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A Practical Implementation of Deep Learning Method for Supporting the Classification of Breast Lesions in Ultrasound Images

Seokmin Han*, Suchul Lee* and Jun-Rak Lee†

**Department of Computer Science and Information Engineering, Korea National University of Transportation, Korea*
†Division of Liberal Studies, Kangwon National University, Korea
**seokmin.han@ut.ac.kr, *sclee@ut.ac.kr, †jrlee@kangwon.ac.kr*

Abstract

In this research, a practical deep learning framework to differentiate the lesions and nodules in breast acquired with ultrasound imaging has been proposed. 7408 ultrasound breast images of 5151 patient cases were collected. All cases were biopsy proven and lesions were semi-automatically segmented. To compensate for the shift caused in the segmentation, the boundaries of each lesion were drawn using Fully Convolutional Networks(FCN) segmentation method based on the radiologist's specified point. The data set consists of 4254 benign and 3154 malignant lesions. In 7408 ultrasound breast images, the number of training images is 6579, and the number of test images is 829. The margin between the boundary of each lesion and the boundary of the image itself varied for training image augmentation. The training images were augmented by varying the margin between the boundary of each lesion and the boundary of the image itself. The images were processed through histogram equalization, image cropping, and margin augmentation. The networks trained on the data with augmentation and the data without augmentation all had AUC over 0.95. The network exhibited about 90% accuracy, 0.86 sensitivity and 0.95 specificity. Although the proposed framework still requires to point to the location of the target ROI with the help of radiologists, the result of the suggested framework showed promising results. It supports human radiologist to give successful performance and helps to create a fluent diagnostic workflow that meets the fundamental purpose of CADx.

Key words: *Breast Cancer, Deep Learning, FCN, segmentation.*

1. Introduction

Breast cancer is known to be one of the most common cancers in women worldwide and it is considered as the second leading cause of female cancer deaths[2]. In addition to mammography, which is the primary imaging modality for screening, ultrasound (US) imaging is performed in breast imaging protocol as a

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Corresponding Author: jrlee@kangwon.ac.kr
Tel: +82- 33-570-6608, Fax: +82- 33-570-6604
Division of Liberal Studies, Kangwon National University, Korea

diagnostic tool[3]. Double-reading the same mammograms by two radiologists independently has been reported to reduce the occurrence of missed cancers and it is included in most screening programs[4]. Because double-reading requires additional work load and costs, computer-aided diagnosis (CADx) is considered to provide radiologists with a second opinion for the medical image interpretation and diagnosis[5-14]. In many cases, CADx is applied to differentiate malignancy or benignancy for tumors or lesions[7, 8, 15- 20]. Because these systems can provide a second opinion to radiologists in a cost-effective way, they can help detect breast cancer in early stage and reduce the breast cancer death rate among women[21].

A wide variety of machine learning methods have been researched for early detection of breast cancer[22-24]. Recently, deep learning methods have been widely adopted in perception-related problem[25]. The deep learning methods have been introduced to the medical imaging field with promising results on various applications, such as organ segmentations[26] and detection[27-30], tissue classification in histology and histopathology images[31-32], ultrasound standard plane selection[33],and knee cartilage segmentation[34], the computer aided prognosis or diagnosis for Alzheimerâ€™s disease[35- 38] and so forth.

In terms of breast cancer, there are some previous works that applied deep learning methods to classify the identified lesions in breast images[39-40]. In this study, we exploit the performance of several reputational CNNs to differentiate the distinctive types of lesions and nodules acquired with ultrasound imaging, using relatively large size database. Its performance and accuracy in classifying and discriminating breast lesions were evaluated. The proposed framework is a component algorithm of S-Detect technology, which is implemented in RS80A(Samsung Medison, Inc.) This research is an practically implemented method of the authors' previous method[42] and a substantial extention of [43]. Differently from the previous research of the authors[42], we employ a segmentation method instead of translation augmentation of the training data..

2. Method and Materials

The proposed procedure is in Fig.1.

