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Classification of histological images of thyroid nodules based on a combination of Deep Features and Machine Learning

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Abstract

Background: Thyroid nodules are a prevalent worldwide disease with complex pathological types. They can be classified as either benign or malignant. This paper presents a tool for automatically classifying histological images of thyroid nodules, with a focus on papillary carcinoma and follicular adenoma.

Methods: In this work, two pre-trained Convolutional Neural Network (CNN) architectures, VGG16 and VGG19, are used to extract deep features. Then, a principal component analysis was used to reduce the dimensionality of the vectors. Then, three machine learning algorithms (Support Vector Machine, K-Nearest Neighbor, and Random Forest) were used for classification. These investigations were applied to our database collection,

Results*:* The proposed investigations have been applied to our private database collection with a total of 112 histological images. The highest results were obtained by the VGG16 transfer deep feature and the SVM classifier with an accuracy rate equal to 100%.

Keywords: Thyroid nodules, Papillary carcinoma, Follicular adenoma, Deep feature, Support Vector Machine learning, K Nearest Neighbor, Random Forest, supervised machine learning, transfer learning,

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1. Introduction

The thyroid gland can develop solid or fluid-filled nodules, which are common disorders with clinical symptoms of various pathological kinds. There are two types of thyroid nodules: benign thyroid nodules and malignant thyroid nodules. Thyroid adenoma and nodular goiter are benign thyroid nodules. The thyroid's papillary carcinomas, follicular, medullary, and anaplastic carcinomas are all examples of malignant nodules. The differential diagnosis of thyroid nodules is crucial because thyroid cancer requires surgery while benign nodules just require follow-up. The pathological evaluation of tissues from resected tumors is the gold standard for tumor diagnosis. Currently, pathologists obtain the vast majority of abnormal tissue cuts, and clinical diagnosis is based on long-term collections of samples. In spite of this, manual differential diagnosis of thyroid tumor histological images is still challenging for three main reasons: first, the ability to accurately diagnose samples depends greatly on the pathologist's professional training and experience, and such experience cannot be quickly acquired; second, the task is time-consuming, expensive, and boring; and third, it is challenging for the human eye to distinguish subtle changes in the tissues. As a result, pathologists may become exhausted, which might lead to an incorrect diagnosis.

Thus, determining the correct histological diagnosis of thyroid nodules is difficult and requires an automatic system that aids in diagnosis [1].

Machine learning algorithms (ML) are used to allocate test data to specified groups in classification tasks. Deep learning algorithms are being applied to the pathological diagnosis of various diseases and are being employed more and more in the field of medical imaging recently. But the DL algorithms require a large database to give us satisfactory and accurate results, especially in the field of medicine, and unfortunately, this is not the case in our work, because we do not have a large database.

Transfer learning is a popular and efficient method where the information gained by a DL model while addressing a source problem S is applied to address a separate or related target problem T. In this work, we studied the impact of deep features on three machine learning algorithms, namely: Support Vector Machine (SVM), K Nearest Neighbor (KNN), and Random Forest (RF) on our database. The winning model of the ImageNet competition at ILSVRC-2014 provided the deep features used in this work, which is the Visual Geometry Group's abbreviation VGG16, where 16 denotes the number of layers. The second architecture applied in this study is the Visual Geometry Group abbreviation VGG19, and the 19 indicates the number of layers. Our method is divided into four steps: first, we applied pre-processing operations to the data then we transferred the initial layers from the pre-trained VGG16 and VGG19 models to our datasets. Additionally, we optimized the vector features using principal component analysis, and then the classification models are applied.

The main contribution of this work is focused on the realization of an automatic system that makes the classification of the histological images of the thyroid pathology accurate, to enable histological doctors to make their diagnosis or validate their microscopic diagnosis.

The remainder of this document is organized as follows: Section 2 details related work; Section 3 details the dataset and the method used; Section 4 presents the results and discusses the obtained results; and Section 5 concludes the study.

2. Materials and Methods

In this research study, we explored the deep Convolutional Neural Network of two pre-trained models as a features extractor, the VGG16 and the VGG19, which would contribute to the construction of a system for identifying the classes of thyroid nodules based on histological images, stained with H&E. For this investigation, we used a private dataset of 112 histological images of the thyroid. The proposed method is illustrated in Figure 1 (Fig.1).

