ULTRASOUND AS USEFUL TOOL FOR EVALUATION AGE-RELATED CHANGES AND PATHOLOGICAL LESIONS OF THE FACE SKIN

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SUMMARY

Introduction. Various skin parameters such as the thickness of the epidermal echo, dermis and subcutaneous tissue, the surface area of individual layers, the thickness of the subepidermal layer with a low echogenic effect, the caliber of blood vessels, as well as the presence or absence of blood flow in the vessels, can be investigated with ultrasound. The **aim** of our investigation was to evaluate age-related changes and pathological lesions of the face skin using ultrasound examination of the different anatomical areas of the face in young and older women.

Materials and methods. The thickness of different skin layers (epidermis, dermis, hypodermis) was measured in the area of the interbrow zone, chin, nasolabial folds and cheeks in 52 patients aged 15 to 75 years (mean age 44.3±11.9 years) using an ultrasound scanner Mindray DC-8. The study was carried out in Department of Fundamental Medicine of the Immanuel Kant Baltic Federal University. Statistical processing for the study results was performed in Microsoft Excel 2017 using average values (M), the reliability was determined using Student's criterion, and its critical level in this study was taken to be 0.05.

Results and its discussion. The thickness of the epidermis was minimal in the nasolabial fold (0.039 cm) and the maximum (0.043 cm) in the chin. The thickness of the dermis was maximal in the interbrow zone (0.081 cm) and the smallest in the chin (0.062 cm). The thickness of the hypodermis was the biggest in the

cheeks area (0.136 cm and 0.137 cm to the right and left, respectively), the smallest hypoderm thickness was recorded in the chin area (0.019 cm). A thickening of the dermis was established in patients after 40 years in all anatomical areas of the face with the achievement of a statistically significant difference in the nasolabial folds ($p = 0.027$) and cheeks ($p = 0.01$). It was found that the dermis was thickened in patients who used fillers in all anatomical areas of the face with a statistically significant ($p < 0.05$) difference in the nasolabial folds. **Conclusion**. Until now, little attention has been paid to the study of age-related changes and some pathological lesions in the face skin by using ultrasound, so there are no standard parameters for assessing its thickness, which requires further research.

Keywords: facial skin, epidermis, dermis, hypodermis, age, ultrasound examination of the skin, women older than 40 years, fillers.

Introduction. Facial aging is the result of the interaction of changes occurring in the skeleton, ligaments, muscles, adipose tissue of the face and, of course, the skin [1, 2, 3]. These changes occur with each mentioned structure at a different rate, begin in each person at different ages, and differ depending on ethnic origin [1, 3].

Age-related skin changes, known as "chronological aging", are modulated by genetic, behavioral, catabolic, endocrine, and gravitational factors [4, 5]. Besides, chronic exposure to sunlight causes many clinically important degenerative changes in various parts of the skin, the so-called photo-aging [4, 5].

Skin ultrasound study is becoming an increasingly popular method of research, as evidenced by the growing number of scientific publications, as well as the number of scanners for skin imaging available on the marketplace [4, 6]. Ultrasound images of healthy skin show three main layers: the epidermal echo, dermis, and subcutaneous tissue, which correspond to the anatomical structure of the skin [4, 6, 7]. Various parameters are taken into account for ultrasound skin assessment: the thickness of the epidermal echo, dermis and subcutaneous tissue, the surface area of individual layers, the thickness of the subepidermal band with a low echogenic effect, the caliber of blood vessels, as well as the presence or absence of blood flow in the vessels.

The study of all face layers thickness using ultrasound is a topical issue of contemporary medicine since age-related skin changes can be slowed down or prevented by appropriate clinical procedures (dermatological and surgical interventions). Even though cosmetic fillers are increasingly applied to improve the aesthetic characteristics of the skin, several authors have noted the growth of complications associated with their usage [8, 9, 10, 11]. At the same time, ultrasound has been successfully used to detect and identify common types of fillers and has become a first-line visualization method for working with these exogenous components [8].

The **aim** of our investigation was to evaluate age-related changes and pathological lesions of the face skin using ultrasound examination of the different anatomical areas of the face in young and older women.

