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Classification of Breast Cancer Histology Images Using Transfer Learning

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***Abstract*— Breast Cancer is a most common form of cancer among women and life taking disease around the globe. Histopathological imaging is one of the methods for cancer diagnosis where Pathologists examine tissue cells under different microscopic standards but disagree on the final decision. This is a tiresome task and for that reason, Deep Neural Networks are being used for the supervised classification. We have used Breast Histology dataset having 240 training and 20 test images for classification of the histology images among four classes, i.e. Normal, Benign, In-situ carcinoma and Invasive carcinoma. The dataset was preprocessed for proper classification. We have applied transfer learning based on AlexNet, GoogleNet, and ResNet that can classify images at multiple cellular and nuclei configurations. This approach has resulted in 85% accuracy in case of ResNet as the highest among others and further research is being done to increase its efficiency and reduce the human dependency. The proposed design can also be enhanced for automation of other medical imaging methods.**

Keywords—Deep learning, AlexNet, GoogleNet, ResNet. Breast Cancer

I. INTRODUCTION

Around 1.7 million women annually are diagnosed with breast cancer around the globe and its most frequent cause of death than other types of cancer [1], [2]. It's causes are still not precisely known but early diagnosis and treatment have increased its cure up to 85% while in later stages it decreases to only 10 %[3].

Breast cancer is divided into two major types; carcinoma and non-carcinoma, which further has its own sub-types and properties. Carcinoma has two basic types, normal and benign. Benign is explained as little change in breast tissue structure but it cannot be classified as cancer and in most cases, it is not even harmful to the health. In-situ and invasive are two further types of carcinoma. Invasive carcinoma cancer has a tendency to spread among other organs as well while in-situ (non-invasive) cancers remain in the mammary ductal-lobular system and do not affect others organs. In-situ carcinomas can be cured if timely diagnosed.

Breast cancer is initially diagnosed via palpation (self-assessment) followed by ultrasound imaging and mammography in routine checkups. In case of the possibility of malignant tissue growth, the case is verified by needle biopsy which is considered as one of the very reliable method of breast cancer diagnosis [4]. The microscopic structure and elements of tissues are assessed by the pathologists histologically. This breast tissue histological examination helps to distinguish between the types of cancer explained above [5]. The process of staining with Hematoxylin and Eosin (H&E) is performed on tissue before the visual analysis. Nuclei (purple) and cytoplasm (pinkish) structure and other regions of interest on that tissue slide are enhanced by H&E staining [6].

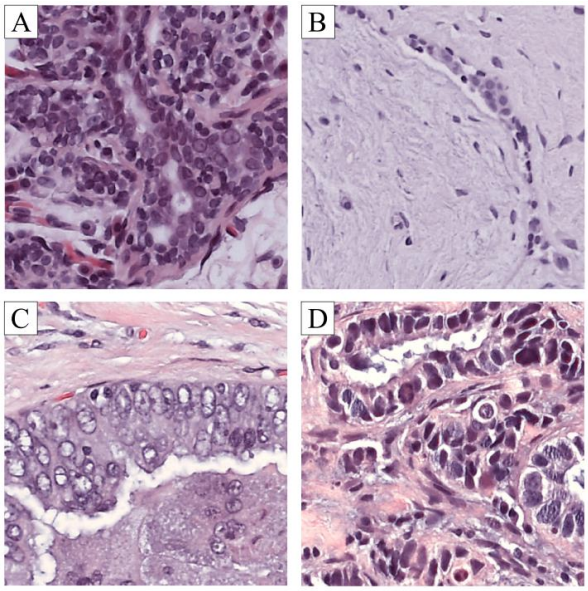

Figure 1. Examples of the patches extracted from used dataset. Due to the hematoxylin and eosin staining, Purple and pink structure explains Nuclei and cytoplasm, respectively. **A** Normal tissue; **B** Benign abnormality; **C** In-situ carcinoma; **D** Invasive carcinoma

During the analysis, pathologist assesses the relevant regions of whole slide images and analyze the overall tissue architecture and distribution of cells in the tissue along with nuclei organization, density, regularities of cell shapes and variability of the stained tissue [7]. Figure 1 explains different types of breast cancer tissue structures. Higher nuclei density and variability along with distorted structure is termed as invasive carcinoma. This analysis procedure is not trivial and the specialist may disagree on the final conclusion [8]. The manual examination is a tiresome work and requires a lot of time and expertise due to inter-class variability. The advancements in science and technology motivate us to develop computer-aided diagnostic(CAD) systems for the improvement in the efficiency and help pathologists in case of disagreement [9].

