Proceedings of the Fourth International Conference on Trends in Electronics and Informatics (ICOEI 2020)
IEEE Xplore Part Number: CFP20J32-ART; ISBN: 978-1-7281-5518-0

Detection of Nuclei Cell in Histopathological Images of Uterine Cancer: Adenocarcinoma of Endometrium

Dr. Shoba. R Patil
Department of Information Science and Engineering
Basaveshwar Engineering College, (Affiliated to Visvesvaraya Technological University, Belagavi-590018)
Bagalkot, India
Srpatil19@gmail.com

Veena. I Patil
Department of Computer Science and Engineering
B.L.D.E.A's V. P. Dr. P. G. Halakatti College of Engineering and Technology, (Affiliated to Visvesvaraya Technological University, Belagavi-590018)
Vijayapur, India
vapatil@bldeacet.ac.in

***Abstract*— Pathologist visual inspection of Histopathological uterine tissue sample is still considered as confirmatory test for uterine cancer finding. Manual assessment depends upon the knowledge and experience of pathologist. Hence subject of concern is objective analysis. An effective way of diagnosis, grading and classification of endometrium adenocarcinoma is structural analysis of the tissue sample. The effectiveness of computer assisted diagnosis, grading and classification depends on glandular structure and detection of individual nuclei cell. Hematoxylin channel from H&E stained image is extracted using color deconvolution algorithm. Morphological operation and thresholding are carried out in this work for structural analysis of glandular region and for detection of nuclei cell. To rise the effectiveness of the system elimination of cell nuclei from stroma is done before feature extraction is also described.**

Keywords— Adinocarcinoma; endometrium; uterus; color deconvolution; nuclei cell

I. INTRODUCTION

Endometrial cancer is the most occurring type of uterine cancer. As endometrium is part of the uterus it is often referred to as uterine cancer. The most frequently diagnosed gynecologic cancer is endometrial cancer which contains cancers of uterus, ovaries, cervix, vagina, vulva and fallopian tubes. 80 percent of endometrial cancer are Adenocarcinomas of the endometrium. This type of cancer forms when inner lining cells of the uterus i.e. endometrium start to grow uncontrolled [1]. During pregnancy Endometrium thickens to hold the fetus and is shed during menstrual period. Pelvic examination, endometrial biopsy/fractional dilation followed by curettage i.e. microscopic analysis of biopsy samples has to be done for diagnosis, grading and classification of uterine cancer. Visual understanding of biopsies is time consuming, labor intensive and highly depends on the knowledge and experience of the medical professional. If such a responsibility of analysis can be done by computer systems, then diagnosis, grading and classification could be done easily through textural or architectural analysis of biopsies. This work supports medical professionals in making their analysis work simpler and easier.

II. RELATED WORK

Various related works were proposed with different methods for segmentation of different specimens of microscopic images. Some of the methods are morphological operation, thresholding, watershed transformation, k-mean clustering, active counters, region growing, edge based etc. Faliu Yi et al. [2] proposed automatic system to extract cell nuclei from hematoxylin and eosin (H&E) stained images of cancer Genome tissue. As pre-processing the method starts with a color deconvolution separates hematoxylin H channel and eosin E channel. Morphological operation and thresholding technique are applied on H channel to segment the nuclei along using marker-controlled watershed transform algorithm. Khin Yadanar Win et al. [3] used OTSU thresholding to segment cell nuclei from images of cytology pleural fluid. In this method, the image is enhanced using median filter. l* and b* components are extracted from the image by converting it to l*a*b* color space. OTSU thresholding is used to segment cell nuclei. Lastly, morphological operation is performed to remove unwanted artifacts and reconstructed into color segmented image. The method was tested on 25 images of Pap stain. V. B. Surya Prasath et al. [4] proposed color decomposition-based method for segmenting cell nuclei from Glioma histopathology images. Izzati Mubimmah et al. [5] projected a nuclei segmentation method. The method uses morphological operation and watershed transformation. In this contrast enhancement and edge sharpening are used to find the boundary of nuclei. Then morphological operations and thresholding are performed before applying watershed transformation. Pedro Quelhas et al. [6] introduced a method for cell detection and shape estimation using slide band filter on multivariate of images. Han Yeong Oh et al. [7] developed algorithm and application program for extraction of cellular area of uterine cervical cancer cell depending on the basis of size of cell nucleus. Hough transform is used to measure the radius of the nucleus area. If nucleus area < 25 μm^2, it is