Materials and methods. The thickness of different skin layers (epidermis, dermis, hypodermis) in the area of the glabellar area, chin, nasolabial fold and cheeks (salivary gland) was measured in 52 patients aged 15 to 75 years (average age 44.3±11.9 years) using the Mindray DC-8 ultrasound scanner. There was group I of 21 women under 40 years (average age 32.4±1.8 years) and the group II of patients over 40 years consists of 31 women (average age 50.0±2.4 years).The study was carried out in Department of Fundamental Medicine of the Immanuel Kant Baltic Federal University. Statistical processing of the obtained research results was conducted in the Microsoft Excel 2017 software using average values (M), the reliability was determined using the Student's criterion, and its critical level was assumed to be equal to 0.05.

Results.

The results of the facial skin layers in different anatomical areas are presented in table 1.

Table 1.

Thickness of facial skin layers, depending on the anatomical area (M)

Skin layer	Thickness of skin layer (cm) and anatomical region					
	Interbrow zone	Chin	Left nasolabial fold	Right nasolabial fold	Right cheek area	Left ~~Salivary gland~~
Epidermis	0,040	0,043	0,039	0,039	0,040	0,040
Dermis	0,081	0,062	0,069	0,069	0,069	0,070
Hypodermis	0,126	0,119	0,128	0,131	0,137	0,136

We found that the thickness of the epidermis was minimal in the nasolabial fold (0.039 cm) and the maximum (0.043 cm) in the chin area. Analysis of the dermis thickness indicates the largest size was in the interbrow area (0.081 cm) and smallest in the chin (0.062 cm). The hypodermis thickness was greatest in the area of the salivary glands (0.136 cm and 0.137 cm on the left and right sides, respectively). The smallest thickness of the hypodermic, according to the obtained data, is registered in the chin area (0.019 cm).

It should be noted that in the surveyed patients, the thickness of the dermis and hypodermis was the smallest in the chin area in comparison with other investigated areas of the face, and the epidermis thickness was the largest.

The analysis of the thickness assessment of all skin layers (epidermis, dermis, hypodermis) shows that it's thickening with age occurs due to the dermal layer. We found a thickening of the dermis in patients after 40 years in all anatomical areas of the face with a statistically significant difference in nasolabial folds (p=0.027) and cheeks (p=0.01) (Fig.4). We had found that in patients under 40 years of age, the smallest thickness of the dermis was diagnosed in the nasolabial folds area – 0.043 cm, and over 40 years – it was 0.067 cm (Fig. 4). The maximum thickness of the dermis is documented in the interbrow area, regardless of age.

