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ANALYSIS OF MORPHEA INDUCED CHANGES OF SKIN BASED ON ULTRASONOGRAPHIC IMAGES

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Abstract - The study presents a mathematical modelling aimed at detection of morphea-induced changes in high-frequency ultrasonographic (USG) images of the skin and a discrimination procedure. The novel 25-35 MHz USG scanner with Golay codes transmission mode was used to examine the skin. The images were recorded from patients with limited cutaneous scleroderma (morphea). Images of the affected skin and a healthy one from opposite side of the body were collected. The differences of thickness of dermis and epidermis were analyzed. A mathematical model was fitted to the measured values revealing statistically significant relation between the measurements and state of the skin. These results were in a good agreement with visual expertise made by an experienced dermatologist.

Keywords - High-frequency USG, morphea, atrophodermia, autoimmune diseases, mathematical modelling.

I. INTRODUCTION

Ultrasonography, a non-invasive method of visualization of body structures and tissue, is currently a standard imaging technique in many branches of medicine, providing diagnostic data, valuable in clinical practice. Depending on the frequency of the ultrasound different parts of the body can be visualized. High frequency USG scanners, which operate above the frequency of approximately 20 MHz, can be used to visualize tissue lesions a few millimetres deep and are typically used to investigate the skin, making that technique applicable in dermatology [1], [2].

Limited cutaneous scleroderma (morphea) is a skin disease of auto-immunological origin. As visible symptoms, on the body of a patient an area of a changed skin appears. Typically a diagnosis in such case is made by visual inspection of the sick areas with checking some other (e.g. mechanical) properties of the skin. To find more objective properties of diagnostic value, physically measurable parameters should be chosen. USG imaging can be a valuable extension of diagnostic possibilities. Research based on the analysis of USG images of the skin can be found in the literature [3]–[6]. In our study we focused on the most distinguishable features of the images, namely on the thicknesses of epidermis and the generalized dermis layers. They can be relatively easy distinguished on most of the pictures and the objective measurements of these quantities can be made. The USG hardware allows for storing images and then making computer post-processing analysis.

The standard 3-10 MHz ultrasound does not allow precise, high resolution estimation of the epidermis layer. Instead, only a thin line with no structure, known in the literature as an entrance echo, is visible [2]. However, when frequencies higher than 20 MHz are used, the epidermis layer starts to be distinguishable and its thickness can be determined. Next layer below the epidermis is the dermis layer. Although the dermis may exhibit more detailed structure (depending on the conditions of the measurement), we look for its total thickness up to the border with subcutaneous tissue. An example of high frequency USG image of a healthy skin is presented in Fig. 1

Dermatologists with an expertise in USG image analysis, in many cases are able to determine which image describes a morphea case by its visual inspection. These observations formed the basis for our studies. We applied a mathematical model describing the measured properties of the images which should be consistent with the description made by an expert.

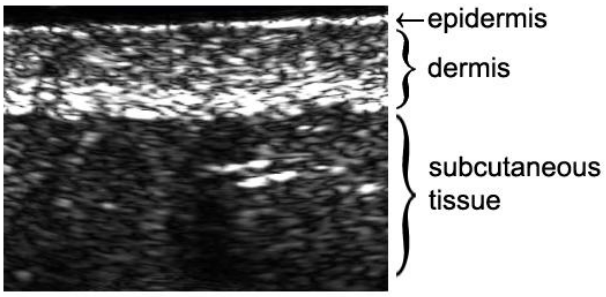

Fig. 1. Example of a 32 MHz USG skin image. The measured skin layers are marked. The observed depth in the skin is from 6 to 8 mm, depending on the local attenuation.

II. MATERIAL AND METHODS

For images acquisition we used the uSCAN high-frequency ultrasound scanner (developed in the Institute of Fundamental Technological Research, Polish Academy of

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Sciences, Warsaw, Poland) equipped with a B-mode sector probe working in the frequency range of 20-35 MHz.

The uSCAN is a versatile high-frequency ultrasound scanner with implemented coded excitation [7]. The application of the Golay codes offers higher signal-to-noise ratio (+14 dB for 16-bit Golay codes at 20 MHz) while preserving the axial resolution. The device works with a single element wobbler type focused transducer made in thick-film technology supporting resolution up to 50 μm. The system is well suited to research and development of new imaging algorithms as well as real-time image and radio frequency (RF) processing, thanks to direct RF sampling.

