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## High-frequency ultrasound in the 21<sup>st</sup> century

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### Abstract

The beginnings of skin ultrasound date back to about 50 years ago. However, the dynamic progress of skin ultrasound took place in the last twenty years, when the unprecedented development of computer technologies occurred, which resulted in the popularization of and easier access to modern ultrasound equipment. Skin tests can be performed with both classic scanners equipped with broadband transducers with a minimum frequency of 15 MHz, and specially dedicated skin systems with high-frequency scanners, which are equipped with mechanical transducers with a frequency of 20 MHz to up to 100 MHz. Owing to technologically advanced machines, ultrasonography has proved to be useful in many areas. The aim of this study was to present the current knowledge and possibilities of skin imaging using high-frequency ultrasonography. The paper discusses technical aspects, types of devices available on the market, as well as methods for the analysis of ultrasound skin images and parameters useful in their interpretation. We also present current applications of skin ultrasound, with particular emphasis on dermatology and aesthetic medicine. In the field of dermatology, we discussed imaging of focal lesions as well as an assessment of pathologically changed skin and treatment monitoring. We also focused on the use of high-frequency ultrasonography in aesthetic medicine and cosmetology. The popularity of this method is constantly growing in these fields, and ultrasound is now used in everyday practice to assess the skin, plan and monitor procedures, as well as to treat potential complications. High-frequency ultrasonography is a highly effective method for skin evaluation, although still underappreciated in many fields. Further research is needed to standardize this modality, as well as to implement training for operators, and to popularize this imaging technique.

## Introduction

The skin, which is the largest human organ, has aroused interest for centuries. Thus, skin lesions, which can be easily seen with the naked eye, have been the subject of investigations since ancient times. Despite the great interest in the appearance of both healthy and diseased skin, there had been no separate field devoted to this human body layer for many centuries. It was not until the 18<sup>th</sup> and 19<sup>th</sup> centuries, when modern dermatology developed with the emergence of pathological anatomy

and the use of a microscope to investigate body tissues. Along with the development of this field, dermatological diagnostic possibilities have also expanded. Currently, dermatology and the related fields use advanced methods of skin diagnosis, with skin ultrasound playing an important role<sup>(1)</sup>.

The beginnings of skin ultrasound may be sought in the 1970s. A paper on ultrasound measurement of skin thickness using a 15 MHz mechanical ultrasound transducer published by Alexander and Miller in 1979 was the first

scientific report in this field<sup>(2)</sup>. This paper became an impulse for other researchers to develop this method and construct scanners specialized in skin imaging. It should be noted, however, that the dynamic development of skin ultrasound took place at the turn of the 20<sup>th</sup> and 21<sup>st</sup> centuries, which was significantly influenced by the progress in the field of new computer technologies. This resulted in a dramatic increase in scientific publications on this subject. Ultrasonography is eagerly employed for skin examination as compared to other diagnostic methods as it is easier to use, cheaper, and most of all reliable and safe for the patient<sup>(3)</sup>. Ultrasonography of the skin is currently used in dermatology<sup>(3,4)</sup> and in related fields, such as aesthetic medicine and cosmetology<sup>(4,5)</sup>. It has also found its place in phlebology and even in gynecology<sup>(6,7)</sup>. The aim of this study was to comprehensively present issues related to skin ultrasonography, to discuss its current applications and to evaluate its usefulness.

## The frequency and scanners used

Considering the essence of ultrasound imaging, transducers with a higher frequency rather than those used for classic ultrasound examinations (e.g. abdominal cavity) should be used for skin imaging. The use of a higher frequency allows for higher image resolution and assessment of fine skin structures, however, at the expense of the depth of ultrasound penetration. The use of 10 MHz, 20 MHz, and 50 MHz transducers will allow for tissue penetration of about 35 mm, 10 mm and only 3–4 mm, respectively<sup>(8,9)</sup>. Details are summarized in Table 1. Frequencies ranging from about 15 MHz to 100 MHz are usually used for skin imaging; however, most skin ultrasound examinations are performed at about 20 MHz<sup>(10)</sup>. Nevertheless, it should be noted that the choice of frequency for a given examination depends on its purpose. A 75–100 MHz transducer will be the best option for the monitoring of epidermal lesions, whereas a 20–30 MHz transducer is a better option if the imaging also involves the dermis and the subcutaneous tissue. According to the latest guidelines of the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB), the minimum frequency for skin imaging should be 15 MHz, which is high-frequency imaging. Transducers with a frequency >20 MHz are referred to as high-frequency transducers. Transducers with a frequency of 30–70 MHz are classified as ultra-high-frequency transducers, which allow for the assessment of small adnexal structures,

such as sebaceous glands, as well as apocrine and eccrine glands<sup>(10)</sup>.