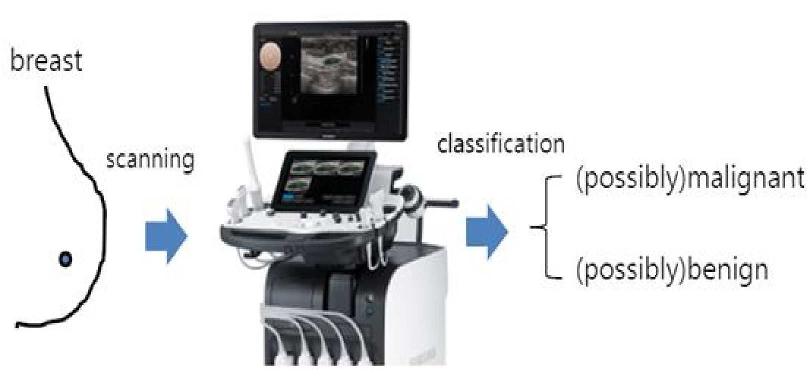


Figure 1. The conceptual architecture of the proposed deep learning CAD framework

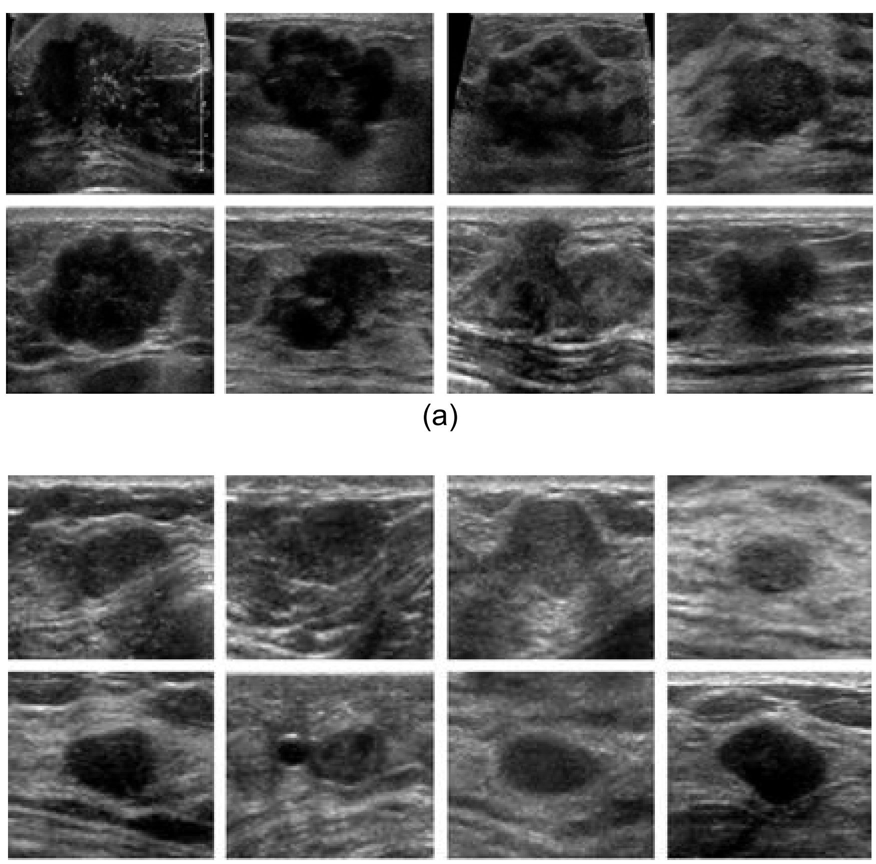
For this research, 7408 ultrasound breast images of 5151 patients cases were gathered. All cases have been proven in all biopsies and semi-automatically segmented lesions have been associated with the masses. All images were histogram-equalized, and each image was cropped to match the input image size. In 7408 ultrasound breast images, 6579 images were used for training, and 829 images were used as test set. The training dataset consists of 3765 benign and 2814 malignant mass images. Then, the training images were augmented by varying the margin between the boundary of each lesion and the boundary of the image itself.
Optimal parameters were selected based on 10-fold cross validation with the training data.

2.1 Data Preparation

7408 breast ultrasound images were scanned from 5151 patients, in Samsung Medical Center(Seoul, South Korea). 5254 images were acquired with IU22(Philips, Inc.) and 2154 images were acquired with RS80A(Samsung Medison, Inc.). Histopathological characteristics of all breast lesions were biopsy proven. Some examples of malignant lesions and benign lesions are in Fig.2. All experimental protocols were approved by Samsung Medical Center, Seoul, South Korea. Informed consent was obtained from all patients for their consent to use their information in the research without violating their privacy. Among the images, 829 lesions(489 benign lesions and 340 malignant lesions) were randomly selected as a test set. We selected those test data so that the train and test set were separated at the patient level to avoid bias. In Table.1, an overview of the lesion size attributes of training data and test data is presented.

Table 1. Overview of the lesion size attributes of training data and test data.

