Oral Epithelial Dysplasia Computer Aided Diagnostic Approach

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***Abstract*—The main purpose of this research is to establish a Computer Aided Diagnositic (CAD) approach for the detection and classification of Oral Epithelial Dysplasia. The disturbances that occur in the epithelial layers is diagnosed as premalignant dysplasia. The epithelial dysplasia diagnosis, in-terms of accuracy, is pathologically difficult and contributes to main challenges to oral pathologists due to the multiple dysplastic criteria of the disease such as the loss of polarity of the basal cells and other cellular and nuclear changes. A new approach has been developed based on different selections and magnifications of stained microscopic images. The approach extracts a set of features that would automatically diagnose the image supplying its condition and the category it has reached so far. The resulted analysis from our research will enable the pathologists in classifying cells abnormalities. Feature extracted using Oriented FAST and Rotated BRIEF (ORB) algorithm with the Support Vector Machine (SVM) as a classification algorithm. The proposed approach achieved an accuracy of 92.8% in classification of Oral Epithelial Dysplasia. The system was trained and tested on a total of forty-six cases of magnification 100x levels of 70% and 30% respectively. This research presents for the first time a diagnostic approach for grading oral epithelial dysplasia according to sixteen extracted features with the given experimented accuracy rates on different magnification levels.**

***Index Terms*—Oral Cancer, Medical Image Analysis, Oral Epithelial Dysplasia, Segmentation, ORB Feature extraction, SVM classifier**

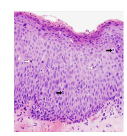
I. Introduction

Oral diseases are widely spread around the globe, as a fact most of the adults have dental cavities abnormalities [1]. According to WHO, oral diseases are included in the list of major health problems that humans face; especially periodontal diseases, dental caries, and epithelial abnormalities [1]. The epithelial surface is the transparent thin tissue forming the outer lining layer of the oral cavity. Lesions with epithelial dysplasia, sometimes referred as "Potentially malignant lesions", are basically various disturbances in the epithelial tissue with benign morphological change having high intention to turn into malignancy because of its unpredictable course of progression.

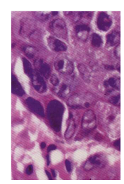
Identifying these processes along with the knowledge of these lesions is very important in prevention and early diagnosis and hence treatment. Epithelial dysplasia is divided into three categories of severity: mild, moderate, and severe. According to the latest studies made by the WHO in 2017 [2], the severe category in epithelial dysplasia is identified as Carcinoma in-Situ.

The cells are manipulated using three different magnification levels for each case; 40x, 100x, and 400x. Throughout each magnification level has certain features that can be extracted from as mentioned in Figure 1. As the magnification increase there are more details that arise in the cell image as shown in Figure 1, where Figure 1a shows the 40x magnification image, Figure 1b shows the 100x magnification image and Figure 1c shows the 400x magnification image.

(a) Photomicrograph showing the normal epithelial



(b) Photomicrograph showing mitotic figures



(c) Photomicrograph showing dyskaryosis and aypical nuclear architecture

Fig. 1: A sample image of different magnifications

A number of 300-400 new cases and 145,400 deaths from oral cavity cancer (including lip cancer) occurred in 2012 worldwide [3]. There are several risk factors that play a role in oral cavity cancer occurrence including the following: smoking, alcohol use, smokeless tobacco use [3]. A national survey by the Egyptian Smoking Prevention Research Institute (ESPRI) revealed that among males aged 18 and older, 13.6% in rural areas reported current use of the water pipe, compared to 10% in the urban areas. These statistics stated that 20.3% of Egypts population overall are daily tobacco smokers [4]. As per the National Cancer Institute in Egypt (NCI) [5], Oral cavity cancer in Egypt is the 5^{th} common malignant tumor in males, however in females, it is in the 8^{th} place. The proposed approach shall have a great impact upon not only Egyptian community but also the African and regional communities.

