Automatic Segmentation of Abnormal Cell Nuclei from Microscopic Image Analysis for Cervical Cancer Screening

Chin-Wen Chang¹, Ming-Yu Lin¹, Horng-Jyh Harn², Yen-Chern Harn³, Chien-Hung Chen¹, Kun-His Tsai², and Chi-Hung Hwang¹

¹Instrument Technology Research Center, National Applied Research Laboratories, Taiwan
²Department of Pathology, China Medical University Hospital, Taiwan
²Department of Computer Science and Information Engineering, National Taiwan University, Taiwan

Abstract — In this paper, two methods of microscopic image analysis were presented to classify the abnormal cells in Papanicolaou(Pap) smear for cervical cancer screening. Our goal is to extract those cell nuclei which are abnormally large size, bizarre shape as well as hyper density and we hope to apply this method to the different kinds of abnormal cells. The global information of the image and the local image condition were meantime considered. The reported method searched whole picture by scanning on different axes and determined the locations of abnormal cell nuclei with high contrast This developed method is also able to find cell nuclei, those were almost as bright as the background. Using the reported cytological image analysis, we successfully recognized the abnormal cells such as squamous intraepithelial neoplasia (SIL) and differentiated them from the normal epithelial cells.

Keywords — automatic segmentation, abnormal cell nuiclei, cervical cancer, line scanning, energy method

I. INTRODUCTION

Cervical cancer is the second most common cancer in woman's cancer diseases and yield over 500,000 new striking cases worldwide each year [1]. Pap smear, the cytological gynecological investigation is the first-step routine method to diagnose the cervical cancer. In clinical diagnostics, cytotechnologists are responsible for examining Pap smear. It is time-consuming and the accuracy of diagnosis is dependent on training experience of cytotechnologists. Therefore there are increasing needs from cytotechnologists for the development of automated cytological classification system.

Different researchers have been studying on segmentation of cell tissues. Deformable model was presented to cell nuclei segmentation by M.E. Plissiti [2]. Fuzzy logic engine was applied by Grigory Begelman to handle the noise and uncertainty in cell nuclei data [3]. Gradient vector field was used for building 3D model [4]. Xiaowei Chen presented an automated segmentation, classification, and tracking of cancer cell nuclei in time-lapse microscopy [5].

Enlargement and deformation of cell nuclei are two major criteria to recognize the abnormal cells in Pap smear exam. Recently, automatic cell nuclei segmentation has been made much more attraction and also provided one of the most interesting topics in cytological image analysis. The inherent problems due to the video microscopy and the smear make this work a challenge. We attempt to identify and label those

abnormal cells with enlarged and deformed nuclei in order to simplify the recognition process as screening purpose.

II. MATERIAL AND METHODS

A. Material

The smear images used in this work are provided by Pathology department, China Medical University Hospital, Taichung, Taiwan. All tumor cells are confirmed by two independent pathologists. These images are captured under 400x magnification lens and stored with 1280x960 pixels. The flowchart of reported automatic microscopic image analysis is shown in Fig 1.

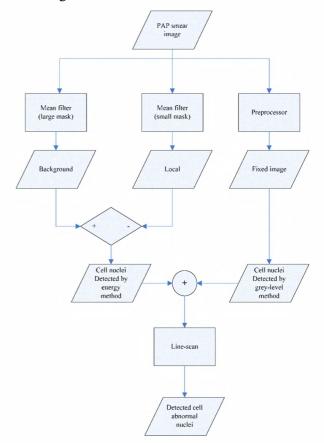


Figure 1. The flowchart.

^{*}Contact author: Chin-Wen Chang is with the Instrument Technology Research Center. 20, R&D Rd. VI, Hsinchu Science Park, Hsinchu, 300, Taiwan.(phone:+886-3-5779911 #580; fax:+886-3-5773947; e-mail: fifer@itrc.org.tw)

B. Grey-Level Method

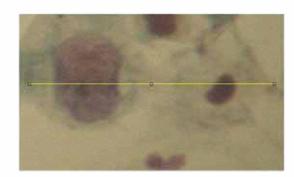
In an image, cell nuclei are generally darker than the other parts of the image. Thus, most of the time, we can tell where the cell nuclei are by grey level. However, in the PAP smear images we have, it's always lighter in the center and darker at the corner. This phenomenon makes it difficult to distinguish where the cell nuclei are by grey level. The promble comes from the light source and needs to be fixed.

