BIOCYBERNETICS AND BIOMEDICAL ENGINEERING 38 (2018) 684–690

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/bbe

Original Research Article

Discriminant analysis of neural style representations for breast lesion classification in ultrasound

Michał Byra *

Department of Ultrasound, Institute of Fundamental Technological Research, Polish Academy of Sciences, Warsaw, Poland

ARTICLE INFO

Article history:
Received 13 December 2017
Received in revised form
5 May 2018
Accepted 11 May 2018
Available online 14 June 2018

Keywords:
Breast lesions classification
Deep learning
Discriminant analysis
Transfer learning
Ultrasound imaging

ABSTRACT

Ultrasound imaging is widely used for breast lesion differentiation. In this paper we propose a neural transfer learning method for breast lesion classification in ultrasound. As reported in several papers, the content and the style of a particular image can be separated with a convolutional neural network. The style, coded by the Gram matrix, can be used to perform neural transfer of artistic style. In this paper we extract the neural style representations of malignant and benign breast lesions using the VGG19 neural network. Next, the Fisher discriminant analysis is used to separate those neural style representations and perform classification. The proposed approach achieves good classification performance (AUC of 0.847). Our method is compared with another transfer learning technique based on extracting pooling layer features (AUC of 0.826). Moreover, we apply the Fisher discriminant analysis to differentiate breast lesions using ultrasound images (AUC of 0.758). Additionally, we extract the eigenimages related to malignant and benign breast lesions and show that these eigenimages present features commonly associated with lesion type, such as contour attributes or shadowing. The proposed techniques may be useful for the researchers interested in ultrasound breast lesion characterization.

1. Introduction

Breast cancer is one of the most common causes of death for women in the western world [1]. Ultrasound imaging plays an important role in breast lesion detection and diagnosis. This imaging modality is safe, low cost, widely available and can discriminate breast lesions with high accuracy. However, ultrasound imaging is highly operator dependent. Diagnosis of breast lesions by ultrasound imaging requires experienced

* *Corresponding author at*: Department of Ultrasound, Institute of Fundamental Technological Research, Polish Academy of Sciences, Pawińskiego 5b, 02-106 Warsaw, Poland.
E-mail address: mbyra@ippt.pan.pl
https://doi.org/10.1016/j.bbe.2018.05.003

radiologist who know how to operate ultrasound scanner and possess deep knowledge of characteristic image features related to lesion type [2]. This requirement results in high inter-observer variation rate among the radiologists. Moreover, low specificity of examination results in high number of unnecessary performed biopsies. To support the radiologists, computer-aided diagnosis (CADx) systems have been used to help differentiate benign and malignant breast lesions [3].

There are various approaches to breast lesion CADx system development [4,5]. Usually the features are extracted manually from ultrasound images and then the classification is performed with machine learning methods. In this case, the performance of a CADx system relies mainly on well-chosen handcrafted features developed by researchers. Those features are usually divided into texture and morphological features [4]. In the review paper [5] a large number of handcrafted features were evaluated for classifying breast lesions in ultrasound. The study demonstrated that the morphological features are the best for breast lesion classification. The aim of these features is to quantify shape and contour attributes of breast lesions [6–8]. Usually more regular and well-defined contours are expected in the case of benign lesions [9].

Nowadays, with the rise of the deep learning (DL) methods, CADx systems with automatic feature extraction have been proposed for classification of medical images [10,11]. These systems commonly use convolutional neural networks (CNNs) to transform input images into a single decision as output, which corresponds to the probability that the examined image contains pathology. However, datasets in medical imaging are usually too small to train a DL model from scratch. This issue makes the researchers turn to transfer learning methods for CADx system development [12,11]. In this case, a DL model pre-trained on a large dataset is used as a feature extractor for the task of interest. The performance of the pre-trained model relies on the similarity of the medical images at hand to those from the training dataset. In [13] the authors applied several transfer learning techniques to extract features for breast classification using the VGG19 neural network. In [14] the authors proposed to use a modified and fine-tunned version of the Inception neural network. Both studies reported good results and depicted the usefulness of transfer learning in breast lesion classification.

