Original paper

High-frequency ultrasonography in monitoring the effects of treatment of selected dermatoses

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Post Dermatol Alergol 2011; XXVIII, 4: 255–260

Abstract

Introduction: High-frequency ultrasound provides a modern, non-invasive method of skin visualization used for many years in dermatology. In this paper, we present the use of high-frequency ultrasound in monitoring the effects of treatment of selected dermatoses and a review of the literature on this topic.

Material and methods: Ultrasound examination of the skin using a 20 MHz linear probe (Dermascan C, Cortex) was performed twice: before the introduction of a specific treatment and after therapy in patients treated at the Department of Dermatology, Poznan University of Medical Sciences, with a diagnosis of atopic dermatitis, T-cell cutaneous lymphoma, eosinophilic fasciitis, limited cutaneous scleroderma (morphea), plaque psoriasis and chronic cutaneous graft versus host disease.

Results: In each of the patients presented in this study ultrasound skin imaging made it possible to visualize the clinical improvement by analyzing the degree of echogenicity, the thickness of the dermis, hypoechoic band and the entrance echo.

Conclusions: We demonstrated the usefulness of 20 MHz ultrasound in monitoring the treatment of different dermatoses.

Key words: high-frequency ultrasound, skin USG, atopic dermatitis, psoriasis, skin lymphoma, morphea, fasciitis eosinophilica, cutaneous graft versus host disease (cGvHD).

Introduction

Ultrasonography has been a well-recognized method of organ and tissues imaging in medicine for about 60 years. Numerous applications (fetal imaging, evaluation of lymph nodes, examination of abdominal organs, and others) are associated with its non-invasiveness and reproducibility as well as relatively low cost. In routine gynaecological and internal practice frequencies from 3.5 MHz to about 7.5 MHz with a resolution of 2-3 mm are used. Imaging of the skin requires the use of substantially higher frequencies between 15 MHz and 20 MHz, providing a resolution of 60-120 µm. The term high-frequency ultrasound (HF USG) was introduced for ultrasound using frequencies above 15 MHz [1-3]. Currently, it is possible to achieve even higher resolution images using modern probes of a frequency of 50 MHz or even 100 MHz.

The first attempt to use ultrasonic beams for experimental dermatology was conducted in 1979 by Alexander and Miller. Using the presentation of type A (from amplitude) the researchers performed measurement of skin thickness [4]. There has been intensive development of imaging techniques in subsequent years. A special contribution to the improvement of this method of visualization was made by researchers from Germany, Denmark and Japan [5]. The result of ultrasound examination of the skin may be presented in the form of presentation A (A-scan, measurement at one point), type B (B-scan, two-dimensional, 2D) and type C (2D image at a certain depth parallel to the skin surface). Modern ultrasound devices are also capable of 3-dimensional image reconstruction (3D) [3, 5, 6].

High-frequency ultrasonography is a method of imaging with multiple indications in clinical and experimental dermatology. Table I shows the possible use of 20 MHz

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Table 1. Possible applications of HF-USG in dermatology

Preoperative assessment of skin tumours' size
Evaluation and monitoring of treatment of scleroderma-like diseases, e.g. morphea, eosinophilic fasciitis, cutaneous graft versus host disease
Evaluation and monitoring of treatment of inflammatory skin diseases, e.g. psoriasis, atopic dermatitis, eczema
Assessment of skin photoaging
Evaluation of wound healing
Assessment of the adverse effects of topical drug therapy, e.g. posteroid skin atrophy
Assessment of the effects of cosmetics, e.g. anti-cellulite

ultrasound in dermatology. In this paper, we present the use of high-frequency ultrasound in monitoring the effects of treatment of selected dermatoses and a review of the literature on this topic.

Material and methods

The paper presents the sonograms of 5 patients treated at the Department of Dermatology, Poznan University of Medical Sciences due to atopic dermatitis (AD), cutaneous T-cell lymphoma, eosinophilic fasciitis, limited cutaneous scleroderma (morphea), plaque psoriasis and chronic cutaneous graft versus host disease (sclerodermoid, cutaneous graft versus host disease – cGvHD). The diagnosis of each dermatoses was established according to accepted standards. Therapy for each patient was applied depending on the diagnosis and clinical status. Characteristics of each patient are presented in Table 2.