For skin imaging, not only the frequency, but also the type of ultrasound scanner should be appropriately chosen. Classic scanners equipped with broadband linear transducers with a frequency from about 10 MHz to more than 20 MHz, as well as specialized ultrasound scanners for skin examinations may be used. As opposed to classic scanners, ultrasound machines for skin imaging use single element mechanical transducers with a constant frequency >20 MHz, i.e. high-frequency transducers. Currently, there are several manufacturers of this type of scanners. DermaScan C (Cortex Technology, Hadsund, Denmark) and DUB-USB (Taberna Pro Medicum, Lüneburg, Germany) are the best known ultrasound scanners. Researchers also use Episcan I-200 (Longport, Inc., Silchester, Great Britain) in their studies. Also, a Polish high-frequency ultrasound scanner DermaMed (Dramiński S.A., Olsztyn, Poland) has been manufactured for several years now. The characteristics of high-frequency transducers available on the market is summarized in Tab. 2<sup>(9)</sup>.

There is no consensus among researchers on which type of ultrasound scanner is a better option for skin imaging. The use of classic scanners is supported by the fact that they have a varying frequency and thus allow for imaging at different depths<sup>(11)</sup>. Color and Power Doppler options are also their great advantage. Furthermore, increasingly effective broadband transducers, e.g. for microflow assessment, which, supported by highly technologically advanced options to improve imaging (such as harmonic imaging, cross-beam imaging and speckle noise suppression), allow for obtaining high-resolution skin images, have appeared on the market. High-frequency scanners, on the other hand, are best suited for epidermal and dermal imaging<sup>(3,9)</sup> (Fig. 1). Mobility and small size, allowing for transportation and use in many settings, are advantages of this type of devices. Therefore, it is important to choose the type of scanner primarily based on the purpose of the examination. The use of both types of scanners would be the most optimal option for skin imaging.

## Ultrasound image of healthy skin

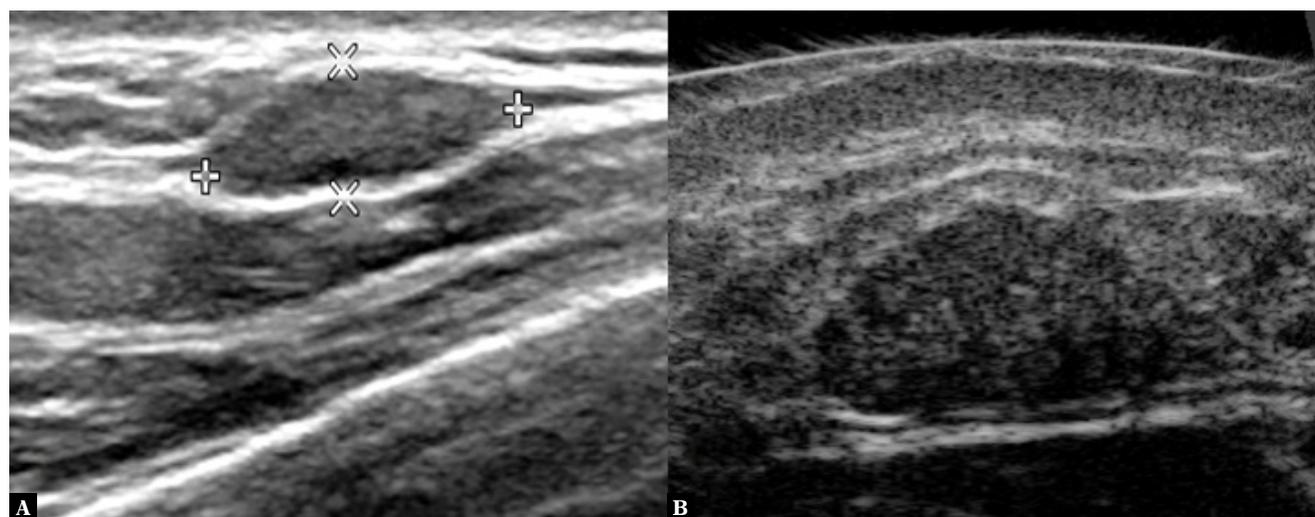
In the ultrasound image of healthy skin, three basic layers may be distinguished (Fig. 2)<sup>(3,4,11)</sup>:

**Tab. 1.** Varying ultrasound penetration depth depending on the frequency used

No.	Frequency [MHz]	Penetration depth [mm]	Structures that can be visualized
1	7.5	>40	Deep structures, lymph nodes
2	10	35	The epidermis, dermis, subcutaneous tissue
3	20	10	Epidermis and dermis - a fragment of the subcutaneous tissue
4	50	3–4	Epidermis and dermis
5	75	3	The epidermis and a fragment of the dermis
6	100	1,5	Epidermis only

