STATISTICAL PROPERTIES OF ECHOSIGNAL OBTAINED FROM HUMAN DERMIS IN VIVO

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ABSTRACT: The paper presents the classification of the healthy skin and the skin lesions (basal cell carcinoma and actinic keratosis), basing on the statistical parameters of the envelope of ultrasonic echoes. The envelope was modeled using Rayleigh and non-Rayleigh (K-distribution) statistics. Furthermore, the characteristic parameter of the K-distribution, the effective number of scaterrers was investigated. Also the attenuation coefficient was used for the skin lesion assessment.
The comparison of the results obtained for the region of skin where the pathological states were diagnosed with the results obtained for healthy skin has shown differences in the values of attenuation coefficient and effective number of scatterers (M). The attenuation coefficient was higher in the case of pathological state of the skin. The effective number of scatterers, obtained for the skin cancer was lower comparing to the value obtained for healthy skin. No differences were found in the values of M parameters calculated for healthy skin and precancerous state. The results, indicate that the combination of quantitative ultrasound parameters, has the potential for extracting information useful for the skin conditions characterization.

KEYWORDS: statistics, K-distribution, Rayleigh distribution, ultrasonic scattering, human dermis

INTRODUCTIONS

The ultrasonic echo-signal, received by transducer, is formed from the summation of partial echoes scattered from the tissue inhomogeneities. The interference of waves, reflected from the randomly located scatterers results in speckles formation, which in ultrasonic images can be modeled as random process whose statistical features depend on the tissue class. When the number of scatterers contained in the resolution cell and involved in the signal formation is large, speckles intensity (signal envelope) is Rayleigh distributed. In a case when scatterers number is low the Rayleigh distribution is not applicable. In this case the envelopes of echoes from tissue may be modeled in terms of non-Rayleigh statistics.

Although, the examinations of statistics of the ultrasonic signals for their potential to classify the tissues types have been studied [1],[2], in the case of the skin tissue such studies have not been widely carried on. Raju and Srinivisan [3] studied *in vivo* the statistics of envelope of high-frequency ultrasonic backscatter signal from normal human dermis and subcutaneous fat. They found that the Generalized Gamma, K and Weibull distributions modeled the envelope statistics well while the Rayleigh distribution provided poor fit. Raju and Swindells [4] noted the need of diffraction correction during the statistical analysis of echo signal. They showed that diffraction affects the echo statistics parameters due to variation in the beam size with the distance.

Our research was concentrated on the K distribution as a suitable description for modeling statistics of envelope of signal obtained from human dermis *in vivo*. Also, the classification of healthy skin, skin with actinic keratosis and basal cell carcinoma based on the characteristic parameter of K distribution - the effective number of scatterers and the attenuation coefficient is presented. The methods used for the determination of the attenuation coefficient were developed in our previous study [5].

Figure 1 presents histological images of healthy skin (a) basal cell carcinoma (b) and precancerous state of skin – actinic keratosic(c). The structural differences between (a) and (b) are clearly visible, while the differences between (a) and (c) are not evident.

a) b) c)

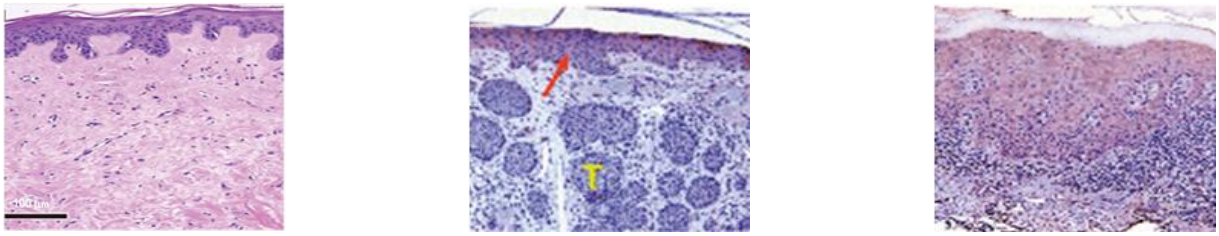

Fig.1 The histological pictures of healthy skin (a) basal cell carcinoma (b) and precancerous state - actinic keratosis (c).
Pictures adapted from:
http://www.nature.com/jid/journal/v125/n4/fig_tab/5603564f4.html#figure-title