II. RELATED WORK

With the advancements in Image Processing and Machine Learning tools, biotechnology has become an interesting area for research and development. Scientists are developing algorithms for the reduction in the workload of the pathologist and to increase the diagnostic efficiency by automating the traditional methods using CAD systems. For instance, to classify a tissue as malignant or benign, nuclei morphological analysis is conducted[10]. Kowel et al. used handcrafted features, like morphological, topological, and texture to train a classifier on 500 images from 50 patients and achieved an accuracy between 84 to 93% [11]. Flipczuk

and George used nuclei related features, shape, and texture of nuclei, by performing a circular Hough transform and Otsu-thresholding [12]. George further refined nuclei segmentation using watershed and achieved accuracy between 71.95% to 97.15% while Filipczuk algorithm of majority voting among eleven images achieved an accuracy of 98.51%[12]. Belsare used the architecture of the tissue organization for the classification of histology images [13]. He extracted spatio-color-texture graphs to segment the epithelial layers the lumen of the cells and final classifier was trained on statistical texture features reporting an accuracy between 70% to 100%.

Brook and Zhang worked on 3-class classification approach for breast histology dataset published by the Israel Institute of Technology[14], [15]. They classified the histology images in normal, invasive and non-invasive carcinoma. Brook used connected components to train a support vector machine (SVM) classifier on the binarized images[14]. He achieved an accuracy of 93.4% to 96.4%. Zhang used cascaded classification approach and trained an SVM on Curvelet transform and local binary images resulted in an accuracy of 97% [16]. He also incorporated the rejection method in case of disagreement.

Recent advancements in the image processing techniques and artificial intelligence, problems related to image classification are also being solved. Previously used handcrafted features are now being replaced by features extracted by Convolutional Neural Networks (CNN) on training image patches by classification loss function. These methods have outperformed in the image classification challenges [17] including medical image analysis[18] as well as histopathological images[19]. CNN's does not rely on the in-depth field knowledge for the classification and produce unbiased results for any dataset. Good results can be achieved using similar networks. Spanhol used CNN architecture used in IMAGENET Classification challenge [20] to classify his breast cancer dataset containing images of 82 patients. Authors used a total of 7909 H&E stained tissue biopsy images in different magnifications i.e. 200x, 400x etc [21]. He extracted patches of 32 × 32 and 64 × 64 from sliding window and random extraction. These patches were used to train a classifier. Patch probabilities with maximum, product, and sum rule were used for the classification. They also concluded that higher magnification decreases the achieved accuracy.

Researchers have made a successful modification to the CNN architectures for the breast histology related problems. Ciresan won the ICPR 2012 Contest with an accuracy of 78% [17]. Authors used 101×101 patches for the training of CNN which helps in the study of the nuclei of different sizes and their neighborhood. The size and complexity of the training dataset were increased by arbitrary rotations and mirroring the images. Cruz-Roa extracted patches of 100×100 from breast histology images using grid sampling for the classification of invasive carcinoma [22]. They extracted features from both nuclei and overall tissue organization resulted in an accuracy of 78%. Both, Cireson and Cruz-Roa, used probability map and thresholding techniques for the detection[17], [22].

III. Transfer learning

Deep Convolutional Neural Networks have provided revolutionary assistance to a lot of classification related problems up till now and are widely used in modern research but they have a drawback as well; they require a large amount of data for efficient training along with significant computing capability. The issue of this computing has been partially resolved with the dawn of modern GPUs but the collection of a large amount of data is tiresome and it still persists.