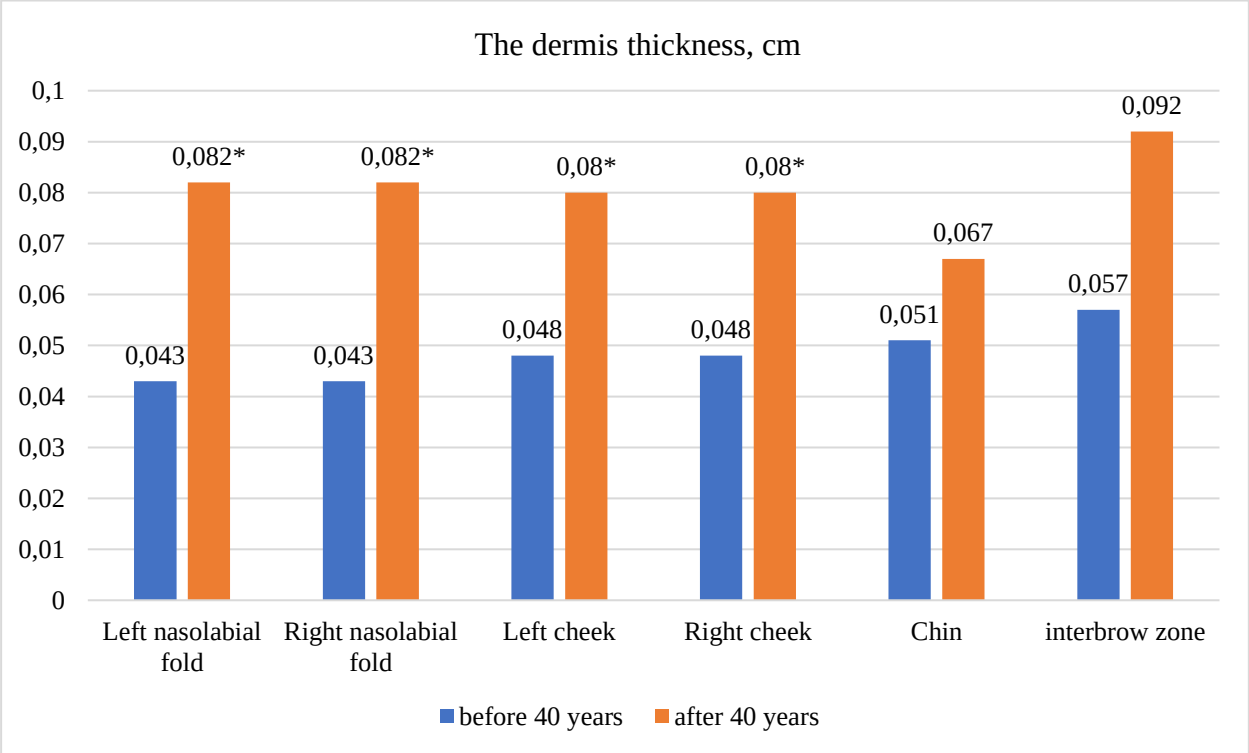

*Fig. 1. Comparative analysis of the dermis thickness of different face anatomical areas in surveyed patients under and over 40 years. *- p<0.05*

We had revealed that the dermis is thickened in patients who use injectable cosmetology (fillers and filaments) in all face anatomical areas with the achievement of a statistically significant (p<0.05) difference in the area of nasolabial folds (Fig. 2).

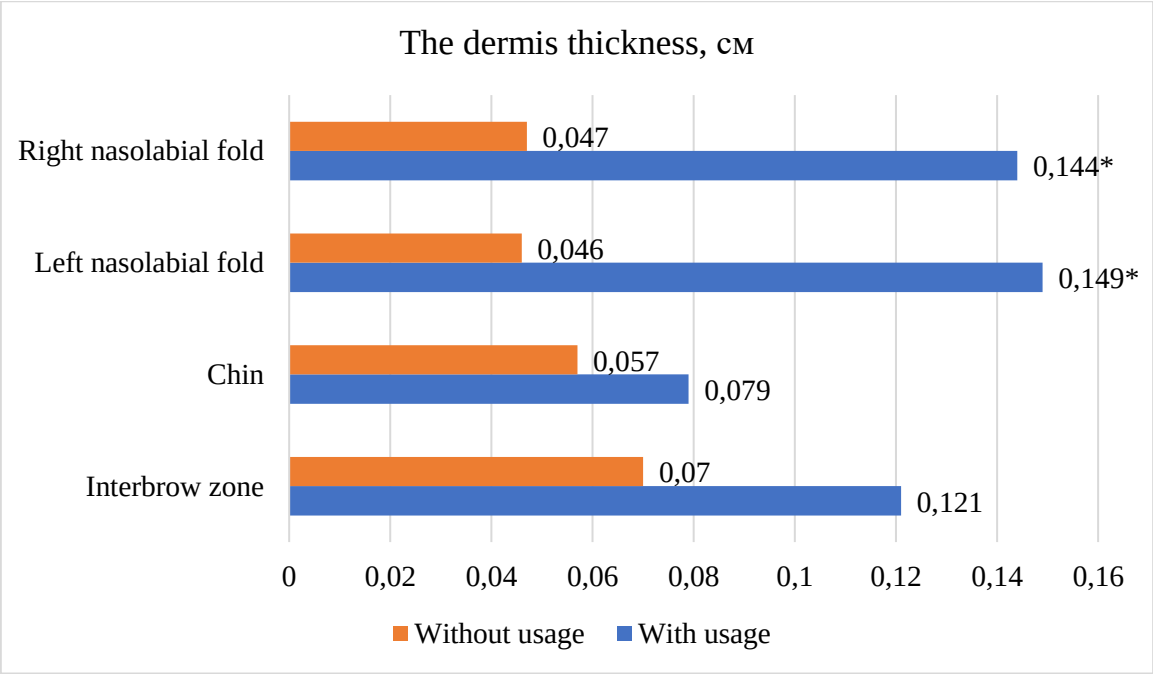

*Fig. 2. Comparative analysis of the dermis thickness of different face anatomical areas in patients depending on the use of injectable cosmetic procedures. *- p<0.05*

It should be noted that the thickness of the dermis in nasolabial folds in patients using dermal fillers was more than 3 times greater in comparison with surveyed women without it.