STATISTICS OF THE ECHO-ENVELOPE

The echo signal from the biological tissue can be modeled as the sum of individual backscattered signals from the single scaterers within the medium. Backscattered signal of each individual scatterer can be represented as a phasor. The components may have both, random lengths (amplitudes) and random direction (phases) in a complex plane. When amplitude and phase are the random variables due to scatterers properties and position, the sum is also random. In this case, the tip of phasor representing echo signal is found at the "random walk", corresponding to the end-to-end sum of N random phasors . Using the phasor notation [6,7] echo signal can be described as resulting random phasor sum:

$$\mathbf{S} = Se^{j\theta} = \sum_{i=1}^{N} \mathbf{s}_i = \sum_{i=1}^{N} s_i e^{j\varphi_i} \tag{1}$$

where **S** (a complex number) represents the resulting phasor, *S* describes the amplitude and θ describes the phase. The $\mathbf{s}_i$ represents *i*th component of phasor in the sum (s_i and φ_i are the amplitude and phase $\mathbf{s}_i$, respectively).

If amplitudes s_i and phases φ_i are statistically independent, uniformly distributed and assuming that the $N \to \infty$, then using the central limit theorem, the joint probability distribution function *p(S)* for the real (*Re*(**S**)) and imaginary (*Im*(**S**)) parts of the resulting phasor becomes:

$$p(S) = \frac{1}{2\pi\sigma^2} e^{-\frac{(\mathrm{Re}(\mathbf{S}))^2 + (\mathrm{Im}(\mathbf{S}))^2}{2\sigma^2}} \tag{2}$$

It follows, that the envelope is statistically described by the Rayleigh distribution, whose probability density function (pdf) is given by:

$$p(S) = \frac{S}{\sigma^2} e^{-(\frac{S^2}{2\sigma^2})} \tag{3}$$

In typical medical applications the envelope of the backscatter signal is Rayleigh distributed but in case of skin tissues the following conditions leads to the necessity of applying another kind of distribution: the number of scatterers per resolution cell might not be large enough or the scatterers might not be located randomly (due to periodicity, clusterings, etc.).
Therefore, in this study also non-Rayleigh probability density function was tested. The distribution, which is able to model the statistics of envelope of signal under varying conditions, is the K distribution [8][9], which pdf is given by:

$$p(S) = 2(\frac{S}{2})^M \frac{b^{M+1}}{\Gamma(M)} K_{M-1}(bS) \tag{4}$$

where $b = \sqrt{\frac{4M}{E[S^2]}}$ and $K_\beta(\cdot)$ is modified Bessel function of the second kind of order β, $\Gamma(\cdot)$ is the standard Gamma function. Jakeman and Pusey [8] have shown that the parameter M which can be treated as the "effective number of scatterers" per resolution cell, is given as:

$$M = N(1+v) \qquad v > -1 \tag{5}$$

where N is the number of scatterers in resolution cell of echo imaging system, the parameter v modulates the number of scatterers to give the „effective" numbers of sctterers affecting the echo envelope statistics.
One of the method of estimation of the M parameter, is the "method of moments" proposed by Jakeman and Pusey [8] and Weng et al.[10]. In this paper, second and forth order moment method was used.
The η th central moment of envelope *S* for the K-distribution, has a form:

$$E[S^\eta] = (\frac{E[S^2]}{M})^{\frac{\eta}{2}} \frac{\Gamma(\frac{\eta}{2} + M)\Gamma(\frac{\eta}{2} + 1)}{\Gamma(M)} \tag{6}$$