Skin ultrasonography was performed using a probe with a frequency of 20 MHz, Dermascan C, Cortex Technology (Hadsund, Denmark), twice, before and after treatment. Ultrasound beam penetration into the tissue is approximately 10 mm, with axial resolution of 80 µm, and lateral resolution of 200 µm. Ultrasound examination in the form of presentation B was performed in a selected, representative region (twice in the same location – before and after treatment). The results are presented in the form of ultrasound images.

Dermascan C in creating the image uses an arbitrary adopted scale of intensity of the reflected wave from 0 to 255 pixels and it is considered that the intensity of < 30 indicates low echogenicity. Echogenicity reflects the average intensity of the reflected wave for each pixel in the field under examination.

Results

In the sonogram of the AD patient before UVA1 phototherapy the presence of a wide hypoechoic band just below the echo entry and decrease of total skin echogenicity were revealed (Fig. 1 A). After completion of planned therapy, ultrasound examination showed the reduction of hypoechoic band thickness and an increase of skin echogenicity (Fig. 1 B).

The ultrasound examination of T-cell lymphoma (Figs. 2 A, B) before turning the planned therapy revealed the presence of a hypoechoic band in the upper part of the dermis and its disappearance was observed in the sonogram made on the last day of therapy.

Similar observations were made in relation to sonograms of a patient with plaque psoriasis. In ultrasound pictures taken before treatment (Fig. 3 A) a highly echogenic, thickened entrance echo as well as streak, perpendicular to the entry echo shadowing, were visualised. The presence of a hypoechoic band in the upper part of the dermis, as in the case of AD, was also revealed. However, in the sonogram made on the last day of treatment (Fig. 3 B) the entry echo has been smoothed, the streak shading disappeared, the entire skin thickness was thinner, and, as in the case of the AD patient, the skin echogenicity increased.

In the sonogram of patients suffering from sclerodermic diseases (fasciitis eosinophilica, morphea, cGvHD) as a result of a UVA1 irradiation cycle, the reduction of both analysed parameters (skin thickness and echogenicity) was observed in comparison to the analysis before treatment (Figs. 4 A, B, 5 A, B, 6 A, B).

Table 2. Patients characteristics

Diagnosis	Sex	Age [years]	Therapy
AD	M	16	Mild/moderate topical glucocorticosteroids/antihistamines
Cutaneous T-cell lymphoma	M	52	UVA1 phototherapy
Fascitis eosinophilica	F	54	UVA1 phototherapy
Morphea	F	27	UVA1 phototherapy
Plaque psoriasis	M	32	Etanercept (16 weeks)
cGvHD	F	40	UVA1 phototherapy

M – male, F – female

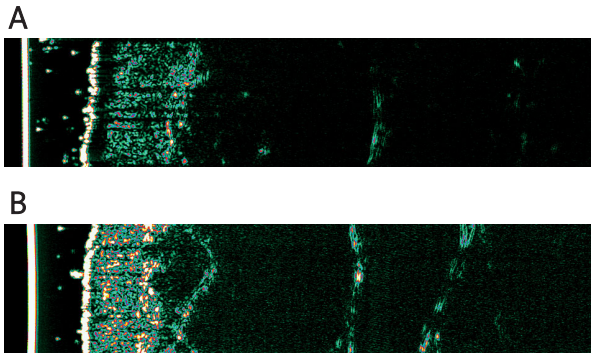

Fig. 1. Sonogram of AD: **A** – before treatment, **B** – after treatment

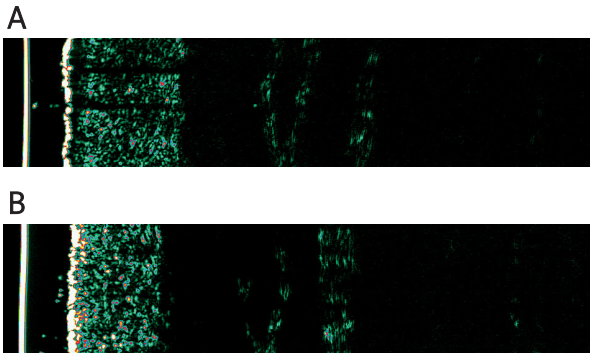

Fig. 2. Sonogram of T-cell lymphoma: **A** – before treatment, **B** – after treatment