Discussion. The first layer visible in the place if the contact of the ultrasound probe is a hyperechoic line that histologically corresponds to the epidermis [4]. Under the epidermis is the dermis, which is anatomically divided into papillary (the upper part of the dermis lying under the epidermis) and reticular (the layer located under the papillary dermis) layers [4]. The papillary part makes up about 20% of the dermis and contains blood vessels and irregularly located thin collagen and elastin fibers [4]. On the other hand, the reticular dermis, which composes approximately 80%, regularly contains collagen, elastin and reticular fibers [4]. The third layer, visible in ultrasound images, is subcutaneous fat.

The first age-related changes of the facial skin in women (the roughness and wrinkles appearance) are already noticeable at the age of 20-30 years, and the most significant occur in the postmenopausal period, which is mainly due to the influence of hormonal status [12]. According to Lephart E. D. [13] and Tobin D. J. [14], degenerative changes in the skin of the face associated with the loss of basic collagen (sagging skin, reducing its thickness, etc.) may be due to an age-related decrease in the level of estrogen. It is proved that 30% of skin collagen is lost in the first five postmenopausal years with an average decrease of 2% per year for 15 years [15]. Marcos-Garcés V et al. [16] using methylation levels as markers of epigenetic aging, menopause was found to accelerate biological aging.

The thickness of the facial epidermis *stratum corneum* does not change significantly with aging, but there is a decrease in the number of lipids in it [14]. It has been proved that in middle-aged people (50 to 80 years), abnormal acidification of the *stratum corneum* leads to deferred lipid processing, slowed restoration of the permeability barrier and violation of its integrity, and delays in ion transport [17].

In contrast to the stratum corneum, keratinocytes in the basal layer of the epidermis show increasing atypia with age [17]. Tobin D. J. [14] notes that basal keratinocytes suppress the expression of certain β-1 integrins, which indicates their pathological proliferation and adhesion in photo-damaged elderly skin, what also confirms the data of Kawabata K. et al. [18].

The organization of the papillary part of the dermis also changes with age (Fig. 3) [14, 19]. In the area of wrinkles in the dermis, there is the disappearance of chondroitin sulfates, which are known to provide water retention in the skin, and a change in the oxytalane fibers - thin fibers of an elastic network organized perpendicular to the skin surface [19]. In the area of wrinkles, the number of oxytalane fibers decreases significantly, or they disappear altogether; a change in the orientation of collagen fibers is also noted [19]. Humbert P. et al. [20] proved the presence of atrophic changes in both the dermis and hypodermis at the location of wrinkles. Marcos-Garcés V. et al. [16] during histological examination of skin biopsies of 45 people aged from several months to 95 years revealed a significant increase in the thickness of the papillary part of the facial dermis after reaching the age of about 50 years. According to the authors, the thickness of the reticular dermis increases by about 2 times, while the average thickness in the first months of life is about 1.6 mm, reaching about 3.2 mm by the age of 50 [16]. Our results on the thickening of the dermis in patients after 40 years in all anatomical areas of the face with the achievement of a statistically significant ($p<0.05$) difference in the nasolabial folds and cheeks confirm

the data of Humbert P. et al. [20] and Marcos-Garcés V. et al. [16].

As for the macroscopic organization of collagen bundles, the papillary and reticular areas of the dermis also develop differently. While the average thickness of the collagen bundle decreases from 1.0 mkm to 0.8 mkm in the papillary area, this parameter increases from 5 mkm to 10 mkm in the reticular area [16]. The thickness of the collagen bundles decreases simultaneously with dermal atrophy, and the space between the bundle's increases, what leads to a decrease in tissue density in both the papillary and reticular areas (Fig. 3) [16].

