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Quantitative ultrasound examination of peritumoral tissue improves classification of breast lesions

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***Abstract*— Quantitative Ultrasound (QUS) methods showed high suitability for classifying malignant and benign tumors based on ultrasound data from suspicious breast lesions. Apart from differences in internal structure, malignant and benign tumors have been also shown to have different effects on neighboring tissues. In our previous work we investigated the usefulness of QUS methods based on ultrasound data from surroundings of breast tumors. The present study is an attempt to answer the question of the optimal area of the surroundings to be used. The study included 116 tumors whose malignancy was determined by histopathological examination of biopsy samples. The parameters used in tumor classification were the shape parameter of the Nakagami distribution and ten texture parameters. The Linear Discriminant Analysis and the Leave-One-Out cross-validation were used to classify tumors. Classification results were assessed based on the area under the ROC curve (AUC). The best multi-parametric classifier for intra-tumor data has reached AUC = 0.82. In case of the data from the tumor surrounding area the best classification result was AUC = 0.89 and it was obtained for the surroundings range of 5 mm.**

Keywords — quantitative ultrasound, tumor classification

I. Introduction

Breast cancer is still one of the leading causes of cancer-related death for women worldwide [1]. Early and accurate diagnosis can significantly affect further therapy. Ultrasound imaging is one of the most common techniques used in breast tumor diagnosis due to its availability and relatively low cost. Evaluation of breast tumors can be improved using quantitative ultrasound (QUS) techniques. These techniques are based on the analysis of raw ultrasound data to determine the statistical and structural parameters which characterize the tissue properties. For example, the scattering properties of a tissue can be evaluated by modelling the probability density function (PDF) of the signal envelope. Several statistical models are commonly used. One of the most often used distributions for modeling soft tissue scattering is the Nakagami distribution [2] which became very common in QUS techniques [3-10]. The texture of the ultrasound image is another property that can characterize a tissue. Some of the texture parameters can be extracted from the gray-level co-occurrence matrix (GLCM). This method was described by Haralick et al. [11] and also can be used in ultrasound classification of tumors [7, 12].

Tumor classification is generally based on data from within the lesion. There are reasons however, to also use data from a neighboring tissue [13], as it often differs in morphological features depending on the malignancy of the tumor. Benign tumors usually have a covering made up of normal cells and their borders are mostly well-defined. In turn, malignant tumors are not encapsulated and have an irregular pattern of growth. Their borders are often not well defined and they spread into adjacent tissue rather than displacing or pushing it aside.

In our previous work [14] we confirmed that that for the examined QUS parameters the classification brings better results if the data from the tumor surrounding tissue rim is used. In the present study, the efficiency of classification of breast changes using classifiers determined from the data collected from the tumor and from the data from the tissue surrounding the tumor, depending on the size of the peritumoral tissue was examined. The parameters used in tumor classification were the shape parameter of the Nakagami distribution and ten parameters determined from GLCM matrix.

II. Methods

A. Data acquisition

The acquisition of ultrasound data was carried out in the Department of Radiology, Maria Skłodowska-Curie Memorial

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Institute of Oncology in Warsaw. The study protocol was approved by the institutional review board and all patients signed the informed consent for the study. A total of 116 patients diagnosed with a suspicious breast lesion of solid BI-RADS category 3, 4, or 5 participated in the study. Each lesion was subjected to a biopsy (fine needle aspiration biopsy for BI-RADS 3, core-needle for BI-RADS 4 and 5). Based on the histopathological examination of the samples taken, 57 lesions were categorized as malignant and 59 as benign.

Each lesion was also subjected to ultrasound examination performed in accordance to the American College of Radiology BI-RADS guidelines, using longitudinal and transverse scan planes [15]. Classical B-mode data and radio-frequency (RF) post-beamformed data were acquired using a commercial ultrasound scanner (Ultrasonix SonixTouch-Research, Ultrasonix Medical Corporation, Richmond, BC, Canada) and a L14-5/38 linear probe. The transmitted pulse frequency was set at 10 MHz and the focus was set at the area within the tumor.