For $\eta = 2$, $E[S^\eta] = E[S^2]$, the normalized central moment $\eta = 4$ is given by:

$$r_4 = \frac{E[S^4]}{[E[S^2]]^2} = 2(1+\frac{1}{M}) \tag{7}$$

so

$$M = \frac{2}{r_4 - 2} = \frac{2}{\frac{E[S^4]}{[E[S^2]]^2} - 2} \tag{8}$$

In equation (5), it is easy to see, that the "effective number of scatterers" estimated by the K distribution model, depends on the actual number of scattering sites per resolution cell as well as the uniformity of backscatter coefficient. The type and distributions of scatterers are intrinsically related to the type of tissues that the ultrasound beam is passing through. Therefore, the M parameter can be used to distinguish between regions differing in special density of scatterer or between regions of varying scatterer's cross-section and in consequence can be used as a parameter for tissue characterization.
By comparing the distributions of the skin data envelopes to the K distribution, and Rayleigh distribution, the validity of both distributions as the accurate descriptors of the skin scattering was investigated in this work.
The goodness of the fit of K-distribution and Rayleigh distribution to the empirical histograms was evaluated using the mean square error (MSE). The small value of MSE indicates the good fit of the distribution to the empirical data.

MEASURMENT PROCEDURE

Skin tissues were examined *in vivo*. The measurements were performed in the dermis at the various parts of the body of the patients of Dermatology Clinic. Three kinds of data was obtained. The measurements were carried out in the regions of skin where the basal cell carcinoma was diagnosed and in the regions where the precancerous states of the skin were localized. Also, for all the patients the data from healthy fragments of skin was recorded.
Figure 2 illustrates the examples of the B-mode images obtained for the analyzed states of the skin. Figure 2 shows a B-scan of the healthy skin (a), precancerous state of skin (b) and basal cell carcinoma (c), (the white frame indicates the ROI).

a) b) c)

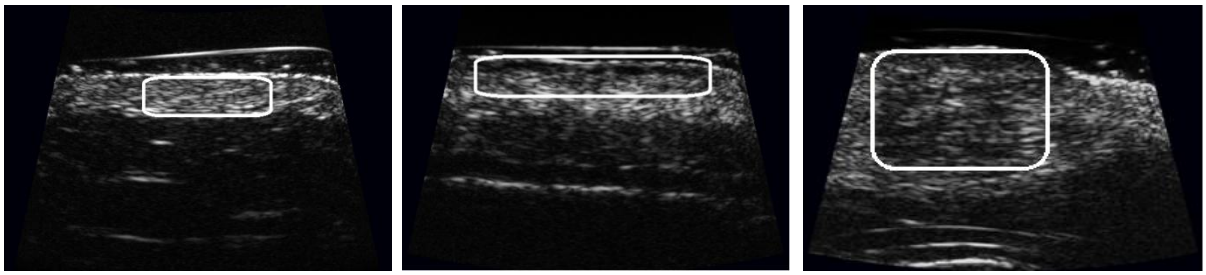

Fig.2 B-mode images of healthy human dermis (a) precancerous state of skin (b) and basal cell carcinoma (c) with marked the ROI

The skin echoes were acquired with the skin scanner, operating at the frequency of the 25 MHz. The scanner was developed in our laboratory [11]. It performed a sector scan with the image frame rate up to 10 Hz. The transmitted signal and scattered echoes were sampled at 200 MHz frequency with 12 bits resolution. In this study we have used a 20 μm thick

spherical transducer (with 3 mm diameter, 8.6 mm focal length) made of the modified PZT 37 deposited on the PZT substratum using the thick-film technology (Ferroperm, Denmark).

SIGNAL PROCESSING

Prior to the statistical evaluation of the received RF signals it was necessary to compensate the signal for the Time Gain Control (TGC) and for the attenuation in the tissue.

