CONSTRUCTION OF AN ORAL CANCER AUTO-CLASSIFY SYSTEM BASED ON MACHINE-LEARNING FOR ARTIFICIAL INTELLIGENCE

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ABSTRACT

Oral cancer is one of the most widespread tumors of the head and neck region. An earlier diagnosis can help dentist getting a better therapy plan, giving patients a better treatment and the reliable techniques for detecting oral cancer cells are urgently required. This study proposes an optic and automation method using reflection images obtained with scanned laser pico-projection system, and Gray-Level Co-occurrence Matrix for sampling. Moreover, the artificial intelligence technology, Support Vector Machine, was used to classify samples. Normal Oral Keratinocyte and dysplastic oral keratinocyte were simulating the evolvement of cancer to be classified. The accuracy in distinguishing two cells has reached 85.22%. Compared to existing diagnosis methods, the proposed method possesses many advantages, including a lower cost, a larger sample size, an instant, a non-invasive, and a more reliable diagnostic performance. As a result, it provides a highly promising solution for the early diagnosis of oral squamous carcinoma.

KEYWORDS

Oral Cancer Cell, Normal Oral Keratinocyte (NOK), Dysplastic oral keratinocyte (DOK),Gray-Level Co-occurrence Matrix (GLCM), Scanned Laser Pico-Projection (SLPP), Support Vector Machine (SVM), Machine-Learning.

1. INTRODUCTION

Oral cancer is a common neoplasm worldwide. Over the past decades, it shows a progressive increment in its incidence and mortality. Though there'are some surgical and radiotherapeutic improvements, it still shows a poor prognosis and also low survival rate. As the development of oral cancer, the cell will first become dysplastic, a pre-cancerous stage. Later, the cells will turn into carcinoma *in situ*, that is, the cells are abnormal cells, which might have a high speed of DNA/RNA duplication and undergo ultimate replication out of control. Most importantly, the cells are still in place, an indication of high curabilty after removal and a smaller excition area for faster recovery. Finally, the cells become cancerous, not only carcinomatous, but also gains the ability to move and invade into other tissues, more precisely, metastasis. Earlier detection of the

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abnormal growth of oral tissue can provide a promising future for a better therapy planing and a higher survival rate.

For many years, many non-invasive imaging techniques have been proposed for the clinical diagnosis of cancers, including X-rays, computed tomography (CT), positron emission tomography (PET), ultrasonography (US), magnetic resonance imaging (MRI), and tissue polarimetry. For oral cavity, Dental Cone Beam CT, and impression scan with CAD/CAM is also a new era of making a computed 3D oral model. Recently, due to the higher computing power and smarter artificial intelligence, many computing techniques are now adding to help analyzing the medical images and aid the doctors in diagnosing diseases. Therefore, an urgent requirement exists for more timely, non-invasive, and quantitative system for detecting the presence of abnormal cells and classification of the different stage of oral cancer.

With the scanned laser pico-projection (SLPP) system, Chuang[1]*et al*. put out a method for extracting the two-dimensional (2-D) nanoparticle concentration of solid and liquid solutions through an inspection of the speckle contrast of the images obtained. The feasibility of the proposed approach was demonstrated by measuring Type I collagen concentrations ranging from 0.025 ~ 0.125%.There are many practical benefits, such as infinite focus, inherent high image contrast and also good power efficiency thatSLPP systems can provide in optical diagnosis[2].

Gray-Level Co-occurrence Matrix (GLCM) functions characterize the texture of an image by adding up how often pairs of pixel with specific values and in a specified spatial relationship occur in an image, creating a GLCM, and then extracting statistical measures from this matrix. D. Molina *et al.*[3] used GLCM to analyze the medical imaging on brain tumor heterogeneity obtained from magnetic resonance images (MRI) and find its potential relationship with tumor malignancy. In the past years, the author has proved that image obtained with SLPP and process with GLCM can successfully provide a great discrimination between low metastatic cancer cells and high metastatic cancer cells[4], and the combination of the two techniques is also useful in distinguishing oral pathological sections[5].