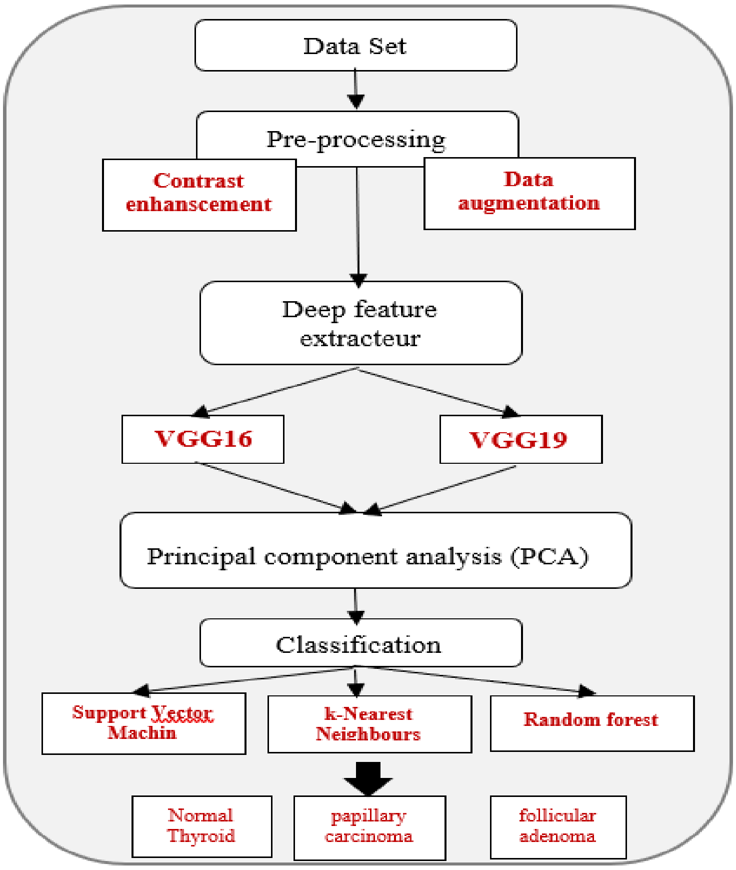
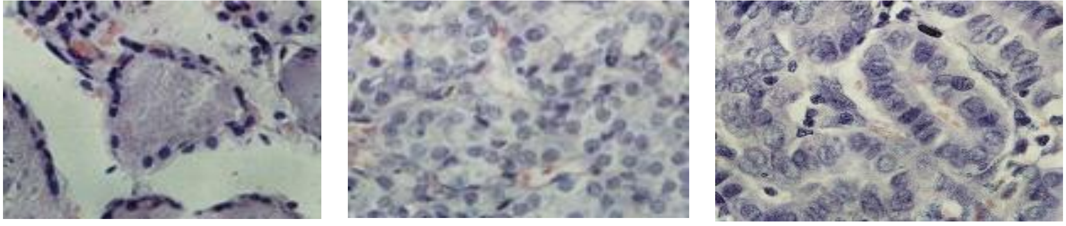


Fig. 1. The diagram of the proposed method

2.1 Data acquisition

We used a real dataset (self-collected from several laboratories) of 28 thyroid histology images for this research study with the consent of the patients and the preservation of their anonymity. These images were taken with an Olympus CX41 microscope and a DP12 camera at the histology lab of the University of Tlemcen's Faculty of Medicine. Pathological slides were stained with hematoxylin and eosin (H&E) for morphological evaluation. All images were scanned at ×40 magnifications. Three classes were used to categorize each image: normal thyroid (NT), follicular adenoma (FA), and papillary carcinoma (PC). A pathologist was responsible for labeling. 10 images were classified as normal thyroid, 10 images were classified as follicular adenoma and 8 images were classified as papillary carcinoma.

Figure 2 (Fig.2) presents some images from our private database.



(a) normal thyroid (b) follicular adenoma (c) papillary carcinoma

Fig. 2. Example of images from the database

2.2 Pre-processing

Pre-processing, which is a part of data preparation, refers to any type of processing done on raw data in order to get it ready for another data processing technique. It is a crucial phase for image processing and computer vision. In this study we have used two processes: 1) contrast enhancement method and 2) database augmentation method.