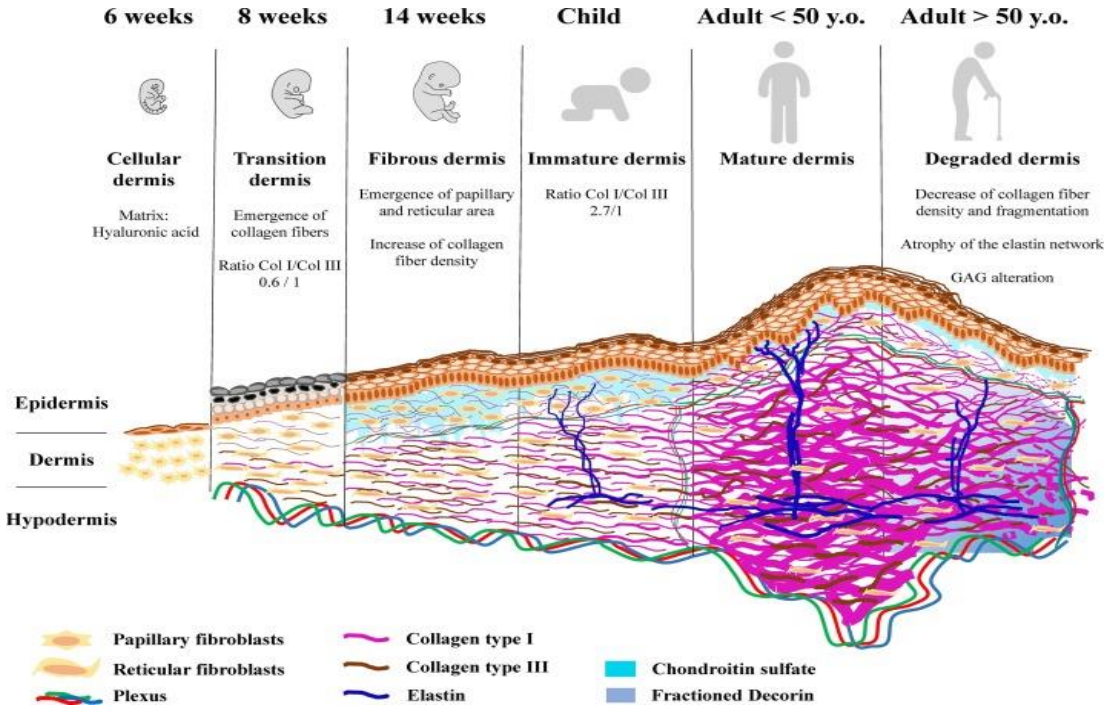

Fig. 3. Schematic representation of the dermis evolution in the process of human development and aging [adopted from 19].

Mizukoshi K. et al. [21] claim that after 50 years, the quality of the dermis gradually deteriorates: the thickness decreases, in parallel with the progressive weakening and loss of fibrous dermal-epidermal connection. Age-related changes in the dermis papillary area were confirmed by ultrasound: echogenicity changes and a subepidermal anechoic band appears between the epidermal echo and the dermis in aging skin, the so-called SLEB (subepidermal low-echoic band) or SENEB (subepidermal non-echoic band) [19]. It should be noted that in our patients' cohort under 40 years of age, the smallest thickness of the dermis was diagnosed in the nasolabial folds area – 0.043 cm, and over 40 years – it was 0.067 cm. The maximum thickness of the dermis is documented in the glabellar area, regardless of age. In addition, according to Mlosek R. K. et al. [4] increased SLEB thickness is associated with water retention in the papillary dermis. Oh J. H. et al. [22] and Ahmed T. et al. [23] consider that this modification of the echogenic properties of the tissue may indicate changes in the organization and composition of the matrix with a decrease in the density of perlecan and hyaluronic acid and the density of collagen fibrils.

Age-related changes are not only limited by structural elements of the entire skin dermis, including the face but also by the vessels located in it [24]. Results of the study by Gomi T. et al. [25] testify to the general deterioration of blood vessels in the upper lip dermis during aging. The authors found that both the area and number of blood vessels in the upper lip dermis decreased with age [25].

