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Breast cancer diagnosis using deep belief networks on ROI images

ROI görüntülerinde derin inanç ağları kullanarak göğüs kanseri teşhisi

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Abstract

Hand-crafted features are efficient methods for image processing, recognition, and computer vision. However, the advancements in data size and image resolution lead to inconvenience in feature extraction. Moreover, they are unstable, method-dependent, and computationally intensive due to high dimensions. Especially, big data on image datasets causes unpredictable long process. It is a definite necessity to adjust the feature extraction algorithms to computer-assisted methods for image processing. Generative representational learning algorithms have been emerging approaches with the advantages of Deep Learning. In this study, I proposed employing Deep Belief Networks (DBN) for breast cancer diagnosis on ROI images. DBN models were iterated on different image sizes to evaluate the impact of dimensionality on ROI images. The proposed DBN model has achieved performance rates of 96.32%, 96.68%, 95.93%, and 96.40% for accuracy, specificity, sensitivity, and precision, respectively. Consequently, the proposed DBN with detailed representational learning is an efficient and robust algorithm for the classification of breast cancer and healthy tissues on mammograms by the advantage of generative architectures.

Keywords: Deep Learning, representational learning, Deep Belief networks, breast cancer, DDSM.

Öz

Elle çıkarılan öznitelikler, görüntü işleme, tanıma ve bilgisayarlı görü için etkili yöntemlerdir. Ancak, veri boyutu ve görüntü çözünürlüklerindeki artış, özniteliklerin elde edilmesinde zorluklara sebep olmuştur. Kararsız, yönteme bağımlı ve hesaplama açısından yoğundurlar. Özellikle, görüntü veri kümelerindeki büyük veriler, öngörülemeyen uzun süreçler doğurur. Görüntü işleme için öznitelik çıkarma algoritmalarının bilgisayar destekli yöntemlere uyarlanması kesin bir ihtiyaçtır. Üretken temsili öğrenme algoritmaları, Derin Öğrenmenin avantajları ile son yıllarda ortaya çıkan yaklaşımlardır. Bu çalışmada, ROI görüntülerinde meme kanseri teşhisi için Derin İnanç Ağlarının (DBN) kullanılmasını önerdim. DBN modelleri, boyutun ROI görüntüleri üzerindeki etkisini değerlendirmek için farklı görüntü boyutları üzerinde tekrarlanmıştır. Önerilen DBN modeli doğruluk, özgüllük, duyarlılık ve kesinlik için sırasıyla %96.32, %96.68, %95.93 ve %96.40 performans oranlarına ulaşmıştır. Sonuç olarak, önerilen ayrıntılı temsili öğrenmeye sahip DBN, üretici yapıların avantajı ile meme kanseri ve sağlıklı dokuların mamogramlarda sınıflandırılması için verimli ve sağlam bir prosedürdür.

Anahtar kelimeler: Derin Öğrenme, Temsili öğrenme, Derin İnanç ağları, meme kanseri, DDSM.

1 Introduction

Breast cancer is one of the most frequently studied fields due to the increasing number of deaths with the prevalence of the disease. Therefore, early diagnosis of breast cancer is a crucial stage in treatment processes to prevent disease progression in medicine. Whereas mass detection and complete analysis on mammograms were performed using hand-crafted features and advanced image processing [1], the developments on Deep Learning (DL) techniques lead to novel popularity on detailed analysis without hand-crafting on medical images [2],[3]. DL is a contemporary tool in the segmentation, classification, and detection of the pathologies on various types of medical images [3]-[5].

The researchers utilized histology, histopathology images, mammograms, and tomography images to diagnose breast cancer. Alanazi et al. split high-resolution histopathology images into small boxes to identify cancer tissue using the Gaussian mixture model and DL algorithms [6]. However, the mammogram is the most frequently used diagnostic tool to assess pattern, mass, and tissue variations by color-based characteristics [7]. Furthermore, the remaining diagnostics need expensive medical devices with high charges. Hence, mammograms have a usage in literature and open-access databases instead. Pardamean et al. identified cancer and non-cancer mammograms using transfer learning on the Digital Database for Screening Mammography (DDSM) database by fine-tuning classification parameters on pre-trained DenseNet convolutional neural networks (CNN) architecture [8]. Zeng et al. proposed a region of interest (ROI) pooling stage for CNN to identify abnormal pathologies on mammograms [9]. Yu et al. extracted the ROI images using conventional image processing, including morphological opening and intensity thresholding. They fed 330 ROIs into DenseNet201 architecture and highlighted the effect of different depth sizes in fine-tuning [10]. Ertosun and Rubin integrated a probabilistic technique into CNN for mass identification on mammograms. They reported the highest capability for GoogleNet architecture among various pre-trained CNN architecture using transfer learning [11]. Xi et al. re-trained the popular pre-trained CNN architectures to detect the mass on mammograms. They highlighted the highest performance for VGGNet among various pre-trained CNN architecture comparing feature activation maps [12]. Moreover, Agarwal et al. already performed a transfer learning approach using ResNet architecture on ROIs from the DDSM database [13]. Suzuki et al. classified the ROIs from mammograms into mass and non-mass on the DDSM database by re-training the AlexNet architecture with transfer learning on CNN [14]. Touahr et al. experimented on the effect of local binary patterns on CNN to detect tumors on