2.2.1 Contrast enhancement

In this work, the images used are color images. These images are not of good quality; this is due either to the poor quality of the slide or to the acquisition device (DP12). To improve the quality of these images we tested some filters like the median filter and the Gaussian filter...ect, but unfortunately, we did not obtain satisfactory results (loss of information), so we opted for contrast enhancement. Figure 2 (Fig.2) shows the result of such processing.

2.2.2 Data augmentation

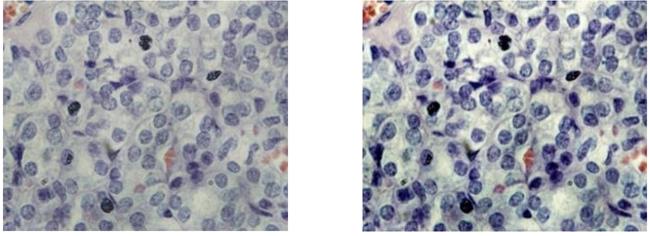
In our work, we have a very small database that contains 28 images. The work done on this database does not give good results because of its size. To slightly increase the number of images in our database, we used the process of flipping and rotating images.

The images were rotated and flipped to enhance the data. Each image fragment was rotated 0°, 90°, 180°, and 270° in addition to being flipped horizontally. We've quadrupled the size of the data by flipping and rotating it in this manner.

We obtained a total of 112 images: 40 NT images, 40 FA images, and 32 PC images.

2.3 Feature extraction VGG16 and VGG19

Pre-trained models frequently aid in improved initialization and convergence when the dataset is less than the dataset of natural images, and this outcome has also been widely applied in other fields of imaging [32]. We employed two pre-trained CNN-based models that were suggested by the Visual Geometry Group (VGG) of the University of Oxford to achieve this[33].



(a) original image (b) image improved

Fig. 3. Contrast enhancement

VGG16 and VGG19, two separate deep CNNs, were used as feature extractors in this work. These designations were chosen because the basic architectures of VGG16 and VGG19 each have sixteen weight layers and nineteen weight layers, respectively [33]. Acquiring the feature vector from convolutional layers rather than using the model's classification phase is the notion behind exploiting the deep functionality of both models.

2.4 Principal component analysis (PCA)

In a multivariate analysis method known as principal component analysis (PCA), observations are defined by a number of quantitative dependent variables that are connected with one another. With the aid of additional orthogonal variables referred to as principle components, it is intended to extract key information from the array and display it as points on maps to show how well observations and variables match up with each other [34].

PCA enhances machine learning accuracy and efficiency while preventing over-fitting [35].

Principal component analysis can be broken down into five steps:

1-Normalize the gamut of initial continuous variables.

2-Determine correlations by calculating the covariance matrix.
3-Identify the primary components by computing the eigenvectors and eigenvalues of the covariance matrix.
4-Build the features vector (choose the key elements to be maintained).
5-Recasting of data according to the axes of the principal components [35].

2.5 Classification

For this research, the classifier receives the deep characteristics that were extracted in order to conduct various machine learning models. We begin by presenting the classification models that we have selected for this study, and then we will talk about the evaluation parameters that allow us to estimate the performance of each model, which will lead to the choice of the optimal solution.

a. The classification models used

1. *Support Vector Machine (SVM)*

SVM is a supervised machine learning method that produces excellent accuracy while using little processing power. It is straightforward and widely used. It can be used for problems involving regression and classification [36].

SVM does not inherently allow multi-class classification in its most basic form. It facilitates categorizing data points into two classes and binary classification. Calculations of data-point separation rely on a kernel function. There are various kernel functions, including sigmoid, linear, polynomial, Gaussian, and radial basis functions (RBF). The fluidity and effectiveness of class separation are determined by these functions, and tinkering with their hyper-parameters can result in either an over- or under-adjustment. After dividing the multi-class problem into many binary classification problems, the same method is applied to multi-class classification.

The most often used multi-class SVM techniques include: the One-to-One approach breaks down the multi-class problem into several binary classification problems. With a binary classifier for each pair of classes, and the One-to-Rest approach, in this approach, the distribution is defined on a binary classifier for each class [37].

In this particular work, we chose the first approach to apply the classification between normal thyroid, papillary carcinoma, and follicular adenoma with the linear nucleus function

2. *k-Nearest Neighbours (KNN)*

K-Nearest Neighbors (KNN) is a group of techniques for regression, and classification. Since the nearest K-neighbors are a non-parametric learning approach, there is no restriction on the number of parameters. However, the extent of the learning base will determine how complicated they are.