	~0.5	*~1.0*	*~2.0*	*~3.0*	*~4.0*	*~5.0*	*~5.5(cm)*	*total*
Train	672	2134	2433	846	355	132	6	6579
Test	88	343	314	58	16	9	1	829



(a)

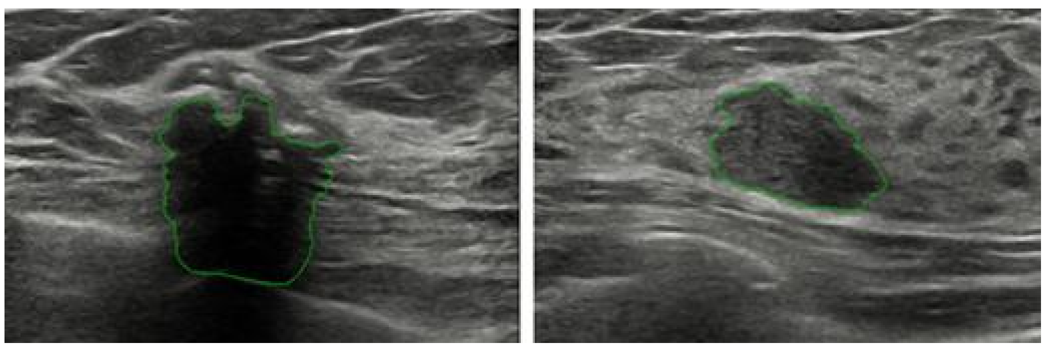
(b)

Figure 2. The conceptual architecture of the proposed deep learning CAD framework

The suggested CADx method aims to classify an identified ROI as benign or malignant lesion. In this research, the ROI location was provided by six radiologists first, then an automatic segmentation method followed to draw the boundary of lesions. Based on the resultant boundary, the ROI was cropped with a margin, which is defined as the distance between the lesion boundary and the boundary of the cropped image itself.

2.2 Lesion Boundary Segmentation

In classifying the ROI of an input image with benign or malignant lesion, the shift of each lesion from the imagecenter may affect the performance of the classification. To compensate for the shift, the boundary of each lesion is drawn using Fully Convolutional Networks(FCN) segmentation method[1] based on the radiologist specified points.



(a) (b)

Figure 3. (a) and (b) are examples of segmented boundaries of breast lesion.

In Fig.3(a) and Fig.3(b), we presented examples of breast lesion images. After applying FCN segmentation, the boundary of the lesion can be drawn as in Fig.3. Taking advantage of the drawn boundary, the center position of the breast lesion can be estimated as the median of the boundary. The ROI can be cropped centered based on the estimated center position of the breast lesion. This process matters in that in the real clinical situation, the radiologist provides the input image after pointing the seed point to the area of the potential lesion. It can be possibly anywhere in the acquired US image. After operating FCN segmentation method considering the point provided by a radiologist, we can center the lesion on the center of the input image and crop the input image based on the result of the segmentation result.

2.3 Data Augmentation by Image Cropping with Margin

The margin is defined as the distance between the lesion boundary and the boundary of the cropped image itself in this research. To figure out how the size of the margin affects the overall performance, we created a database without a margin, a database with a margin of 50 pixel. The performance using each database was compared to each other so that we could figure out whether image cropping with a margin is better than image cropping without a margin or not. With the margin, the image contains information about the breast lesion as well as the background. If the dataset with a margin shows better result than the result of the dataset without a margin, it indicates that the information in the background also affects the overall classification performance. In addition to the performance comparison, we made the network feed backward to create the saliency map[41]. The final label evaluation is inversely fed back to determine what part of the input image affects the final label evaluation. To do that, the derivative of each layer is obtained. Derivatives at each layer is the gradient of that layer with respect to the output of the layer. To construct the saliency map, we obtained derivatives with respect to the input layer. In the saliency map, the portion of the input image that affects the estimated label is enhanced. This result may explain why the margin affects the performance. If the information to classify the lesion exists outside the lesion as well as the lesion itself, the margin will surely affect the performance. To create the training dataset, the images that were cropped with a margin of 30 pixels and 70 pixels were added to the images cropped with a margin of 50 pixels for data augmentation. However, the margin was set to 50 pixels in test data set. All ROI images have been resized to 255x255 because the input size of the network is set to 255x255. Because the input image size is fixed at 255x255, this augmentation affects and determines the relative size of the breast tumor in the images. Differently from the previous research of the authors[42], we have nont adopted translation augmentation. With FCN segmentation, the center of the lesion is displayed at the center of the training image and the input image. Thus, rather than the translation augmentation, we moved the image to the center through the segmented boundary.