predicted as normal, if nucleus area > 25 μm^2 and < 30 μm^2, then the nucleus is predicted as Atypical Squamous Cells of Undetermined Significance (ASCUS). Else if nucleus area > 30 μm^2 and < 40 μm^2 is predicted as low grade squamous intraepithelial lesion (LSIL). In other cases, it is predicted as high grade squamous intraepithelial lesion (HISL). Pegah Faridi et al. [8] developed system for detecting and segmenting of cancerous nuclei. This method segments deformed cell nuclei boundary. The system first detects center of cell nuclei then level set algorithm is used to detect boundary of cell nuclei and then boundary segmentation is performed. In this method, first step of pre-processing is bilateral filtering. Next, to extract the cell nuclei gamma correction function is applied on filtered green channel image. Then thresholding is applied to binarize the image. A structuring element of radius one is used to perform Morphological operators dilate and erode. Detected blobs are passed through 2D Difference of Gaussian filter CDoG. Nuclei center are gained by thresholding. Yue Cui et al. [9] developed a system to detect abnormal nuclei cell from microscopic images of cervix uteri. In this method tumor marker Ki-67 stained microscopic images of cervix uteri are used. Abnormal nuclei are stained brown and normal bluish color. A multilevel segmentation is used for abnormality identification and segmentation of nuclei. First goal of segmentation is to partition nuclei regions. In next level segmentation the under segmented nuclei cluster is further partitioned to segment nuclei. To classify and separate touching regions of clustered nuclei feature extraction is applied on regions of interest. Sonal Kothari et al. [10] proposed semi-automatic method for cell cluster segmentation and counting cell from digital tissue image. Cell clusters are a prominent feature in tissue samples. For accurate cell counting segmentation of clusters is a challenge. Nuclei cluster boundary are obtained in pre-processing stage from RGB tissue sample. To segment overlapped nuclei edge concavity is detected. In third step ellipse-fitting technique is used to segment nuclei at these concavities. After cluster segmentation, each nucleus is counted. The method was applied on four different types of cancerous tissue samples and it gives promising results. Thiran et al. [11] developed a method to recognize cancerous tissues from microscopy image. The method is based on mathematical morphology, and more specifically on the use of Geodesy. The method removes the background noise and then segments the nuclei of the cells from the image. Then the shape, size and texture of the nuclei are analyzed. Metin N. Gurcan et al. [12] developed a method which automatically segments cell nuclei for neuroblastoma, an adrenal gland cancer. This method uses morphological top-hat by reconstruction algorithm with hysteresis thresholding to identify and segment cell nuclei. Youyi Song et al. [13] presented a method to segment cervical cytoplasm and nuclei using multiscale convolution network (MSCN) and graph partitioning. Shape, texture, contextual information is used to locate the boundary of nuclei. Touching nuclei are separated using markers. Instead of raw pixels super pixel are used for segmentation which reduces the computational complexity. Rahmadwati et al. [14] proposed an algorithm for classification of cervical cancer using microscopic biopsy images. The image is segmented into normal, abnormal, background, basal and stromal cells making use of texture classification and Gabor filters. To find degree of malignancies global classification algorithm is used. Kaaviya S et al. [15] developed a technique that segments single cell using Fuzzy C-means (FCM) clustering. Nosrati M. S et al. [16] segments overlapping cells of pap smear images using star-shape prior segmentation framework with directional derivatives. Das A et al. [17] discussed approaches for segmentation and analysis of Cervix image. Numerous image processing methods and mathematical operations are exploited and applied in this work. Guo P et al. [18] used Support Vector Machine (SVM) and Linear Discriminant Analysis (LDA) approaches for classification of epithelium. Leave-one-out is used for training and testing for cervical intraepithelial neoplasia (CIN) classification.

III. Adenocarcinoma Histopathology

Endometrium the inner lining of uterus nourishes a fetus during pregnancy and is shed during menstruation. Endometrium is glandular tissue layer rich with blood vessel. It thickens during the menstrual cycle. The two chief constituents of endometrium are the endometrial glands and endometrium stroma Fig. 1 shows microscopic image of normal endometrium.