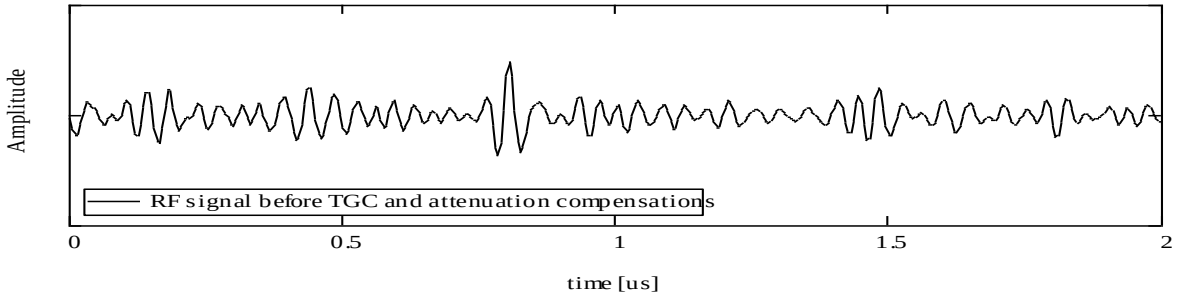

Fig.3 RF signal before the TGC and attenuation compensations and its envelope

The attenuation coefficient $\alpha(f)$ of the skin was determined for every case separately, using the spectral difference technique based on the comparison of the power spectra of the signals backscattered at different depth in the tissue [5].
For the compensation of attenuation the following algorithm was used [12]. First, the spectrum of attenuated signal (FA) was calculated. Next, the synthesis of a new signal $F(\cdot)$ on the basis of spectral components of the backscattered signal was performed. During the synthesis, the amplitudes of spectral components were increasing with the increasing value of the depth co-ordinate corresponding to the penetration depth and the value of attenuation coefficient α_0. This process is described by the formula:

$$F(t_i) = \sum_{k=1}^{G} FA_k \exp(\alpha_0 \cdot f_k \cdot v \cdot t_i) \cdot \exp(-j \cdot 2 \cdot \pi \cdot f_k \cdot t_i) \tag{9}$$

where k stands for the index of the spectral component, f_k denotes frequency, FA_k is a complex spectrum of backscattered signal, v denotes phase velocity of the longitudinal acoustic wave in the skin and α_0 is the attenuation coefficient, $t_i = i \cdot \delta t$ stands for time, where δt is a time step given by the signal sampling rate. The summation is carried over the whole range of frequencies of backscattered signal (G). The real part of $F(\cdot)$ is the desired backscattered signal compensated for attenuation.
After applying the compensation procedures the Hilbert transform was used to obtain signal envelope. Fig.4. shows signal after the TGC and attenuation compensation and its envelope.

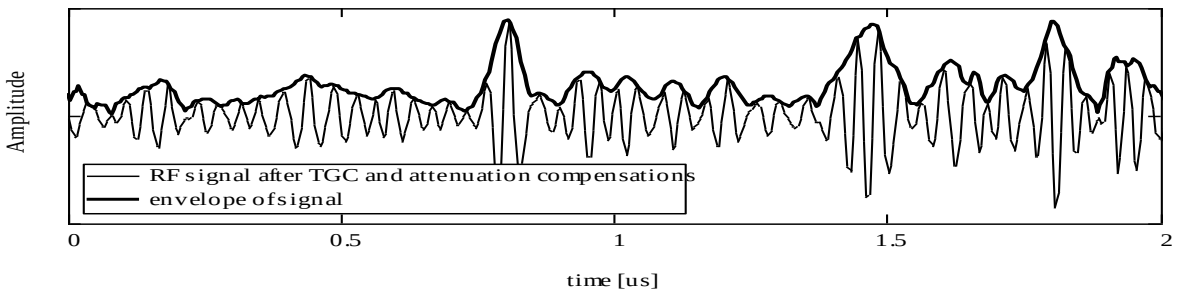

Fig.4 RF signal after the TGC and attenuation compensations and its envelope

THE INFLUENCE OF FOCUSING ON THE M PARAMETER

The computation of quantitative parameters requires compensation for the system dependent effects, because the recorded signal is dependent on both the tissues, as well as the device used in recording the signals. When focused transducer is used, variations in beam size along the path of the beam, would lead to changes in the number of scatterers contributing to resultant echosignal from the tissues (at the focus, the beam size is small and hence smaller number of scatterers contribute to the resultant signal comparing to the place away from the focus where the beam is broader). Therefore, the zone near the focus where the influence of the focusing on the results (the effective number of scatterers) is negligible was determined empirically.

