

# Breast carcinoma tissues characterization using statistics of ultrasonic backscatter

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## Summary

The Ultrasonix SonixTouch scanner with the special RF block was used to collect B-mode images together with appropriate RF echoes from the pathological and healthy breasts regions of patients with diagnosed malignant and benign breast lesions. The RF data were processed for the statistics of the backscattered echo signals assessment (K distribution and effective density of scatterers –  $M$  and Nakagami distribution and its shape parameter  $m$ ). The comparison of signals recorded from malignant and healthy tissues showed, that in 80% of examined cases the values of the statistical parameters  $M$  were higher for carcinomas tissues than for healthy tissue. Beside of that in the case of benign lesions obtained results was able to distinguish the fibroadenoma from the other with probability of 75%.

ACS no. xx.xx.Nn, xx.xx.Nn

## 1. Introduction

Breast cancer is the most frequently diagnosed cancer among women between 40 and 60 years old. According to the report of the World Health Organization WHO, 0.5 million women die each year because of it. Breast cancer is the second – after lung cancer – cause of death of Polish women.

In Poland, data from 2010 indicate that there were 15 784 new cases of breast cancer, and 5226 deaths of women [1]. In the world the breast cancer is also considered as the most widespread neoplasm – based on the reports, as much as 34% of women with neoplasm is suffering because of breast cancer. This number puts the breast cancer in the first place among the causes of mortality in middle-aged women. Lowering a scale of disease incidences can be achieved by prevention, early detection of lesions as well as proper treatment [2]. According to the American Cancer Society, the mammographic examination is now one of the main non-invasive imaging methods used for diagnosis of breast cancer. Mammography (MMG)

is a screening method, its use reduced mortality of women with breast cancer. However, the sensitivity of MMG in the breast glandular structure is 30-48 % and 80-90 % in women with fatty breast [3, 4]. About 50 % of women under 50 years old and 30 % of women over 50 years old have glandular breasts. In addition, this type of breast structure quadruples the risk of breast cancer compared to women with fatty breasts construction.

At present, a growing importance of tissue imaging on the basis of the ultrasound techniques is being noted. The main trend of the ultrasound research refers to the improvement of images in order to identify pathologically altered areas. For example Zhang et al. and Shi et al. [5,6] have proposed a number of algorithms for improving the quality of the B-mod images. Then, on the sonograms generated by this method many research groups [7,8,9] applied different techniques, such as EPSO (*Eliminating Particle Swarn Optimalization*) [10] or MFPCT (*Modified Fuzzy Possibilistic C-Means*)

*Technique*) [11] algorithms to provide an improvement in detecting the boundaries of the tissue regions affected by cancer.

Nevertheless, only a small part of information contained in the ultrasound echoes is used in the imaging of tissues. Up to now the only one extended clinical trial is dated from 1995, [12]. The authors have analyzed seven hundred fifty ultrasound images in order to determine whether the “raw” ultrasound images enable accurate distinguishing between benign breast tumors of an undefined character or malignant nature, and whether these differences can be determined at a level which ensures avoiding thin-needle biopsy. The results confirmed that the method based on the imaging only, does not always enable an adequate classification of lesions as well as a correct diagnosis. Due to limitations of the diagnostics resulting from the fact that only the B-mode images are analyzed, the quantitative ultrasound techniques (*QUS-Quantitative Ultrasounds*) for parameterization of tissues, gain a special significance, mostly assessing breast lesions using a parameter called *backscatter coefficient* (BSC), in particular for identification of differences between three types of tissues: adipose tissue, breast parenchyma and invasive ductal carcinoma of breast. The obtained results revealed differences in values of the BSC parameter and its frequency dependencies. In the case of the analysis of breast parenchyma the backscatter coefficient reached one order higher values than the values obtained in the case of the adipose tissue or carcinoma. This coefficient exhibited increased frequency dependence as well. There is another approach to characterization of breast tissue besides analyzing the frequency dependence - a method based on modeling the tissue as a medium of stochastically variable function of probability density. Molthen et al., [13] showed that the Rayleigh distribution commonly used in statistical analysis of ultrasound signals is not appropriate for the breast tissue. Shankar et al., [14, 15, 16] applied the K and the Nakagami distributions in order to distinguish benign changes from the malignant lesions occurring in breasts. The Nakagami distribution has been the most frequently adopted model in the context of tissue characterization, probably due to its simplicity.