3. Experimental Results

We employed GoogLeNet, which is established in 2014, and modified the network for our purpose. Two Auxiliary classifiers were removed in this research as in the authors' previous research[42]. In this research, we have just 2 class problem, benign and malignant lesion. Because GoogLeNet has 1000 class outputs, we reduced the output to 2 class outputs. All pixels in each patch are treated as the input neurons. This modified GoogLeNet was set as a reference network in this research. We evaluated the performance of the proposed deep learning framework of breast cancer classification in terms of accuracy, sensitivity, specificity, and AUC(area under curve). Optimal parameters were chosen based on 10-fold cross validation with the training data. Then, the optimized parameters were applied to evaluate the performance on the test dataset.

First, we compared the number of the training images and the required time of the proposed method to those of the previous method of the authors[42] in Table.2. As can be seen in Table.2, the proposed method has a much shorter learning time compared to the previous method. Using the proposed method, we could train the network within a day, while we should spend more than a month to train the network using the previous method, which makes the proposed method much more practical than the previous one in terms of implementation efficiency.

Table 2. Comparison of the required time for learning and the number of training images.

	proposed method	*previous method[42]*
Benign images	11295	553455
Malignant images	8842	413658
learning time(1000 epoch)	7 hour	42 day

Fig.4 shows ROC(Receiver-Operating Characteristic) curves for the evaluated CNNs. One neural network is trained and tested on the images without a margin. The other neural network is trained and tested on the images with 50 pixel margin.

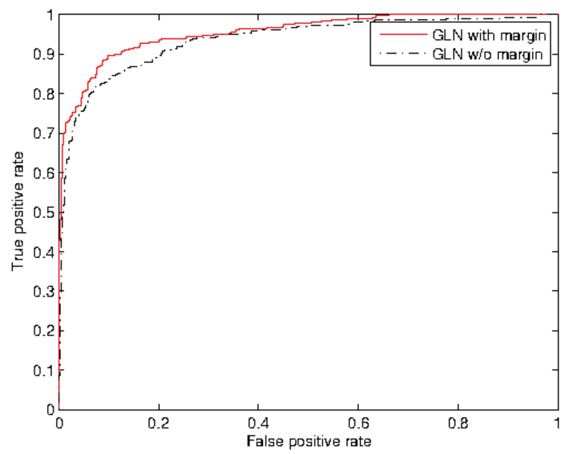


Figure 4. ROC curves of GoogLeNets trained and tested on the images without a margin(black) and with a margin(red).

Table 3. Performance comparison of a CNN trained on the images with a margin to a network trained on images without a margin. GLN refers to GoogLeNet.

	accuracy	*sensitivity*	*specificity*	*AUC*
GLN with margin	88.41%	0.7676	0.9652	0.9551
GLN w/o margin	87.9%	0.8029	0.9324	0.9361

As can be seen in Fig.4 and Table.3 training and testing the neural network on the images with a margin seem to improve the performance of the neural network. To figure out if the information to classify the lesion exist outside the lesion as well as in the lesion, we implemented the saliency map[41] and applied it to the trained network. In Fig.5, four resultant examples are presented. In each example, the input image is on the right side while the saliency map corresponding to the input image is on the left side. The black region indicates the pixels that affect the label estimation. As can be seen in Fig.5, the black region seems to exist also in the boundary of the lesion as well as in the lesion itself.

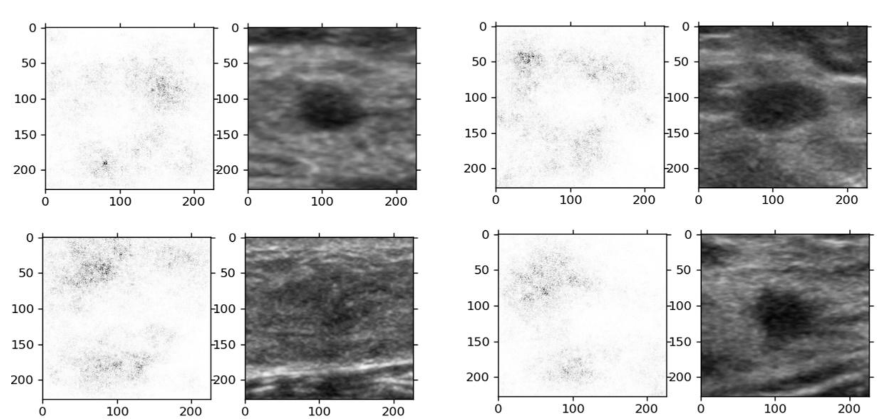


Figure 5. Saliency map examples that shows where the important information exists in the image.