Machine-Learning is a part of Artificial Intelligence (AI) that the computer learns without manifestly programmed. With the data inputted and the task set, as the computer programmed learned, the performance of the program is said to be improved as the data increased. In other words, the program optimizes itself to reach a higher performance, that is, accuracy in classify tasks. Support Vector Machine (SVM) is a basic yet clever script used in machine-learning. With label assigned, and data taken as vectors, the SVM is solving the following mathematic problems to find the greatest margin when classify each labels and thus creating a classify model. For the past decades, many more optimization options occured to strengthen the SVM, including the kernels and cross-validation. Kernels are ways to project the data into a higher dimensional space, creating a better distribution for classification. The most common ones are the linear, the polynomial, the radial basis function (RBF), and the sigmoid kernels. Due to the parameters inside the kernel, it needs to be optimized for a better projection. Cross-validation devides the data into several groups, and use one as a testing set, the re

mainings as the training set each time. It is a method for the computer to test itself, and eliminate the effect of some unusual data's. Otherwise, it will create a over-fitted model.

$$\min \frac{\|w\|^2}{2} \quad subject\ to\ \ y_i(w^T x_i + b) \geq 1, i = 1,2, \ldots\ldots, n \quad \{1\}$$

In our study, we will use 2 cell lines to verify the validity of our system. The system is first comprised of a SLPP technique to obtain image, then with GLCM to process the image, extracting some figures out, finally the SVM calculation to create a classification model to achieve the detection of oral cancer. Compared to the existing diagnostic process, the proposed method provides a highly promising solution for the faster, non-invasive, and early diagnosis of oral cancer.

2. MATERIALS AND METHODS

2.1 Sample Preparation

Cell lines were incubated at 37°C with 5% CO_2, and cultured in 2 well silicone separator 48hrs before taking image. Each well was filled with $3x10^4$ cells to form a uniform monolayer. While taking images, the separator is pulled off, forming a blank region on the slide. Then, the samples were washed twice using phosphate buffered saline solution (PBS, 0.1 M, pH = 7.4) or Hank's Balanced Salt Solution (HBSS, no calcium, no magnesium) depending on the cells. The details of each cell line are described in the following.

1. **NOK**, Normal Oral Keratinocyte: The cell line was established from human normal oral mucosa and grown in keratinocyte serum-free medium (KSFM) with low calcium.
2. **DOK,** Dysplastic Oral Keratinocyte: When normal oral keratinocytes go wild and becoming cancerous, it first turn dysplastic, or pre-malignant. This cell line, DOK, was obtained from heavy smoker's dysplastic dorsal tongue epithelium and cultured in Dulbecco's Modified Eagle Medium (DMEM), with 2mM Glutamine, 5μg/ml Hydrocortisone, and 10% Foetal Bovine Serum (FBS).

2.2 Experimental Setup

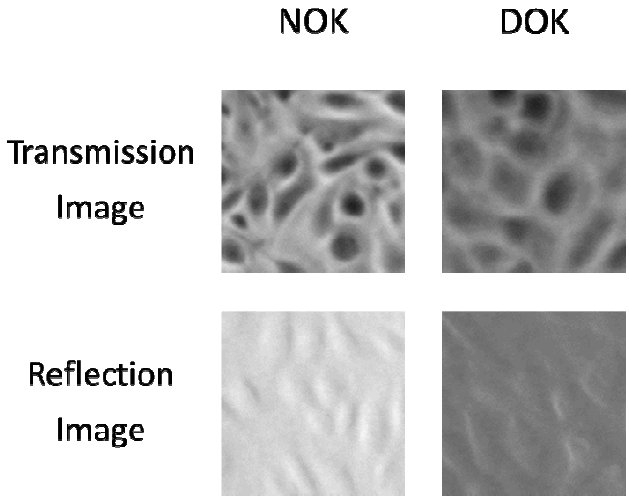
The optical diagnosis system used in this study comprised a SLPP (SONY; Model: MP-CL1A; Resolution: 1920 × 720; Aspect Ratio: 16:9 Widescreen; Contrast Ratio: 80,000:1; Image Size: 40 inch @ 1.15 m) and a microscope (Nikon Eclipse TS-100). In accordance with the findings of a previous study, the samples were illuminated using a green laser source (wavelength = 532 nm) in order to enhance the sensitivity of the reflection image measurements. In obtaining the transmitted images of the cells, the samples were illuminated using a halogen lamp. The cell images and speckle images were captured using a CCD camera (Model: PMD-500) with IS Capture and View image acquisition software. To calibrate the background noise of different image, we calculate SNR (Signal to Noise Ratio). The images (2592×1944 pixels, about 5 megapixels) were partitioned into 2 files, one with cells is regarded as 'Signal' and the other without cell (the blank area caused by the silicone separator) is regarded as 'Noise'. Thus, the image captured can now stand on the same point for comparison.