Therefore, some preprocessing is necessary. First, we find the barycenter of this image which is weighted by grey level. Second, cluster the pixels according to the distance from the barycenter to each pixel, and then, rescale the grey level to each cluster.

Determining where the cell nuclei are, a threshold has to be given. If the grey level of a pixel is lower than the threshold, it would be taken as a part of cell nuclei. Otherwise, it would be ignored. The threshold is given by the mean value of the image multiplied by a factor. The factor is chosen by experience.

After determining the cell nuclei in the image, we apply line-scanning to the image. On a chosen axis, if there are sufficient number of pixels belongs to cell nuclei and continuously connected together, these pixels are marked as abnormal cell nuclei. If there are only several pixels, they would be taken as noise. By scanning on different axis, those large cell nuclei would be marked and smaller ones would be ignored. Line-scanning works as shown in Fig 2.

This method is applied Fig 3 and the fixed image is shown in Fig 4. The result is shown in Fig 5.



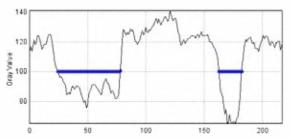


Figure 2. Line-scanning.

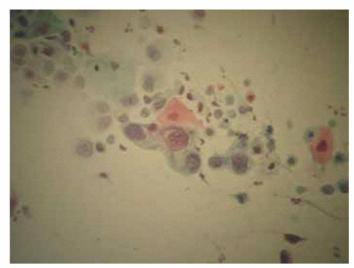


Figure 3. The original PAP smear image provided by China Media University Hospital.

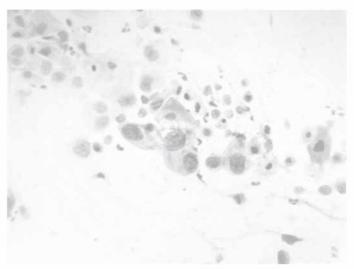


Figure 4. This image is rescaled by clusters.

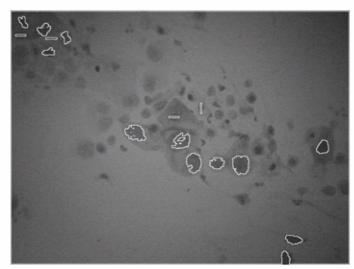


Figure 5. The cell nuclei detected by grey-level method.

C. Energy Method

Enlarged cell nuclei with lower grey level are a type of abnormal cell nuclei, but these abnormal cell nuclei cannot be captured by grey level method due to their low grey level. Therefore, energy method is provided. Energy method enhances these cell nuclei which have low grey level.

Energy method works with two mean filters. One of them has a larger mask and is taken as a background-energy operator. The other has a smaller mask and is taken as a local-energy operator. By subtracting local energy from background energy, cell nuclei in the image would be enhanced. And then, there should be a threshold to decide which pixel is part of cell nuclei and which is not.

The size of the filters and the threshold for the subtracting result are important factors. The size of the filters is chosen according to the size of normal cell nuclei. The threshold for the subtracting result is zero, since cell nuclei in the image are considered to be darker than the background.

Comparing the enhanced image to the original image, cell nuclei are clearer in the enhanced image. It's as shown in Fig 6. The image on left side is a original image and the other is the enhanced image. Obviously, the enhanced image has a higher contrast and is easier for setting threshold.

This method is also applied to Fig 3 and the enhanced image is as shown in Fig 7. The result of line-scanning is shown in Fig 8.

Some of the abnormal cell nuclei are not captured here, but are captured by the grey-level method. Combing these two methods, most of the abnormal cell nuclei are captured.

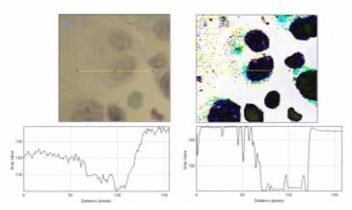


Figure 6. On the left side, it's a original image. On the right side, it's the enhanced image of the left one. In the plot of the left side image, it's obvious that choosing a threshold to determine whether a pixel is a part of cell nuclei is difficult. However, the enhanced image has high contrast and is easy for choosing threshold..