The data were recorded from 14 morphea patients during their medical examination. The patients gave written consents to participate in the study. In order to see the changes between healthy and sick skin, in each case a pair of images was used; one image of a sick area and the second image of a healthy skin from the opposite side of the body. Several images for each of the skin areas were recorded. Because the parameters for the healthy skin did not differ much, in each case one healthy skin picture (with the most distinguishable features) was selected as a reference for a series of measurements made on various places of the sick area. All the measurements were made with the same settings of the USG apparatus.

For the analysis only newly (a few months old) created skin changes were selected. An expert selected a set of images based on blind diagnostic attempts made only by looking at the images with names of patients removed. Additionally, the images were selected to be clear, not containing structures or parts disturbing the measurements. The final set chosen for the further analysis contained 79 pairs of images from 11 subjects.

The measurements were made by an expert using a software written for that specific purpose. The software allowed to display the given images and then to mark directly on the screen linear dimensions of skin layers (epidermis and dermis) using a computer mouse. The measured distances were stored for further calculations.

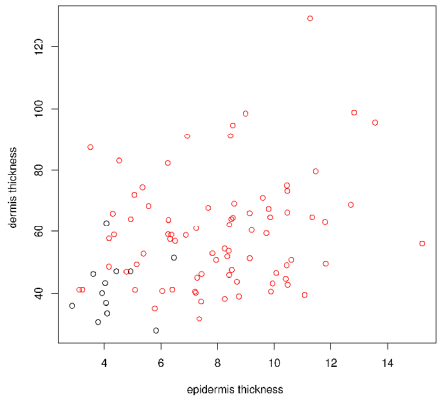

Fig. 2. Epidermis and dermis thicknesses measurements presented in *xy* plane in arbitrary units, dermis thickness on vertical axis, epidermis thickness on horizontal axis. Color circles depict measurements for the images: black—healthy skin, red—changed skin.

The results of the measurements are presented in Fig. 2. They are shown on a *xy* graph, with epidermis thickness on the horizontal axis and dermis thickness on the vertical axis in arbitrary units unified for all pictures. It means that a measurement of both thicknesses for each image is described by one point (*x*,*y*) on the graph. As can be seen in Fig. 2, when full information for the pair of images is not used, it is difficult to find a regular pattern in the picture. On the other hand, in Fig. 3 we can see the same data presented in form of vectors describing changes, pointing from the healthy condition to the sick condition for a given pair of measurements. Specific trends of changes are now visible.

A. Modelling of changes

Due to variability in measured skin thickness between different patients, areas on the skin and even places in the USG image, the measured values always fall in a certain range of values. We need to apply a stochastic model, able to describe the change related to the skin state and a random component in the measured quantities.

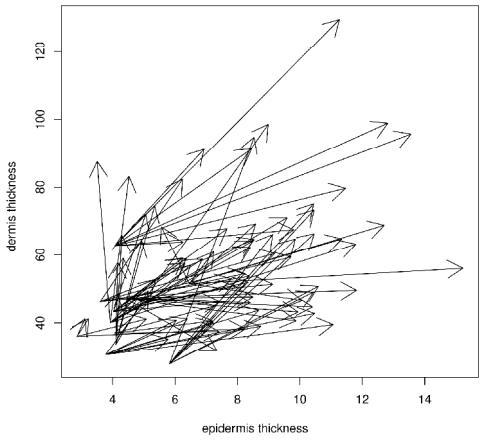

Fig. 3. Vectors of thicknesses' change for pairs of healthy skin-sick skin. Arrows show changes during the disease process. Organization of the plot similar to Fig. 2.

To come up with a statistical model able to provide a diagnosis based on thicknesses of epidermis and dermis we tried to fit a generalized linear model for Bernoulli distributed response variable [8]. It allows to describe an influence of many parameters (input variables) on the final condition (output variable). The parameters were chosen as follows: as the input variables, explaining in the model the value of the output variable, thicknesses of epidermis and dermis were used. Additionally we tried a model including an interaction between epidermis and dermis. As the output parameter the skin status: observed morphea or healthy skin was selected. The calculations were conducted using the "R" statistical package [9]. As both models (with and without interaction between predictors) were fitted and there was no significant difference in the quality of models, we settled with "status explained by epidermis and dermis measurement" as a minimal adequate model.

