; 25%-30% humidity). The measurements occurred in the same room (the room that was used for rest and relaxation) and chair, with the same ambience and room setting, and all measurements were performed between 9:00 a.m. and 12:00 p.m.

Measurements were done on one of the prominent LP lesions and on perilesional and symmetrical uninvolved skin. The selection of these three sites for measurement was done by the same dermatologist (A.F.) who confirmed the diagnosis. Generally, the active border of a lesion was selected as the lesional skin, and the normal-appearing skin in the same location on the other side of the body (if not involved) was selected as symmetric. The normal-appearing skin at least 3 cm away from the active border of the lesion was selected as perilesional uninvolved skin.

The measurements were done with the Multi Probe Adapter system (Courage + Khazaka Electronic GmbH, Cologne, Germany) and included SC hydration (using the Corneometer CM 825), TEWL (using the Tewameter TM 300), pH (using the Skin-pH-Meter PH 905), erythema and melanin indices (using the Mexameter MX 18), sebum (using the Sebumeter SM 815), friction value (using the Frictiometer FR700), elasticity parameters including R0, R2, and R5 (using the Cutometer 580), and skin temperature (using the Skin-Thermometer ST 500).

The Frictiometer measures the torque as friction index and is related to elasticity and plasticity of the skin. R0 (Uf) shows total elastic and plastic deformation of the skin, and the value of R0 is opposed to firmness. R2 shows gross elasticity ($R2 = Ua/Uf$, where $Ua =$ viscoelastic/plastic recovery or final retraction of the skin, and $Uf =$ total deformation of thw skin). R5 shows the net elasticity of the skin ($R5 = Ur/Ue$, where $Ur =$ immediate elastic recovery or immediate retraction, and $Ue =$ immediate extensibility or elastic deformation; Neto et al., 2013).

A high-frequency skin ultrasonography was performed using 22- and 50-MHz probes of DUB skin scanner (tpm Company, Germany) for dermis and epidermis, respectively, to assess the thickness, echo-density, and subepidermal low-echogenic band (SLEB) on the three sites of measurement. The SLEB was defined as a clearly visual low-echogenic band in the upper dermis, directly underneath the epidermal entrance echo. 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.

All statistical analyses were performed using SPSS software, version 18 (SPSS Inc., Chicago, IL). Mean and standard deviation (SD) were used for the description of the quantitative data, and a comparison of the quantitative data between the two groups was performed with a paired sample t test. The statistical significance level was defined as $p < .05$.

Results

Twenty-one patients with classic LP were included in this study, including 8 male and 13 female patients. The age of the participants was between 18 and 74 years (mean: 47.62 years; SD: 15.36). The Fitzpatrick skin types were III in 4 patients and IV in 17 patients. The duration of the lesions was from 0.5 to 240 months (mean: 23.07 months; SD: 56.06), and the lesions were located on the hands in 10 patients, feet in 6 patients, face in 3 patients, and trunk in 2 patients.

There was no statistically significant difference in SC hydration ($p = .97$), TEWL ($p = .07$), pH ($p = .42$), erythema index ($p = .07$), melanin content ($p = .55$), sebum ($p = .16$), friction value ($p = .54$), R0 ($p = .61$), R2 ($p = .80$), R5 ($p = .54$), skin temperature ($p = .14$), thickness of epidermis ($p = .98$), density of epidermis ($p = .82$), thickness of dermis ($p = .37$), density of dermis ($p = .16$), thickness of SLEB ($p = .79$), and density of SLEB ($p = .48$) between perilesional and symmetrical uninvolved skin. The average of these parameters was used as the control and compared with lesional skin (Tables 1 and 2).

According to the Table 1, SC hydration, sebum content, and R0 were significantly lower in LP skin, but pH, melanin content, erythema index, and temperature were significantly higher in LP skin compared with normal skin. No significant differences were found in TEWL, friction index, R2, and R5 between LP and normal skin.

The thickness of the dermis and SLEB in LP skin was significantly higher and the echo-density of the dermis in LP skin was significantly lower than that of normal skin (Table 2). No significant difference was found in the thickness of the epidermis, density of the epidermis, and density of SLEB between LP and normal skin. SLEB was found in 76.2% of LP lesions, 28.6% of perilesional uninvolved areas, and 19% of symmetrical uninvolved areas.