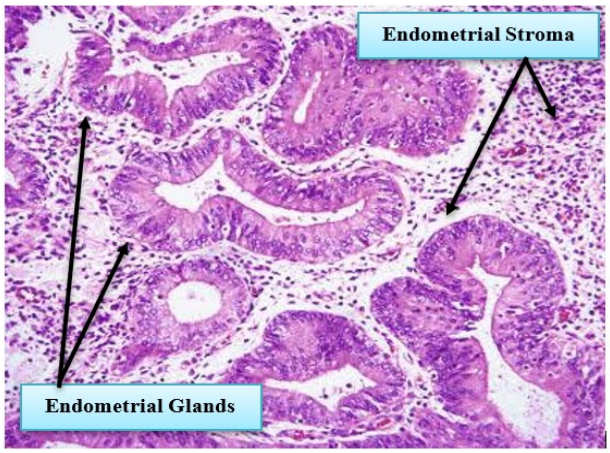


Fig.1 Normal Endometrium

Usually the regular glandular structure is destroyed by adenocarcinoma, damaging regular architectural arrangement of tissue components. The glands are well-differentiated and show angulation/branching. Cytologic atypia is small. International Federation of Gynecology and Obstetrics (FIGO) system is used for grading endometrioid adenocarcinoma. FIGO assigns a grade to endometrial endometrioid carcinomas (EECs) depending on the extent of glandular diversity. Grade1 tumors show less than or equal to 5% solid non-glandular, non-squamous growth; grade2 tumors form between 6% to 50%; and grade3 tumors greater than 50% [19].

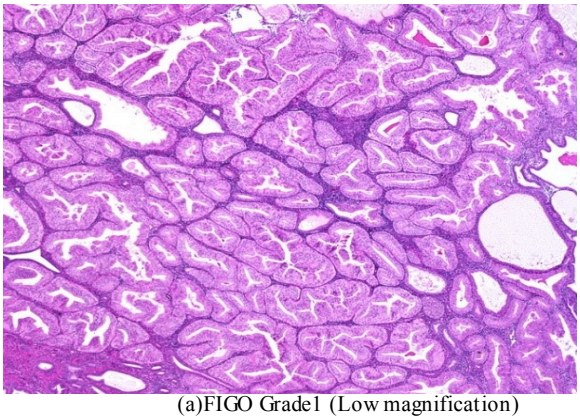
IV. Experimental Results Material

Generally histopathological digital images are obtained from biopsies samples stained using hematoxylin and eosin (H&E) technique. Hematoxylin (H) acting as blue stain on the nuclei, eosin (E) acting as pinkish(magenta-red) color stain on cytoplasm and stromal region and lumen region will be in white color. The goal of this work is to pick the pattern of

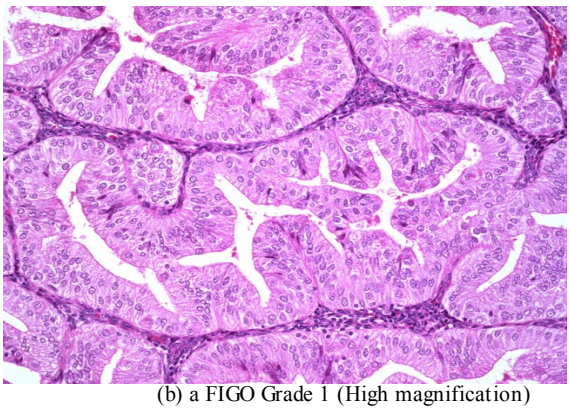
gland like structure i.e. the amount of regular distribution of epithelial nuclei in the image. For this region, color deconvolution is used to decompose the image into stroma, nuclei and lumen regions. The following section describes the datasets, experimental methodology and experimental results.

A. Datasets

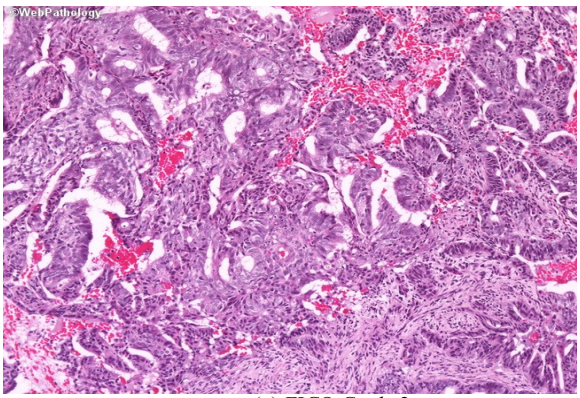
Dataset of Endometroid consisted of 17 samples, 10 samples of Endometroid Adenocarcinoma FIGO Grade1, 1 Endometroid Adenocarcinoma FIGO Grade2 and 5 Endometroid Adenocarcinoma FIGO Grade3. The dataset was downloaded from the Web Pathology visual survey of surgical pathology available at the address (https://www.webpathology.com/case.asp?case=569).