The simplicity in the identification of the dysplasia on spot will insure the fastest responses from the pathology experts in treatment the cases. There has been an increase in the cancer of the oral cavity in the recent years and each year more than over 450,000 new cases [6] of oral cancer are reported. A high incidence of oral cancer [7] is mainly due to late diagnosis of potential precancerous lesions and conditions. In 1984, this disease became a public health issue in many regions of the world including the UK [8], South Africa, and many Southeast Asian countries [9], [10].

TABLE I: Criteria of the Epithelial Dysplasia [2]

Architecture	Cytology
Irregular Epithelial Stratification	Abnormal variation in nuclear size (anisonucleosis)
Loss of polarity of basal cells	Abnormal variation in nuclear shape (nuclear pleomorphism)
Basal cell hyperplasia	Abnormal variation in cell size (anisocytosis)
Drop-shaped rete ridges	Abnormal variation in cell shape (cellular pleomorphism)
Increased number of mitotic figures	Increased nuclear-cytoplasmic ratio
Abnormally superficial mitoses	Increased nuclear size
Pre-mature keratinization in single cell (dyskeratosis)	Atypical mitotic figures
Keratin pearls within rete ridges	Increased number and size of nucleoli (Hyperchromatism)

Criterion of the epithelial dysplasia are divided into two-groups; The architectural group which is the structure and the look of the epithelial tissue; the cytological group which is the structure and function of the cell and nucleus; as mentioned in Table I. There are sixteen different extracted features from the epithelial microscopic images. Mainly, for the extracted features implying the disturbance in the epithelial layer are; the dropped rete ridges which are the U shaped figures as highlighted and shown in Figure 2, the existence of the rounded loops as called Keratin Pearls as shown in Figure 7, the increased number and size of the nucleoli as shown in Figure 9. Moreover, each extracted criteria is explained in detail in Section III-B3 which presents our Approach. There are certain features that require certain magnification levels in order to be detected and extracted from the biopsy tissues collected from the patients.

The paper is organized as follow, Section II discusses similar related researches. The proposed approach is explained upon different feature extracting algorithms and presented in Section III. Section IV discusses our data set collection work. Our implemented experiments and results are presented in Section V. Finally, Section VI presents our conclusions and future work.

II. Related Work

An approach was proposed by Sami et al. [11] to work on hematoxylin-eosin stained microscopic images of the epithelium. These researches have chosen this topic to assist other

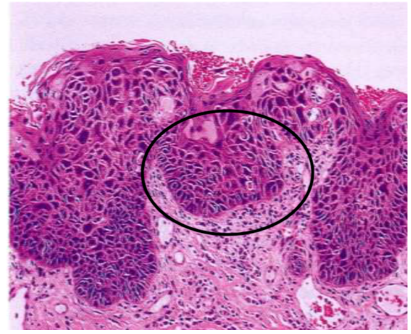


Fig. 2: The roundness of the U shaped figures are diagnosed as Dropped Rete Ridges

doctors in their justification of the oral epithelial diseased patients. They mainly have detected the dysplasia along with analysis that would benefit the physicians in the medical field. The system basically focuses on the region of interest which is the twin pairs in the epithelial. The image then passes through multiple pre-processing algorithms to be prepared for further mathematical calculations. The calculations done target providing differences in the roundness of the left and right pair. As per the generated experiments, the higher the rate of roundness of the pair, the more severe the case and dysplasia grows to. They were capable of categorizing the case to Normal, Dysplasia, or Carcinoma In-Situ.

SVM based classification of the epithelial is proposed by P.Aurchana et al. [12] to detect the Leukoplakia; which is the white or grayish keratotic patch in the oral cavity. Their main objective was to design an application to help in early detection of the epithelial dysplasia. Their system deals with microscopic images. Firstly, they convert the RGB image to HSV image for a better color space. Moving on to the feature extraction, they've used two algorithms for comparisons later on; the SURF Feature Extraction, and the SIFT Feature Extraction. They have used SVM (Support Vector Machine) which is a machine-learning classifier. They've established high accuracy rate of 91.4% in terms of the SURF algorithm, and 84% in terms of the SIFT algorithm.