**Tab. 2.** Characteristics of high-frequency ultrasound scanners

Parameter	Episcan I-200 (Longport)	DermaScan C (Cortex Technology)	DUB-USB Skin Scanner (Taberna Pro Medicum)	DermaMed (Dramiński)
Analog-to-digital converter	200 MHz, 8-bit (256 levels)	No data	100 MHz, 8-bit (256 levels)	96 MHz, 8 bit (256 levels)
Penetration depth [mm]	3.8–22.4	10–20 (depending on the transducer)	15–3 (depending on the transducer)	4–20
Axial resolution [ $\mu\text{m}$ ]	Up to 40	60	Up to 21 at 75 MHz	15
Lateral resolution [ $\mu\text{m}$ ]	–	130	–	50
Frequency [MHz]	20, 50	20	18, 22, 33, 50, 75	35 (Pulse Frequency 48 MHz)
Lateral scan length [mm]	15	–	12,8	15 mm focal length (scanning angle 30°)
Scanning speed [images/s]	1	8	2.5	8
Imaging modes	A-scan, B-scan	A-scan, B-scan	A-scan, B-scan	B-scan
Computer connection	Permanently connected, a built-in computer	Permanently connected, a built-in computer	A separate device connected to a computer via USB 2.0 or 3.0	A miniature, handheld device with a built-in USB port connected to a laptop

**Fig. 1.** Comparison of resolution between classic scanner (Epiq5) **A**, and a high-frequency scanner (DermaMed) **B**, based on an example of a granuloma. More details can be seen in the **B** image due to the use of a 48 MHz transducer

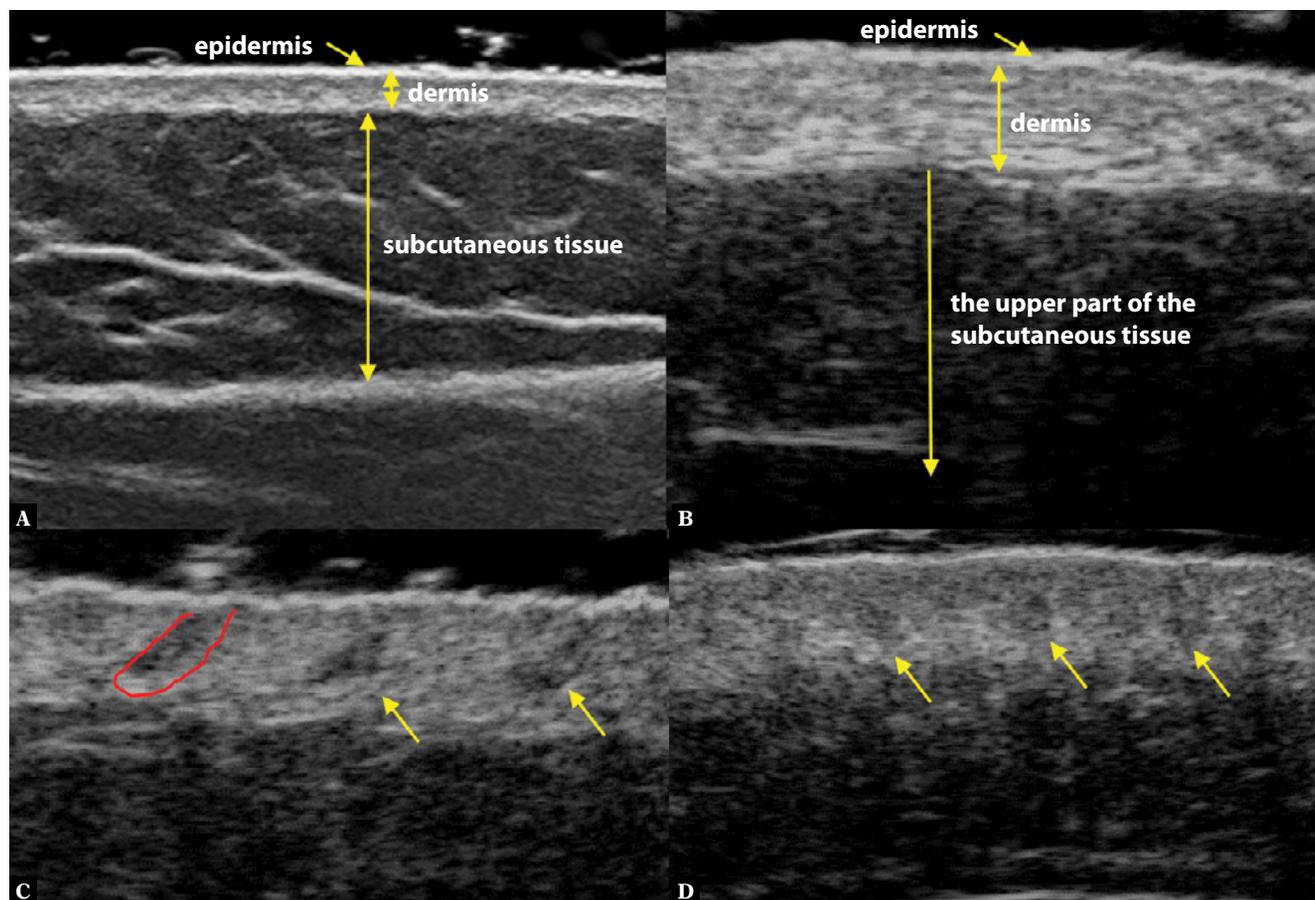
- **epidermis** – a thin, strongly hyperechoic layer,
- **dermis** – a heterogeneous layer with hyperechoic reflections of the collagen fibers and hypoechoic ones from the extracellular matrix. In the dermis, it is also possible to visualize hair follicles, glands, and vessels.
- **subcutaneous tissue** – a hypoechoic layer composed of hyperechoic reflections originating from adipose lobules separated by thin linear hyperechoic reflections running in different directions, corresponding to thin fibers of connective tissue. Depending on the frequency of the transducer, the ultrasound image may show a fragment of or the entire subcutaneous tissue. The latest generation ultrasound scanners also allow for visualization of the veins and arteries.