To deal with the issue of the small dataset, data augmentation techniques are used by extraction of overlapping patches and creating its copies via mirroring and rotation. Tissue patches are rotation invariant and pathologists can analyze the patch from any side/angle. So this rotation technique increases the dataset by eight folds and has worked successfully. Transfer learning is stated as an improvement in parameters of classification of a new task through the transfer of knowledge from a model trained for some other task of similar nature [23] and has successfully resulted in overcoming the issue of computation. Some state-of-the-art existing pre-trained Deep Neural Network models are AlexNet, GoogleNet and ResNet. They just need modifications in their architecture according to the application. For Alexnet, GoogleNet and ResNet50 remove last fully connected layer and replace it with new layers; Fully connected layer containing number of classes according to the dataset, softmax layer and classification output layer. After little modifications in the training parameters, we can save a lot of training time with better results.

IV. Proposed Solution

We have applied different transfer learning-based approaches to the Breast Histology dataset for the improvement in classification process of breast histology images. We have tested and fine-tuned multiple algorithms starting with AlexNet and modifying it to our dataset. Initially the removal of last fully connected layer was performed as it was trained on IMAGENET classification challenge having 1000 categories while the dataset that we are using is comprised of four distinct classes. A similar approach is employed on GoogleNet and ResNet50. Achieved outcomes are explained in the results section.

A. Dataset Description

The dataset is collected and published by Araujo and team [24] and available publically at https://rdm.inesctec.pt/dataset/nis-2017-003. The dataset contains high-quality non-compressed (2048 x 1536 pixels) images of breast tissues. These are H&E stained labeled images processed under the same digitization and acquisition technique; pixel size contains 0.42 x 0.42 µm and 200x magnification.

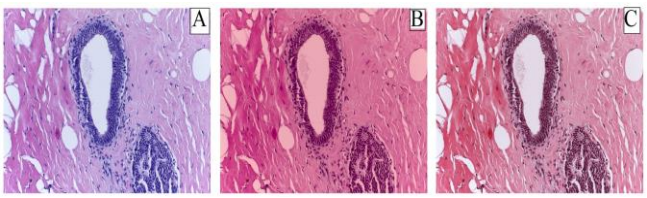

Figure 2: Histology Image Normalization,
A Original image, **B** Reinhard Normalized image,
C Macenku Normalized Image

There are total 260 images and labels are assigned to every image. An issue associated with the dataset is that the label is assigned to whole slide and region of interest is not identified which can contribute to error. The dataset is labeled by two experienced pathologists in four classes; Normal, Benign, In Situ Carcinoma, Invasive Carcinoma. Images having a difference of opinion were excluded and published separately as an extended dataset.

B. Preprocessing

Dataset was preprocessed before the training procedure. Two types of stained image normalization techniques proposed by Macenku [25] and Reinhard [26] were performed. Figure 2 shows the results from both. Recurrent experiments of without image normalization and with these techniques yield good results of Macenku's [25] method on our dataset as this image normalization technique helps in the better quantitative analysis. Steps proposed by Mackenku are explained in the flowchart in figure 3.

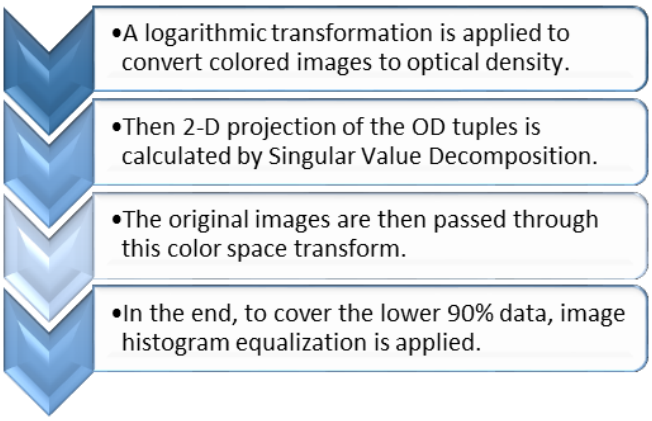

Figure 3: Steps of Macenku's preprocessing method of Histology Images

C. Augmented patch dataset

As mentioned in the dataset section, the dataset contains 260 whole slide high-quality images which are very less for the deep learning algorithms and transfer learning. So, we use the technique of augmented patch dataset to decrease the effect of overfitting and increasing the size and dimensions of the dataset. Also, patch rotation and mirroring have also contributed to efficient results in similar image histology problems, as the patches are rotation invariant and pathologists can identify cancer and region of interest from any viewing angle by analyzing the cellular architecture. To achieve the overall strategy, the methods proposed by [24] is to slide a window of k × k with a stride s over the image. This will make a total number of patches according to the equation below, where I_w and I_H are image width and height respectively.