In this paper we combine two pattern recognition techniques to characterize breast lesions in ultrasound images. The first one is related to eigenfaces and Fisherfaces which have been used for human face recognition [15]. These methods of image decomposition relies on the idea of a template that match a specific object, e.g. the human face. Our first aim is to apply Fisher linear discriminant analysis (FLDA) to ultrasound images of malignant and benign lesions in a similar fashion as performed in face recognition. The second pattern recognition technique is related to the concept of neural transfer of artistic style [16]. As reported in several papers, DL models can be used to separate the content and the style of a particular image [17]. Neural style transferring has been applied to create appealing images that combine paintings of well-known artists with regular photos [16]. In this work, we extract the neural style representations corresponding to malignant and benign breast lesions. We assume, that there exist a universal style connected with the lesion type. Next, we apply the FLDA on these neural style representations for classification. It is presented that the decomposition of the style is much more effective for classification than the decomposition of ultrasound images. The proposed approach may serve as a general method of transfer learning.

This paper is organized in the following way. First we describe the dataset used in this study. Second, the concepts of Fisherimages and eigenimages are introduced. Next, we explain how the neural style representation can be extracted using a deep neural network. Our approach to analysis is described. The results are presented and discussed.

2. Materials and methods

2.1. *Dataset*

In this study we used the freely available breast lesion dataset, the OASBUD (Open Access Series of Breast Ultrasonic Data, https://doi.org/10.5281/zenodo.545928) [18]. The dataset contains raw ultrasound data recorded from breast focal lesions and was originally used to test quantitative ultrasound techniques [19,20]. It includes 52 and 48 scans from malignant and benign lesions, respectively. For each lesion, two orthogonal scans were acquired. Moreover, for each scan a region of interest (ROI) was determined by a radiologist to correctly indicate lesion area. The study protocol was approved by The Institutional Review Board. Additional informations about the dataset and the study can be found in the original paper [18].

To reconstruct the ultrasound B-mode images based on raw data, we employed the approach proposed by the authors [18]. First, the envelope of ultrasonic signals was calculated using the Hilbert transform. Lesion area was cropped using the ROI provided by the radiologist to contain the lesion plus 5 mm of the surrounding tissue area. Second, the envelope was log compressed to 40 dB dynamic range. Next, the data were resized using the bicubic interpolation to 224×224 and normalized.

2.2. *Discriminant analysis*

The eigenimages and the Fisherimages were extracted using the standard approach known from face recognition [15]. Each image was vectorized and the principal component analysis was applied to determine the eigenimages (eigenvectors) corresponding to malignant and benign breast lesions. The eigenimages are related to the directions with the greatest variance in the data. In comparison, the FLDA finds a direction, called the Fisherimage, that best separates the classes. This direction is expected to maximize the ratio of the variance between the classes to the variance within the classes. In the case of binary classification there is only one Fisherimage.

2.3. *Neural style transfer*

To build the style representation of an image we used the style transferring method proposed by Gatys [16]. This method utilizes the VGG19 CNN pre-trained on the ImageNet dataset