The ultrasound image of healthy skin also shows a subepidermal low echogenic band (SLEB, also known as

subepidermal non echogenic band, SENEb) (Fig. 3)<sup>(12,13)</sup>. SLEB is usually found in the skin exposed to sunlight, and therefore regarded as a marker of skin photoaging<sup>(11,13)</sup>.

### An analysis of ultrasound images and ultrasound-assessed parameters

The skin images obtained during the examination are analyzed quantitatively and qualitatively<sup>(14)</sup>. Qualitative analysis is performed by the operator (or a few independent experts) and it involves a comparison of images. Depending on the purpose of the examination, images of diseased vs healthy skin at a synonymous site or images of the same site but at different time points are compared. In this type of analysis, the operators often refer to echogenicity, i.e. the brightness of different skin layers



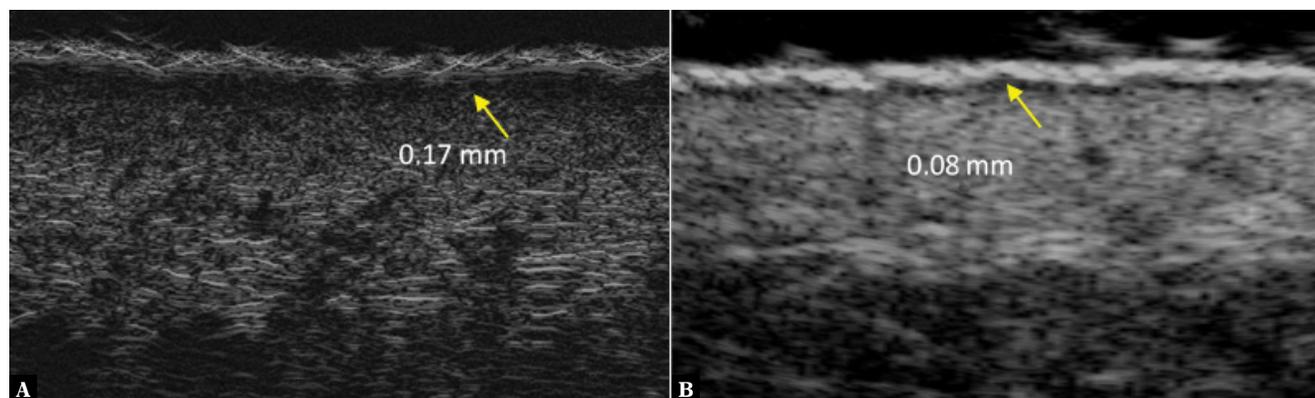
**Fig. 2.** Ultrasound image of healthy skin: **A.** Classic ultrasonography, Philips Epiq5 with a linear 5–18 MHz transducer. **B.** High-frequency DermaMed ultrasound, 48 MHz transducer. **C.** Hair follicles, DermaMed. **D.** Sweat glands – forehead, DermaMed

or structures. In recent years, in addition to the qualitative assessment of echogenicity, attempts have been made to quantify this parameter. In the case of scanners with mechanical transducers, it is possible to measure the number of pixels from a given gray scale range in the region of interest.

Quantitative analysis is also used for such parameters as:

- **thickness:** of the epidermis, dermis and subcutaneous tissue, SLEB and other evaluated structures. This assessment

is the primary measurement parameter. Since thickness measurements of thin structures (such as epidermis) are highly prone to measurement error, and may even be impossible in the case of classic scanners, it is important to use a reliable measurement method. This problem was solved by introducing a software for automatic measurement of the thickness of a given structure in several ultrasound scanners with mechanical transducers in recent years (Fig. 4). It is an innovative measurement method that significantly facilitates the work of the operators and



**Fig. 3.** An anechoic subepidermal band (SLEB/SENEB) in an ultrasound image of healthy skin. **A.** The skin of the forehead, Episcan, 50 MHz transducer. **B.** The skin of the hands, DermaMed, 48 MHz transducer