Automated classification of cells in sub-epithelial connective tissue is a system proposed by M. Muthu Rama et al. [10]. They used segmentation and classification of sub-epithelial connective tissue. Segmentation has been carried out using multi-level thresholding and the cell population has been classified using support vector machine (SVM) based classifier. They filtered the cells and converted them to grayscale, hence the threshold was assigned at the valley between lower and higher gray level intensity in the histogram, resulting in the segmentation of target features from input image. They got a sensitivity of 90.469%; specificity of 87.54% and classification accuracy of 88.69%

A Detection and Diagnosis of Colitis on Computer Tomography system was proposed by Jiamin Liu et al. [13]. They discussed the inflammation of the inner linning of the colon wall due to different reasons such as; ischemia, infection, neutropenia, or irritable bowel disease. They concluded that colitis detection and diagnosis by deep neural networks is accurate and promising for future clinical application. They have used the RCNN algorithm and improved their accuracy and efficiency by applying Faster RCNN. As per their results, they have calculated the mean of average precision of 48.7% and 50.9% for RCNN and Faster RCNN, respectively.

A detection of thyroid papillary cancer system was proposed by Hailiang Li et al. [14] for the thyroid cancer. They discussed the detection of the thyroid papillary cancer through ultrasound images. They weren't very satisfied with the results of using the CNN with the ultrasound images. Mainly, the accuracy of thyroid ultrasound diagnosis is closely depended on the experience and cognitive ability of diagnosticians which isn't accurate enough for judgment. There are several techniques that they have used including CNN, RCNN, and KNN. They stated that they're aiming in the future to generate a practical diagnostic report.

III. Proposed Approach

In the current work, we have utilized the 100x zoom level microscopic images. Through this magnification level some of the features explained in table I can be extracted. The images pass through pre-processing phase to prepare the image for the feature extraction phase. Apply the feature extraction algorithm and finally apply the classification algorithm in the classification phase. Figure 3 shows the proposed approach different phases and stages.

A. preprocessing phase

The pre-processing phase is responsible for enhancing, modifying and preparing the image for feature extraction. As pre-processing phase is successful this means better feature extraction then better classification [15].

1) Image Cropping: At this stage, images are cropped to keep a unified size of 600 pixel width and 600 pixel height. Keeping the same image size to facilitate the process of feature extraction.

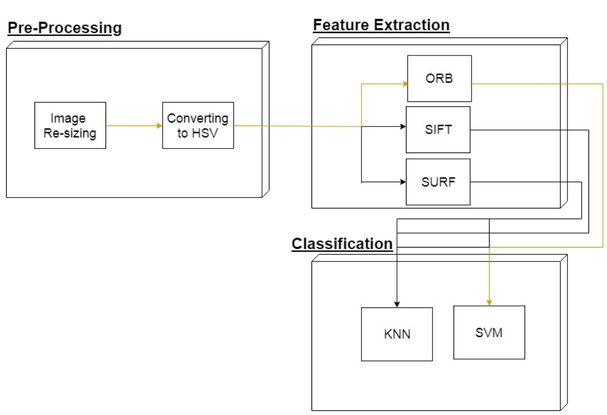


Fig. 3: The proposed approach block diagram

2) Color conversion: Images are converted from RGB color space to Hue, Saturation and Value (HSV) color space. HSV color space describes colors in terms of the Hue which is the color itself, Saturation is the colorfulness of the Hue, and Value describe the darkness of the color. In situations where color description plays an integral role, the HSV color model is often preferred over the RGB model [16]. Figure 4 shows a microscopic image with 100x magnification level in its original RGB color space. Meanwhile in Figure 5 the same image after converting it to HSV color space.