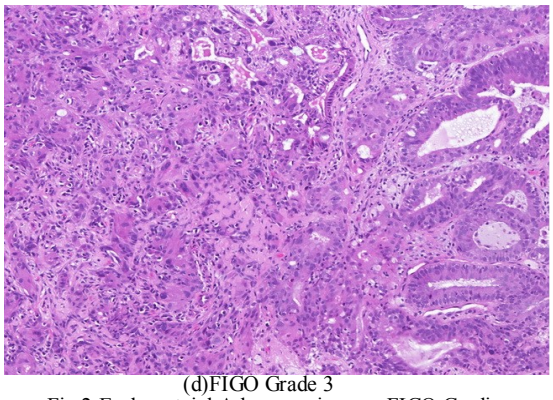
(a)FIGO Grade1 (Low magnification)



(b) a FIGO Grade 1 (High magnification)



(c) FIGO Grade 2



(d)FIGO Grade 3

Fig.2 Endometrial Adenocarcinoma, FIGO Grading

B. Methodology

In this work, it is proposed to develop a system for recognition of glandular structure and nuclei cells in histopathological image of endometrium adenocarcinoma (uterine tissue) to assist grading of carcinoma. The proposed system comprises of several phases which include: Color deconvolution method which separates the hematoxylin and eosin stained image into hematoxylin H channel & eosin E channel. Then median filtering is applied on hematoxylin channel followed by thresholding to binarize the image and connected component Analysis to find the blobs, boundary detection of cells, segmentation of cells. Fig.3 gives block schematic of the model.

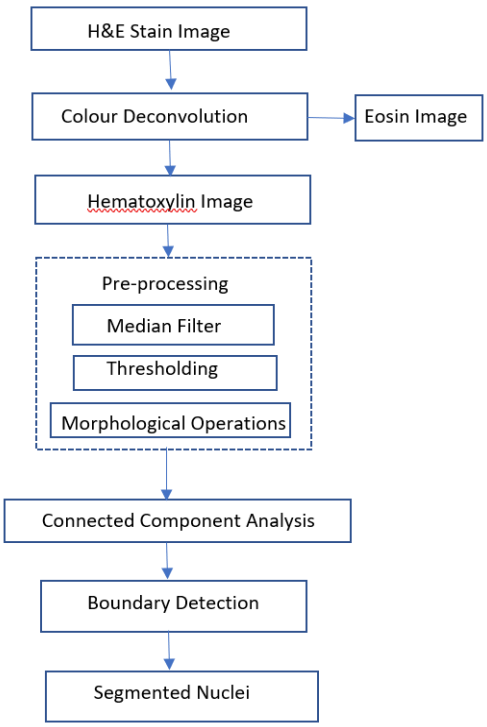


Fig.3 Projected segmentation algorithm

C. Color Deconvolution

Ruifrok and Johnston [20] proposed color deconvolution framework in 2001 and was successfully used in extraction of cells from microscopic biopsy images [21]. Technique color

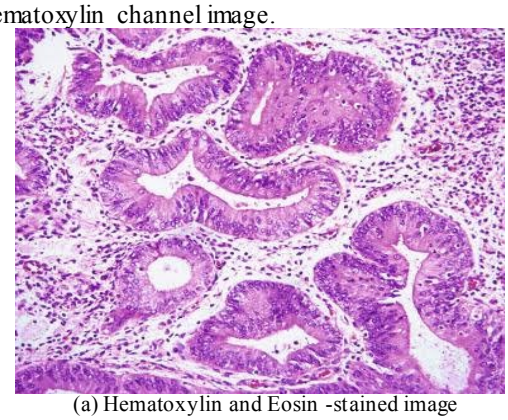
deconvolution is based on the fact that the imaging process can be simulated with the Lambert–Beer law [20]. For a RGB image with known optical densities using M the stain matrix or convolution matrix the relation between RGB color space ℧ and a new color space ¥ is defined by