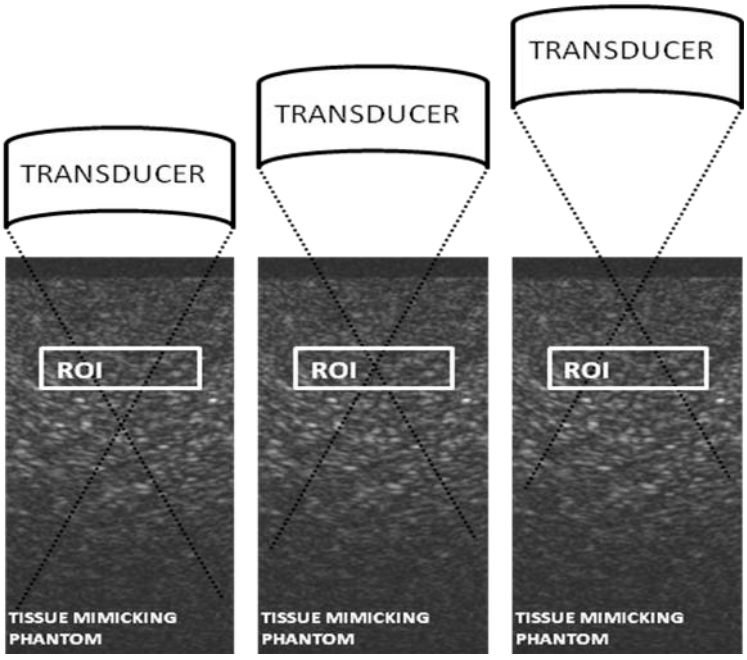

Fig.5 The diagram of measuring system which was used in experiment to determine influence of focusing on the value of the M parameter. The data was collected from the same ROI placed at varying distances from the focus.

For each of the 20 transducer settings the same ROI of tissue mimicking phantom was analyzed to study the variation of statistical parameters with the change of distance from the focus. The transducer was axially moved and the data was collected from 20 locations spaced 0.25 mm. The measurements were done so that the transducer was focused at different depths. For one of them, the ROI was positioned at the transducer's focal zone and for the other the ROIs were positioned above and below focal zone.

The effective number of scatterers was computed for all the 20 locations using the methods described in previous section.

The experiment has shown the influence of the focusing on the variations of the values of M parameter. Figure 6 illustrates the changes of the effective number of scatteres as a function of the distance from the focus. The curve was helpful in the determination of the zone where the influence of focusing on the value of M parameter could be neglected. We have found that in the 2 mm length zone centered at the focus the M parameter is almost constant ($\pm$20%). So, during analysis of data from the skin tissues, the effective number of scatteres was calculated for the ROIs which were localized in the distance from the focus of the transducer not exceeding 1mm.

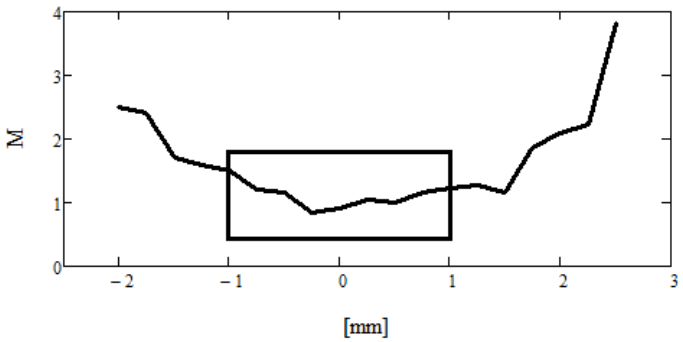

Fig.6 The curve illustrates the variation in the value of the effective number of scatters as a function of the distance from the focus

RESULTS

To determine the applicability of the K distribution in modeling the statistics of the ultrasonic backscatter from human dermis, a comparison between histogram of experimental data obtained from healthy human skin and the K and Rayleigh distributions were done. Fig. 7 shows that the histogram of echo-envelope signal of the dermis is well described by K distribution, whereas the Rayleigh distribution does not successfully fit the experimental data.