B. *Data processing*

Further data processing was performed offline using Matlab® (The MathWorks, Inc., Natick, Massachusetts, United States). For each image the tumor region was marked by an experienced physician. Next, its neighborhood of a certain range *r* (from 1 to 10 mm) was determined. These regions of interest (ROI), i.e. tumor and its surroundings were then a base for estimation of QUS parameters representing backscatter signal statistics and image textural features.

The backscatter statistics were assessed with use of the Nakagami distribution shape parameter μ. Its value was estimated using method of moments according to the following formula:

$$\mu = \frac{\left(E\left[A^2\right]\right)^2}{V\left[A^2\right]} \tag{1}$$

where A is the signal amplitude while E and V denote mean and variance respectively.

The textural features were represented by parameters extracted using the Gray Level Co-occurrence Matrix (GLCM) [11]. The GLCM is a matrix that contains probabilities of occurrence of certain gray tones in a pair of pixels being in a particular relative spatial position. This spatial relation was defined as vertical or horizontal displacement by 0.3 mm. The considered parameters were the contrast, correlation, energy, homogeneity, and variance. Each parameter was calculated for vertical and horizontal spatial relations separately, which gives a total of ten texture parameters.

Each parameter was calculated using a sliding window technique, which resulted in parametric maps. Pixel values of parametric maps were then averaged for both longitudinal and transverse scans together to obtain a single QUS parameter value for a given ROI type, i.e. the tumor or its surroundings.

C. *Statistical analysis*

The QUS parameters are intended to be used in tumor classification into benign and malignant groups. To assess which ROI is best for this purpose, a set of tumor classifiers was created basing on various QUS parameters for each ROI (tumor and its neighborhood of various ranges *r*). An ‘exhaustive search’ approach [16] was applied, i.e. all possible parameter combinations were included. The classifiers were obtained through the Linear Discriminant Analysis (LDA) algorithm. Cross-validation was done using the Leave-One-Out technique. Classification results were assessed based on the Area Under the ROC (Receiver Operating Characteristic) Curve (AUC).

III. Results

In the first step an overall performance of single-parameter classifiers was evaluated. The results (Fig. 1) show that the classification based on tumor surroundings is more precise than basing on the tumor itself, regardless of the surrounding rim thickness *r*. The AUC values grow until *r* reaches 4 mm, and stay stable for higher *r* values.

In case of the multi-parameter classifiers (Fig. 2) the AUC continues to growth until *r* reaches 5 mm, and decreases slightly for larger rims.

The best multi-parameter classifier was obtained for rim thickness of 5 mm. This classifier was compared with best classifiers for each r value. As shown in Fig. 3, this classifier is best or is close to the best for r ≥ 2.5 mm.

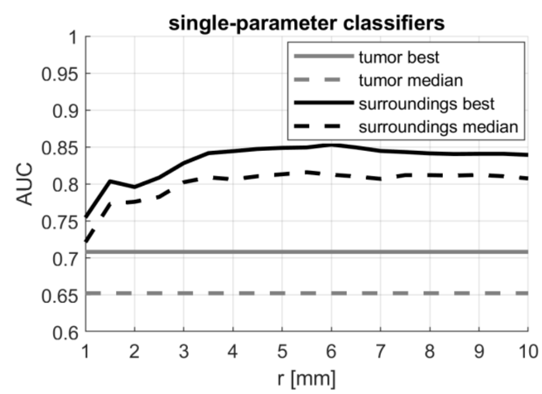

Fig. 1. AUC values for single-parameter classifiers for various ROIs: tumor and its surroundings of range r.