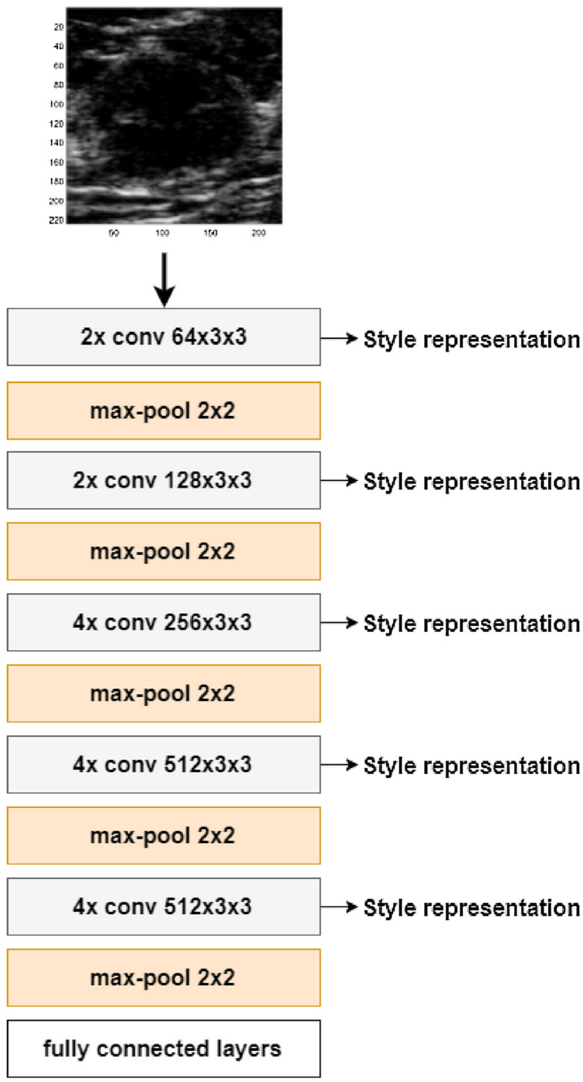

Fig. 1 – The architecture of the VGG19 neural network.

[21,22]. The architecture of the VGG19 neural network is depicted in Fig. 1. The network includes large blocks of convolutional layers that code different information from images. In our study we used the implementation of the VGG19 model publicly available in Keras [23].

The style representation captures information on texture but not the image content or arrangement. This representation is obtained using the feature space built on top of filter responses in network layers. The style of an image is captured using the Gram matrix that determines the correlations between the filter responses in a convolutional layer. Feature correlations in the ith convolution layer can be expressed by the Gram matrix $G^i \in R^{n_i \times n_i}$, where n_i is the number of distinct filters in the ith layer and the matrix G of inner products is equal to:

$$G^i_{jk} = \sum_l F^i_{jl} F^i_{kl}, \tag{1}$$

where F_{jl} stands for the lth position in the jth vectorized feature map. The Gram matrix is unique for each image and can be considered as a transformation of the input image, see Fig. 2.

2.4. Method validation

In our study, the FLDA was applied to ultrasound images and the Gram matrices calculated using several convolutional layers. Patient specific leave-one-out cross-validation was performed to evaluate the classification. In each case, the test set consisted of 2 images from the same patient and the training set consisted of all remaining images. After the training phase, the FLDA was used to calculate the projection for the data in the test set and the results were averaged. Final results were used to determine the receiver operating characteristic (ROC) curve. To evaluate the breast lesion classification performance, the area under the ROC curve (AUC) was calculated. The sensitivity, specificity and accuracy of were determined based on the ROC curve for the point on the curve that was the closest to the upper left corner [24]. All calculations were performed in Python with the scikit-learn package.

3. Results

The FLDA algorithm was applied to classify breast lesions using different image representations. First, we used the ultrasound images. This approach corresponded to the classic method of using Fisherimages for classification. In this case, we obtained AUC value of 0.758. Next, the style representations coded by Gram matrices were extracted using the VGG19 neural network. In [16] the layers conv1_1, conv2_1, conv3_1, conv4_1 and conv5_1 were used for neural style transferring. In our study we employed all convolutional layers of the VGG19 neural network. For each layer, the Gram matrix was calculated and the FLDA algorithm was applied for classification. For each classifier the AUC value was calculated. Fig. 3 shows that the AUC value increases approximately monotonically as deeper layers are employed for classification. The worst classification performance was obtained for the classifier trained using ultrasound images with AUC value of 0.758. The highest AUC value was equal to 0.847 and was obtained for the classifier developed using layer conv4_4. The ROC curves calculated for the worst and the best performing classifiers are shown in Fig. 7. The difference between AUC values was statistically significant according to the Delong test (p-value < 0.001) [25].

In the next step our approach to transfer learning was compared with the best performing transfer learning method proposed in [13]. Features were extracted from the max pooling layers of the VGG19 neural network. Next, features were average-pooled, normalized and concatenated to form the final feature vector. The FLDA classifier was applied. In this case, the AUC was equal to 0.826. According to the Delong test, this method achieved better performance than the classifier trained using ultrasound images (p-value = 0.007) and statistically similar performance to our approach (p-value = 0.26). Results are depicted in Table 1.