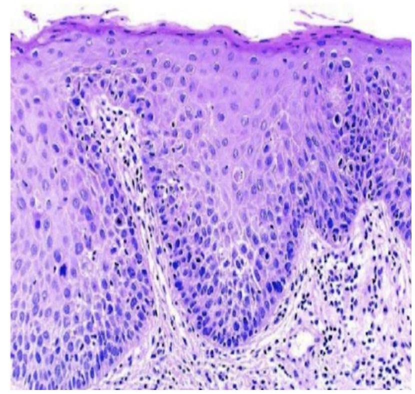


Fig. 4: A microscopic images of 100x magnification with RGB color format

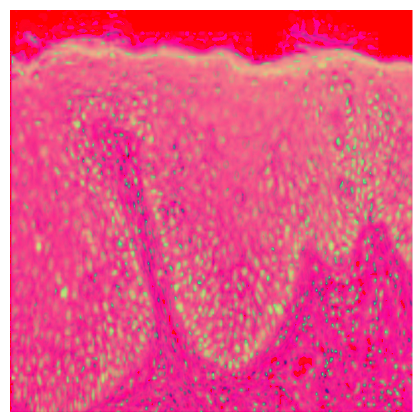


Fig. 5: A microscopic images of Figure 4 after converting to HSV format

B. Feature Extraction phase

We applied different feature extraction algorithms in order to capture the highest accuracy rate.

1) SIFT: (Scale Invariant Feature Transform) algorithm proposed by Lowe in 2004 [17] to solve the image rotation, scaling, and affine deformation, viewpoint change, noise, illumination changes, also has strong robustness. The SIFT algorithm has four main steps: First, Scale Space Extrema Detection, Second, Key point Localization, Third, Orientation Assignment, and Finally, Description Generation and the main advantage of SIFT that it is rotation and scale invariant [18].

2) SURF: (Speeded Up Robust Features) algorithm is based on the same principles and steps as SIFT; but details in each step are different. The algorithm has three main parts: First, interest point detection, Second, local neighborhood description and Finally, matching. SURF was used because it is better at handling images with blurring and rotation [19].

3) ORB: (Oriented FAST and Rotated BRIEF) algorithm was brought up by Ethan Rublee, Vincent Rabaud, Kurt Konolige and Gary R. Bradski in 2011. ORB is basically a fusion of FAST key point detector and BRIEF descriptor. The ORB algorithm has three main steps: First, Uses FAST to find key points, Second, Apply Harris corner measure to find top N points, Third, Pyramid to produce multi-scale features. Except for one disadvantage which is that FAST doesnt compute the orientation. So the algorithm computes the intensity weighted centroid of the patch with located corner at center. The direction of the vector from this corner point to centroid gives the orientation. To improve the rotation invariance, moments are computed with x and y which should be in a circular region of radius r, where r is the size of the patch and also ORB steer BRIEF according to the orientation of key points to get higher performance with rotation and the main advantage of the ORB is that is a good in computation cost and matching performances [20].

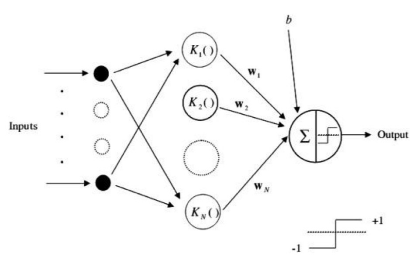


Fig. 6: Architecture of the SVM. [12]

C. Classification phase

The classification phase responsible for defining the object the on the test image with that learned during the feature extraction phase. The better features selection and extraction leads to better classification accuracy. Two classification approaches was tested to get the best performance from them.

1) SVM: (Support Vector Machine) is a statistic machine learning technique that has been successfully applied in the pattern recognition area and, is based on the principle of structural risk minimization. SVM builds a straight model to assess the choice capacity utilizing non-direct class limits in light of help vectors [21]. SVM learns an optimal separating hyper plane from a given set of positive and negative as shown Figure 6, the architecture of the SVM. It maps the input patterns into a higher dimensional feature space through some nonlinear mapping chosen a priori. A linear decision surface is then constructed in this high dimensional feature space. Thus, SVM is a linear classifier in the parameter space, but it becomes a non-linear classifier as a result of the nonlinear mapping of the space of the input patterns into the high dimensional feature space.