Considering the result in Fig.4 and Fig.5, we augmented the training dataset by adding images cropped with a margin of 30 pixels and 70 pixels. Thus, we present the evaluation results of the GoogLeNet CNNs with the data augmentation and without the data augmentation in Fig.6.

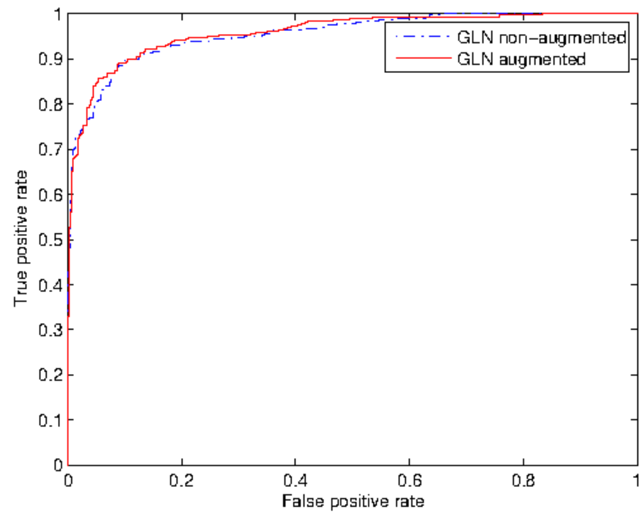


Figure 6. ROC curves of GoogLeNet without the data augmentation and with the data augmentation.

Table 4. Diagnostic performances of CNN networks.

	accuracy	*sensitivity*	*specificity*	*AUC*
GLN with augmentation	90.46%	0.8588	0.9365	0.9589
GLN w/o augmentation	88.41%	0.7676	0.9652	0.9551

As we can see in Table.4, the performance of CNN is very promising. The networks trained on the data with augmentation and the data without augmentation both show AUC over 0.95. The network showed about 90% accuracy, 0.86 sensitivity and 0.95 specificity. The result shows that the data augmentation in terms of the margin improves the performance of classification. Considering the large number of the images in the training set and the test set, the proposed framework seems to be very helpful to classify benign or malignant breast tumor in real clinical application. Although it is assumed that the lesion should be centered on the basis of the segmentation result, there is a possibility that each radiologist may have differently specified the center point which affects the performance of the proposed framework. Thus we also simulated that situation. We have made the center position of each test image unstable by random vertical and horizontal movements that are uniformly distributed between 0 and 32 pixels (one pixel corresponds to about 0.3 mm). In Fig.7 shows the result. As can be seen in Fig.7 and Table.5, the perturbed unstable position by the radiologist may affect the performance. Centered image indicates the result without unstable movement in Table.4. Perturbed image in Table.5 indicates the result with perturbation recovery based on FCN segmentation. Some performance may have been lost, but the proposed method was able to recover the perturbation. Modified GoogLenet was employed for this simulation test.