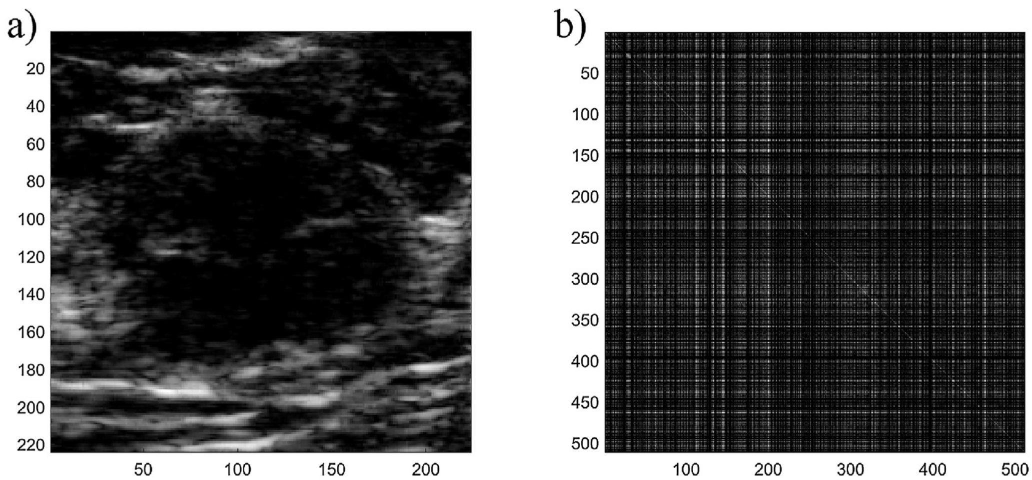

Fig. 2 – An example of a B-mode image of a benign breast lesion and the corresponding Gram matrix calculated using VGG19 layer conv4_4.

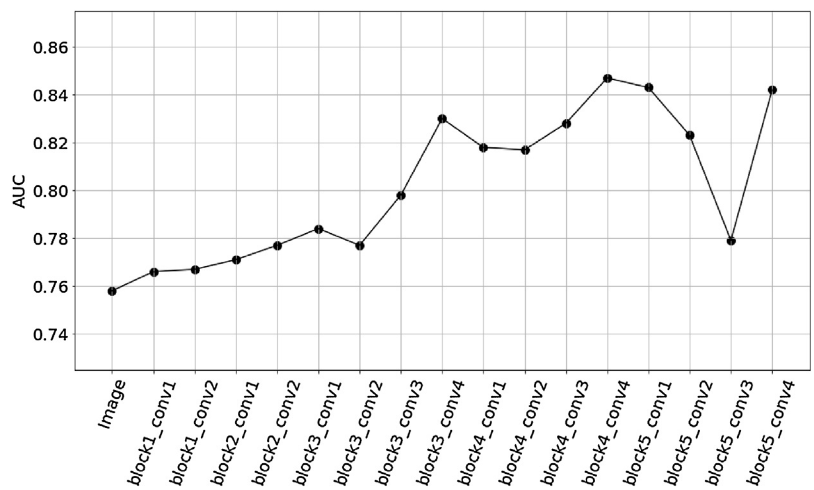

Fig. 3 – AUC values for the classifiers developed using ultrasound images and convolutional layers of the VGG19 neural network.

To illustrate class specific patterns the eigenimages were extracted separately for the benign and malignant breast lesion ultrasound images. For this task the entire dataset was used. Fig. 4 shows the first two eigenimages of both classes. Additionally, the PCA was applied to decompose the Gram matrices of benign and malignant lesion images calculated for features in layer conv4_4. Fig. 5 presents the scatter plots of the first two principal components. In the case of the ultrasound images, first two components explained around 16% of variance while for the second approach this factor was higher and equal to 29%. Fisherimages for the ultrasound images and Gram matrices from layer conv4_4 are presented in Fig. 6.

Table 1 – Classification performance.