The kernel function may be any of the symmetric functions that satisfy the Mercer's conditions. There are several SVM kernel functions [22].

Polynomial function as shown in equation 1 where x is the input stream and x_i is the support vector.

$$(x^T x_i + 1)^p \tag{1}$$

Gaussian function as shown in equation 2 where σ^2 is a variance, $1 \leq i \leq N_i$, and N_i is the number of support vector.

$$\exp\left[-\frac{\left[x^T - x_i\right]^2}{2\sigma^2}\right] \tag{2}$$

Sigmoidal function as shown in equation 3 where β_0, β_1 are constant values and P is degree of the polynomial.

$$\tanh(\beta_0(x^T x_i) + \beta_1) \tag{3}$$

2) KNN: K-Nearest Neighbor classify images based on the training instances in feature space and based on a similarity measure which is distance functions. We used the distance function as the Euclidean distance since it is the most commonly used distance metric in KNN classifier [23]. The KNN classifier takes only one parameter which is K. The prediction of data is done based on its neighbor set. Rank is based on the minimum distance between data sets samples [24].

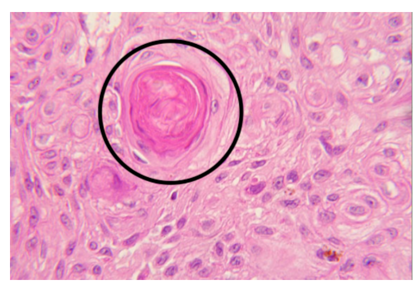


Fig. 7: The rounded-looped shapes are diagnosed as Keratin Pearl

D. Oral Epithelial Dysplasia classification

Oral Epithelial Dysplasia is classified and graded according to two types of classifications, architectural property and cytological property in total of 16 extracted features as mentioned in Table I. Briefly explaining each of the extracted features for the architectural properties, The Drop-shaped Rete Ridges, as shown in Figure 2, it is the abnormal rounded part dropped from the epithelial layer, unlike the normal epithelial layer shown in Figure 1a. One of the most noticeable features are the Keratin Pearls shown in Figure 7, they appear in the epithelial in a form of a recognized-sized pearl that effectively help determining the case.

Accordingly, the basal level of the epithelial cells should fall in perpendicular to the base, however; this is when the loss of polarity appears, leaning to either sides, changing the normality of the epithelial shown in Figure 8. Secondly, as for the cytological changes, starting by the mitotic figures shown in Figure 1b, The five nuclei pointed by the sign, this is a very abnormal feature as it is not supposed to have five abnormal nuclei in a very small region like this, for a more clear view of the abnormal nucleus architecture, it is shown in Figure 1c.

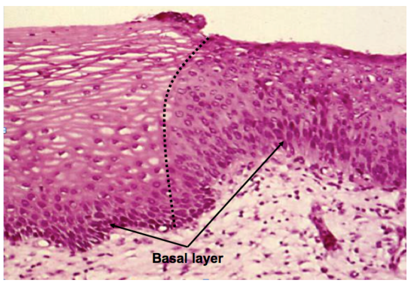


Fig. 8: The cells on the basal layer are not perpendicular on it, diagnosed as Loss of Polarity

Moreover, for the cytological changes we have increased number and size of nucleoli, the normal nucleolus is a small darkly stained body inside the nucleus, and it is supposed to be only one, but in Figure 9, there are numerous huge size nucleoli and some of the nucleus have multiple nucleoli not only one, which is considered as abnormal feature. In addition, supposedly each cell is rounded, containing nucleus that sizes one-third of the whole cell. However, in some cases the size of the nucleus increases, resulting in a size of almost equal ratio between them. Accordingly, the cell shape changes as well as the size as shown in Figure 1c.

Thirdly, to be capable of establishing all of the previously mentioned characteristics and features from the given different magnification types of images, clustering is used in order to combine the selected features, resulting in an accurate grouping of the epithelial cases in a form of clusters that represent the severity of the supplied case.

