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Classification of Pathological Images Using Convolution Neural Networks

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***Abstract*— Cancer can now be counted in the deceases with high mortality rate. Oral cancer is the cancer originating or affecting the oral cavity. Oral cavity consists of the inner part of the open mouth which is visible. Gold standard available for the detection of the oral cancer is through analysis of the microscopic obtained from the Hemotoxilin and Eosin (H&E) staining of the tissue biopsy images. In this paper trying to automate the classification of the above mentioned images with the help of Convolution Neural Networks and Support Vector Machines. The collection used for training the CNN for the feature extraction consists of 300 cancerous images and 60 normal images. Through the proposed approach we achieved the Sensitivity of 80 percent and the specificity of 60 percent.**

Keywords*— Oral Cancer, Pathological images, Convolutional Neural Network

I. INTRODUCTION

Cancer is described as an abnormal uncontrolled division of cells. Cancer can affect or origin in any part of the body. Cancer associated with oral cavity is termed as Oral Cancer. Oral cancer accounts for over 30% of all cancers in the India and the mortality because of oral Cancer is 20 per 100,000 populations[1]. In this work we are restricting our scope to only one type of oral cancer: Squamous Cell Carcinoma(SCC) as it comprise of around 78% of all oral malignancies[3]. Oral squamous cell carcinoma is a malignant neoplasm of the oral Mucosa. Oral mucosa is divide in to Sqamous Epithelium as the outer part and Lamina Propria or the connective tissue as the inner part. The outer surface of Squamous Epithelium may be cover with a thin layer of Keratin.

As of now the diagnosis of oral cancer through the analysis of microscopic images of H&E stained tissue biopsy samples is done completely by the humans. Doing biopsy and getting the biopsy tissue sample is generally done by the Dentists and the H&E staining of these biopsy tissue samples are done by the lab technicians. We require specialist (Pathologist or Oncologist) to classify these H&E stained tissue samples into either the malignant class or the benign class. In this paper we are trying to automate the work of the above mentioned specialist.

However the following are the other two adjunctive diagnostic measures which are not very widely used techniques as they are still in the experimental phase.

- Staining the tissues in-vivo with the staining agents like Toluidine blue, Methylene blue or Lugol's iodine solution and noting down the change in the color and the intensity of the color on the stained tissues.
- Use of autofluorescence of the tissue i.e. the absorption of a particular wavelength and emission of a different wavelength when exited by a specific wavelength.

II. DISTINGUISHING FEATURES

There are two main features to distinguish the cancerous photomicrograph from the benign one. They are (a) Presence of Keratin Pearl in the tissue and (b) Invasion of malignant epithelial cells in the connective tissue. These two features are discussed in brief in the remaining part of this section.

A. Presence of Keratin Pearl in the tissue.

Keratin is the protein that protects epithelial cells from damage or stress. Keratin influences the mitotic process of the epithelium cells[2] and hence its presence, area of presences and the quantity dominates the features of classification of tissue into malignant or benign. A keratin pearl is a keratinized structure found in regions where abnormal squamous cells form concentric layers. Its appearance is that of a pearl and hence the name. Usually it is dark pinkish or reddish in color. Figure 1 and Fig. 2 depicts the keratin pearls as seen in the Photomicrographs pointed by the yellow arrows.

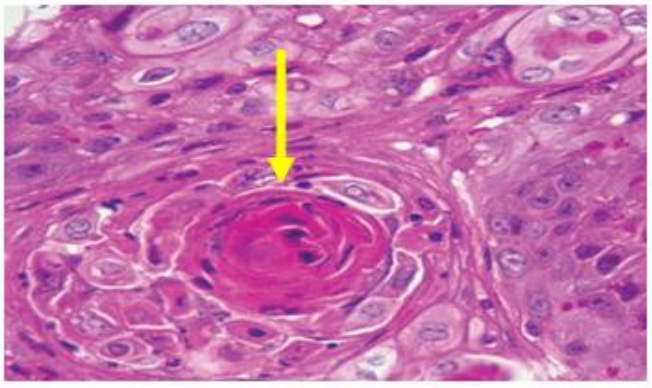

Fig. 1. Keratin pearl (sample1)

B. Invasion of malignant epithelial cells in the connective tissue

The outermost layer of oral mucosa is the epithelium. After this epithelium layer we have the Besal layer which differentiates the epithelium layer from the connective tissue.