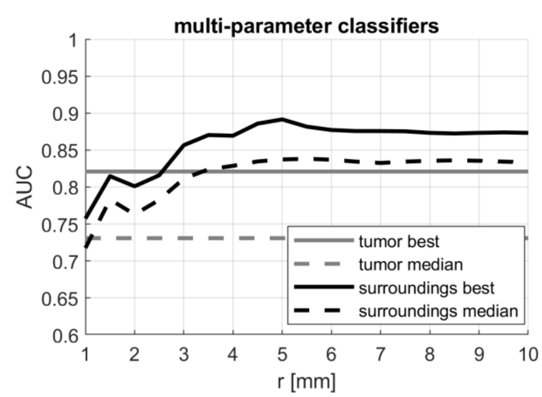

Fig. 2. AUC values for multi-parameter classifiers for various ROIs: tumor and its surroundings of range r.

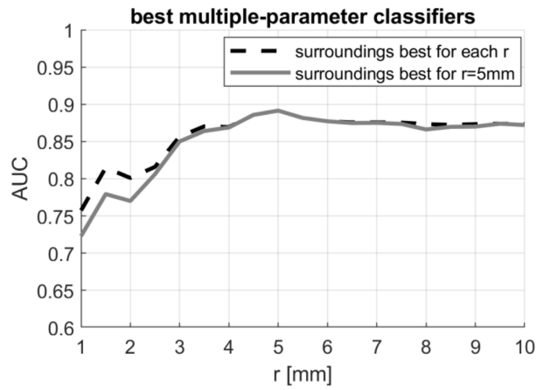

Fig. 3. AUC values for best multi-parameter classifiers optimized for each r value (dashed line) and optimized for r = 5 mm (continuous gray line).

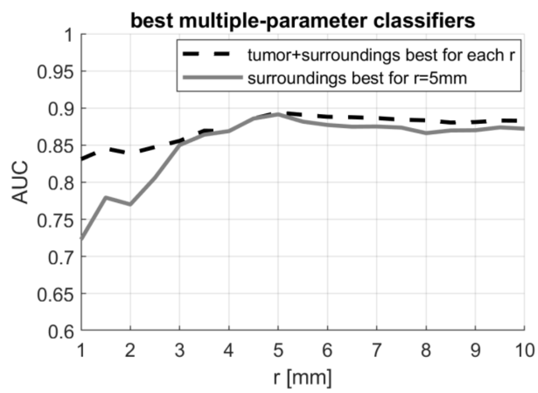

Fig. 4. AUC values for best multi-parameter classifiers: based on combined tumor and surroundings parameters optimized for each *r* value (dashed line) and based on surroundings parameters optimized for *r* = 5 mm (continuous gray line).

The last step was to check the performance of the best classifier making use of both tumor and its surroundings. When compared to the best multi-parameter classifier obtained for the tumor surrounding rim of *r* = 5 mm, the additional use of the tumor related QUS parameters does not introduce significant improvement (except for low *r*, where classification based on the surroundings only is generally poor).

IV. Discussion

The obtained results show that the optimal thickness of the tumor surrounding rim equals 5 mm. This may be explained as an interaction of two factors. The first one is the actual range of influence of the tumor on the surrounding tissue. This influence includes spreading the cancer cells into adjacent tissue, damaging it and causing inflammations. The second factor is the variance of the QUS parameters estimates. If the area of the ROI is small, then the QUS parameter value resulting from averaging of the QUS parameter map is highly uncertain. This in turn limits the classification efficiency. It appears that the 5 mm rim thickness provides enough data for averaging while still covering the area of actual tumor influence.

References

[1] J. Ferlay, I. Soerjomataram, R. Dikshit, S. Eser, C. Mathers, M. Rebelo, D. M. Parkin, D. Forman, and F. Bray, “Cancer incidence and mortality worldwide: sources, methods and major patterns in globocan 2012”, International journal of cancer, vol 136, no. 5, pp. E359-E386, 2015.

[2] M. Nakagami, “The m-distribution-a general formula of intensity distribution of rapid fading”, Statistical Method of Radio Propagation pp. 3-36, 1960.

[3] P. M. Shankar, “A general statistical model for ultrasonic backscattering from tissues” IEEE transactions on ultrasonics, ferroelectrics, and frequency control, vol. 47, no. 3, pp. 727–736, 2000.