The Nakagami model was then systematically used in various medical ultrasound imaging fields; ophthalmology [17], vascular [19, 20, 21], and breast cancer [22]. The K-distribution was used in the context of breast cancer and skin lesions [23]

classification. More recently, the homodyned K-distribution was used for cardiac tissue characterization [24] and cancerous lesion classification [25,26,27,28] and a model of mixtures of Rayleigh distributions was adopted for liver fibrosis quantification [29]. The Nakagami distribution besides providing purely quantitative information was applied also as a tool for the development of the so-called Nakagami's images. Procedures for developing the images of this type were presented by Tsui et al.[22]. This tool was applied by Liao et al. [30] as a method providing more precise determination of the contours of lesions. In recent paper Shankar [31] is developing a new model for tissue with microcalcifications. He modified the Nakagami model to the McKay type I density function for speckle factor exceeding 2, so for situation approaching breast calcification. This hypothesis was not as yet verified in *in vivo* examinations.

In diagnostic process of breast diseases, the basic role is attributed to unification of examination reports both mammographic and sonomammographic. The crucial role in this regard is attributed to BIRADS classification that has been already implemented by Polish Ultrasound Society. BIRADS classification, based on morphological features of breast structures and pathological lesions, enables the sharp demarcation of benign lesions from malignant ones and constitutes the group of suspicious lesions. It evaluates in % the risk of malignancy and precisely forms the recommendations for subsequent follow up and diagnostic procedures.

In BIRADS classification category 3 denotes lesions probably benign with probability of malignancy to approximately 2% and the recommends the choice of biopsy of imaging follow up. The group 4 denotes the suspicious lesions with probability of malignancy in the range from 2% to 95%. In this group the procedure of choice is biopsy of the lesion.

The optimal solution would lead to to eliminate the biopsies completely or to a large degree. However, the classical ultrasound in B-mode enriched with evaluation of blood flow using power Doppler and even with elastography, is not accurate enough to differentiate between benign and malignant breast lesions and cannot replace biopsy, which is an invasive procedure with error burden.

The goal of this study was to find the quantitative measure of the breast tissue backscattering properties for differentiating the changes of tissue structure induced by benign and malignant breast lesions.

Presented approach constitutes the progress that is hoped to bring new solutions in ultrasound diagnostics of breast masses. The description of relation of characteristics of ultrasound echo signals to the structure of the tissue under examination will eventually enable objective and reproducible characterization.

## 2. Materials and methods

### 2.1 Data Acquisition

The ultrasound radio-frequency signals were acquired using a ultrasound scanner (Ultrasonix SonixTouch), with the raw RF data digitalized at the sampling frequency 40MHz. The linear array with the central frequency 10MHz and 128 elements was used.

Breast tissues were examined in vivo. A group of women with diagnosed benign and malignant breast lesions participated in this study (30 and 13 cases, respectively). Three types of data: traditional B-mode image set of RF echo-lines, TGC gain curve were stored for the breast regions where the tumors were localized. For all cases, the data were recorded from two perpendicular sections (vertical and horizontal). For all the patients the reference data from the healthy fragments of the breast tissues were also recorded. The examples of B-mode images of breast lesions in two sections: horizontal and vertical are shown in Fig. 1.

The received sequences were first logcompressed and next envelope detected and displayed. The compressed RF data were stored separately, together with TGC (Time Gain Control) curve that was used to increase the quality of breast images. One image consists of to 500 RF echo lines. The number of samples in every RF signal was depending on the choice of the depth of examination. Once the RF data were collected the

further processing and analysis was done off-line Mathcad (Mathsoft PTC, USA) software.