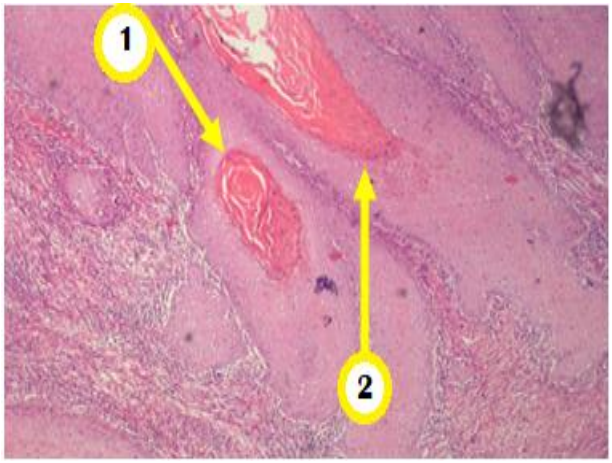

Fig. 2. Keratin pearl (Sample2)

Connective tissue is the inner most layer of the oral mucosa. When the squamous cells of this epithelium become cancerous cells, they break the middle Besal layer and invade the connective tissue. There for if the epithelial cells are found in the connective tissue then the photomicrograph can be classified as cancerous or else it is benign. Such invasion of the epithelial cells into the connective tissue can be seen in the Fig. 3 and Fig. 4.

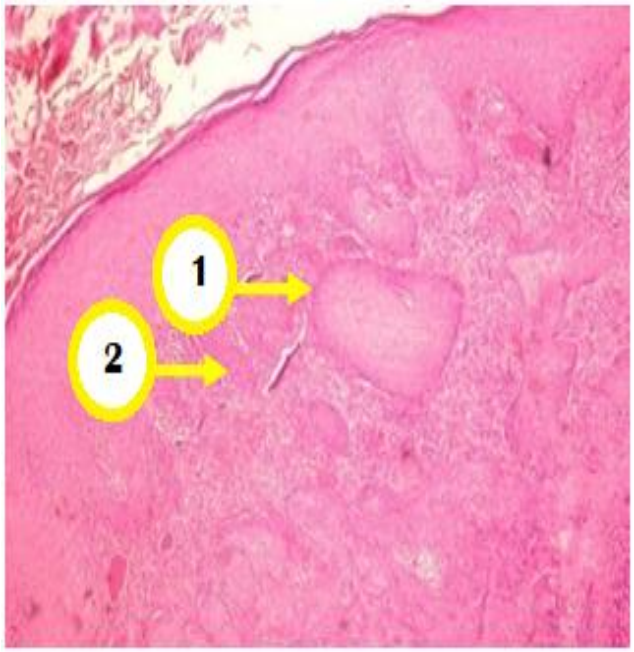

Fig. 3. The invading epithelial cells (Sample 3)

The first distinctive feature may or may not be present in the photomicrograph to be classified as cancerous but the second distinctive feature should be present to identify it as malignant.

III. Proposed Approach

Training photomicrographs of three different zoom (10X, 20X and 40X) of Malignant type are kept in one folder and those of Benign type are kept in another folder. These two folders are given as input to the convolution neural network for the extraction of the features. The test image is also given to the CNN module to extract the test image features. The preprocessing stage resizes the photomicrographs to appropriate size. Resizing is applied to the training data set as well as for the testing image.

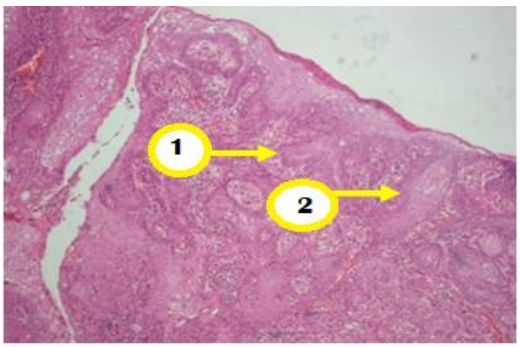

Fig. 4. The invading epithelial cells (Sample 2)

The process of extracting the features are done by custom tuned convolution neural network which is already trained for classification of some other objects. This type of fine tuning the already trained convolution neural network is known as transfer learning[4][5]. which we have used composes of more than 20 hidden layers which comprises of Convolution layer, Rectified Linear activation Function (ReLu) layer, along with the Max Pooling layer.