[4] P. M. Shankar, V. A. Dumane, J. M. Reid, V. Genis, F. Forsberg, C. W. Piccoli, and B. B. Goldberg, “Classification of ultrasonic b-mode images of breast masses using nakagami distribution”, IEEE transactions on ultrasonics, ferroelectrics, and frequency control, vol. 48, no. 2, pp. 569–580, 2001.

[5] P. H. Tsui, C. C. Chang, M. C. Ho, Y. H. Lee, Y. S. Chen, C. C. Chang, N. E. Huang, Z. H. Wu, and K. J. Chang, “Use of nakagami statistics and empirical mode decomposition for ultrasound tissue characterization by a nonfocused transducer”, Ultrasound in medicine & biology, vol. 35, no. 12, pp. 2055–2068, 2009.

[6] P. H. Tsui, C. K. Yeh, Y. Y. Liao, C. C. Chang, W. H. Kuo, K. J. Chang, and C. N. Chen, “Ultrasonic nakagami imaging: A strategy to visualize the scatterer properties of benign and malignant breast tumors”, Ultrasound in medicine & biology, vol. 36, no. 2, pp. 209–217, 2010.

[7] Y. Y. Liao, P. H. Tsui, C. H. Li, K. J. Chang, W. H. Kuo, C. C. Chang, and C. K. Yeh, “Classification of scattering media within benign and malignant breast tumors based on ultrasound texture-feature-based and nakagami-parameter images”, Medical physics, vol. 38, no. 4, pp. 2198-2207, 2011.

[8] H. Y. Ma, Y. H. Lin, C. Y. Wang, C. N. Chen, M. C. Ho, and P. H. Tsui, “Ultrasound window-modulated compounding nakagami imaging: Resolution improvement and computational acceleration for liver characterization” Ultrasonics, vol. 70, pp. 18–28, 2016.

[9] P. H. Tsui and Y. L. Wan, “Application of ultrasound nakagami imaging for the diagnosis of fatty liver”, Journal of Medical Ultrasound, vol. 24, no. 2, pp. 47–49, 2016.

[10] K. Dobruch-Sobczak, H. Piotrzkowska-Wróblewska, K. Roszkowska-Purska, A. Nowicki, and W. Jakubowski, “W. Usefulness of combined bi-rads analysis and nakagami statistics of ultrasound echoes in the diagnosis of breast lesions”, Clinical radiology, vol. 72, no. 4, pp. 339-e7, 2017.

[11] R. M. Haralick, K. Shanmugam, and I. H. Dinstein, “Textural features for image classification”, IEEE Transactions on systems, man, and cybernetics, vol. 6, pp. 610–621, 1973.

[12] A. Sadeghi-Naini, H. Suraweera, W. T. Tran, F. Hadizad, G. Bruni, R. F. Rastegar, B. Curpen, G. J. Czarnota, “Breast-lesion characterization using textural features of quantitative ultrasound parametric maps”, Scientific reports, vol. 7, 13638, 2017.

[13] S. R. Lakhani, “WHO Classification of Tumours of the Breast” International Agency for Research on Cancer, 2012.

[14] Z. Klimonda, P. Karwat, K. Dobruch-Sobczak, H. Piotrzkowska-Wróblewska, J. Litniewski, “Breast-lesions characterization using Quantitative Ultrasound features of peritumoral tissue”, Scientific Reports, vol. 9, 7963, 2019.

[15] E. B. Mendelson, M. Böhm-Vélez, W. A. Berg, G. J. Whitman, M. I. Feldman, H. Madjar, G. Rizzsatto, J. A. Baker, M. Zuley, A. T. Stavros, C. Comstock, and V. Van Duyn Wear, “Acr bi-rads® ultrasound. ACR BI-RADS Atlas, Breast Imaging Reporting and Data System”, Reston, VA, American College of Radiology 149, 2013.

[16] I. Guyon, S. Gunn, M. Nikravesh, and L. A. Zadeh, “Feature Extraction, Foundations and Applications”, vol. 207, Springer, 2008.