Discussion

This study showed that skin with classic LP is characterized by certain changes in biophysical and biomechanical properties compared with uninvolved normal skin, including lower SC hydration, sebum content, and R0 elasticity and higher pH, melanin content, erythema index, and temperature.

The SC hydration of the LP skin lesion was significantly lower than that of normal skin. SC hydration is an indicator of skin barrier function, and this finding is compatible with the pathophysiology of the disease. The decrease in SC hydration might also be due to defects and/or alterations in SC proteins (Baroni et al., 2012).

Table 1

Comparison of biophysical and biomechanical parameters between lesion and control skin in patients with classic lichen planus

Parameter (unit)	Lesion Mean ± SD	Control (Mean of perilesion and symmetric skin) Mean ± SD	*p*-value (paired *t* test)
Hydration (arbitrary)	39.12 ± 14.12	51.41 ± 16.83	.002
TEWL (g/m²/h)	13.04 ± 13.20	9.67 ± 10.68	.11
Friction (arbitrary)	173.23 ± 197.52	221.29 ± 176.82	.21
pH (arbitrary)	5.81 ± 0.86	5.46 ± 0.83	.007
Sebum (μg/cm²)	4.67 ± 11.61	10.24 ± 16.53	.04
Melanin content (arbitrary)	300.47 ± 101.25	173.58 ± 51.23	< .001
Erythema index (arbitrary)	403.55 ± 83.24	273.04 ± 138.07	< .001
Temperature (centigrade)	31.39 ± 1.32	30.99 ± 1.26	.01
R0 (arbitrary)	0.12 ± 0.08	0.17 ± 0.078	.005
R2 (arbitrary)	0.63 ± 0.17	0.72 ± 0.16	.05
R5 (arbitrary)	0.53 ± 0.22	0.57 ± 0.19	.37

SD, standard deviation; TEWL, transepidermal water loss

There was no significant difference between the plasticity (friction index) of the lesional skin and the control, but a decrease in lesion was not significantly. In a normal population, the skin friction coefficient varies with age, sex, and body site, and positively correlates with SC hydration on some body sites (Zhu et al., 2011). No significant decrease of friction index in LP lesions correlates with a SC hydration decrease. Friction assessment is also a simple and fast method that significantly correlates with elasticity evaluation results (Neto et al., 2013).

We did not find a significant difference in gross elasticity (R2) and net elasticity (R5) of the skin between LP and control skin, but both R2 and R5 decreased in lesions. However, R0 (reciprocal of firmness) was significantly reduced in lesions compared with that of the controls. The cutometer has been shown to be a reliable instrument for the objective and quantitative evaluation of skin elasticity and related parameters (Kawakita et al., 2004).

In a study by Baek et al. (2011), R2 (gross elasticity) was correlated with skin hydration. In our study, this parameter was lower in the lesional area (but not statistically significant), which also had a lower hydration rate than the control areas.

Koseoglu et al. (2016) reported decreased aortic elasticity and increased aortic stiffness in patients with LP. In our study, skin elasticity was decreased, but not significantly, and skin firmness (reciprocal of R0) was significantly increased, which suggests that the mechanisms through which LP affects collagen and elastin and thus elasticity/firmness might be the same in the skin and aortic intima.

Skin pH was significantly higher in LP compared with normal skin. The TEWL and increase in skin dryness has been shown to be accompanied with an increase in pH values (Choi et al., 2003; Firooz et al., 2007; Ring et al., 2000), and LP lesions had more dryness and TEWL as well as a higher pH in this study. Moreover, Darlenski et al. (2011) revealed that a reduced amount of sebum (fatty acids) and hydration (natural moisturizing factor) of the skin leads to an increased pH. A reduction in sebum and stratum corneum hydration of LP lesions was shown in our study, which can justify the increase in lesion pH.

We found less sebum content in LP skin compared with normal skin. In lichen planopilaris (Weston and Payette, 2015) and LP pigmentosus (Romiti et al., 2017), the sebaceous glands have been shown to be damaged, and sebaceous glands may be disturbed in classic LP as well.

The Mexameter is a sensitive and precise instrument to analyze skin color and erythema (Matias et al., 2015). Both the erythema index measured by the Mexameter and the temperature of LP lesions were higher than those of control skin in this study. In other inflammatory skin conditions, these findings are indicators of the inflammatory response and correlate with increased vascularity (Rao et al., 2018). The erythema index of the skin affected by radiodermatitis was shown to increase significantly compared with control areas, and the skin surface temperature was also higher, but the difference was not statistically significant (Fukushi et al., 2014). This increase in erythema and temperature corresponds with the inflammation present in LP lesions.