$$℧ = \exp(-M¥), \quad (1)$$

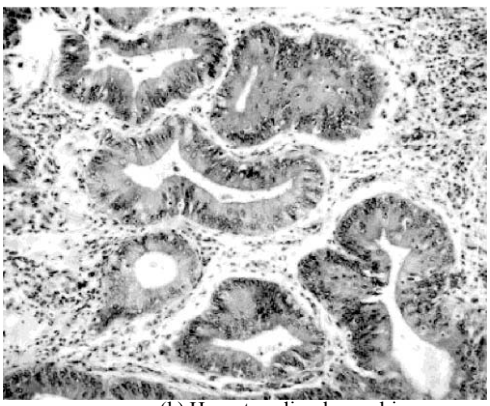
Using optical density E= -log (Ω) and inverse of stain matrix $M = M^{-1}$ intensity of stain concentration in the new color-space € is deduced as

$$€ = M^{-1}E, \quad (2)$$

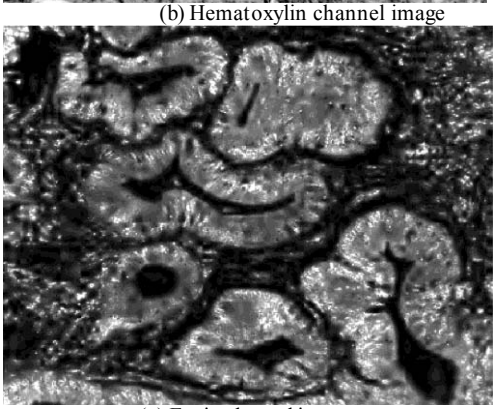
This has information on the absorbance and concentration of stains and can be used to obtain single stain images. [19]. The result of color deconvolution on fig.1.a is shown in fig.4. As Hematoxylin stains cell nuclei in the tissue section, analysis of architectural details of nuclei region is carried out on hematoxylin channel image.



(a) Hematoxylin and Eosin -stained image



(b) Hematoxylin channel image



(c) Eosin channel image

Fig.4 Color Deconvolution

D. Preprocessing

The hematoxylin image contrast is enhanced using histogram equalization then passed through median filter. Filtered image is then binarized after global thresholding. In global thresholding to extract the object from grey background a threshold value T is selected. The image *h(i,j)* is transformed into bi-level image defined as

$$h(i,j) = 1 \text{ for } (i,j) > T$$

$$h(i,j) = 0 \text{ for } (i,j) \leq T$$

The resulting image is a bi-level image. Pixels intensity value of 1 equal to objects and pixels intensity value of 0 equals to background as shown in the Fig. 5(a), (c) and (e) Carcinoma affects epithelial cells so the stromal nuclei were removed by morphological operators dilation and erosion using radius one structuring element.

E. Connected component analysis

Next connected component analysis is done. The matlab bwareafilt command abstracts all connected components from the bi-level image, in the specified range of area of the object, producing another bi-level image. bwareafilt returns a bi-level image containing the objects that meet the criteria as shown in Fig. 5(b), (d) and (f).