Algorithm	AUC	Accuracy	Sensitivity	Specificity
FLDA images	0.758	0.71	0.596	0.833
FLDA conv4_4	0.847	0.80	0.808	0.792
FLDA pooling layers, see [13]	0.826	0.77	0.865	0.666

4. Discussion

The proposed transfer learning method utilizes Gram matrices that capture correlations between the filter responses in the VGG19 neural network [16]. Our study shows the usefulness of this approach. Table 1 indicates that the classification performance increases as the deeper layer is employed for training. Moreover, Fig. 5 shows the scatter plots of the first two principal components determined for the ultrasound images and the Gram matrices calculated using conv4_4. In the case of the neural features, the malignant and benign lesions are easier to separate visually. Fig. 5 depicts that the AUC value

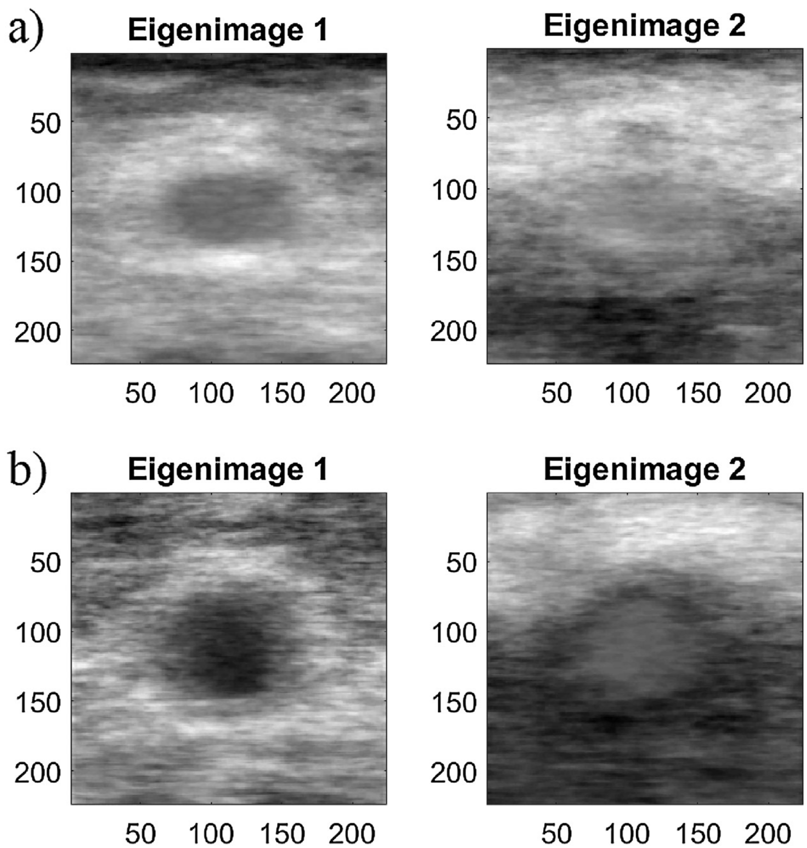

Fig. 4 – The two first eigenimages corresponding to: (a) benign and (b) malignant breast lesions.

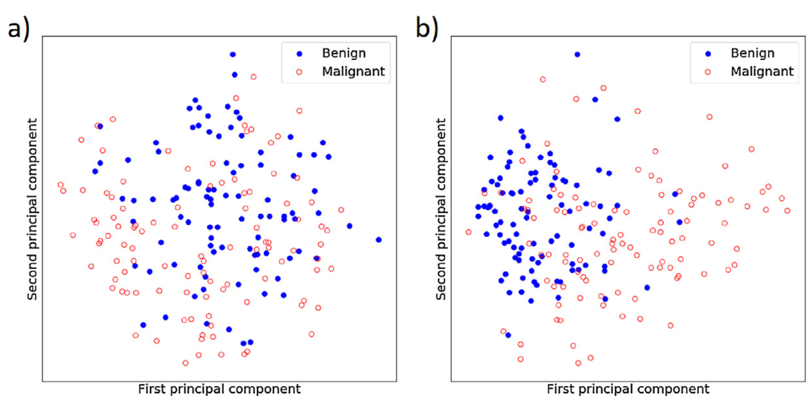

Fig. 5 – The scatter plots of the first two principal components obtained using: (a) B-mode images and (b) Gram matrices from layer conv4_4.