Until now, little attention has been paid to the study of age-related changes in the skin of the face using ultrasound. Pellacani G. et al. [5] evaluated the echographic aspect of the facial skin in young people at different sites and changes in the thickness and echogenicity of the skin that develop with age. The authors found that the thickness of the skin is significantly higher on the upper and lower lips, chin and under-eye area than on the forehead and cheeks. In older people, an increase in the thickness of the facial skin on the forehead, cheeks, lips, chin and nose and thinning of the sub-ocular areas were verified compared to younger subjects. The increase in skin thickness values was statistically significant in the lateral areas of the forehead, upper and lower lips, and nose [5]. According to Pellacani G. et al. [5], skin echogenicity was higher in the upper part of the face (forehead, infraorbital areas and cheeks) than in the lower part (lips and chin), as evidenced by a decrease in hyporeflective echo and an increase of 30-100 and 100-200 pixels. That also proved by our results.

We found in surveyed patients, that the thickness of the dermis and hypodermis was the smallest in the chin area in comparison with other studied areas of the face, and the thickness of the epidermis was the largest. According to the morphometric study of facial skin

features by Karymov O. N. et al. [26], the thickness of the epidermis in the chin area is significantly more ($p<0.05$) than other anatomical zones.

In 70% of elderly people, a subepidermal hypoechoic band was visualized in the central area of the forehead and cheeks, in 80% - on the infraorbital areas, in 100% - on the upper lips. In the elderly, there was an increase in values related to the expansion of areas of medium and high amplitude (amplitudes 30-100, 100-200, and 201-255) and a decrease in the elongation of areas that affect hyporeflectivity [5]. The differences were significantly significant in the under-eye area (for band 0-30), on the cheek (for band 100-200), and on the upper lip (for all intervals). The lower lip and chin showed the lowest reflectivity with small hyperreflective areas (intervals of 100-200 and 201-255), especially in young subjects. A subepidermal hypoechoic band was documented on the lower lip in 50% of elderly subjects and on the chin in 70%. The ultrasound image of the nasal skin had a special picture: the lower part corresponding to the skin covering the cartilage was visualized poorly echogenic in both young and elderly people, while the upper part representing the skin above the bone shows a hypo-echogenic subepidermal area, which is especially pronounced in the elderly people [5].

Currently, age-related skin changes can be slowed down or prevented by appropriate clinical procedures: dermatological, surgical, and cosmetic interventions [27]. At the same time, skin examination is an effective and reliable tool for real-time diagnostics of the implant used type, its location, and the study of possible complications [28].

Considering the literature data that dermal fillers used for the treatment of age-related skin atrophy lead to the dermis thickening by neocollagenogenesis, it was interesting to assess the presence of changes in the thickness of skin layers depending on the use of injectable cosmetic procedures by patients. Chiang Y.Z. et al. [9] identify the following key complications associated with the use of fillers: pigment changes, hypersensitivity reactions, infections, nodule formation, granulomatous reactions, vascular occlusion, and filler migration. However, quite often patients do not know or remember the exact details of the procedure or the filler used type [29, 30]. Therefore, the usage of such an accurate and non-invasive diagnostic tool as ultrasound can help clarify the relationship between the procedure and the resulting pathology [29, 30]. We found that the dermis thickness in the area of nasolabial folds in patients using dermal fillers was more than 3 times greater in comparation with surveyed women without it. The obtained data are comparable with the results of Kim JS. [31] and Kim JA et al [32], who with histological examination of dermal biopsies, found its thickening lasting up to 4 years or more after intradermal cosmetic injections with polycaprolactone-based drugs.

Conclusion. We have detected a thickening of the dermis in patients over 40 years old and in surveyed women that using injection cosmetology methods. The results obtained in relation to the difference in the thickness of the skin layers depending on the anatomical area of the face, confirm the previously conducted morphometric measurement of the skin, and the detected changes in the dermis as a result of fillers – histological studies of its biopsies, which indicates the reliability of the ultrasound method for assessing the state of the organ under discussion. The advantages of this method are its non-invasiveness, the possibility of repeated research, and mobility. Until now, little attention has been paid to the study of age-related changes and some pathologic lesions in the face skin using ultrasound, so there are no standard parameters for assessing its thickness, which requires further research.

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ПРИМЕНЕНИЕ ЛЕКАРСТВЕННЫХ РАСТЕНИЙ В СТОМАТОЛОГИЧЕСКОЙ ПРАКТИКЕ

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