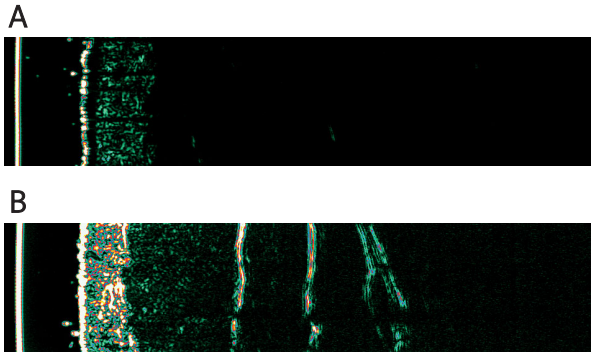

Fig. 3. Sonogram of plaque psoriasis: **A** – before treatment, **B** – after treatment

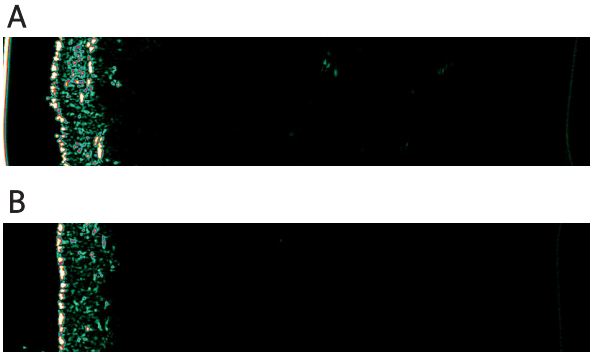

Fig. 4. Sonogram of fasciitis eosinophilica: **A** – before treatment, **B** – after treatment

Fig. 5. Sonogram of morphea: **A** – before treatment, **B** – after treatment

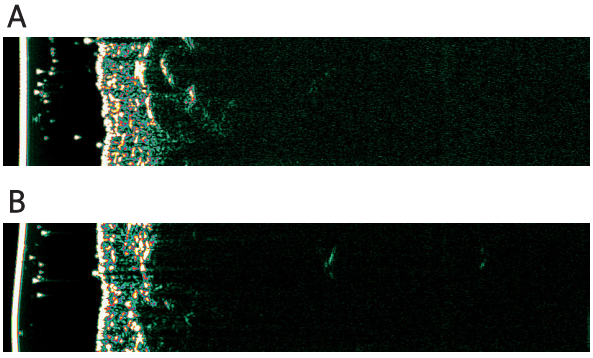

Fig. 6. Sonogram of cGvHD: **A** – before treatment, **B** – after treatment

Discussion

Healthy skin sonogram consists of three layers (Fig. 7):

- entrance echo – a strongly echogenic band,
- the dermis – a layer rich in echoes of the scattered reflections,
- subcutaneous tissue – a layer of low echogenicity with well-reflecting wave compartments.

According to Gniadecka *et al.*, thickness of the entry echo does not correspond to the thickness of the epidermis [5]. Using a 20 MHz probe it is not possible to illustrate the various layers of the epidermis, or dermal-epidermal junction, due to insufficient resolution. In accordance with the observation of researchers, the entry echo is formed as the sum of echoes from the stratum corneum, the rest of the epidermis and dermal-epidermal junction [6]. The epidermis (mainly low in the water stratum corneum layer) can only be visualized in diseases presenting with thickening of the stratum corneum, such as