increased from 0.758 for the image based FLDA algorithm to 0.847 for the classifier developed using layer conv4_4. This result illustrates the discriminative power of the VGG19 neural network. However, the classification performance does not increase in the case of the classifiers developed using Gram matrices from the 5th block of the VGG19 neural network. In the case of the layer conv5_3, the AUC value actually decreased to around 0.78. This could be caused by the fact that the last convolutional block is more tuned to recognize objects contained in the ImageNet dataset. The classification performance is presented in Table 1. The method proposed in [13] achieved slightly lower, but comparable performance, with the AUC value equal to 0.826. In the original paper higher AUC value of 0.872 was reported. This difference was caused probably by the datasets, in the original paper, 1125 breast lesions were used to develop classifiers. The methods proposed in our study and in [13] require averaging across filter responses and work with the VGG19 neural network. This neural model employs large blocks of uniform convolutional layers that code different level information from images.

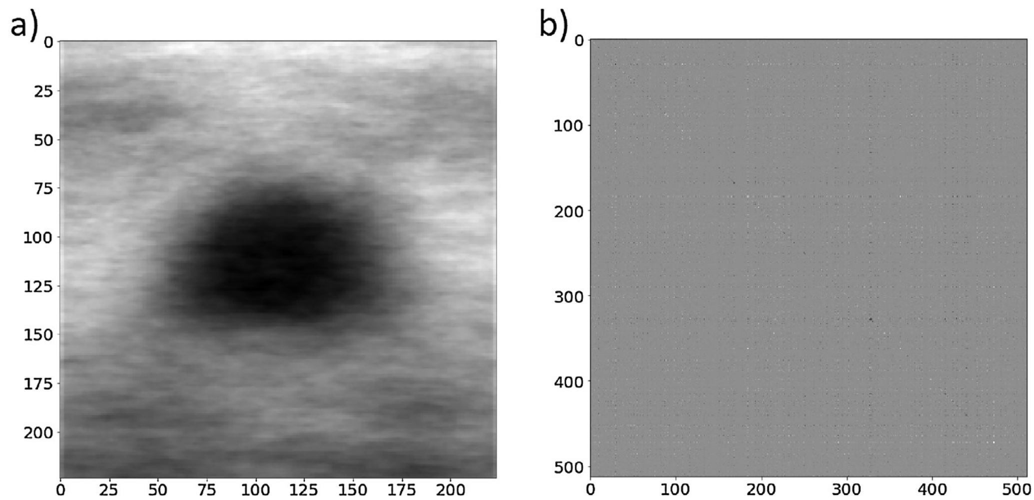

Fig. 6 – Fisherimages corresponding to: (a) ultrasound images and (b) Gram matrix from layer conv4_4.

The use of these transfer learning methods in the case of more complex neural architectures is not straightforward and is out of the scope this study.

The eigenimages in Fig. 4 reveal important features related to malignant and benign breast lesions. Supposedly, the first eigenimages in both cases refers to the shape of the lesion. In both cases lesion boundaries are clearly depicted. Several papers on CADx systems for breast lesions classification reported that the morphological features related to lesion contour are the most useful for lesion differentiation [5]. Another factor is related to the observation that the brightness of malignant lesions is usually smaller in comparison to the brightness of surrounding tissue than in the case of the benign lesions. This feature is connected to the fact that the malignant lesions highly attenuate ultrasound waves [26]. This phenomenon is clearly depicted in the second eigenimage in Fig. 4. A large difference in brightness is observed between the region above and below the lesion. As the wave propagates through the tissue, it is attenuated in the lesion area. As a result, the tissue below the lesion seems to be darker than the tissue above. The same issue can be observed in the Fisherimage in Fig. 6a). The impact of the attenuation may be important for the researchers who would like to apply data augmentation to train a DL model from scratch. Rotation of ultrasound images can produce images without the dark region below the lesion. Such images would loose one of the characteristic physical features related to malignancy.