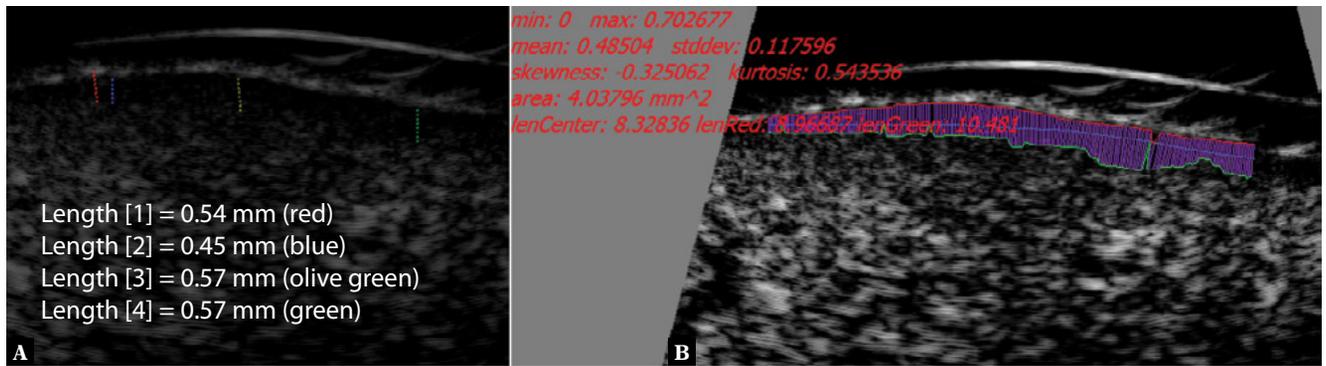


Fig. 4. SLEB thickness measurement. A. Manual measurement. B. Automatic measurement with the use of software available in the ultrasound (DermaMed)

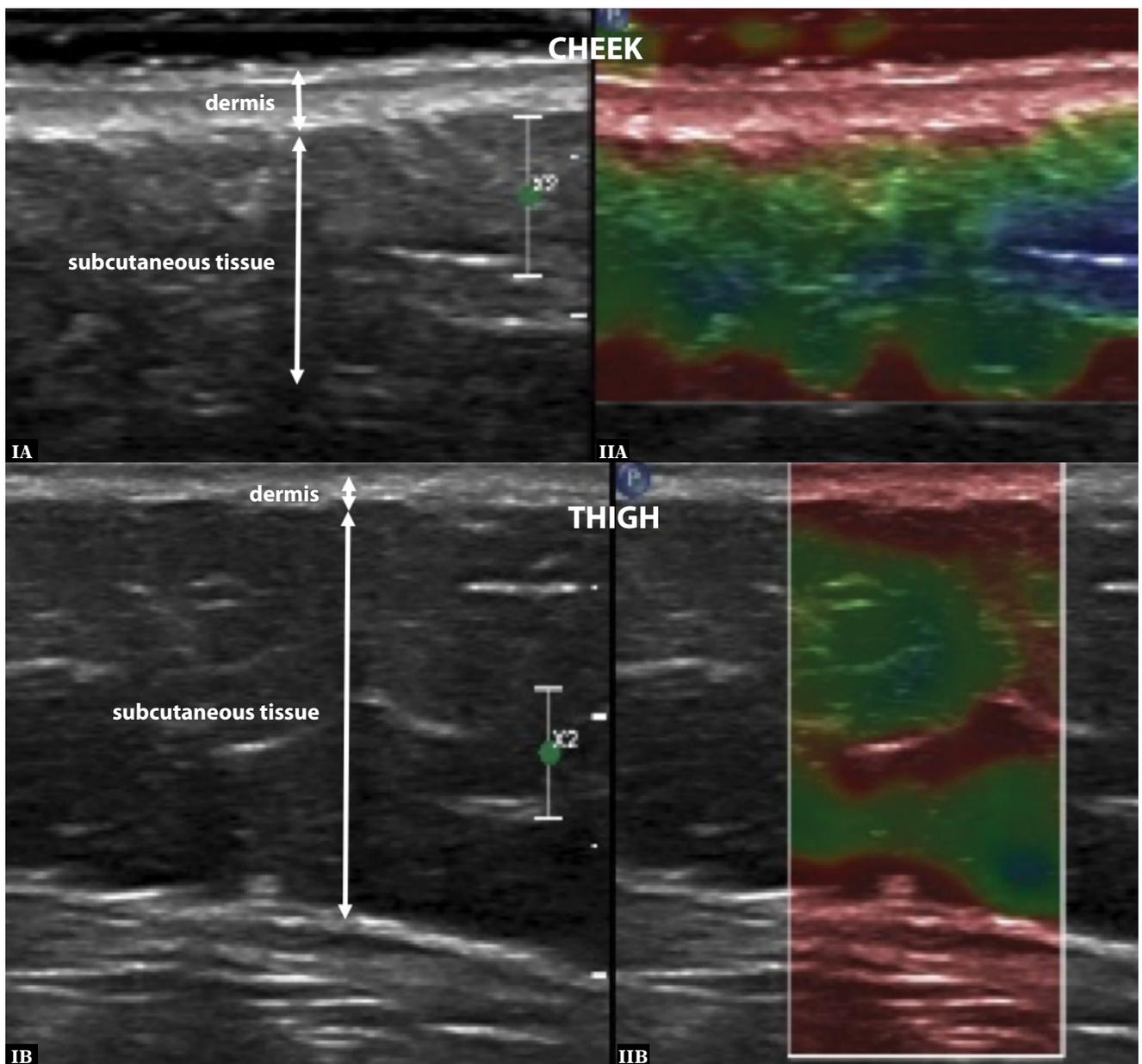
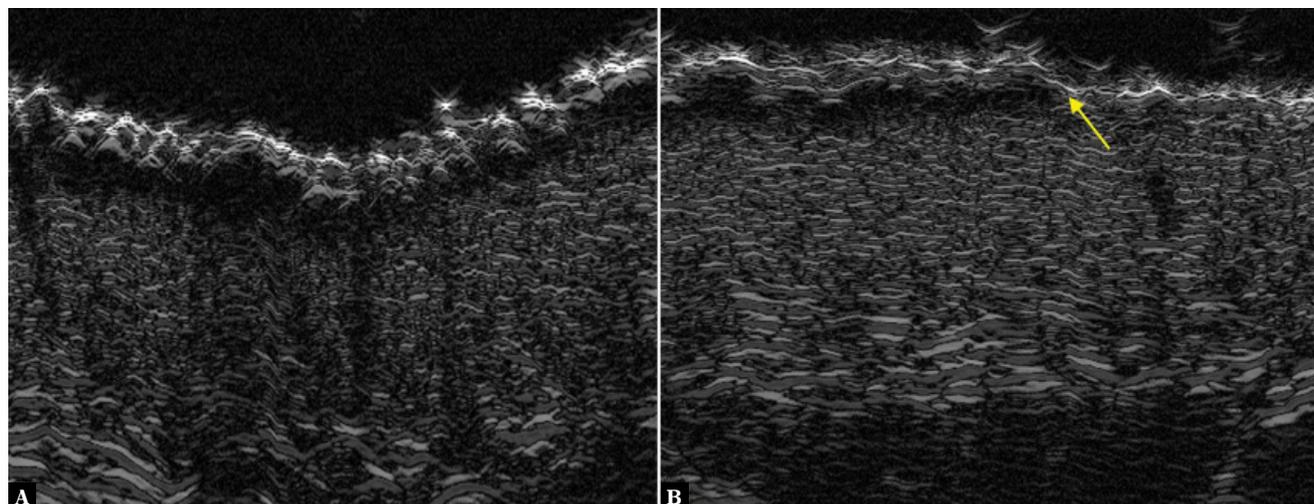