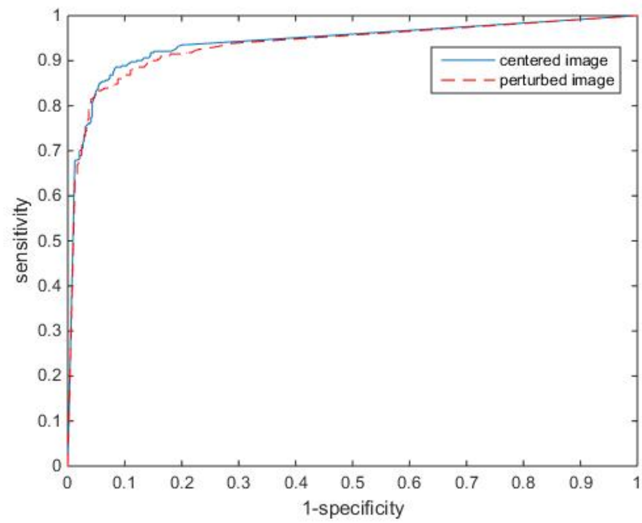
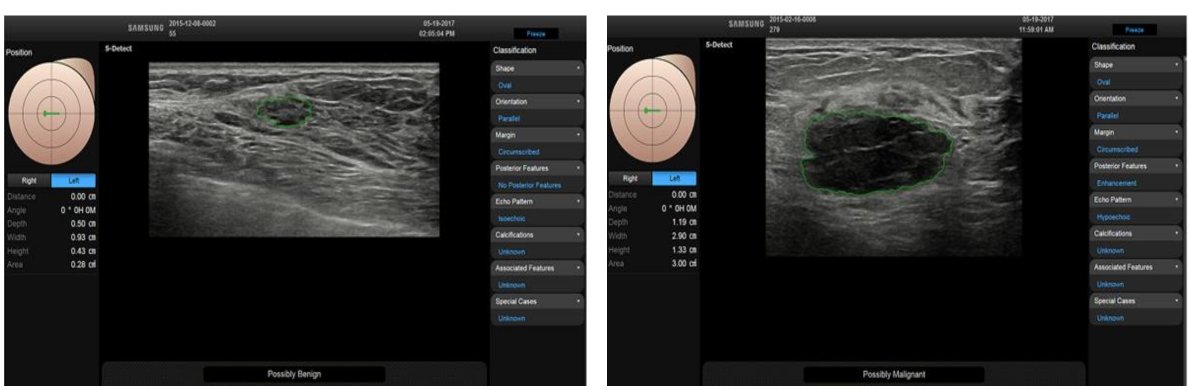


Figure 7. The perturbation in the center location by radiologist does not affect the performance much

Table 5. Diagnostic performances on centered images, and perturbed images.

	accuracy	*AUC*
centered image	90.46%	0.9589
perturbed image	90.58%	0.9477

In Fig.8, we presented some implementation examples.



(a) (b)

Figure 8. An implementation examples of (a)a possibly benign lesion, (b)a possibly malignant lesion.

In this research, the threshold was set to 0.1 for high sensitivity model, and 0.6 for high specificity model. CNN training is implemented with the Caffe[44] deep learning framework, using a NVidia K40 GPU on Ubuntu 14.04. A model snapshot with low validation loss is taken for the final model. Learning hyperparameters are set as follows: momentum 0.9, weight decay 0.0002, and a poly learning policy with base learning rate of 0.0001.

The image batch size is 32, which is the maximum batch size that works in our system circumstances.

4. Discussion

The proposed method could accurately distinguish malignant lesions from benign lesions when the location of the tumor was given by a radiologist. Thus, the proposed framework can help radiologists make accurate decisions about the next procedures. This research applied a deep learning method to data sets collected by over 1000 patients. Considering the number of images and patients, the results of the proposed framework may be reproduced in different data sets, demonstrating the benefits of clinical application of deep learning methods. Unlike our previous research[42], we have not adopted translation augmentation. With FCN segmentation, the center location of the lesion centered in the training images, as well as the input images. This reduced the number of the training images. In Reference[42], we had to increase the number of training images for translation augmentation as well as margin augmentation. This research is very useful and practical for implementation because it reduces the number of the training images and makes the data set preparation much easier. The neural networks trained on the data with augmentation and the data without augmentation both showed AUC over 0.9. We added the images cropped with a margin of 30, 50, and 70 pixels to the input image data for data augmentation. Trying more data augmentation in terms of margins may improve results.

The difficulty comes from the fact that the number of malignant tumor images is smaller than the number of benign tumor images. Increasing the number of malignant tumor images can reduce the loss of accuracy. If the proposed framework is applied to the actual clinical situation by radiologist, it can classify the malignant lesions in a short time and support the diagnosis of radiologist who discriminates malignant lesions. Therefore, it is possible to give successful performance in cooperation with human radiologist as a second opinion, which meets the fundamental purpose of CADx.

5. Conclusion

In this research, we used a deep learning framework to differentiate the distinctive type of lesions and nodules in breast acquired with ultrasound imaging. Biopsy-proven benchmarking datasets were created to evaluate the proposed method. The proposed framework consists of histogram equalization, image cropping, and margin augmentation. Optimal parameters were selected based on 10-fold cross validation with training data. The networks showed AUC of 0.95, about 0.9(90%) accuracy, 0.86 sensitivity and 0.95 specificity. Although the proposed framework still requires to point to the location of the target ROI with the help of radiologists, the result of the suggested framework showed promising results. Using this method in conjunction with a radiologist in a clinical setting can assess the malignancy of the lesion and the radiologist can identify malignant lesions at the right time. Therefore, the proposed framework can support human radiologist to give successful performance and help to create a fluent diagnostic workflow that meets the fundamental purpose of CADx

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