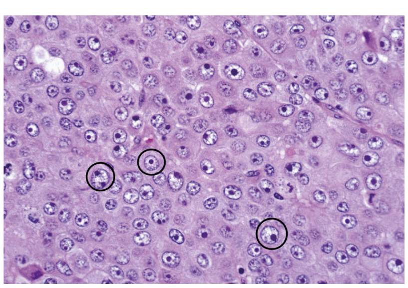


Fig. 9: Increase in Size and Number of Nucleoli

IV. Dataset Collection

Oral Epithelial Dysplasia is a new research topic in the field of computer science and especially image processing. Consequently, there is no dataset for the Oral Epithelial Dysplasia that can be used for the training and testing of our approach. Although, there are some images in the Internet, but most of them miss any sort of ground truth. So, we decide to generate our own dataset.

Our dataset is collected from two main sources: First, the the histopathology lab at the Faculty of Oral & Dental Medicine in Misr International University and Secondly, the Faculty of Dentistry, Alexandria University. A total number of forty-six cases, each with three magnified microscopic images. Seven of the specimens were normal cases while the other thirty-nine were diagnosed as oral epithelial dysplasia with different grades. The dataset cases are from different age and gender category.

V. Experiment & results

The proposed system was implemented on forty-six cases of 100x magnification zoom level. First of all, the images pass through the pre-possessing phase which is divided into two steps; Firstly, converting each image from RGB to HSV format.

Secondly, the system re-sizes the images to 600 pixel width and 600 pixel height.

The pre-processed images were trained on three different features extraction algorithms which are SIFT , SURF and ORB establishing the results in Table II.

Secondly, the features extracted from each image is divided into two random training and testing groups 70% and 30% which are equivalent to 32 pictures and 14 pictures respectively. KNN classifier uses the extracted features and the value of K was set with 1,3 and 5.Moreover, the SVM classifier uses the extracted features from the two groups. We have varied the values of the gamma and constant C multiple times in order to achieve the best results as occurred with 0.001 for the gamma and 100 for the constant C.

The results of the features extracted with SIFT and SURF Algorithm and with SVM classifier were the same achieving 71.4% and for the features extracted with ORB Algorithm with SVM Classifier 92.6%, furthermore, the results of SIFT and SURF with KNN classifier with K=1 was 71.6% and for k=3 the accuracy was 74.5% for both features extraction algorithms and ORB with KNN where k=1 gave accuracy 78.5% and for k=3 the accuracy was 71.4%

VI. Conclusions and future work

In the current work, we developed an automated system that classifies the epithelial dysplasia disease. The system extracts multiple number of features and characteristics, classifying them into two groups according to the severity of the extracted characteristics. The system works on Hematoxylin and Eosin stained microscopic images of 100x zoom level. The classification method passes by different stages, starting by the pre-processing, feature extraction, and finally classification. In the

TABLE II: Experimented Results on forty-six cases

Feature Extraction Algorithm	Classifier Algorithm	Accuracy Achieved
ORB	SVM	92.8%
SIFT	SVM	71.4%
SURF	SVM	71.4%
ORB	KNN, K=1	78.6%
ORB	KNN, K=3	71.4%
SIFT	KNN, K=1	78.5%
SIFT	KNN, K=3	71.4%
SURF	KNN, K=1	78.5%
SURF	KNN, K=3	71.4%

end, there's a statistical report that contains multiple calculated components in an image as for the length between the basal cell and the bottom of the epithelial. These calculations enormously increases the accuracy rate of the justification of the doctors. Among all of the co-working projects related to the epithelial dysplasia, we have achieved the highest result rates in terms of the oral epithelial dysplasia detection.

For our future work, we are collaborating with different educational institutes to increase our data set with a widespread range of a variety of images. We aim to use clustering techniques in order to combine and compare all the extracted features from all three magnification zoom levels for better accuracy rates. Clustering is hugely beneficial in-terms of determining the epithelial dysplasia levels either Mild, Moderate, or severe Carcinoma In-Situ. The upcoming proposed approach shows a good promise for the automated pathological assessment of oral cancer.

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