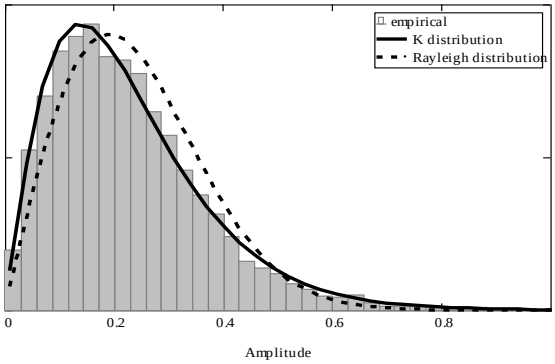

Fig. 7 Theoretical Rayleigh and K distribution and histogram of empirical data obtained at the nape of neck.

Table 1 presents the mean square error (MSE) values for the comparison of the empirical data obtained from healthy skin and the K- and Rayleigh distributions.

	Skin in various parts of body										
	I case	II case	III case	IV case	V case	VI case	VII case	VIII case	IX case	X case	MEAN
K	0.014	0011	0.013	0.009	0.011	0.013	0.011	0.008	0.014	0.021	**0.012**
R	0.087	0.085	0.09	0.084	0.076	0.081	0.087	0.089	0.073	0.078	**0.083**

Table 1 MSE coefficient calculated for the histograms of the signal envelopes measured from the skin backscatter and theoretical K and Rayleigh (R) distributions

On average, the error (mean MSE) between the K-distribution and empirical data was eight times lower than the error between the Rayleigh distribution and experimental data, pointing to a closer fit of data to the K-distribution.

Next the attenuation coefficient and the M parameter were calculated, using ultrasonic signals obtained, from the pathological region of skin and for comparison for region with non pathological changes. The results, obtained for the four cases of the BCC are presented in the table 2.
For all patients, the attenuation coefficient calculated for the fragments of the healthy skin was significantly lower than for basal cell carcinoma and ranged from 1.98 dB/(cm·MHz) to 2.25 dB/(cm·MHz) with the mean value of 2.17 dB/(cm·MHz). The data obtained from the BCC lesions showed the attenuation coefficient value from 3.12 dB/(cm·MHz) to 3.9 dB/(cm·MHz) with the mean value of 3.48 dB/(cm·MHz).

BCC	AC	M	Healthy skin	AC	M
I	3.12 dB/(cmMHz)	1.117	**I**	1.98 dB/(cmMHz)	1.989
II	3.4 dB/(cmMHz)	1.165	**II**	2.25 dB/(cmMHz)	1.611
III	3.9 dB/(cmMHz)	0.908	**III**	2.25 dB/(cmMHz)	1.611
IV	3.5 dB/(cmMHz)	1.192	**IV**	2.2 dB/(cmMHz)	1.929

Table 2 The AC (attenuation coefficient) and M (effective number of scatterer) calculated for basal cell carcinoma and healthy skin.

Fig.8 shows examples of the histograms determined for the healthy skin (b) and for the basal cell carcinoma (a). It's easy to see that the shapes of histograms are different. The values of the effective number of scatterers also were different for healthy skin and for skin with the BCC.