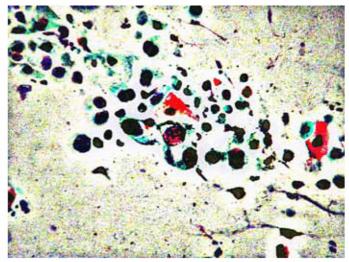


Figure 7. The enhanced image.

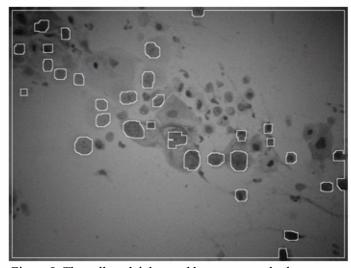


Figure 8. The cell nuclei detected by energy method.

III. CURRENT RESULT AND FUTURE WORK

We have come up with an efficient method capturing abnormal cell nuclei. All the suspicious cell nuclei in Fig 3 are found by combining Fig 5 and Fig 8. Even though the quality of the image is limited, we can still detect the abnormal cell nuclei. The reported automatic cytological specimen classification system is successful to recognize abnormal cells from normal cells with low complexity and high sensitivity from those low contrast images.

Applying our methods to different images, these methods still work as shown in Fig 9, but some special issues are disturbing us. Take Fig 10 as an example, the abnormal cell nucleus E is not captured. And the captured cell nucleus D is enlarged. The half on the right side shouldn't be involved. Figuring out the problem, we look into Fig 113, the enhanced image of Fig 10. It shows that the cell nucleus E can be seen in the enhanced image, but not as dark as other cell nuclei.

In the future, we will be working on recognizing the pattern of color in the enhanced images, or taking different imaging

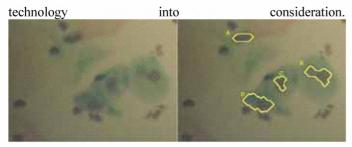


Figure 9. Four abnormal cell nuclei are captured.

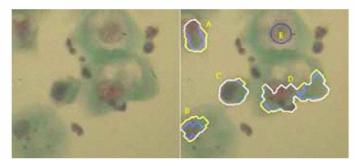


Figure 10. The image with several problems.



Figure 11. The enhanced image of Fig 9.

ACKNOWLEDGMENT

This work cannot be done without the help of the research team of Advanced Electronic System Division of Instrument Technology Research Center. Special thanks to T.S. Liao, C.F. Lin, R.C. Weng, S.J. Jou, and T.L. Huang. This project is also supported by the research team of Department of Pathology of China Medical University Hospital. Special thanks to Hung-Juan and Jia-Hui.

REFERENCES

- [1] Paavonen J, "Human papilloma virus infection and the development of cervical cancer and related genital neoplasias", Int. I. Infect. Dis., 11, Supp 2:S3-9, Review, 2007.
- [2] M.E. Plissiti, A. Charchanti, O. Krikoni and D.I. Fotiadis, "Automated segmentation of cell nuclei in PAP smear", Greece, in proc.IEEE International Special Topic Conference of Information Technology in Biomedical, Oct. 26-28, 2006
- [3] Begelrnan G, Gur E, Rivlin E, RudzskyM and Zalevsky Z, "Cell nuclei segmentation using fuzzy logic engine", Proceedings of International Conference on Image Processing, Volume 5, 2937 - 2940, 2004.
- [4] Gang Li, Tianming Liu, Jingxin Nie, Lei Guo andWong STC, "Segmentation of touching cells using gradient flow tracking", Proceedings of International Symposium on Biomedical Imaging 2007, 77-80
- [5] Xiaowei Chen, Xiaobo Zhou, Stephen T.C. Wong, "Automated Segmentation, Classification, and Tracking of Cancer Cell Nuclei in Time-Lapse Microscopy", IEEE Transactions on Biomedical Engineering, VOL. 53, No. 4, April 2006, 762-766