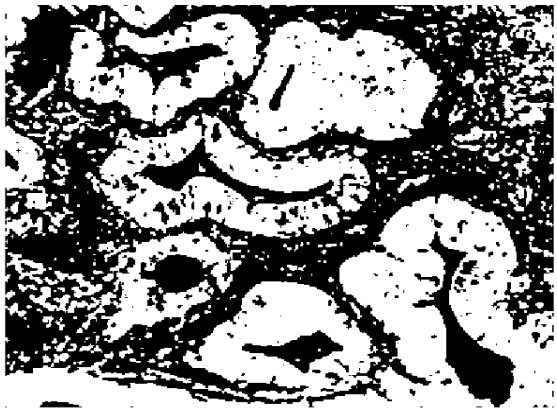


Fig. 5(a) Binarized image

Fig. 5(b) After Connected component analysis

Well differentiated adenocarcinoma

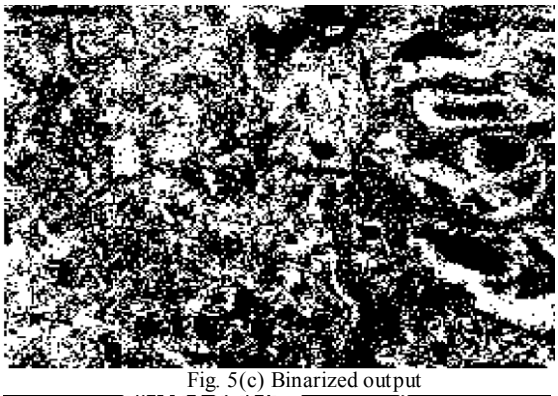


Fig. 5(c) Binarized output

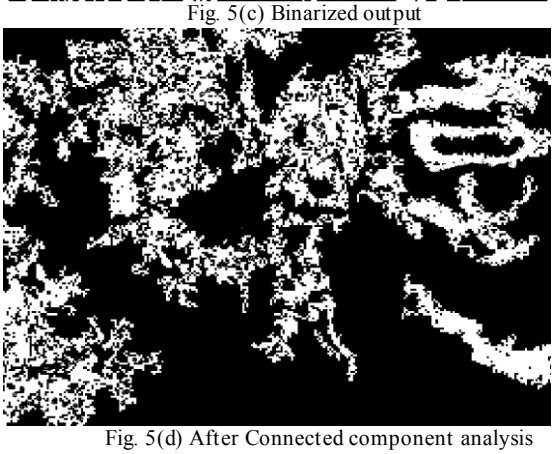


Fig. 5(d) After Connected component analysis

Moderately differentiated adenocarcinoma

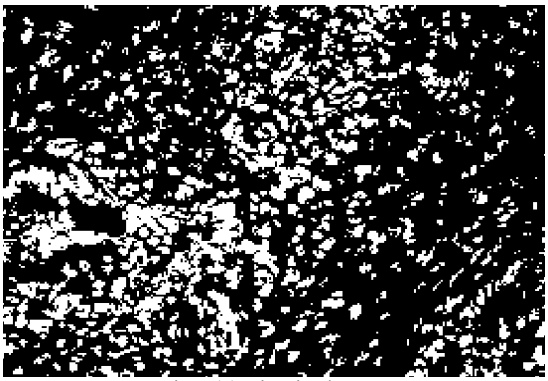


Fig. 5(e) Binarized output

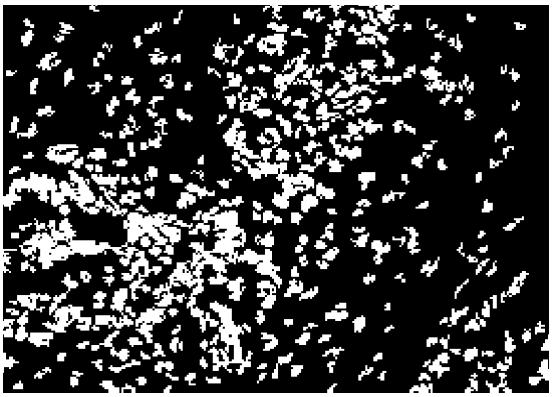


Fig. 5(f) After Connected component analysis

Poorly differentiated adenocarcinoma

F. Segmentation of nuclei

After application of thresholding to identify the nuclei a series of morphological operations and connected component analysis on the image, the perimeter of the nuclei is detected Fig. 6(b). The perimeter is used as the marker on the original image Fig. 6(a) to segment the nuclei in the image. The result is shown in Fig. 6(c).