$$\left[1+\frac{I_w-k}{s}\right] \times \left[1+\frac{I_H-k}{s}\right] \quad \text{---- (1)}$$

Considering k = 512 and s = 256 as of [24], patches of 512 × 512 are extracted from the whole slide image on 50% overlap rule in immediate patches resulted in 35 patches from a single slide as shown in figure 4.

Then each patch is converted into eight different patches by 0, 90, 180, 270-degree rotations and vertical reflections as explained in figure 5. The augmentation converts every single image into 8 × 35 patches resulting in the original dataset of 260 images to 72800 images which somehow can be used for transfer learning as explained in Table 1. Each patch label is assigned on the basis of the original image.

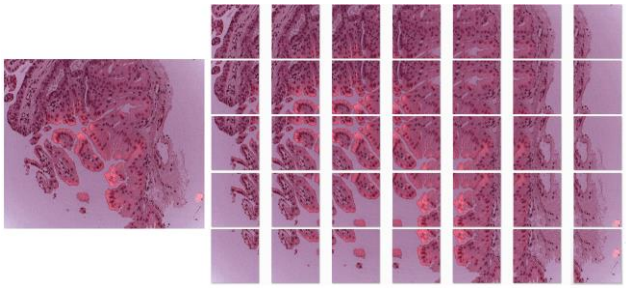

Figure 4: Thirty-five patches extracted from original whole slide image

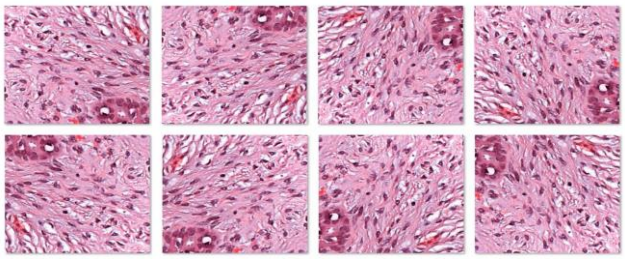

Figure 5: Eight transformations of a single patch

TABLE I. AUGMENTED PATCH DATASET DETAILS

Before Augmentation.				
Normal	***Benign***	***InSitu***	***Invasive***	***Total***
51	74	68	67	260
After Augmentation				
Normal	***Benign***	***InSitu***	***Invasive***	***Total***
14280	20720	19040	18760	72800

D. Experimental Platform

Experimental Platform consists of MATLAB 2017b as a software and NVIDIA graphic card having 12GB memory with computing capacity of 3.5. Training of the model was carried out on the GPU instead of CPU.

E. Model Training

We did transfer learning on AlexNet, GoogleNet and ResNet50 architectures using augmented patch dataset. As Alexnet takes image input of 227×227 while GoogleNet and ResNet take 224×224 and 299×299 patch size image so we used bi-cubic interpolation to resize the patch of 512×512 at first place. Then layers of the architectures were modified according to the setting of transfer learning explained in the transfer learning section.

V. PERFORMANCE EVALUATION

Performance evaluation of our proposed methods is conducted on the basis of accuracy and sensitivity.

A. *Patch-wise Classification*

Patch-wise classification accuracy of four classes is calculated by creating twelve non-overlapping patches from the whole slide images of the total size of 512×512. The results are shown in table 2 and the comparison is presented in figure 5.

B. *Image-wise Classification*

Image-wise classification accuracy is calculated by passing the twelve non-overlapping patches extracted from open slide images and image label is decided on the basis of the majority voting rule among these twelve. For this, we have used mode function as it gives the output of most voting. Results of Image-wise classification has been mentioned in table 2. While the comparison of patch-wise and image-wise has been shown in figure 5.