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mammograms using malignant and benign mass [15]. Swiderski et al. adapted non-negative matrix factorization on ROIs as a preprocessing stage before feeding the CNN architecture [16]. Nguyen and Lim adapted region of analysis filters into the feature learning stage of CNN on ROIs to separate multi-class cancer types on DDSM database. They highlighted the impact of Gabor filter on the extraction of pathological tissue on mammograms [17].

Hand-crafted feature extraction is an efficient method for image processing, recognition, and computer vision. However, data size and image resolution advancements lead to extracting hand-crafted features, including morphology, area, shape, and more [18],[19]. Moreover, they are not robust, method dependent, and are computationally intensive due to high dimensionality. Especially, big data on image datasets causes unpredictable long progress [20]. On the other hand, CNN architectures were applied as feature extractors to characterize the cancerous mass for breast cancer [21]. It is a definite necessity to adjust the feature extraction algorithms to computer-assisted methods for image processing. Yoon and Kim utilized features extracted with conventional image processing techniques on mammograms. They fed hand-crafted features into support vector machines (SVM) with nonlinear kernel and the Adaboost technique [1]. Sarosa et al. analyzed ROIs on mammograms from the DDSM database to separate the malignant and benign mass using hand-crafted features, including gray-level co-occurrence matrix features. They reported average performances feeding SVM with a nonlinear kernel [22]. Hekal et al. extracted CNN-based features using ResNet and AlexNet on ROIs for multi-case cancer classification. They experimented on the feature activation maps with SVM and highlighted the capabilities of DL algorithms on the early diagnosis of breast cancer [21].

With the developments in GPU technology in recent years, the generation of these representations and transfer learning with multilayered models, generating dominant features, and the gradual extraction of low-, middle-, and high-level features have become possible with Deep Learning algorithms. Deep Belief Networks (DBN) is one of the most common classifiers among these algorithms. DBN is a classifier that examines the weights of connections between adjacent sequential layers during pre-training using Restricted Boltzmann Machines (RBM) [23]. Random weights are determined depending on the number of neurons between the layers with representations before the RBM. The initial determination of the random weights is performed by probabilistic and energy functions depending on the input and subsequent layer structure. The DBN was frequently utilized in image processing, including handwriting recognition [23], 3D object recognition [24], medical image analysis [25], and more. In addition to the prosperity of the DBN model on the image processing, it was also used in the classification of time-series using the fiducial and non-fiducial features extracted using various signal analyzing methods as input to the DBN model. Altan et al. provided a classification model on five arrhythmia types using statistical features of different modulation signals sifted by Hilbert-Huang transform to ECG signals [26]. Altan et al. also applied a second-order difference plot to the ECG signals and quantified chaos distribution. Using quantization features with various shape types as input to the DBN model, they separated patients with coronary artery disease and healthy subjects with high classification performances [27].

Altan et al. applied the Hilbert-Huang transform to the EEG signals and extracted the statistical feature from the intrinsic mode functions. In their proposal, they fed the statistical feature dataset to the DBN model with two hidden layers. They reported that positive and negative brain activity trails could be determined successfully for stroke patients with the DBN classifier. The literature shows that the DBN performed very successful classification performances in hand-crafted features and direct images. DBN had already proved the efficiency of mammograms. Abdel-Zaher and Eldeib analyzed the Wisconsin breast cancer dataset using various back-propagation techniques on the supervised stage of DBN. They reached high accuracy rates for a small-scale dataset [28].