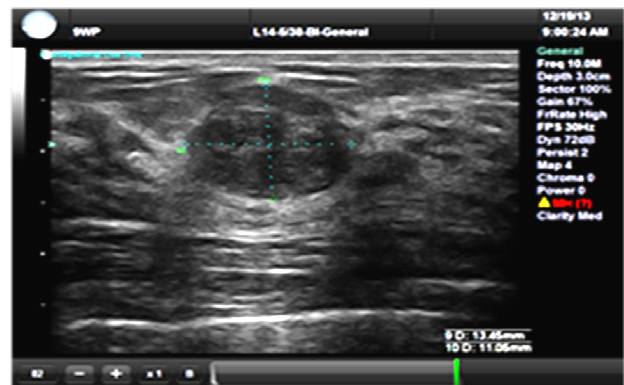


Figure 1. B-mode images of the lobular tumor

### 2.2 Quantitative parameters –Attenuation coefficient

The attenuation coefficients of the breasts tissues were determined using the spectral difference technique based on a comparison of the power spectra of the backscattered signals recorded at two different depths and denoted as and respectively, where  $i$  stands for the number of considered echo line and  $f$  denotes frequency. Only the RF data from selected regions of interest (ROI) were used. The procedure was as follows: first, from the selected part of the scattered echo-signal, two segments,  $0.45 \mu s$  long and separated by distance , were weighted, using a Hanning window. These segments were next Fourier transformed and the power spectra were calculated. The spectra from the same depth were averaged over all echo lines within the ROI (not less than 25 lines) yielding two averaged spectra and and the attenuation coefficients were estimated from their log-ratio. The longitudinal wave velocity of 1540m/s was assumed. The following formula was used to determine the attenuation coefficient:

$$\alpha(f) = -\frac{10 \log \left( \frac{\left| \frac{1}{N} \sum_{i=1}^N S_{B_i}(f) \right|}{\left| \frac{1}{N} \sum_{i=1}^N S_{A_i}(f) \right|} \right)}{4\Delta z} = -\frac{10 \log \left( \frac{S_B(f)}{S_A(f)} \right)}{4\Delta z} \quad (1)$$

where  $N$  is the number of echo lines in ROI.

### 2.3 Data preprocessing

Attenuation in the examined tissue results in the decay of the wave amplitude with depth. The latter is reduced by a TGC system of the receiving amplifier, what is useful for B-mode imaging, but disturbs the estimation of quantitative parameters. The influence of the system TGC on RF echoes was compensated prior to the processing that was carried out in order to determine the attenuation coefficient of the breast and the statistical properties of the breast backscatter.

The acquired echoes, first corrected for TGC, were subsequently compensated for attenuation. A method proposed by Litniewski et al [40] was implemented. For each measured RF line the following attenuation compensating algorithm was applied. First, the spectrum of the recorded RF signal was calculated. The amplitude of each spectral component was individually compensated by increasing its value along with an increase of the pulse penetration and value of the frequency-dependant attenuation  $\alpha(f)$ . Next, a compensated signal  $RF_c$  on the basis of compensated spectral components was constructed. The process is described by the formula:

$$RF_c(z_i) = \sum_{k=0}^M FFT_k \exp(\alpha(f_k)z_i) \exp(-2\pi j f_k t_i) \quad (2)$$

where  $k$  stands for the index of the spectral component,  $f_k$  denotes the spectrum frequency component,  $FFT$  is a complex spectrum of backscattered signal.  $z_i = t_i \cdot c$  where  $c$  denotes velocity of the longitudinal wave in skin, and  $t_i = i\delta t$  stands for time while  $\delta t$  is sampling interval. The summation is carried over the whole range of frequency components of the transmitted signal (from 0 to  $M$ ). The real part of  $RF_c$  is the desired backscattered signal compensated for attenuation.