Melanin content was significantly higher in LP compared with normal skin. Basal layer damage and melanin incontinence are characteristic pathologic features of LP. A study on the automatic detection of erythemato-squamous diseases using adaptive neuro-fuzzy inference systems showed that melanin incontinence was a diagnostic feature for LP (Übeylı and Guler, 2005).

A high-frequency ultrasound is a simple noninvasive method to evaluate skin thickness and echo-density (Firooz et al., 2017). With a high-frequency ultrasonography, normal skin is composed of an epidermal entry echo, dermis, and SC tissue. There are also small hypo-echoic areas that correspond to hair follicles, vessels, and sebaceous glands (Szymańska et al., 2011). In LP lesions, epidermal

Table 2

Comparison of high frequency ultrasonographic findings between lesion and control skin in patients with classic lichen planus

	Lesion Mean ± SD	Control (Mean of perilesion and symmetric skin) Mean ± SD	*p*-value (paired *t* test)
Thickness of Epidermis(μm)	128.00 ± 24.52	120.18 ± 12.93	.18
Density of epidermis	76.39 ± 19.22	85.75 ± 25.54	.07
Thickness of dermis (μm)	1512.55 ± 303.68	1355.70 ± 330.82	.02
Density of dermis	24.71 ± 12.17	33.37 ± 13.58	.005
Thickness of SLEB	346.33 ± 281.55	22.64 ± 38.58	< .001
Density of SLEB	4.30 ± 1.04	5.99 ± 3.16	.17

SD, standard deviation; SLEB, subepidermal low-echogenic band

thickness was higher and epidermal density was lower compared with normal skin (but neither was significant).

On the other hand, dermal thickness was significantly higher and dermal density was significantly lower in LP lesions compared with control skin. This finding can be justified by the existence of SLEB in the dermis. SLEB represents infiltration of inflammatory cells and papillary edema (Polańska et al., 2013a, b). Moreover previous ultrasound studies have revealed a sound shadow in the dermis in LP (El-Zawahry et al., 2007).

Some of the similar symptoms of inflammatory skin diseases result in diagnostic problems (Norman and Blanco, 2003), and invasive histopathology is usually needed to differentiate (Younas and Haque, 2004). Noninvasive monitoring of lesions would benefit patient care by helping with diagnoses. Various simple, noninvasive methods have been employed to make clinical diagnoses with more certainty so far (Calzavara-Pinton et al., 2008). Currently, novel and noninvasive in vivo methods to measure skin biophysical properties can be used to elevate diagnostic accuracy without the requirement for a biopsy (Cal et al., 2010).

A high-frequency ultrasonography can be used as another noninvasive method to evaluate a response to treatment and disease progression in cutaneous lesions (Dasgeb et al., 2013; El-Zawahry et al., 2007; Polańska et al., 2011, 2015) and is an established diagnostic tool in dermatology (El-Zawahry et al., 2007).

Skin biophysical parameters change with age, sex, season, and so on (Firooz et al., 2012; Galzote et al., 2014), and patients' noninvolved skin needs to serve as a control in the evaluation of skin biophysical characteristics (Sugarman et al., 2003). To our knowledge, no previous study has made these complete comparisons of skin biophysical characteristics between affected and nonaffected skin of patients with LP and considered the mean of both perilesional and symmetrical uninvolved skin as a control.

Conclusion

Skin with classic LP is characterized by certain changes in biophysical and biomechanical properties. An evaluation of the biophysical and ultrasonographic characteristics of the skin is an objective, noninvasive, and quantitative measuring tool in dermatology that can be used to provide valuable information about diseases. The findings in our study could help in the development of new treatment strategies, with the purpose of correcting damaged skin's biophysical properties. Similar studies on other inflammatory skin diseases should be conducted to make comparisons, which may help in differential diagnoses of inflammatory skin disorders.

References

Baek J, Lee M, Koh J. Relationship between clinical features of facial dry skin and biophysical parameters in Asians. Int J Cosmet Sci 2011;33(3):222–7.

Baroni A, Buommino E, De Gregorio V, Ruocco E, Ruocco V, Wolf R. Structure and function of the epidermis related to barrier properties. Clin Dermatol 2012;30(3):257–62.