The popularity of DL on mammograms is accelerated with the developments of CNN. Whereas CNN is an effective way of comprising convolution-based feature extraction and classification stages with novel adaptive optimization techniques, using a pooling layer has caused disagreements on the idea that it may cause significant data loss during down-sampling. Moreover, training of fully connected layers is a time-consuming process that requires high computation capabilities. Therefore, I decided to use DBN due to the advantages of using generative graphical representational learning with fast and robust training. A mammogram is a medical image type that is hard to process owing to different tissue density, small pathologies, and prone to noise. Therefore, I decided to use ROIs in various dimensions (64x64, 128x128, and 224x224), which are precisely related sections for the cancerous tissue, instead of complete mammograms for a more characteristic cancer generalization.

This study aims to compare the advantages and efficiency of the DBN classifier on the classification of breast cancer and generate representation capabilities of DBN on ROIs. In order to implement a complete comparison, limited classification parameter ranges, such as model hidden layers, neuron numbers, and activation functions on DBN, were iterated for representational learning. The analysis was performed by reducing the image dimensions as much as possible to cause the feature size to become closer. The remaining of the paper is organized as follows: The DDSM database and DBN are detailed in materials and methods. Experimental setup for various classification parameters is explained, and the achievements for different DBN models are evaluated in experimental results. The advantages and disadvantages of the proposed model are handled with a detailed comparison in the discussion section.

2 Materials and methods

2.1 The digital database for screening mammography database

DDSM is an open-access large-scale mammogram database [29]. It is comprised of a total number of 2620 cases from different medical imaging devices. The DDSM was collected within the scope of the project by multiple organizations. The capabilities of different resolutions and bit specifications are the powerful aspects of the database. Therefore, DDSM provides analyzing opportunities on mammograms from three different devices (DBA, Lumisys, and Howtek) with lesion ROIs.

Normal and cancer cases in DDSM were handled in the analysis. The variety of medical devices contributes to the generalization capability of the proposed DBN models. The benign cases were excluded from the dataset. The ROIs of lesions were extracted from mammograms with cancer using bounding boxing in the

DDSM and cropping. I augmented the ROI images using cropping, vertical-, and horizontal-flipping due to the necessity of wider databases for the DL algorithms and abstaining from overfitting. Table 1 presents the diversity of mammograms and ROIs with cancer and non-cancer distribution in the analysis considering medical devices.

Table 1. Data variety for DL experiments.

	Mammograms		ROIs	
Devices	Cancer	Normal	Cancer	Normal
DBA	97	430	117	457
Howtek	424	183	435	317
Lumisys	393	82	421	278

The analyzed ROI dataset comprises 2,025 images, including 973 ROIs with lesions and 1052 ROIs with normal tissue.

2.2 Deep belief networks

The DBN is a specified model of Deep learning algorithms with the advantages of fast training and representational learning. While the first layers of the DBN model are used to learn low-level features, high-level features are obtained as the number of layers moves towards the top layer [30]. The DBN is a statistical and probabilistic model. It is performed by calculating the conditional probabilities of the other inputs in case the input state is binary. Unlike common deep learning algorithms, it can achieve very high training performance for a low number of datasets. The DBN is a two-stage classifier that starts with an unsupervised stage to predefine the weights by generating different presentations using RBM and supervised model by unfolding the pre-trained weights into the neural network model for fine-tuning [23]. The RBM-based predefined weights are updated using greedily layer-wise training of the DBN model. Each RBM has a connection between adjacent layers as n^{th} and $(n+1)^{th}$ layers. For instance, the first RBM consists of an input layer $h_0 = v$ (for visible units) and first hidden layer h_1. The bias parameters are b_n and c_n for h_n and h_{n+1}:

$$E(h_n, h_{n+1}) = -h_{n+1} W h_n - b_n h_n - c_n h_{n+1} \quad (1)$$

$$P(h_n, h_{n+1}) = \frac{e^{-E(h_n, h_{n+1})}}{\sum e^{-E(h_n, h_{n+1})}} \quad (2)$$

$P(h_n, h_{n+1})$ is the joint distribution of the RBM and $E(h_n, h_{n+1})$ is the energy function between nth and $(n+1)^{th}$ layers. The DBN model generates high-level features at the top levels of the DBN by generating RBM-based representations [31]. The more detailed presentations can be generated using more hidden layers in the network [23].

3 Experimental results

The DBN enables generating various representations of the input data using different layer models. The number of the layers and neurons at each layer provides learning the descent features and transferring them to the next latent layer using the unsupervised methods. Using time-frequency features as the input of the DBN defines relational parameters in this way pre-training correlated weights.