TABLE II. ACCURACY COMPARISON

Methods		**Accuracy**	
		Patch-wise Classification	***Image-wise Classification***
Araujo et al.[24]		66.7	77.8
Nawaz et al.[27]		75.73	81.25
Proposed Methods	AlexNet	79.84	82.3
	GoogleNet	81.07	83.6
	ResNet50	**83.60**	**85.0**

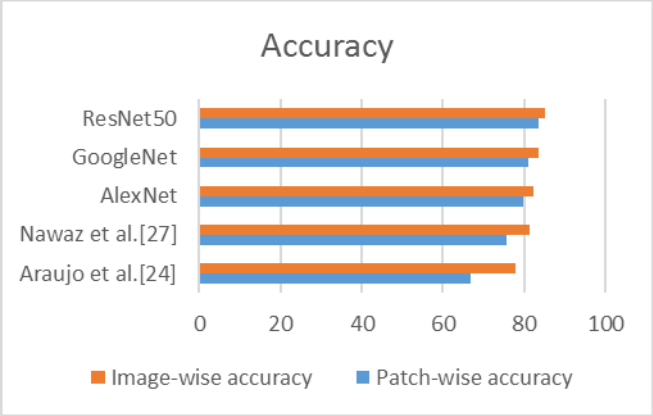

Figure 6: Comparison of accuracy of different architectures in %

VI. ANALYSIS CONCLUSION

This paper presents the use of transfer learning for the classification of Breast Cancer type on Histopathological images. We have modified the pre-trained networks; AlexNet, GoogleNet, and ResNet for the classification of dataset published by [24] and promising results have been achieved as 85 % which were previously 66.7 % from the authors. This technique has resolved the issue of computing time and small training set effectively. For future, we are working to improve further accuracy by employing other architectures as well as improving preprocessing techniques. Also, improvements in the image-wise classification methods are under experimentation. We are also testing the system on mammograms [28].

VII. REFERENCES

[1] R. L. Siegel, K. D. Miller, and A. Jemal, "Cancer statistics, 2016," *CA. Cancer J. Clin.*, vol. 66, no. 1, pp. 7–30, 2016.

[2] "Breast Cancer Statistics." Breast Cancer Research Foundation, 2012.

[3] R. A. Smith *et al.*, "American Cancer Society guidelines for the early detection of cancer," *CA. Cancer J. Clin.*, vol. 52, no. 1, pp. 8–22, 2002.

[4] "Breast Cancer Diagnosis." NationalBreastCancerFoundation, 2015.

[5] C. W. Elston and I. O. Ellis, "Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer: experience from a large study with long-term follow-up," *Histopathology*, vol. 19, no. 5, pp. 403–410, 1991.

[6] P. P. Rosen, *Rosen's breast pathology*. Lippincott Williams & Wilkins, 2001.

[7] M. N. Gurcan, L. Boucheron, A. Can, A. Madabhushi, N. Rajpoot, and B. Yener, "Histopathological image analysis: A review," *IEEE Rev. Biomed. Eng.*, vol. 2, p. 147, 2009.

[8] J. G. Elmore *et al.*, "Diagnostic concordance among pathologists interpreting breast biopsy specimens," *Jama*, vol. 313, no. 11, pp. 1122–1132, 2015.

[9] J. Tang, R. M. Rangayyan, J. Xu, I. El Naqa, and Y. Yang, "Computer-aided detection and diagnosis of breast cancer with mammography: recent advances," *IEEE Trans. Inf. Technol. Biomed.*, vol. 13, no. 2, pp. 236–251, 2009.

[10] M. Veta, J. P. Pluim, P. J. Van Diest, and M. A. Viergever, "Breast cancer histopathology image analysis: A review," *IEEE Trans. Biomed. Eng.*, vol. 61, no. 5, pp. 1400–1411, 2014.

[11] M. Kowal and P. Filipczuk, "Nuclei segmentation for computer-aided diagnosis of breast cancer," *Int. J. Appl. Math. Comput. Sci.*, vol. 24, no. 1, pp. 19–31, 2014.