### 2.4 Statistics of echo envelope

The statistics of echo signals backscattered by a medium depends on both medium structure and spatial resolution of the scanning system that is defined by the size of the resolution cell. This size varies with pulse length and acoustic beam cross-section.

The soft tissue is often modeled as a collection of spatially distributed small scatterers [32, 33]. It can be shown that for the large number of scatterers within the resolution cell, the signal

amplitude statistics follows the Rayleigh distribution. However in biological tissue the spatial distribution of scattering elements is not uniform. Also, the scatterer density and size vary throughout the tissue. Thus, the effective number of scatterers in the resolution cell may not fulfill Rayleigh statistics condition, particularly when the resolution cell is small. In this case non-Rayleigh statistics are considered [34].

Jakeman and Tough [35] pointed out that for the low effective density of scatterers, the PDF (Probability Density Function) of the backscatter amplitude is given by the K distribution. More recently, it was shown that the K distribution describes well the statistics of the skin backscatter [36]. The K distribution is defined by:

$$p(A) = 2 \left( \frac{A}{2} \right)^M \frac{b^{M+1}}{\Gamma(M)} K_{M-1}(bA) \quad (3)$$

where  $A$  is amplitude,  $p(A)$  is probability density,  $b = \sqrt{\frac{4M}{E[A^2]}}$ ,  $K_\beta(\cdot)$  is the modified Bessel function of the second kind of order  $\beta$ ,  $\Gamma(\cdot)$  is the standard Gamma function,  $E[\ ]$  is the expectation operator,  $M = N(1 + v)$  is the effective density of scatterers within the resolution cell,  $N$  is the number of scatterers and  $v$  is the constant, depending on scatterer characteristic [37].

The effective density of scatterers estimated from 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 spatial density of scatterer or between regions of varying scatterer's cross-section, and in consequence can be used as a parameter for tissue characterization.

The effective density of scatterers ( $M$ ) can be estimated from the fourth normalized moment ( $r_4$ ) of the K-distribution [38]:

$$M = \frac{2}{r_4 - 2} \quad (4)$$

where

$$r_4 = \frac{E[A^4]}{[E[A^2]]^2} \quad (5)$$

The moments  $E[A^n]$  were directly computed from the envelopes of RF signals enclosed in ROI. Next the  $r_4$  was determined, and the  $M$  parameter was calculated using Eq. (5).

In the case when coherent component is present the K distribution is not able to model the statistics

of envelope of signal well. In that case simple but nonetheless extremely versatile solution seems to be the use of the Nakagami distribution, which enables to emulate several other distributions such as Rayleigh, Rician or homodyned K-distribution [39].

The probability density function of the Nakagami distribution  $p(A)$  calculated from the backscatter envelopes is given by:

$$p(A) = \frac{2m^m A^{2m-1}}{\Gamma(m)\Omega^m} e\left(-\frac{m}{\Omega}r^2\right) \quad (6)$$

Where  $\Gamma(\cdot)$  is the standard Gamma function. Two of the parameters, the Nakagami parameter  $m$  and scaling parameter  $\Omega$ , can be calculated using:

$$m = \frac{[E[A^2]]^2}{[E[A^2 - E[A^2]]]^2} \quad (7)$$

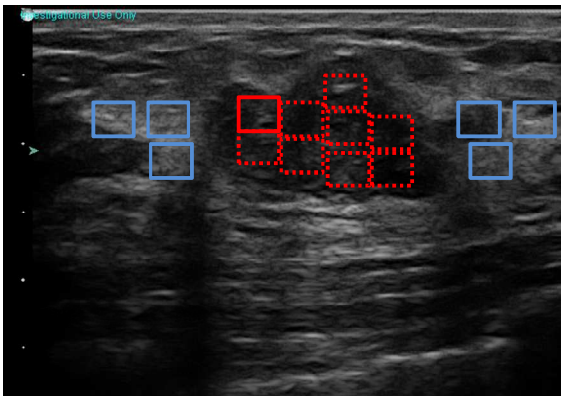
and

$$\Omega = E[A^2] \quad (8)$$

where  $E[\cdot]$  is the statistical mean.