Cal K, Zakowiecki D, Stefanowska J. Advanced tools for in vivo skin analysis. Int J Dermatol 2010;49(5):492–9.

Calzavara-Pinton P, Longo C, Venturini M, Sala R, Pellacani G. Reflectance confocal microscopy for in vivo skin imaging. Photochem Photobiol 2008;84(6):1421–30.

Choi SJ, Song MG, Sung WT, Lee DY, Lee JH, Lee ES, et al. Comparison of transepidermal water loss, capacitance and pH values in the skin between intrinsic and extrinsic atopic dermatitis patients. J Korean Med Sci 2003;18(1):93.

Curto L, Carnero L, López-Aventin D, Traveria G, Roura G, Gimenez-Arnau A. Fast itch relief in an experimental model for methylprednisolone aceponate topical corticosteroid activity, based on allergic contact eczema to nickel sulphate. J Eur Acad Dermatol Venereol 2014;28(10):1356–62.

Darlenski R, Kazandjieva J, Tsankov N. Skin barrier function: morphological basis and regulatory mechanisms. J Clin Med 2011;4(1):36–45.

Darlenski R, Sassning S, Tsankov N, Fluhr J. Non-invasive in vivo methods for investigation of the skin barrier physical properties. Eur J Pharm Biopharm 2009;72(2):295–303.

Dasgeb B, Kainerstorfer J, Mehregan D, Van Vreede A, Gandjbakhche A. An introduction to primary skin imaging. Int J Dermatol 2013;52(11):1319–30.

El-Zawahry MB, Abdel El-Hameed El-Cheweikh HM, Abd-El-Rahman Ramadan S, Ahmed Bassiouny D, Mohamed Fawzy M. Ultrasound biomicroscopy in the diagnosis of skin diseases. Eur J Dermatol 2007;17(6):469–75.

Firooz A, Gorouhi F, Davari P, Atarod M, Hekmat S, Rashighi-Firoozabadi M, et al. Comparison of hydration, sebum and pH values in clinically normal skin of patients with atopic dermatitis and healthy controls. Clin Exp Dermatol 2007;32(3):321–2.

Firooz A, Rajabi-Estarabadi A, Zartab H, Pazhohi N, Fanian F, Janani L. The influence of gender and age on the thickness and echo-density of skin. Skin Res Technol 2017;23:13–20.

Firooz A, Sadr B, Babakoohi S, Sarraf-Yazdy M, Fanian F, Kazerouni-Timsar A, et al. Variation of biophysical parameters of the skin with age, gender, and body region. Sci World J 2012:386936.

Fukushi Y, Kitajima M, Itaki C, Noto Y, Mikami K, Hirota Y, et al. Changes in skin surface temperature and erythema intensity during and after radiotherapy for breast cancer patients. Radiat Emerg Med 2014;3(2):47–51.

Galzote C, Estanislao R, Suero M, Khaiat A, Mangubat M, Moideen R, et al. Characterization of facial skin of various Asian populations through visual and non-invasive instrumental evaluations: Influence of seasons. Skin Res Technol 2014;20(4):453–62.

Herrero-González JE, Parera Amer E, Segura S, Mas Bosch V, Pujol RM, Martínez Escala ME. Epithelial antigenic specificities of circulating autoantibodies in mucosal lichen planus. Int J Dermatol 2016;55(6):634–9.

Ireddy SG, Udbalkar SG. Study of lichen planus and its different types and associated conditions. BMR Med 2014;1(1):1–11.

Kawakita T, Takano Y, Asano-Kato N, Tanaka M, Dogru M, Goto E, et al. Quantitative evaluation of eyelid elasticity using the cutometer SEM575 and its clinical application in assessing the efficacy of tacrolimus ointment treatment in eyelid atopic dermatitis. Cornea 2004;23(5):468–71.

Koseoglu C, Erdogan M, Ertem A, Koseoglu G, Akoglu G, Aktas A, et al. Aortic elastic properties and myocardial performance index are impaired in patients with lichen planus. Med Princ Pract 2016;25(3):247–53.

Kwon S, Jeong M, Park K, Youn S, Huh C, Na J. A new therapeutic option for facial seborrhoeic dermatitis: Indole-3-acetic acid photodynamic therapy. J Eur Acad Dermatol Venereol 2014;28(1):94–9.