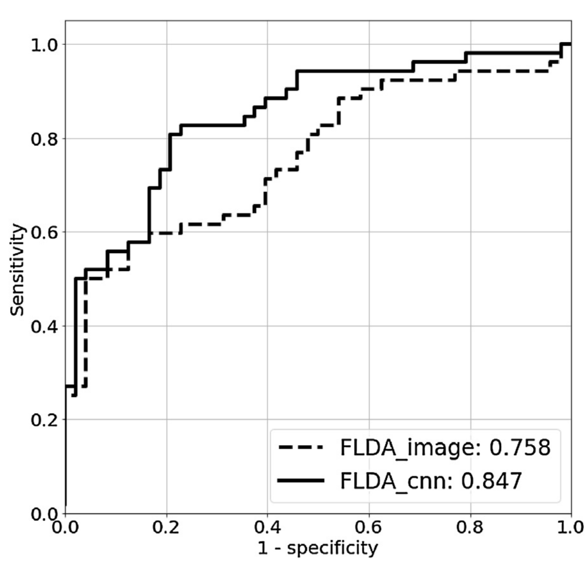

Fig. 7 – The ROC curves for the worst and the best performing classifiers.

The main idea behind the eigenfaces and the Fisherfaces is that there is a universal face template. The concept of template is similar to the concept of style in neural style transfer. Facial images are connected to a certain style specified by color and shape. In the case of breast lesions, the style is related to a specific speckle pattern, echo intensity and lesion shape. Contour attributes are related to lesion type. CNNs are excellent edge detectors and this fact may explain the good performance of the neural transfer learning. Our approach can be considered as a transfer learning technique. A pre-trained neural network is used to extract features for classification and to train another model. In some sense our approach is similar to kernel discriminant analysis but instead of a specified kernel, the neural model is applied to transform nonlinearly the input data. We assume that there is a style space generated by the network and that the images from each class correspond to a different subspace of this space.

To successfully extract eigenimages, the initial images have to be centered, scaled and similarly oriented. These conditions are usually hard to meet in reality. In the case of ultrasound imaging, the lesion appearance in image strongly rely on radiologist performing the examination. In comparison to facial images, the lesion images commonly have different size, orientation and shape. In this study we showed that this problem can be minimized by using a pre-trained convolution neural network. Gram matrices help separate the content from the style. However, this approach is more difficult to interpret. The eigenimages extracted using the ultrasound images presented in Fig. 4 can be assessed by an expert. These eigenimages contain lesion features reported in the literature. In comparison, the Fisherimage obtained using the Gram matrices in Fig. 6b) is difficult to interpret. It is unclear which image features it encodes. However, in a similar way it would be difficult to interpret the Gram matrix corresponding to a Van Gogh painting. We could calculate the Gram matrices corresponding to a set of Van Gogh paintings. Next, it would be possible to extract eigenimages using Gram matrices and transfer the style they represent to regular photos as in the neural style artistic transfer. It could reveal the most important features associated with the Van Gogh paintings.

5. Conclusions

In this paper we proposed a transfer learning method for breast lesion classification. Our approach was based on discriminant analysis. First, the eigen-decomposition and the FLDA were applied to differentiate ultrasound images of malignant and benign breast lesions. Next, the neural style patterns of breast lesions were extracted using the VGG19 neural network. FLDA was used to differentiate style representations obtained for malignant and benign lesions. Our approach may be useful for the researchers interested in breast lesion characterization.

Acknowledgement

This work was partially supported by the National Science Center (Poland), Grant Number UMO-2014/13/B/ST7/01271.