The KNN algorithm can compete with the most accurate models because it makes extremely accurate predictions. Therefore, it can be used for applications that require high precision but do not require the generation of human-readable models, as KNN does not produce comprehensible models. The K-nearest neighbors have been used in several fields and many applications such as statistical estimation and pattern recognition, prediction of economic events, estimation of the capacity of a lithium-ion battery, distance measurement, text categorization, and multi-label classification [38].

The 'k' in the KNN algorithm refers to the number of nearest neighbors to include in the majority of the voting process, making it a crucial parameter for the KNN algorithm.

3. *Random forest*

A supervised machine learning technique called random forest is frequently applied in classification and regression applications [39]. In order to classify a vector input, the classifier comprises of a mixture of tree classifiers, each of which is constructed using a random vector sampled independently from the input vector and casts a unit vote for the most popular class. The RF algorithm's ability to handle data sets with both continuous variables (as in regression) and categorical variables (as in classification) is one of its key characteristics. It's called random forest because we use random subsets of data and features and end up building a forest of decision trees (many trees). RF is also a classic example of a bagging approach because we use different subsets of data in each model to make predictions [40].

b. Classifier performance evaluation

Metrics for assessing our method have been introduced in this section. This is an essential indicator for assessing how well the model predicts the expected outcome. We evaluated the classification performance of the proposed thyroid histology images in our dataset in terms of accuracy (ACC) (equation (1)), precision (Pre) (equation (2)), recall (equation (3)) and score equation F1. (4)).
The evaluation metric definitions are as follows:

$$ACC = \frac{TP+TN}{TP+TN+FP+FN} \qquad (1)$$

$$Pre = \frac{TP}{TP+FP} \qquad (2)$$

$$Recall = \frac{TP}{TP+FN} \qquad (3)$$

$$F1 = \frac{2.Pre.Recall}{Pre+Recall} \qquad (4)$$

In the above formulas, TP, TN, FP, and FN are respectively the numbers of true positives, true negatives, false positives, and false negatives.

3. Results

In this section, we discuss the implement of VGG16 and VGG19 architectures as features extractors combined with machine learning, such as SVM, KNN, and Random Forest, using a real and private database.
Table I presents the classification results using the VGG16 deep feature and SVM, KNN, and RF classifiers, without and with the application of PCA.
According to the result mentioned in Table I, the VGG16 model gave us better results with the use of linear SVM, the accuracy obtained is 100% with and without the use of PCA. We found that the accuracy obtained with PCA (accuracy = 100%) is higher than the accuracy obtained without PCA (accuracy = 95%) when we used the Random forest classifier. Regarding the results produced by using KNN, we obtained poor results, the accuracy reaching 36% with and without the use of PCA.
Then we can say that our method is very effective when we used the VGG16 deep feature and SVM as a classifier, because the results obtained with this experiment are better results compared to the other classifier. Despite we obtained good results when we used the RF classifier but for the classification with RF we obtained an accuracy of 100% with the application of PCA. However, the SVM classifier achieves a high accuracy without using PCA.

TABLE I. CLASSIFICATION RESULT BY USING VGG16 AS FEATURE EXTRACTOR AND SVM, KNN, AND RANDOM FOREST AS CLASSIFIER

	Without PCA			**With PCA**		
	SVM	**KNN**	**Random forest**	**SVM**	**KNN**	**Random forest**
ACC	100%	36%	95%	100%	36%	100%
F1 score	100%	19%	95%	100%	20%	100%
Recall	100%	36%	95%	100%	36%	100%
Precision	100%	13%	95%	100%	13%	100%
Nombre d'erreur	0	14	1	0	14	0

Table II presents the classification results obtained by using VGG19 as a feature extractor and SVM, KNN, and RF as a classifier, with and without the application of PCA.

The best results are obtained by the SVM classifier without and with the application of PCA with an accuracy of 100%.

We noticed that using VGG19 as a feature extractor yielded the same results for the SVM and RF classifiers as using VGG16. But when utilizing the PCA with the VGG19 as a feature extractor, we found that the precision value for the KNN classifier is slightly increased.