The ROIs were augmented by eight times using flipping and rotating. Each ROI was flipped in different directions (vertically, horizontally, and both) and rotated with an angle of 90 degrees. The dataset was enhanced with a total number of 16,200 images. The ROIs have a variety of resolutions. Each image was resized to 64x64, 128x128, and 224x224 pixels in gray-scale format. In this manner, standardized image size and channel for the representational learning were provided for training the DBN models.

The proposed breast cancer identification system (see Figure 1) was tested using a 5-fold cross-validation method on various dimensions of ROIs (64x64, 128x128, and 224x224). The DBN classifiers were modeled with one input layer, 2 or 3 hidden layers, and an output layer with binary outputs (cancer and non-cancer).

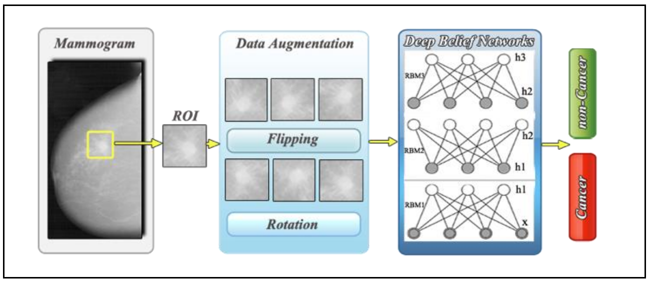

Figure 1. The structure of the proposed breast cancer diagnosis model.

Each ROI was represented with a binary output neuron. Greedily layer-wise pre-training was applied to pre-train the DBN. Each training had 500 epochs. The number of neurons at each hidden layer varied among 50~350 with an increasing size by 10 neurons at each iteration. The learning rate for the supervised training was set as 0.001, the activation function of the output layer was the sigmoid output function. The activation function of hidden layers was established as a sigmoid function. After DBN training was finalized, the remaining fold of the dataset was tested to calculate the classification performance. Statistical test metrics including overall accuracy, precision (PRE), weighted sensitivity (SEN), f1 score, and weighted specificity (SPE) were calculated to evaluate the proposed models. The contingency table of the image fed into DBN is seen in Table 2. Additionally, Table 3 presents the best five cancer identification performances for each ROI size.

Table 2. Contingency table for the DBN model with highest classification performance.

	Cancer	Non-cancer	Total
cancer	7467	279	7746
non-cancer	317	8137	8454
Total	7784	8416	16200

Using the contingency tables, the highest achievements for the DBN on ROI images attained an average accuracy rate of 96.32% using 5-fold cross-validation. The proposal achieved the classification performance rates of 96.68%, 95.93%, 96.40%, and .9616 for SPE, SEN, PRE, and f1 score, respectively. The most successful DBN model is comprised of a deep architecture with three hidden layers of 70-100-240 neurons, respectively. The achievements indicate that the proposal outclasses the state-of-the-art considering identification performance using greedy layer-wise pre-training in DBN. A complete comparison with the state-of-the-art is presented in Table 4.

The proposed DBN model for cancer identification on ROIs has a sparse representation. Deep representational learning has a classification accuracy dominance compared to the state-of-the-art on ROI images.

Table 3. The highest achievements (%) for various DBN models considering accuracy, specificity, and sensitivity.

DBN Model	Image Size	Sensitivity	Specificity	Precision	F1 score	Accuracy
h_1:70, h_2:60	64x64	91.55	82.78	79.03	.8483	86.42
h_1:110, h_2:80, h_3:60		91.16	83.78	80.58	.8554	86.91
h_1:90, h_2:120		93.72	86.77	84.38	.8880	89.78
h_1:210, h_2:180		**94.38**	86.99	84.58	.8921	90.17
h_1:90, h_2:90		92.70	**91.02**	**90.03**	**.9135**	**91.80**
h_1:210, h_2:90	128x128	92.54	95.00	94.48	.9350	93.81
h_1:160, h_2:80, h_3:140		92.38	**96.70**	96.28	.9429	94.62
h_1:170, h_2:110		**97.42**	94.32	94.07	.9571	95.80
h_1:240, h_2:100, h_3:280		95.23	96.34	96.01	.9562	95.81
h_1:70, h_2:100, h_3:240		95.93	96.68	**96.40**	**.9616**	**96.32**
h_1:130, h_2:90	224x224	86.19	82.34	79.55	.8274	84.05
h_1:140, h_2:60, h_3:120		90.83	80.30	75.33	.8236	84.49
h_1:180, h_2:70		91.79	84.57	81.60	.8640	87.65
h_1:230, h_2:180		94.32	88.82	87.05	.9054	91.26
h_1:70, h_2:100		**97.23**	**89.60**	**87.67**	**.9252**	**93.19**

Table 4. A complete comparison with state-of-the-art in terms of classifier, methods, cancer diagnosis accuracy (%) on ROIs.