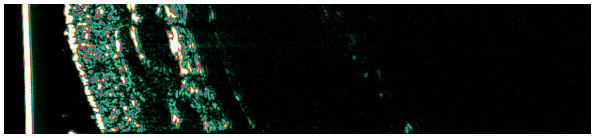

Fig. 7. Sonogram of healthy skin

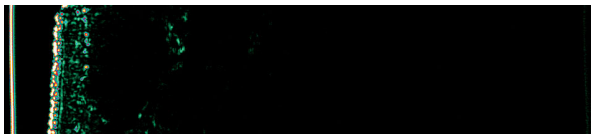

Fig. 8. Sonogram of the palm

psoriasis, as well as within such anatomical locations as the palms and soles [5, 7, 8]. Then in the ultrasound image a strong echogenic band corresponding to the transition between the weakly hydrated stratum corneum and layers of living epidermis rich in water can be observed (Fig. 8). Available literature reports suggest that the visualization of epidermis that is low-reflectant in its internal structure is possible using transducers with much higher frequencies, 100 MHz [5].

The dermis is less echogenic than the entrance echo and consists of multiple echoes of varying intensity [5]. It is believed that the overall echogenicity of this layer is formed as a result of the reflection of the ultrasound wave between collagen fibres, intercellular matrix and cells. As for collagen, the ultrasound image is associated not only with its quantity but also type, orientation and size of its beams [2]. Hence, the upper layers of the skin corresponding to the ultrasound image of papillary dermis usually have lower echogenicity than its deeper layers, the reticular dermis. Therefore, in diseases presenting with excessive accumulation of collagen fibre (for example, in morphea, eosinophilic fasciitis, cGvHD) there is an increase of total skin echogenicity (Figs. 4 A, 5 A, 6 A). As a result of treatment, as in the case of patients presented herein treated with UVA1 (morphea, eosinophilica fasciitis), we observed reduction of skin thickness and decrease of its echogenicity (Figs. 4 B, 5 B, 6 B). It should be noted that the ultrasound image significantly depends on the phase of such disorders. During the inflammatory phase a decrease of echogenicity is observed, while in the sclerotic phase an increase is observed [9, 10].

An interesting observation is sonograms of keloids and hypertrophic scars, although they are composed of fibrous tissue, appear as homogeneous low-reflectant structures. This phenomenon is due to the degree of compaction of the collagen fibres. In keloids we observe tight alignment of collagen fibres, whereas in the scleroderma, because of the presence of larger amounts of intercellular substance, it is looser [5].

Lower skin echogenicity (in comparison to healthy skin) can be observed in the case of oedema, which is probably associated with distension of the fibre network due to the presence of water [5, 8]. Depending on the cause of oedema, areas of reduced echogenicity may be visualized in the upper or lower layers of the dermis. In the case of lipodermatosclerosis hypoechoic areas are primarily localized in the upper dermis, just below the entry echo, while in cardiac insufficiency they occur mainly in the lower portions of the skin [5, 11]. Another cause of reduced echogenicity particularly in the upper layers of the dermis may be, beyond the oedema, infiltration of inflammatory cells [5]. This regularity can be observed in acute and chronic eczema, as well as in the case of AD. There are reports on the use of high-frequency USG in the objective assessment of patch test results [12].

Another sonographic characteristic of inflammatory diseases such as AD is the presence of an echo-poor area underneath the entry echo (called the echolucent area or subepidermal low-echogenic band (SLEB)), which expresses the inflammation process in the epidermis and upper dermis [13]. The SLEB may serve as a parameter showing the resolution of inflammation and at the same time demonstrating the accuracy of the administered therapy. Another interesting observation in our opinion is the possibility of visualization of an echolucent area also within clinically healthy skin in some patients with AD, which may suggest the existence of subclinical inflammation [14-16]. In the case of AD patient presented in this paper treated with narrowband UVA skin sonograms revealed an increase in echogenicity and reduction of the SLEB thickness after completion of therapy. These results are compatible with our previous observations [17, 18]. German researchers conducted a sonographic examination of 20 patients with AD, treated with UVA/UVB therapy and topical steroids, and found that the SLEB disappears completely when the clinical resolution of skin lesions is observed [19].

De Rigal *et al.* first reported the presence of SLEB also in photodamaged skin [20]. It was observed that its thickness correlates with the severity of skin lesions and can be used to assess the effects of treatment with anti-aging formulas. The presence of an echopoor area in photoaging is associated with alterations in skin fibre structure and accumulation of water-binding glycosaminoglycans [21].