Lee HJ, Lee SH. Epidermal permeability barrier defects and barrier repair therapy in atopic dermatitis. Allergy Asthma Immunol Res 2014;6(4):276–87.

Lehman JS, Tollefson MM, Gibson LE. Lichen planus. Int J Dermatol 2009;48(7):682–94.

Manolache L, Seceleanu-Petrescu D, Benea V. Lichen planus patients and stressful events. J Eur Acad Dermatol Venereol 2008;22(4):437.

Matias AR, Ferreira M, Costa P, Neto P. Skin colour, skin redness and melanin biometric measurements: Comparison study between Antera® 3D, Mexameter® and Colorimeter®. Skin Res Technol 2015;21(3):346–62.

Neto P, Ferreira M, Bahia F, Costa P. Improvement of the methods for skin mechanical properties evaluation through correlation between different techniques and factor analysis. Skin Res Technol 2013;19(4):405–16.

Norman R, Blanco P. Papulosquamous diseases in the elderly. Dermatol Ther 2003;16(3):231.

Polańska A, Dańczak-Pazdrowska A, Silny W, Sadowska A, Jenerowicz D, Osmola-Mankowska A, et al. High-frequency ultrasonography in monitoring the effects of treatment of selected dermatoses. Postepy Dermatol Alergol 2011;28:255–60.

Polańska A, Dańczak-Pazdrowska A, Silny W, Jenerowicz D, Olek-Hrab K, Osmola-Mańkowska A. Nonlesional skin in atopic dermatitis is seemingly healthy skin-observations using noninvasive methods. Wideochir Inne Tech Maloinwazyjne 2013a;8(3):192.

Polańska A, Dańczak-Pazdrowska A, Silny W, Wozniak A, Maksin K, Jenerowicz D, et al. Comparison between high-frequency ultrasonography (Dermascan C, version 3) and histopathology in atopic dermatitis. Skin Res Technol 2013b;19(4):432–7.

Polańska A, Silny W, Jenerowicz D, Knioła K, Molińska-Glura M, Dańczak-Pazdrowska A. Monitoring of therapy in atopic dermatitis-observations with the use of high-frequency ultrasonography. Skin Res Technol 2015;21(1):35–40.

Rao A, Khandpur S, Kalaivani M. A study of the histopathology of palmo-plantar psoriasis and hyperkeratotic palmo-plantar dermatitis. Indian J Dermatol Venereol Leprol 2018;84(1):27.

Ring J, Eberlein-König B, Schäfer T, Huss-Marp J, Darsow U, Möhrenschlager M, et al. Skin surface pH, stratum corneum hydration, trans-epidermal water loss and skin roughness related to atopic eczema and skin dryness in a population of primary school children: Clinical report. Acta Derm Venereol 2000;80:188–91.

Romiti R, Biancardi Gavioli CF, Anzai A, Munck A, Costa Fechine CO, Valente NYS. Clinical and histopathological findings of frontal fibrosing alopecia-associated lichen planus pigmentosus. Skin Appendage Disord 2017;3(2):59–63.

Sugarman J, Fluhr J, Fowler A, Bruckner T, Diepgen T, Williams M. The objective severity assessment of atopic dermatitis score: an objective measure using permeability barrier function and stratum corneum hydration with computer-assisted estimates for extent of disease. Arch Dermatol 2003;139(11):1417–22.

Szymańska E, Maj M, Majsterek M, Litniewski J, Nowicki A, Rudnicka L. The usefulness of high frequency ultrasonography in dermatological practice–

ultrasound features of selected cutaneous lesions. Pol Merkur Lekarski 2011; 31:37–40.

Übeylı ED, Guler I. Automatic detection of erythemato-squamous diseases using adaptive neuro-fuzzy inference systems. Comput Biol Med 2005;35(5): 421–33.

Wang J, van der Waal I. Disease scoring systems for oral lichen planus; a critical appraisal. Med Oral Patol Oral Cir Bucal 2015;20(2):e199–204.

Weston G, Payette M. Update on lichen planus and its clinical variants. Int J Womens Dermatol 2015;1(3):140–9.

Younas M, Haque A. Spectrum of histopathological features in non-infectious erythematous and papulosquamous diseases. Int J Pathol 2004;2(1):24–30.

Zhu Y, Song S, Luo W, Elias P, Man M. Characterization of skin friction coefficient, and relationship to stratum corneum hydration in a normal Chinese population. Skin Pharmacol Physiol 2011;24(2):81–6.