The calculations' results are presented in Table I. They can be interpreted that the logarithm of probability *P* of the given

thicknesses values can be attributed to a morphea case is given by the formula:

$$\log\left(\frac{P(\text{new change})}{P(\text{healthy skin})}\right) =$$

$$= B_0 + B_1 \cdot (\text{epidermis thickness}) + B_2 \cdot (\text{dermis thickness})$$

Table I. PARAMETERS OF THE MODEL FOR SKIN CHANGE

Parameter	Value	Std. dev.	*p*-value
intercept (B_0)	11.20061	1.75623	1.80e–10
epidermis thickness (B_1)	–1.18113	0.21004	1.87e–08
dermis thickness (B_2)	–0.09265	0.02213	2.84e–05

The results indicate statistically significant influence of the skin thickness changes for its status. The last column of Table I presents *p*-values describing which variables best explain the result (the variables with lowest *p*-values). It is worth mentioning that *p*-values are below 0.01 which is typically classified as a very significant influence. We can see that both epidermis and dermis thicknesses are important to explain skin status.

Taking into consideration the directions of the changes during the disease process (Fig. 3) together with the presented results it can be concluded that the sick areas are characterized by increased thickness of epidermis with smaller relative changes of dermis thickness in a certain range. The areas in the thicknesses *xy*-space describing the classification of each measurement are presented in Fig. 4. The probability of classification of a given result to "healthy" group (blue) or "sick" (red) is given by an intensity of color. The more intense color means better classification. Whitish areas are border zones, where the classification is unclear.

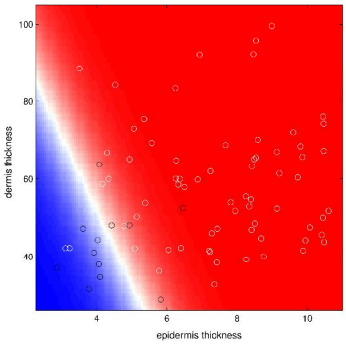

Fig. 4. Classification areas of changes according to epidermis and dermis thicknesses measurements as given by the mathematical model. Black circles—healthy skin, white circles—changed skin measurements. Blue area (bottom left) denotes healthy skin range, red area (center to right and top) denotes sick skin range of parameters.

B. Discrimination procedure

The proposed fitting model, based on simple parameters measured on USG images, helps to determine the factors most influencing the status of the skin. Although it provides a formula to estimate the probability of classification for a given measurement, in practice it is a rather difficult procedure for a routine use. Knowing that both epidermis and dermis thickness should be taken into consideration but with different strength, we propose a simplified approach for classification of the skin status. It may be based on the estimating the Mahalanobis distance [10] of the given measurement from the sick or healthy group of measurements. The Mahalanobis distance measures a distance of a given point from a group of points with correction for the shape of that group. Our measurements for skin areas properly diagnosed as healthy or as sick will form two groups. Classification of a new measurement can be estimated by calculating a difference between distances of that measurement to both groups.

To measure the average discrimination power of the Mahalanobis distance approach we randomly chose groups of 70% measurements of our healthy and sick skin thicknesses, separately. These groups were treated as the learning samples. The rest 30% of measurements were used for testing the method by measuring the Mahalanobis distances of the test points from the previously selected „healthy skin" and „sick skin" learning samples. The point was classified as belonging to the „sick skin" group when the distance from the „sick skin" group was smaller than the one from the „healthy skin" (and vice-versa). After 1000 repetitions of such procedure we got the average result of 81.5% correct classifications.

III.CONCLUSIONS

High frequency ultrasonography is a valuable non-invasive diagnostic technique with applications in dermatology. Some dermatological diseases may be diagnosed not only by skin color or physical parameters on the skin surface, but additionally they exhibit characteristic features or changes in deeper layers when comparing to a healthy skin.

The analysis of diagnostic process on USG images can provide a tool for classification of observed properties based on parameters estimated earlier by an expert. The statistical approach applied here allowed for determination of a relation between measured values and the status of the skin confirming the dermatologist visual expertise. During the model fitting procedure we get information which parameters contribute most to the obtained results, together with their statistical significance level. Later, this methodology can be extended for differentiating more classes of measurements, for instance later stages of morphea or even other diseases, depending on the collected material. When bigger sample of images is available, such analysis may be helpful in quantitative evaluation of advance of the disease or effectiveness of the applied treatment. Moreover, it was shown that the statistical analysis of the sick-healthy skin images with application of the Mahalanobis distance measurements was able to provide over 81% correct skin classifications.

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