The convolutional neural network parameters are as follows. The output of layer l consists of $n_p^{(l)}$ feature maps of size $n_q^{(l)}$ x $n_r^{(l)}$. The input to layer l consists of $n_p^{(l-1)}$ feature maps from the previous layer, each of size $n_q^{(l-1)}$ x $n_r^{(l-1)}$. $Z_i^{(l)}$ is the ith feature map in layer l and can be defined as

$$Z_i^l = A_i^l + \sum_{j-1}^{n_p^{(l-1)}} M_{i,j}^l * Z_j^{l-1} \quad (1)$$

Where where $A_i^{(l)}$ is a bias matrix and $M_i^{(l)}$; j is the size of filter connecting the jth feature map in layer (l-1) with the i^{th} feature map in layer l[6]

We have used ReLU as the nonlinear function for the output of all the convolution layers except for the last one where the Sigmoid function is used. Rectified linear activation function also known as Rectified Linear Unit (ReLU) given by the following expression

$$f(x) = max\ (0, x) \tag{2}$$

$$i.e\ if\ x < 0, f(x) = 0\ and\ if\ x >= 0, f(x) = x.$$

This is the most popularly used activation function in deep learning models. The convergence of ReLU is very much improved over the tanh function. The only limitation of ReLU is that it should be used only within the hidden layers.

In the Max Pooling layer the maximum value of each window is taken. Max Pooling for a 2d image can be better understood by the Fig 5. From the top-left window, value 6 is chosen as it is the maximum in that window.

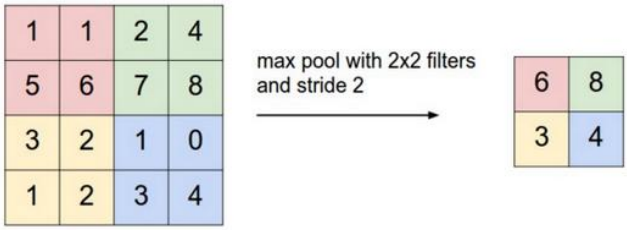

Fig. 5. Demonstration of the Max Pooling layer

A fully connected layer multiplies the input by a weight matrix and then adds a bias vector. Fully Connected layer is a multilayer perceptron which is defined as

$$Z_i^{(l)} = f(y_i^{(l)}) \tag{3}$$

$$y_i^{(l)} = \sum_{j=1}^{n^{(l-1)}} W_{i,j}^{(l)} Z_j^{(l-1)} + W_{i,0}^{(l)} \tag{4}$$

Where where $w_{i;j}^{(l)}$ denotes the weighted connection from the j^{th} unit in layer (l -1) to the i^{th} unit in layer l, and $w_{i;0}^{(l)}$ can be regarded es external input to the unit and is referred to as bias. Here, $n^{(l)}$ denotes the number of nodes in layer l

The proposed approach is summarized through the following points.

1) *Training images (300+ in cancer class and 50+ in Normal class) provided in the training image set and test image is provided in the test image set*
2) *Training images are resized to the desired size*
3) *Step (2) is applied to test images*
4) *Features of training samples of cancer class are extracted using the Convolution Neural networks and are stored in database*
5) *Step (2) is repeated to Normal class*
6) *Compare features of test image with the features of the trained image of both the cancer as well as normal class.*
7) *If the features of the test image are near to that of the training images of Cancer class the goto step (7-a) else goto step (7-b)*
   (a) *Assign the class to test image as probably Malignant*
   (b) *Assign the class to test image as probably Benign*

IV. Results and Discussion

In our case Sensitivity is the probability that a test will indicate cancer among those with the disease, Sensitivity: TP/(TP+FN) × 100 Where TP indicates True Positive, FN indicates False Negative. Specificity is the fraction of those without disease who will have a negative test result, Specificity: TN/(TN+FP) × 100 where TN indicates True Negative and FP indicates False Positive

TABLE I. Tabulation of the result of the testings of the individual images

Image Name	Category	Weight	Classified As
Test Image 1	Cancerous	0.7821	Cancerous
Test Image 2	Cancerous	0.7308	Cancerous
Test Image 3	Cancerous	0.6538	Cancerous
Test Image 4	Cancerous	0.8205	Normal
Test Image 5	Cancerous	0.7564	Cancerous
Test Image 6	Normal	0.6974	Cancerous
Test Image 7	Normal	0.6711	Normal
Test Image 8	Normal	0.7500	Normal
Test Image 9	Normal	0.7368	Cancerous
Test Image 10	Normal	0.8026	Normal