As for psoriasis, its sonographic picture is similar to other inflammatory skin diseases. Hyperkeratotic plaque psoriasis has a thickened entrance echo and also it is possible to visualize streak shading, perpendicular to the entry echo, probably corresponding to bubbles trapped between the scales. It is also possible to observe the presence of SLEB as a parameter indicating the active phase of the disease and on the basis of its changes to evaluate the effectiveness of treatment [8, 13].

In dermatology different scoring systems for evaluation of the effects of various therapies are used, for example PASI (Psoriasis Area Severity Index), whose final value is largely dependent on the subjective assessment of the investigator. More objective evaluation is possible with

20 MHz ultrasound, in which the images entirely correspond to the clinical data. Regarding a patient treated with biologicals, we observed the reduction of SLEB, which was correlated with the improvement in clinical status (Fig. 3 B). In the opinion of other authors, after the removal of scales within psoriatic lesions the reduction of entry echo thickness of 24% and increase of skin echogenicity may be observed [7].

In the ultrasound image of T-cell lymphoma, due to massive lymphocyte infiltration, the dominant feature is the presence of a thick echolucent area under echo entry. Its reduction or disappearance, as in the case of inflammatory diseases, shows the effectiveness of the therapy.

Thus, on the basis of the cases presented in this paper and literature data, high-frequency ultrasound can be considered as a non-invasive method useful in objective evaluation of the course and effectiveness of therapy.

Subcutaneous tissue is a structure of low echogenicity; hence the boundary between it and the dermis can be easily differentiated. Sometimes strands of connective tissue may be visualized as well as in some anatomical locations, such as within the wrist, it is easy to observe the fascia. The average depth of penetration of ultrasound beams for the 20 MHz transducer is approximately 10-12 mm; therefore due to limitations to assessment of the subcutaneous tissue, 7.5-10 MHz transducers seem to be more useful [13].

In conclusion, the usefulness of 20 MHz ultrasound in monitoring the effectiveness of treatment of skin disorders with different aetiologies should be strongly emphasized [15, 16, 20-26]. A particular advantage of this method is its non-invasiveness and the possibility of repeating the skin examination at every stage of therapy. 20 MHz ultrasound of the skin, although it is a method significantly improving dermatological diagnostics, due to the low resolution of obtained images, does not allow for full differentiation of the image to an extent which allows microscopy. Sonography of the skin does not diagnose skin diseases; based on the skin sonograms one cannot make a diagnosis. However, it is an *in vivo* tool which can be performed quickly and automatically, at any stage of treatment, without any special preparation of the patient. Free of contraindications and side effects, ultrasound is particularly relevant in paediatric dermatology. Moreover, it appears that this method will become particularly important in clinical trials of newly introduced drugs. Applications of ultrasound in clinical as well as experimental dermatology are constantly expanding, and certainly this method will complement the modern diagnosis of skin lesions.