The  $m$  parameter is particularly useful for characterizing the probability distributions of ultrasonic backscattered envelopes, including the statistical conditions for pre-Rayleigh, Rayleigh, and post-Rayleigh distributions.

The correct estimation of the shape parameters of probability density functions requires a large number of data samples. To find the size of ROIs that gives the ROI-size-independent parameters  $M$  and  $m$ , the RF data recorded from homogeneous tissue-mimicking phantom was used.



ROI\_tumor  
 ROI\_healthy

Figure 2. The example of ROIs

A set of concentric ROI squares was selected, and each square was analyzed for their respective  $M$  and  $m$  parameters. It was found that a  $4 \text{ mm} \times 4 \text{ mm}$  ROI box, corresponding to a  $3.75\mu\text{s}$  long time

window and averaging over 35 adjacent scan lines, is sufficient to obtain reliable results.

For every lesion the ROIs were chosen in that way to cover all pathological fragment of tissue. The number of ROIs was dependent on the size of the changes. The statistical analysis was done for every ROI separately. These steps were done for every lesion in two dimensions. At the end results obtained for all ROIs were averaged. In the same way the results for the healthy surroundings were calculated.

### 3. Results

The shape parameters of the K and Nakagami distributions were calculated including the compensation of the TGC and the attenuation. The results, obtained for the benign and malignant lesions, for K and Nakagami distributions are presented in Fig. 3 and Fig. 4 respectively.

For 11 patients (from 13 participated in our research), the values of  $M$  parameter calculated for malignant lesions were significantly higher than for healthy tissues.

Similarly (like in the case of the  $M$  parameter), the values of the  $m$  parameter for the Nakagami distribution for the malignant lesions were higher than the value of  $m$  measured for the breast with no pathological changes

In the case of benign lesions the relationships between the state of the tissue and the values of the  $m$  and  $M$  parameters were not observed.

In the case of use of the only one parameter it was possible to distinguish malignant lesions and healthy breast tissue with the diagnostic accuracy of 80%. In order to characterize tumors two parameters were explored:

$$M_{normalized} = \frac{M_{healthy}}{M_{tumor}} \quad (9)$$

and

$$m_{normalized} = \frac{m_{healthy}}{m_{tumor}} \quad (10)$$

The result of  $M_{normalized}$  and  $m_{normalized}$  is shown in Fig. 5. The red and blue points denote the values of parameters obtained for the benign and malignant lesions, respectively.