REFERENCES

[1] Stewart BW, Wild CP. World Cancer Report 2014; 2014.
[2] Bott R. ACR BI-RADS Atlas, no. 1; 2014.
[3] Giger ML, Karssemeijer N, Schnabel JA. Breast image analysis for risk assessment, detection, diagnosis, and treatment of cancer. Annu Rev Biomed Eng 2013;15:327–57.
[4] Cheng HD, Shan J, Ju W, Guo Y, Zhang L. Automated breast cancer detection and classification using ultrasound images: a survey. Pattern Recognit 2010;43(1):299–317.
[5] Flores WG, de Albuquerque Pereira WC, Infantosi AFC. Improving classification performance of breast lesions on ultrasonography. Pattern Recognit 2015;48(4):1125–36.
[6] Bian C, Lee R, Chou Y-H, Cheng J-Z. Boundary regularized convolutional neural network for layer parsing of breast anatomy in automated whole breast ultrasound. International Conference on Medical Image Computing and Computer-Assisted Intervention. Springer; 2017. p. 259–66.
[7] Cheng J-Z, Chou Y-H, Huang C-S, Chang Y-C, Tiu C-M, Chen K-W, et al. Computer-aided us diagnosis of breast lesions by using cell-based contour grouping. Radiology 2010;255(3):746–54.
[8] Chou Y-H, Tiu C-M, Hung G-S, Wu S-C, Chang TY, Chiang HK. Stepwise logistic regression analysis of tumor contour features for breast ultrasound diagnosis. Ultrasound Med Biol 2001;27(11):1493–8.
[9] Chen C-M, Chou Y-H, Han K-C, Hung G-S, Tiu C-M, Chiou H-J, et al. Breast lesions on sonograms: computer-aided diagnosis with nearly setting-independent features and artificial neural networks. Radiology 2003;226(2):504–14.
[10] Cheng J-Z, Ni D, Chou Y-H, Qin J, Tiu C-M, Chang Y-C, et al. Computer-aided diagnosis with deep learning architecture: applications to breast lesions in US images and pulmonary nodules in CT scans. Sci Rep 2016;6:24454.
[11] Shin H-C, Roth HR, Gao M, Lu L, Xu Z, Nogues I, et al. Deep convolutional neural networks for computer-aided detection: CNN architectures, dataset characteristics and transfer learning. IEEE Trans Med Imaging 2016;35(5):1285–98.
[12] Litjens G, Kooi T, Bejnordi BE, Setio AAA, Ciompi F, Ghafoorian M, et al. A survey on deep learning in medical image analysis; 2017, arXiv:1702.05747.
[13] Antropova N, Huynh BQ, Giger ML. A deep feature fusion methodology for breast cancer diagnosis demonstrated on three imaging modality datasets. Med Phys 2017; 44(10):5162–71.
[14] Han S, Kang H-K, Jeong J-Y, Park M-H, Kim W, Bang W-C, et al. A deep learning framework for supporting the classification of breast lesions in ultrasound images. Phys Med Biol 2017;62(19):7714.
[15] Belhumeur PN, Hespanha JP, Kriegman DJ. Eigenfaces vs. fisherfaces: recognition using class specific linear projection. IEEE Trans Pattern Anal Mach Intell 1997; 19(7):711–20.
[16] Gatys LA, Ecker AS, Bethge M. A neural algorithm of artistic style; 2015, arXiv:1508.06576.
[17] Jing Y, Yang Y, Feng Z, Ye J, Song M. Neural style transfer: a review; 2017, arXiv:1705.04058.
[18] Piotrzkowska-Wróblewska H, Dobruch-Sobczak K, Byra M, Nowicki A. Open access database of raw ultrasonic signals acquired from malignant and benign breast lesions. Med Phys 2017;44(11):6105–9.
[19] Byra M, Nowicki A, Wróblewska-Piotrzkowska H, Dobruch-Sobczak K. Classification of breast lesions using segmented quantitative ultrasound maps of homodyned *k* distribution parameters. Med Phys 2016;43(10):5561–9.
[20] Dobruch-Sobczak K, Piotrzkowska-Wróblewska H, Roszkowska-Purska K, Nowicki A, Jakubowski W. Usefulness of combined BI-RADS analysis and Nakagami statistics of ultrasound echoes in the diagnosis of breast lesions. Clin Radiol 2017;72(4). 339.e7.
[21] Deng J, Dong W, Socher R, Li L-J, Li K, Fei-Fei L. ImageNet: a large-scale hierarchical image database. IEEE Conference on Computer Vision and Pattern Recognition, 2009. CVPR 2009. IEEE; 2009. p. 248–55.
[22] Simonyan K, Zisserman A. Very deep convolutional networks for large-scale image recognition; 2014, arXiv:1409.1556.
[23] Chollet. Others, Keras; 2015, https://github.com/fchollet/keras.
[24] Fawcett T. An introduction to ROC analysis. Pattern Recognit Lett 2006;27(8):861–74.
[25] DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics 1988;837–45.
[26] Landini L, Sarnelli R. Evaluation of the attenuation coefficients in normal and pathological breast tissue. Med Biol Eng Comput 1986;24(3):243–7.