The GLCM image-processing and SVM model generation is all coded on Matlab R2018a. For each image, it'll first turned into 8bit gray level image, and crop into several sub-images, size 150 × 150 pixels for better performing speed. Then, we use GLCM to gain the pattern of each sub-image, calculate the SNR and written it into the file. After that, we use LIBSVM[6], a SVM

toolbox developed by National Taiwan University, Department of Computer Science, which provide many useful SVM functions together. Originally written in C+, the LIBSVM toolbox can be translated into Matlab for us to compile everything together. To find the best classify model, we perform cross-validation for self-testing of the machine and prevent over-fitting problems. For better data distribution, we also added some kernels to project the data into a higher dimensional distribution for better solving the non-linear separable problems.

3. RESULTS AND DISCUSSION

Figures 1 shows the transmission and reflection images of these two cell lines (NOK and DOK). As Figure 1 shows, all cells are appeared in squamous shape and firmly attach to their neighbouring cells. Compared to NOK, the normal one, DOK cells become more spindle-shaped. The reflection images were taken from SLPP system. In this study, we try to use a new light source system, SLPP, to provide a routine quality assurance for imaging. The SLPP system can decrease the light intensity with Gaussian distribution from central to the margin via the scanning laser pico-projection technique for wide screen. Moreover, SLPP system is a commercial projection device for wide screen and enhance the usability for imaging. We also do the effort in the case of biopsy from the patients, such as characterization for oral cancer by pathological images. SLPP system with GLCM image processing can differentiate normal & cancerous pathological sections and it works on both full field analysis and specific tissue analysis. The discrimination of normal and cancerous tissues depends on the disorder caused by unusual proliferation and division of the chromosomes and nuclei. Compared to existing methods, the proposed method approach has many advantages, including a lower cost, a larger sample size and a more reliable diagnostic performance.



Figures 1. Transmission and reflection images of these two cell lines (NOK and DOK).

In the subsquent step, we run the classify machine for artificial intelligence to distinguish the NOK and the DOK cells. We use 4 transmission image, 3 reflection image of NOK and 8 transmittion image, 8 reflection image of DOK. For each image, we randomly cropped out 5 areas to go under the GLCM analyzing. Totally, 115 datas, each with 4 features, are sampled and

imported into the SVM. The results are shown below. Table 1 shows the use of different SVM kernels for projecting the data into a higher dimension distribution, except the linear one. Accuracy is from the cross-validation, a self-testing method when forming a classify model. Figure 2 shows the optimization of RBF kernel. When optimized, we add a Cost (C) parameter as penalty of the mis-classified points in the original script, and the RBF kernel uses a gamma(γ) as a parameter in its exponential function. Due to previous studies, the most efficient way to optimized the two parameters is to test it exponentially. Therefore, we briefly searched it once using a bigger grade(as shown in figure 2a) and search it again using a smaller grade in a more targeted range(as shown in figure 2b). Accuracy do raised after the optimization.

Table 1. The classify accuracy of NOK and DOK according to the different SVM kernel.