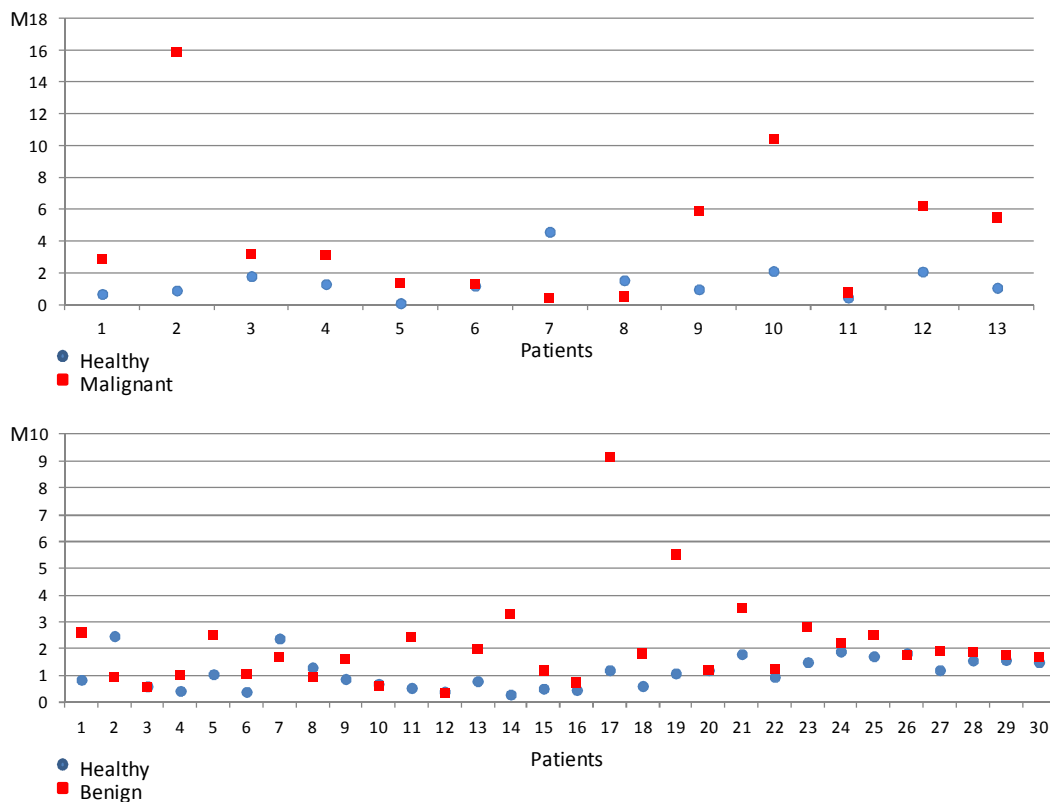


Figure 3. The value of the M parameter obtained for healthy breast tissues and malignant and benign lesions.