Fig. 5. Sonoelastography of healthy skin. IA. The cheek, a grayscale image. IB. The cheek, sonoelastography. IIA. The thigh, a grayscale image. IIB. The thigh, sonoelastography. The subcutaneous tissue is more compliant to strain than the dermis



**Fig. 6.** Ultrasound image of atopic dermatitis (Episcan, 50 MHz transducer). **A.** Active lesion. **B.** The boundary between the lesion and the surrounding healthy tissue

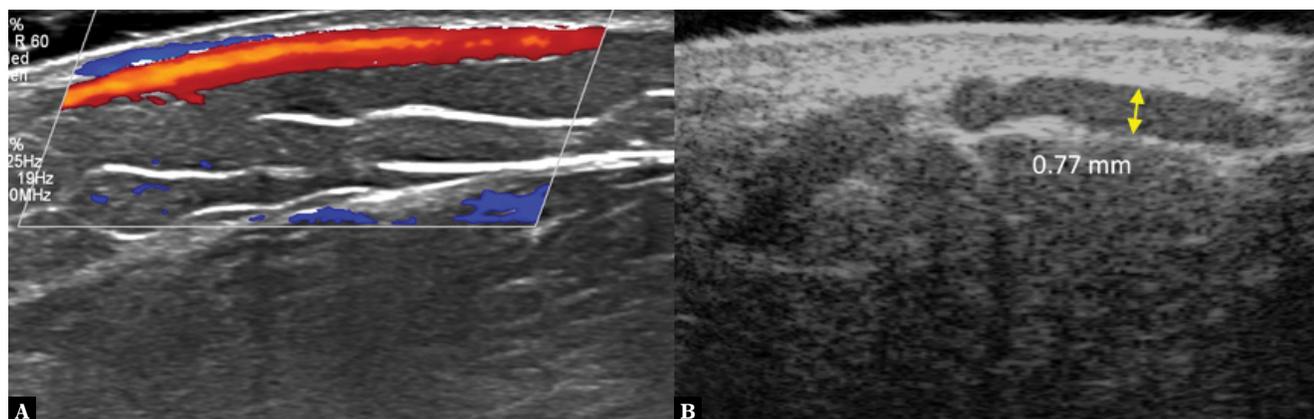
minimizes the risk of error. Research has shown that automatic measurement of tumor thickness was more accurate than manual measurement. Furthermore, there was a significant correlation between tumor thickness and Breslow thickness for melanoma in automatic measurements<sup>(15)</sup>,