Kernels	Linear	Polynomial	RBF	Sigmoid
Parameter number	1	3	2	3
Accuracy	77.3913%	69.5625%	69.5625%	69.5625%

Note: all the samling steps in GLCM is (x,y)=(1,0).

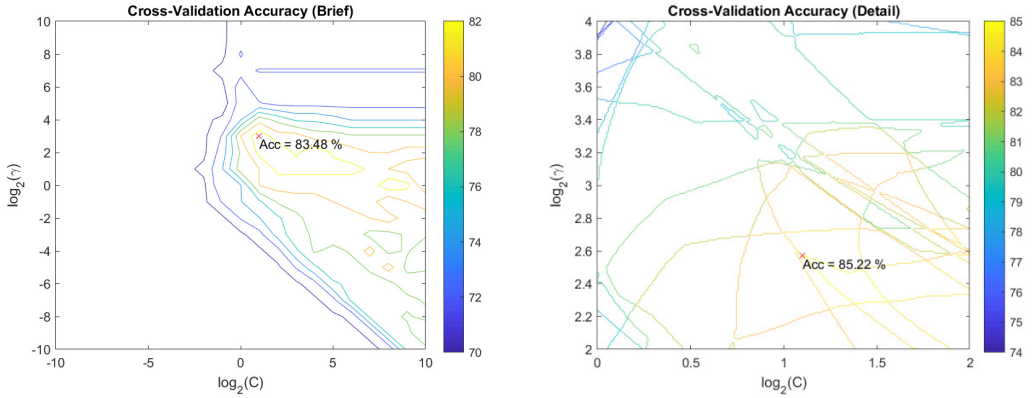


Figure 2a(left)**& 2b**(right) Optimization of RBF kernel with the Cost parameter and gamma optimization.

4. CONCLUSIONS

As the cancer developed, the cells became dysplastic first, turned carcinoma later, and finally invasive. The morphology change of the cells is corresponding to the transformation of cell function. With the aid of SLPP for obtaining a high-resolution image, and the GLCM for better sampling the pattern of the image. With the help of SVM of machine-learning, the system can get the accuracy around 70% in classifying the NOK and DOK. After adding a brief optimization, altering the parameters inside the RBF kernel and the SVM scripts, the classify machine can now reaching 85.22% accuracy, compared to 69.525% without optimization. The result gives out that our method can help to distinguish NOK and DOK, the normal oral keratinocyte and the dysplastic one, providing a promising future of an instant, non-invasive, and early diagnosis of the existing of pre-cancerous cells.

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REFERENCES

[1] C. H. Chuang, T. W. Sung, C. L. Huang, and Y. L. Lo,(2012) "Relative two-dimensional nanoparticle concentration measurement based on scanned laser pico-projection," Sensors and Actuators B: Chemical, vol. 173, pp. 281-287.

[2] K. V. Chellappan, E. Erden, and H. Urey,(2010) "Laser-based displays: a review," Applied Optics, vol. 49, no. 25, pp. F79-F98.

[3] D. Molina et al., (2016)"Influence of gray level and space discretization on brain tumor heterogeneity measures obtained from magnetic resonance images," Computers in Biology and Medicine, vol. 78, pp. 49-57.

[4] C.-L. H. Meng-Jia Lian, (2018)"Texture feature extraction of gray-level co-occurrence matrix for metastatic cancer cells using scanned laser pico-projection images," Lasers in Medical Science, journal article July 24.

[5] C.-L. H. Meng-Jia Lian, Tzer-Min Lee, (2018)"Automation Characterization for Oral Cancer by Pathological Image Processing with Gray-Level Co-occurrence Matrix," Journal of Image and Graphics, vol. 6, pp. 80-83.

[6] C.-C. a. L. Chang, Chih-Jen, (2011) "{LIBSVM}: A library for support vector machines," ACM Transactions on Intelligent Systems and Technology, vol. 2, no. 3, pp. 27:1--27:27.

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