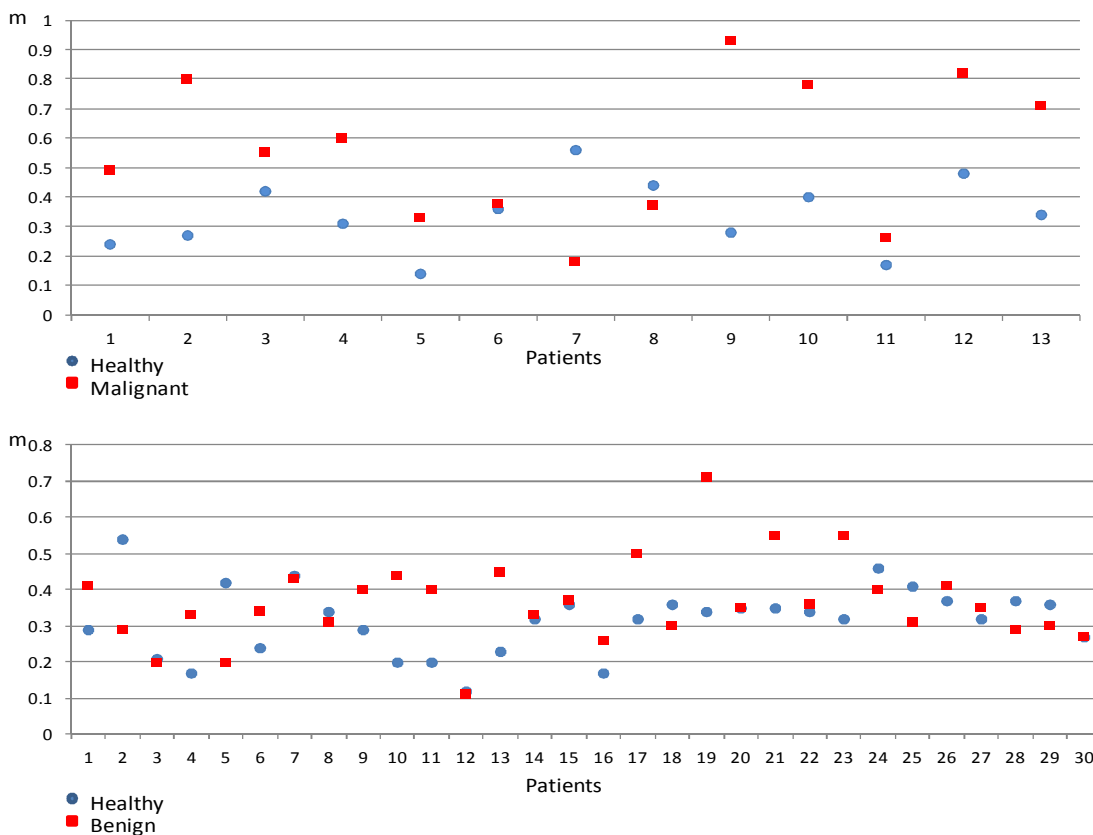


Figure 4. The value of the m parameter obtained for healthy breast tissues and malignant and benign lesions.

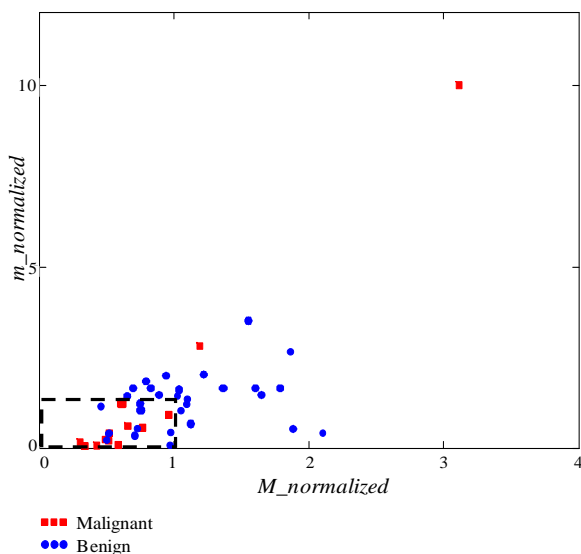


Figure 5. Normalized values of  $M_{normalized}$  and  $m_{normalized}$  parameters for malignant (red points) and benign (blue points) lesions.

#### 4. Conclusions

As it was said, the breast cancer is the most common cancer among women. The imaging techniques that will increase the effectiveness of breast cancer diagnostics are continuously sought. We propose a novel method based on statistical processing of the raw, unprocessed RF echoes signals backscattered in tissue. These data can provide the important information enabling better detection and distinguishing the breast cancer. Hence, it would enable a significant reducing the thin needle and thick-needle biopsies which are invasive procedures with the possibility of errors, as well.

The goal of our study was answering the question whatever the healthy breast tissue, benign lesions and

malignant tumors can be differentiated using, the backscattered properties of breast tissue.

Although the number of 13 malignant and 30 benign cases is rather small to draw definite conclusions, it is worth pointing out that in the 80% of the considered cases we have obtained higher  $M$  and  $m$  values for malignant lesions than the values obtained for healthy reference breast tissues. The increases sensitivity of gives a chance to distinguishing the malignant cases from surrounding healthy tissues, what is significant, especially when the lesions are small and in the standard USG images they look like a lumps of fat.

In the second approach the two normalized parameters were used. The results obtained are very promising. The malignant lesions were localized very close to the origine of the coordinate system. Only two cases were localized outside of the region marked in the Fig. 5 by the dotted lines. In the both cases the cause of that were the specific changes in the microstructure of tumor (it was ascertained by an anatomical pathology), which makes the malignant tumor similar to benign lesions.

We also decided to check various types of benign lesions. The analysis which was carried out showed that 75% of the fibroadenoma (the most common type of benign lesions) cases were localized outside of regions in which were localized malignant tumors.

In conclusion, the two combined normalized statistical parameters together allow to distinguish between malignant lesions from the group of all tumors with diagnostic accuracy of 80%. Within the benign lesions 75% were correctly statistically estimated. However 25% of the tumors were false pointed as a malignant lesions (Fig. 5) The presented approach to is very promising, introducing new information about tumor structure.

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