- **surface area** of structures of interest,
- **sonoelastography** – available in high-class conventional ultrasound scanners, allows for the measurement of tissue stiffness (hardness) and its compliance to strain. This is important for the assessment of both healthy skin and its focal lesions. Skin stiffness changes depending on the layer being evaluated: the dermis is stiffer than the subcutaneous tissue. In the subcutaneous tissue, connective tissue septa are less compliant to strain (Fig. 5)<sup>(16)</sup>. Both, static and dynamic sonoelastography have been used for skin assessment. In the light of the results obtained so far, dynamic sonoelastography has a higher diagnostic value<sup>(17,18)</sup>; however, this topic requires further research due to the relatively small number of papers in this field,
- **microflow** – here, researchers have increasingly modern solutions at their disposal. Recently, classic

scanners have been equipped with the MicroFlow imaging option, allowing to detect slow and weak blood flow even in very small vessels, which is important in skin examination. MFI is characterized by better resolution, sensitivity and it enables imaging of flow patterns that are not visible with the use of Power or Color Doppler<sup>(18–20)</sup>.

### Current applications of high-frequency skin ultrasound

In the initial stage of development of high-frequency ultrasonography, it was mainly intended for skin examinations performed in a dermatological setting. During the first conference on skin ultrasound, which took place in 1990 in Bochum, great hopes were placed in this method and it was permanently linked to dermatology. Ultrasound examination of the skin was to be an “extension of the dermatologist’s hand” and expected to enrich the diagnosis with data from the inside of



**Fig. 7.** Monitoring of the course of small vessels. **A.** Classical scanner (Epiq5), a venous vessel coursing at the border between the dermis and the subcutaneous tissue. **B.** High-frequency 48 MHz scanner (DermaMed), a vessel running under the dermis and descending into the subcutaneous tissue

the skin, to which they had no access when assessing lesions based on visual inspection of the skin surface. Unfortunately, 30 years have passed since this conference and skin ultrasound has not yet become common in dermatological settings, and is still mainly of interest to academic societies. Ultrasound examination of the skin is definitely an underestimated method among many used in dermatology<sup>(4)</sup>, and the many years of our experience show that a large proportion of dermatologists are reluctant to perform it as it is considered difficult to master. Currently, dermatology offices where skin ultrasound is performed are scarce in Poland. Also, skin ultrasound is not a part of curriculum during medical studies or specialization training courses. This situation is incomprehensible given the fact that, as research shows<sup>(3,4,9,11)</sup>, routine high-frequency ultrasound would be particularly useful in:

- the imaging of focal lesions [benign lesions, skin cancers, including melanoma and basal cell carcinoma (BCC)],
- the monitoring of dermatological treatment in a number of conditions [such as scleroderma, psoriasis, and atopic dermatitis (AD)].

Skin focal lesions usually present on ultrasound as oval or circular hypoechoic lesions surrounded by hyperechoic structures; therefore, their differentiation is not fully possible. Although there are reports pointing to the characteristic features of benign tumors and BCC<sup>(10)</sup>, which are helpful in differentiating lesions, histopathological examination remains the gold standard<sup>(11,15,21)</sup>. However, high-frequency ultrasonography is irreplaceable in assessing the size of the lesion, its location in relation to other tissues and structures, as well as potential invasion and its depth. This is particularly important in the case of preoperative assessment of melanoma, where proper determination of the skin margin to be removed along with the lesion significantly influences the patient's further management and prognosis<sup>(4,15,21)</sup>. In the field of dermatology, high-frequency ultrasonography is also useful in the assessment of many diseases and monitoring of their treatment. Diseases that can be assessed with ultrasound include inflammatory skin diseases such as psoriasis, eczema, atopic dermatitis (AD), but also scleroderma. The ultrasound image of inflammatory diseases is characterized by the presence of SLEB and reduced echogenicity of other layers of the dermis, which is due to edema and inflammatory cell infiltration<sup>(4,9)</sup> (Fig. 6). Skin edema, caused by the presence of water, increases the distance between collagen fibers, resulting in a decrease in tissue density<sup>(4)</sup>. As demonstrated by Polańska *et al.*<sup>(22)</sup>, high-frequency ultrasonography proved to be a useful method for long-term treatment monitoring in patients with atopic dermatitis. The ultrasonographic image of localized scleroderma shows significant thickening and increased echogenicity of the skin<sup>(4,9)</sup>. Also, atrophy of skin appendages was observed in the affected skin. Wortsman *et al.*<sup>(23)</sup> showed 100% sensitivity and 98.8% specificity for differentiation between inflammatory and fibrotic phase. Sonoelastography also proved useful for the assessment of scleroderma<sup>(24)</sup>. Introduction

of transducers with a higher frequency allowed for the assessment of wound and burn healing processes, as well as scarring in dermatology<sup>(9,25)</sup>.