References

1. Schmid-Wendtner MH, Dill-Müller D. Ultrasound technology in dermatology. Semin Cutan Med Surg 2008; 27: 44-51.
2. Rallan D, Harland CC. Ultrasound in dermatology – basic principles and applications. Clin Exp Dermatol 2003; 28: 632-8.
3. Jasaitiene D, Valiukeviciene S, Linkeviciute G, et al. Principles of high-frequency ultrasonography for investigation of skin pathology. J Eur Acad Dermatol Venereol 2011; 25: 375-82.
4. Alexander H, Miller DL. Determining skin thickness with pulsed ultrasound. J Invest Dermatol 1979; 72: 17-9.
5. Jemec GB, Gniadecka M, Ulrich J. Ultrasound in dermatology. Part I. High frequency ultrasound. Eur J Dermatol 2000; 10: 492-7.
6. Zmudzinska M, Czarnecka-Operacz M, Silny W. Principles of dermatologic ultrasound diagnostics. Acta Dermatovenerol Croat 2008; 16: 126-9.
7. Hoffmann K, Dirschka T, Schwarze H, et al. 20 MHz sonography, colorimetry and image analysisi in the evaluation of psoriasis vulgaris. J Dermatol 1995; 9: 103-10.
8. Szymanska E, Nowicki A, Mlosek K, et al. Skin imaging with high frequency ultrasound – preliminary results. Eur J Ultrasound 2000; 12: 9-16.
9. Dill-Müller D, Maschke J. Ultrasonography in dermatology. J Dtsch Dermatol Ges 2007; 5: 689-707.
10. Serup J. Localized scleroderma (morphea): thickness of sclerotic plaques as measured by 15-MHZ pulsed ultrasound. Acta Dermatol Venereol (Stockh) 1984; 64: 214-9.
11. Silny W, Osmola-Mańkowska A, Czarnecka-Operacz M, et al. Wąskozakresowa fototerapia UVA-1 w lecznictwie dermatologicznym – pierwsze polskie doświadczenia. Post Dermatol Alergol 2010; 27: 1-10.
12. Gniadecka M. Dermal oedema in lipodermatosclerosis: distribution, effects of posture and compressive therapy evaluated by high-frequency ultrasonography. Acta Derm Venereol 1995; 75: 2: 120-4.
13. Pierzchała E, Lis A, Syguła E, et al. Alergia kontaktowa u personelu medycznego i pomocniczego Kliniki Dermatologii Śląskiej Akademii Medycznej, Katowice. Post Derm Alerg 2004; 21: 9-13.
14. Fornage BD. High-frequency sonography of the skin. Eur J Ultrasound 1995; 2: 173-82.
15. Dańczak-Pazdrowska A, Polańska A, Silny W, et al. Seemingly healthy skin in atopic dermatitis: observations with the use of high-frequency ultrasonography, preliminary study. Skin Res Technol 2011 May 2 [Epub ahead of print].
16. Silny W, Czarnecka-Operacz M, Gliński W, et al. Atopowe zapalenie skóry – współczesne poglądy na patomechanizm oraz metody postępowania diagnostyczno-leczniczego. Stanowisko grupy specjalistów Polskiego Towarzystwa Dermatologicznego. Post Dermatol Alergol 2010; 27: 365-83.
17. Silny W, Dańczak-Pazdrowska A, Osmola-Mańkowska A, et al. High-frequency ultrasonography as a useful device to objective assessment of UVA1 treatment-preliminary study. P208, EADV Gothenburg 2010.
18. Polańska A, Sadowska A, Osmola-Mańkowska A, et al. Ultrasonograficzna ocena atopowego zapalenia skóry. Forum Młodych 2011.
19. Hoffmann K, Dirschka T, Schwarze H. Non-invasive evaluation of inflammation in atopic dermatitis. J Eur Acad Dermatol Venereol 1994; 3: 347-53.
20. De Rigal J, Escoffier C, Querleux B, et al. Assessment of aging of the human skin in vivo by ultrasonic imaging. J Invest Dermatol 1989; 93: 621-5.
21. Gniadecka M, Jemec GBE. Quantitative evaluation of chronological aging and photoaging in vivo: studies on skin echogenicity and thickness. Br J Dermatol 1989; 139: 815-21.
22. Olek-Hrab K, Osmola-Mańkowska A, Silny W, et al. Use of UVA1 in the treatment of mycosis fungoides – case report. Post Dermatol Alergol 2011; 28: 158-64.

23. Unholzer A, Korting HC. High-frequency ultrasound in the evaluation of pharmacological effects on the skin. Skin Pharmacol Appl Skin Physiol 2002; 15: 71-84.
24. Holm EA, Wulf HC, Thomassen L, Jemec GB. Instrumental assessment of atopic eczema: validation of transepidermal water loss, stratum corneum hydration, erythema, scaling, and edema. J Am Acad Dermatol 2006; 55: 772-80.
25. Sadowska A, Polańska A, Dańczak-Pazdrowska A, et al. The assessment of biologic therapy in psoriasis with the use of high-frequency ultrasonography. Karlowe Wary, EADV Spring Symposjum 2011.
26. Silny W, Osmola-Mankowska A, Czarnecka-Operacz M, et al. Eosinophilic fascitis: a report of two cases treated with ultraviolet A1 phototherapy. Photodermatol Photoimmunol Photomed 2009; 25: 325-7.