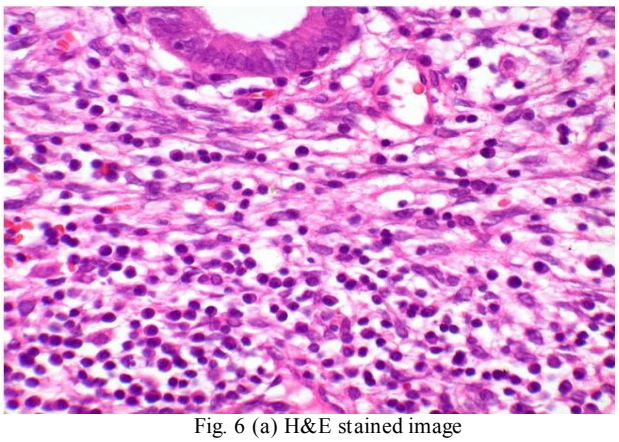
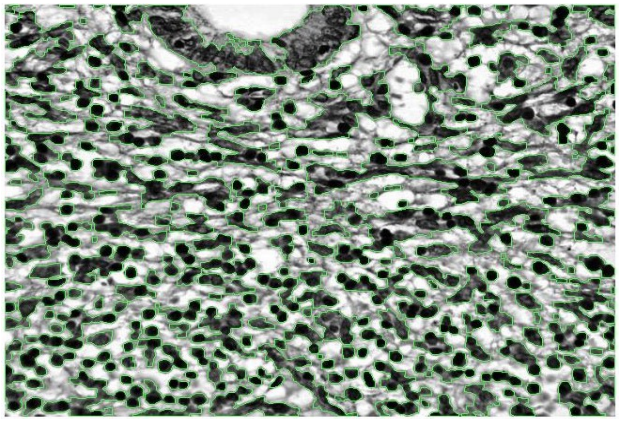
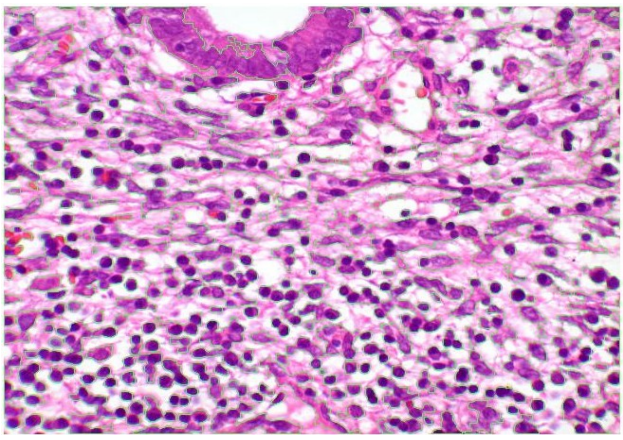


Fig. 6 (a) H&E stained image



(b) Perimeter of nuclei, green line marks the boundary of the cell



(c) Segmented nuclei

V. CONCLUSION

This paper represents a way for structural analysis of glandular region, detecting and segmenting nuclei from the uterine biopsy images. Initially stromal and lumen regions in

the images were separated using H&E stain separation technique. Nuclei images are converted into bi-level image using thresholding. Analysis of Connected component is then performed. The small areas of stromal nuclei were removed. Sequences of morphological operations imfill and imopen are performed. Perimeter of nuclei taken as marker. Marker characterize the nuclei cells. Further touching nuclei can be separated and characteristics of nuclei like shape, size and roundness etc. can be effectively studied to identify cancerous cells.

REFERENCES

[1] Cancer Treatment Centers of America [0nline] Available: https://www.cancercenter.com/cancer-types/uterine-cancer/types [Downloaded on 26/01/2020]

[2] Faliu Yi, Junzhou Huang, Lin Yang, Yang Xie, Guanghua Xiao, "Automatic extraction of cell nuclei from H&E-stained histopathological images," Journal of Medical Imaging vol 4(2), Apr–Jun 2017, pp. 027502.

[3] K. Y. Win, S. Choomchuay, "Automated segmentation of cell nucleiin cytology pleural fluid images using OTSU thresholding", 2017International Conference on Digital Arts Media and Technology (ICDAMT), pp. 14-18, 2017.

[4] V. B. S. Prasath, K. Fukuma, B. J. Aronow, H. Kawanaka, "Cell nuclei segmentation in glioma histopathology images with color decomposition based active contours", *IEEE International Conference on Bioinformatics and Biomedicine (BIBM)*, pp. 1734-1736, 2015.

[5] Izzati Muhimmah, Rahadian Kurniawan, Indrayanti, "Analysis of features to distinguish epithelial cells and inflammatory cells in Pap smear images", Biomedical Engineering and Informatics (BMEI) 2013 6th International Conference on, pp. 519-523, 2013.

[6] P. Quelhas, M. Marcuzzo, A.M. Mendonça, and A.C. Campilho, "Cell Nuclei and Cytoplasm Joint Segmentation Using the Sliding Band Filter", IEEE Trans. Med. Imaging, 2010, pp.1463-1473.

[7] Han Yeong Oh, Seong Hyun Kim, Dong Wook Kim, 2014, "A study on the development of diagnosis algorithm and application program for early diagnosis of cervical cancer using cervix cell", IEEE Fourth International Conference on Innovative Computing Technology (INTECH), 13-15 Aug. 2014, pp. 37 - 40.

[8] Pegah Faridi, Habibollah Danyali, Mohammad Sadegh Helfroush, Mojgan Akbarzadeh Jahromi, "An automatic system for cell nuclei pleomorphism segmentation in histopathological images of breast cancer", Signal Processing in Medicine and Biology Symposium (SPMB), pp. 1-5, 2016.