Aesthetic medicine and cosmetology are also fields that use high-frequency ultrasonography. In these areas, we have observed a dynamic increase in the popularity of this method, with a constantly increasing number of clinics performing this type of examination in the last few years. The popularization of skin ultrasound in the field of aesthetic medicine and cosmetology was influenced by the fact that such offices are very often run by doctors other than dermatologists and cosmetologists who do not have any objective methods for skin assessment. Since many aesthetic interventions interfere with the tissues, it is necessary to monitor these changes. The gap in the dermatological diagnostic methods in aesthetic medicine is perfectly filled by ultrasound, which is safe, reliable and relatively inexpensive<sup>(3)</sup>. In aesthetic medicine, skin examination is useful at every stage of the management: from treatment planning and monitoring to assessing treatment outcomes and possible complications<sup>(4,5,11)</sup>. The EFSUMB<sup>(10)</sup> recommendations published a few months ago pointed to several main areas in aesthetic medicine and cosmetology where skin ultrasound is useful. Although it is not a complete list of applications, it indicates major areas of use. The most important applications include:

- assessment of skin condition and photoaging, followed by monitoring of treatment efficacy. Here, the measurement of SLEB thickness is a useful ultrasound parameter<sup>(10,26)</sup>.
- ultrasonographic assessment of the anatomy of the face and other body parts, which is important for planning procedures and monitoring their correctness. Here, it is possible to assess the thickness of individual structures, as well as their vascularity (Fig. 7);
- assessment and identification of different types of tissue fillers, botulinum toxin, as well as an assessment of their location and expansion<sup>(27,28)</sup>. Fillers are clearly visible on ultrasound images; hyaluronic acid is the most common filler, which can be identified as a round, anechoic space<sup>(4,27,29)</sup>;
- an assessment of complications after different types of aesthetic procedures<sup>(4,10)</sup>. Ultrasonography allows for the monitoring of early complications, such as edema of the skin and subcutaneous tissue, lymphoedema, hematomas, and abscesses. It also enables monitoring of distant complications such as fistulas, fat necrosis, and granulomas<sup>(30)</sup>;
- assessment of the subcutaneous tissue, including cellulite, and monitoring of the effectiveness of interventions<sup>(4,31)</sup>. Cellulite is easy to visualize with ultrasound as it is in the form of characteristic ingrowths of subcutaneous tissue into the dermis what may resemble teeth;
- performing ultrasound-guided procedures, such as administration of hyaluronidase.

In addition to dermatology and aesthetic medicine, skin ultrasound is also used in other fields. Phlebology is one of them. Owing to high frequencies, it is possible to assess the

diameter and the course of small blood vessels, which significantly improves the safety and efficacy of sclerotherapy for reticular veins<sup>(6)</sup>. It is also possible to perform an ultrasound-guided puncture. Gynecology is an interesting and innovative field where high-frequency ultrasound is used. Here, ultrasound is used for vulvar, vaginal and cervical assessment<sup>(7)</sup>. There have also been reports on the imaging of vulvar cancer<sup>(32)</sup>.

## Conclusions

The development of technology witnessed at the turn of the 20<sup>th</sup> and 21<sup>st</sup> centuries had a significant impact on the availability of ultrasound scanners, including high-frequency ones, which are used for skin examination. In this paper, we have shown that skin imaging is used in many fields and, as also pointed out by many other researchers, it shows high usefulness. Unfortunately, easy access to equipment did not contribute significantly to the popularity of ultrasound, which is still underestimated and considered a novelty in offices. This is particularly true for dermatology.

High-frequency ultrasonography is mainly used in scientific and research units. The situation is slightly better in aesthetic medicine and cosmetology, which develop dynamically and implement new therapeutic and

diagnostic methods. High-frequency ultrasound scanners are increasingly used in everyday practice in medical offices. In our opinion, it is aesthetic medicine that will contribute to popularization of skin ultrasonography. However, transparent and comprehensive standards of skin ultrasound need to be developed for this to happen. Such attempts are indeed currently made<sup>(10)</sup>. It is also important to introduce reliable training for operators to popularize ultrasonography. The equipment and software in high-frequency ultrasound scanners with mechanical transducers also require improvement and standardization, so that the obtained results can be compared, especially in terms of echogenicity assessment. The development of ultrasound software should target automation as it allows to avoid measurement errors.

The possible applications of high-frequency ultrasound discussed in this paper should encourage doctors, cosmetologists and other skin specialists to use this method in their daily practice.

## Conflict of interest

*Authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.*

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