TABLE II. CLASSIFICATION RESULT BY USING VGG19 AS FEATURE EXTRACTOR AND SVM, KNN, AND RANDOM FOREST AS CLASSIFIER

	Without PCA			**With PCA**		
	SVM	**KNN**	**Random forest**	**SVM**	**KNN**	**Random forest**
ACC	100%	36%	95%	100%	50%	100%
F1 score	100%	19%	95%	100%	42%	100%
Recall	100%	36%	95%	100%	50%	100%
Precision	100%	13%	95%	100%	70%	100%
Nombre d'erreur	0	14	1	0	11	0

Therefore, we discovered that the best results are obtained when VGG16 or VGG19 are used as feature extractors and SVM is used as a classifier; as a result, we consider this combination to be the study's suggested solution.

We also noticed that the strength of deep approaches emanates from the great capacity of databases, thus reinforcing learning which leads to the adjustment of attributes (automatic), however, guest the acquisition of a large database is often a true technical issue how much even one tries to divert it with software methods such as data augmentation using image transformation tools (rotation, scaling…).

Our work is carried out on a small real database, which we acquired with the Olympus CX41 microscope and the DP12. The images used are obtained from the slides of the patients of the hospital of Tlemcen. We used pre-trained CNN models for feature extraction and ML algorithms for classification. Unfortunately, we couldn't find a public database to apply our work on it, in order to make a comparison between the results. The common point between our work and the works with which we compared is the organ studied and the type of image (histological image).

Table III presents a comparison between our work carried out and existing work in the literature which uses histological images of the thyroid.

4. Discussion

Several new and personalized deep learning models have been proposed by researchers to classify histo-pathological images of cancers of the following organs: bone [2][3], brain [4][5], Breast [6][7][8]), Colon [9][10][11][12], Lung [13], Gastric [14], Pancreas [15] and Prostate [16].

Transfer-learned deep learning models have also been widely used to classify histo-pathological images of cancers of the following organs: blood [17], brain [4][18], breast [19][20][21][22][23], cervix [24] and the colon [25].

In the literature, not many works have been recorded on the classification of thyroid histopathology images using artisanal features and traditional machine learning techniques [26][27][28][29].

Hence, it is evident from the literature that there have been works on the application of deep learning and transfer learning to classify histopathology images. However, to the best of our knowledge, few works have been reported in the literature on the classification of thyroid histopathology images with the application of deep learning methods [30] and transfer learning methods [31]. Therefore we applied pre-trained deep learning models as a features extractor to classify our collected database.

TABLE III. COMPARISON BETWEEN OUR RESULTS AND THOSE OF LITERATURE

Classification method	**Number of images**	**Results**
Closest Matching Rules (CMR)[28]	219 H&E stained thyroid histopathology images.	Accuracy = 100%
multi-classifier system A combination of SVM-L + SVM-Q + SVM-RBF + CMR and SVM-L + SVM-Q + CMR classifiers [29]	219 H&E stained thyroid histopathology images.	Accuracy of combinations = 99.54%
DCNN deep convolutional neural networks with VGG-19, ResNet-v2. [30]	11,715 H&E stained thyroid histopathology images.	Accuracy VGG-19 = 97.34%
Transfer Learning (VGGNet, ResNet, InceptionNet et DenseNet)[31]	221 H&E stained thyroid histopathology images.	DenseNet
Proposed approach: Transfer Learning (VGG16 et VGG19) + PCA + SVM, KNN, CNN.	112 histological images of the thyroid.	SVM Accuracy = 100%

5. Conclusions

The use of deep learning models, that have already been trained to categorize thyroid histopathology images into the three classes of NT, FA, and PC, was experimentally assessed in this study. VGG-16 and VGG-19 pre-trained models were employed in this process. In order to extract features, these pre-trained models are employed. The deep features obtained from the above mentioned model are introduced separately into the classification algorithms such as SVM, KNN and Random forest. The results showed that VGG16 and VGG19 performed best on the dataset using SVM and RF as classifier. Also the PCA improved the RF classifier results.

As a result of the positive findings, a CAD system that applies this model to thyroid histopathology image categorization can be put into place.

This study addresses the medical challenge bur it is also open to further enhancements (more pathologies after expanding the database).

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7. Conflict of interest statement

We certify that there is no conflict of interest with any financial organization in the subject matter or materials discussed in this manuscript.

8. Authors' biography

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