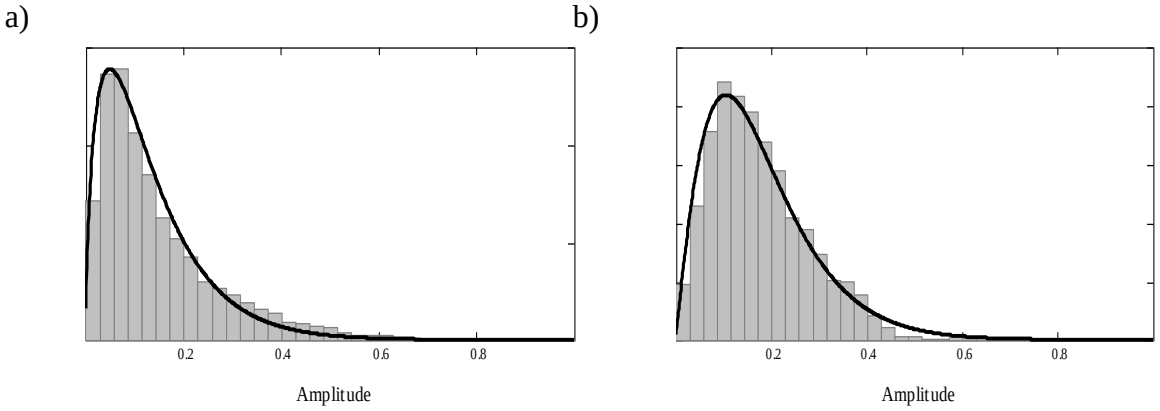

Fig.8 The histograms determined for skin with diagnosed Basal cell carcinoma (a) and for healthy skin (b)

For all patients values of the effective number of scatterers obtained for skin cancer were lower than the values of the M parameters calculated for healthy skin. The mean value of effective number of scatterers for healthy skin was equal to 1.783 and ranged from 1.611 to 1.989 and the mean value of parameter M for skin lesions was equal to 1.095 and ranged from 0.908 to 1.192.
In this study also the precancerous state of skin was analyzed. From medical point of view it is very important to find the methods which may be helpful in detecting the precancerous state of the skin. Two cases of the precancerous skin lesion were analyzed in the same way like basal cell carcinoma. The results are demonstrated in table 4.
Similarly like in the case of analysis of the BCC, the second and fifth column presents values of the attenuation coefficient for the precancerous state of the skin and for the healthy skin

respectively. The values of the AC in the both cases of the precancerous skin lesions are higher than the values of the AC obtained for the fragments of skin with no pathological changes. The mean results, obtained for skin disease and healthy skin were equal to 3.01 dB/(cm·MHz) and 1.927dB/(cm·MHz), respectively. The third and sixth column of the below table, shows values of the effective number of scatterers.

Precancerous state	AC	M	Healthy skin	AC	M
I	3.07 dB/(cmMHz)	1.917	I	2.17 dB/(cmMHz)	2.04
II	2.95 dB/(cmMHz)	1.954	II	2.32 dB/(cmMHz)	1.814

Table 2 The AC and M parameter calculated for the precancerous skin lesion and healthy skin.

Analysis of the two cases of the precancerous skin lesions has demonstrated no significant differences between the effective number of scatteres computed for skin disease and healthy skin. The main value o the M parameter was equal to 1.935 for precancerous skin state and for the healthy skin was just a slightly lower– the main value was equal to 1.927.

CONCLUSION

Our preliminary study shows that the quantitative ultrasound can provide additional information, potentially useful for skin lesions diagnosis. The results are encouraging however a lot of further study must be performed to assess diagnostic usefulness of the proposed method. Medical description of the remodeling of tissue structure in the BCC and AK lesions explains the experimental results. BCC is characterized by the clusters of tumor cells which are much bigger than the healthy skin cells and AK lesion cells too. The K distribution is sensitive to the number and uniformity of scatterers comprised within the resolution cell. The drop of M parameter of K distribution for BCC can be explained by the lower spatial density of scaterrers (cell clusters) comparing to the spatial density of cells in healthy skin and AK lesions. Also, the attenuation coefficient was found to be a significant descriptor of the lesion. The attenuation was higher for carcinoma and precancerous skin lesions comparing to healthy skin. However, the low number of studied cases does not allow us to draw far-reaching conclusions regarding the usefulness of attenuation coefficient and M parameter of K-distribution for skin lesions diagnosis.

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