[9] Yue Cui, Jesse S. Jin, Mira Park, SuhuaiLuo, Min Xu, Yu Peng, W. S. Felix Wong and Leonardo D. Santos, 2010, "Computer Aided Abnormality Detection for Microscopy Images of Cervical Tissue", The 2010 IEEE/ICME International Conference on Complex Medical Engineering, Gold Coast, Australia, Pages: 63 – 68, July 13-15, 2010.

[10] Sonal Kothari, QaiserChaudry, May D Wang, 2009, "Automated Cell Counting and ClusetrSegementation Using Concavity Detection and Ellipse Fitting Techniques",2009 IEEE International Symposium onBiomedical Imaging: From Nano to Macro, June 28 2009-July 1 2009, pp. 795 – 798

[11] Thiran, Jean Philippe, Catholique de Louvain, Macq, B., 2009, "Morphological Feature Extraction for the Classification of Digital Images of Cancerous Tissues",IEEE transactions onBiomedical Engineering,Vol. 43, Issue 10,Oct 1996, pp. 1011 – 1020.

[12] Metin N. Gurcan, Tony Pan, Hiro Shimada, Joel Saltz, 2006, "Image Analysis for Neuroblastoma Classification: Segmentation of Cell Nuclei", 28th IEEE Annual International Conference on Engineering in Medicine and Biology Society, 2006. EMBS '06, 28th IEEE Annual International Conference on Engineering in Medicine and Biology Society, 2006. EMBS'06, Aug. 30 2006-Sept. 3 2006, pp. 4844 – 4847.

[13] Youyi Song, Ling Zhang, Siping Chen, Dong Ni, Baiying Lei, Tianfu Wang, 2015, "Accurate Segmentation of Cervical Cytoplasm and Nuclei Based on Multiscale Convolutional Network and Graph Partitioning", IEEE Transactions on Biomedical Engineering, 07 May 2015, Volume: 62, pp. 2421 – 2433.

[14] Rahmadwati, Naghdy G, Ros M, Todd C, Norahmawati E, 2011, "Cervical Cancer Classification Using Gabor Filters", First IEEE International Conference on Healthcare Informatics, Imaging and Systems Biology (HISB), 26-29 July 2011, pp. 48 – 52.

[15] Kaaviya S, Saranyadevi V, Nirmala M, 2015, "PAP smear image analysis for cervical cancer detection", IEEE International Conference on Engineering and Technology (ICETECH), 20-20 March 2015, pp. 1-4.

[16] Nosrati M. S, Hamarneh G, 2015, "Segmentation of overlapping cervical cells: A variational method with star-shape prior", IEEE 12th International Symposium on Biomedical Imaging (ISBI), 16-19 April 2015, pp. 186 – 189.

[17] Das A, Kar A, Bhattacharyya D, 2014, "Detection of abnormal regions of precancerous lessions in digitised uterine Cervix images", Electrical Engineering Congress (iEECON), 19-21 March 2014. pp. 1-4.

[18] Guo P, Banerjee K, Stanley R. J, Long R, Antani S, Thoma G, Zuna R,Frazier S.R, Moss R.H, Stoecker W.V, 2015, "Nuclei-Based Features for Uterine Cervical Cancer Histology ImageAnalysis with Fusion-based Classification", IEEE Biomedical and Health Informatics, 26 October 2015, pp. 1595-1607.

[19] Robert A. Soslow, Carmen Tornos, Kay J. Park, Anais Malpica, Xavier Matias-Guiu, Esther Oliva, Vinita Parkash, Joseph Carlson, W. Glenn McCluggage, C. Blake Gilks "Endometrial Carcinoma Diagnosis: Use of FIGO Grading and Genomic Subcategories in Clinical Practice: Recommendations of the International Society of Gynecological Pathologists", International Journal of Gynecological Pathology, Jan 2019, pp. S64–S74

[20] A. C. Ruifrok and D. A. Johnston "Quantification of histological staining by color deconvolution", Anal Quant Cytol Histol 23:291-299, 2001.

[21] Mitko Veta, Paul J. van Diest, Robert Kornegoor, Andre Huisman, Max A. Viergever, Josien P. W. Pluim, "Automatic nuclei segmentation in H&E stained breast cancer histopathology images," PLOS ONE, Vol 8, Issue 7, July 2013, pp. 1-12.