[12] Y. M. George, H. H. Zayed, M. I. Roushdy, and B. M. Elbagoury, "Remote computer-aided breast cancer detection and diagnosis system based on cytological images," *IEEE Syst. J.*, vol. 8, no. 3, pp. 949–964, 2014.

[13] A. D. Belsare, M. M. Mushrif, M. A. Pangarkar, and N. Meshram, "Classification of breast cancer histopathology images using texture feature analysis," in *TENCON 2015-2015 IEEE Region 10 Conference*, 2015, pp. 1–5.

[14] A. Brook, R. El-Yaniv, E. Isler, R. Kimmel, R. Meir, and D. Peleg, "Breast cancer diagnosis from biopsy images using generic features and SVMs," Computer Science Department, Technion, 2008.

[15] "Israel Institute of Technology." ftp://ftp.cs.technion.ac.il/pub/projects/medic-image.

[16] B. Zhang, "Breast cancer diagnosis from biopsy images by serial fusion of Random Subspace ensembles," in *Biomedical Engineering and Informatics (BMEI), 2011 4th International Conference on*, 2011, vol. 1, pp. 180–186.

[17] D. C. Cireşan, A. Giusti, L. M. Gambardella, and J. Schmidhuber, “Mitosis detection in breast cancer histology images with deep neural networks,” in *International Conference on Medical Image Computing and Computer-assisted Intervention*, 2013, pp. 411–418.

[18] G. Litjens *et al.*, “Deep learning as a tool for increased accuracy and efficiency of histopathological diagnosis,” *Sci. Rep.*, vol. 6, p. 26286, 2016.

[19] K. Sirinukunwattana, S. E. A. Raza, Y.-W. Tsang, D. R. Snead, I. A. Cree, and N. M. Rajpoot, “Locality sensitive deep learning for detection and classification of nuclei in routine colon cancer histology images,” *IEEE Trans. Med. Imaging*, vol. 35, no. 5, pp. 1196–1206, 2016.

[20] A. Krizhevsky, I. Sutskever, and G. E. Hinton, “Imagenet classification with deep convolutional neural networks,” in *Advances in neural information processing systems*, 2012, pp. 1097–1105.

[21] F. A. Spanhol, L. S. Oliveira, C. Petitjean, and L. Heutte, “Breast cancer histopathological image classification using convolutional neural networks,” in *Neural Networks (IJCNN), 2016 International Joint Conference on*, 2016, pp. 2560–2567.

[22] A. Cruz-Roa *et al.*, “Automatic detection of invasive ductal carcinoma in whole slide images with convolutional neural networks,” in *Medical Imaging 2014: Digital Pathology*, 2014, vol. 9041, p. 904103.

[23] E. S. Olivas, J. D. M. Guerrero, M. M. Sober, J. R. M. Benedito, and A. J. S. Lopez, “Handbook Of Research On Machine Learning Applications and Trends: Algorithms, Methods and Techniques-2 Volumes,” 2009.

[24] T. Araújo *et al.*, “Classification of breast cancer histology images using convolutional neural networks,” *PloS One*, vol. 12, no. 6, p. e0177544, 2017.

[25] M. Macenko *et al.*, “A method for normalizing histology slides for quantitative analysis,” in *Biomedical Imaging: From Nano to Macro, 2009. ISBI’09. IEEE International Symposium on*, 2009, pp. 1107–1110.

[26] E. Reinhard, M. Adhikhmin, B. Gooch, and P. Shirley, “Color transfer between images,” *IEEE Comput. Graph. Appl.*, vol. 21, no. 5, pp. 34–41, 2001.

[27] W. Nawaz, S. Ahmed, A. Tahir, and H. A. Khan, “Classification Of Breast Cancer Histology Images Using ALEXNET,” in *International Conference Image Analysis and Recognition*, 2018, pp. 869–876.

[28] S. Charan, M.J. Khan, K. Khurshid, “Breast cancer detection in mammograms using deep convolutional networks”, *IEEE International Conference on Mathematics and Engineering Technologies*, 2018