TABLE II. Tabulation for the cumulative data for statistical purpose

	Cancerous	Normal	Total Number
Positive	TP = 4	FP = 2	Test Positive = 6
Negative	FN = 1	TN = 3	Test Negative = 4
	Total Cancerous = 5	Total Normal = 5	

Thus our work achieved the Sensitivity of 80% and the specificity of 60%. Table one compares the results delivered by testing of the individual images with that of the category. The category is the class specified by the pathologist and the Classified As column provides the result of our proposed method. Table 2 summarizes the information in table 1 such the sensitivity as well as specificity can be calculated. Sensitivity and specificity are characteristics of the test[6]. The Sample images obtained from the intermediate layers are given in fig. 6, fig. 7, fig. 8, and fig 9.

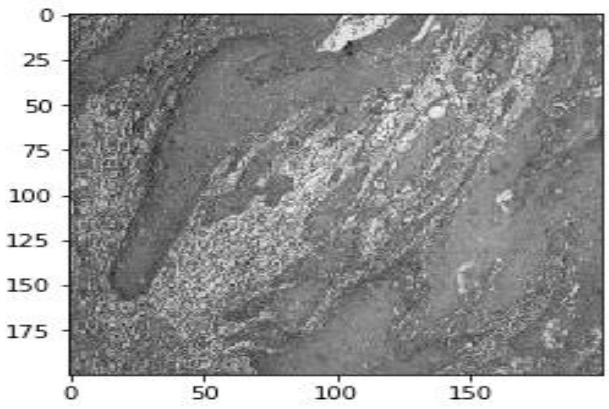

Fig. 6. Gray scale conversion and resizing to 200x200

In our case the number of images taken for training the model is 300 for cancer class and 50 for normal class. As the number of normal images is 1/6th when compared to the number of cancerous images, the training model is subjected to uneven training data and hence the specificity is giving low values.

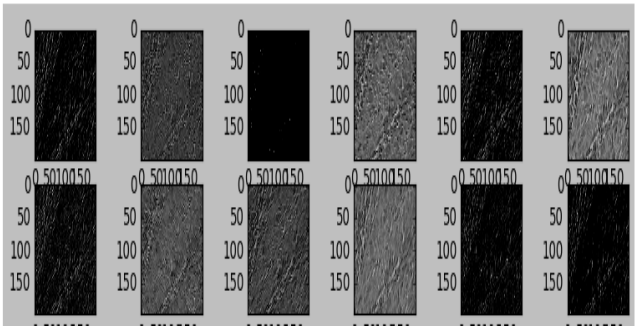

Fig. 7. Visualization of the 3rd Convolution Layer

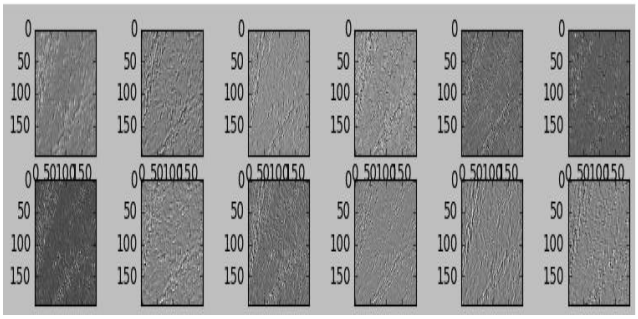

Fig. 8. Visualization of the 5th Relu Layer

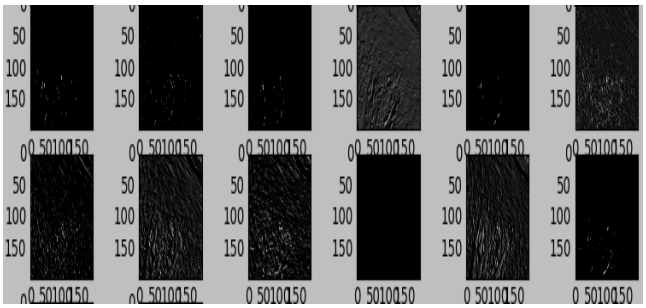

Fig. 9. Visualization of the 3rd Maxpooling Layer

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