Related works	Pre-processing	Data Augmentation	Samples	Classifier	Architecture	Accuracy
Nasir Khan et al.	Contrast enhancement	Shifting, zooming, shearing, rotation	3568	CNN	VGG19	94.45
Ertosun and Rubin	-	Cropping, translation, rotation, flipping	2420	CNN	GoogleNet	85.00
Suzuki et al.	-	-	1656	CNN	AlexNet	85.35
Yu et al.	Morphological thresholding	Rotation	330	CNN	DenseNet	92.73
Altan	-	Cropping, flipping	2025	DAE	-	95.17
Al-antari et al.	Multi-thresholding	Statistical features	672	DBN	-	92.86
Hekal et al.	Otsu thresholding	CNN features	2800	SVM	AlexNet	91.00
This study	-	Flipping, rotation	16200	**DBN**	-	**96.32**

4 Discussion

Whereas Deep learning algorithms provide detailed analysis on image analysis, on the other hand, cause to waste a long time in training. This fact, more emphasis is on developing various accelerator optimization, pruning, transfer learning, and learning algorithms that work in parallel with Deep Learning algorithms that have proven their validity on images.

The majority of literature applied transfer learning on pre-trained CNN architectures to identify breast cancer on mammograms due to the simplicity of frameworks and ease of use. The pre-trained CNN architectures are exclusively the most preferred DL algorithm for even diagnosis of breast cancer by the advantages of transfer learning, including VGGNet, GoogleNet, ResNet [5], DenseNet [8], Resnet-50 [13], and more architectures. In addition to using entire mammograms, some studies focused on using ROIs to identify cancerous tissue using GoogleNet [11], AlexNet [14]. Altan compared the efficiency of DBN and CNN on Deep autoencoder features [32]. Al-antari et al. compared the breast cancer identification performances of DBN and conventional machine learning algorithms using ROIs. They reported DBN as the most successful classifier for statistical features from ROIs [4].

The main advantages of the proposal: (1) A majority of the recent studies focused on the diagnosis of breast cancer on mammograms using CNN. However, CNN applies a down-sampling procedure, pooling, which results in data loss, commonly after each convolution block, whereas the proposal has no down-sampling procedures. (2) The DBN-based cancer diagnosis researches focused on statistical and generative feature extraction from ROIs to feed the DL model. The proposal directly inputs ROI images instead of feature extraction on ROIs. Thus, the proposed DBN model directly relates the cancerous mass in addition to excluding feature extraction stages. Even though the superiority of the proposal in terms of accuracy dominance and contributions, its disadvantages: (1) DBN still needs large-scale datasets to reach a global generalization capability as well as CNN. (2) Using many hidden layers and neurons may cause generating different presentations without cancerous mass for even pathological tissue. Consequently, it is a black box to visualize the learned ROI sections in the proposal to state the clinical relevance.

In future works, it has a possibility to increase the generalization capability using many hidden layers and novel activation functions in the training section by clinical validation of presentations. Furthermore, Deep autoencoders will be integrated to define the pre-trained weights as the unsupervised stage of DBN on large-scale ROI images. Although the classification parameters were limited at a range for the number of hidden layers, the neurons at each layer, DBN had well-enough performances than state-of-the-art. The proposed DBN models have separated ROIs with cancer and normal tissue at the iterated classification parameter range with the rates of 96.32%, 96.68%, 95.93%, and 96.40% for ACC SPE, SEN, and PRE, respectively. Since the DBN is an iterative algorithm in the random weight initialization, it is possible to achieve better breast cancer diagnosis performances using deeper DBN models with novel divergence techniques and experimenting with a variety of classification parameters in the training.

5 Author contribution statement

Gökhan ALTAN conceived of the presented idea and contributed in the titles of literature review, data preparation, modelling deep learning architectures, carrying out the experiments, evaluating the achievements, the writing of the manuscript, and checking the manuscript in terms of spelling and content.

6 Ethics committee approval and conflict of interest statement

The data that support the findings of this study are openly available in Kaggle at https://www.kaggle.com/skooch/ddsm-mammography there is no need to obtain permission from the ethics committee for the article prepared. The author declares that there is no conflict of interest with any person / institution in the article prepared.

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