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Automated analysis of cervix images to grade the severity of cancer

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Abstract— **This paper discusses a method to objectively analyze the severity of cancer in images obtained from cervix. We propose a novel method to identify the transformation zone in post Lugol's iodine images and acetic acid images that are obtained from the cervix to grade the severity of cancer. We segment the Lugol's iodine image to identify the abnormal tissues and map them to acetic acid images to accurately identify the abnormal tissues in post acetic acid images as well. This information is further used to obtain an opacity difference score that could be used for grading the cancer.**

I. Introduction

Cancer arising from cervix is the number two cancer amongst women worldwide and number one cancer in women in developing countries like India. About 30% of cancers in women in India are due to cervical cancer with more than 100,000 new cases diagnosed every year. Unfortunately, there are just twenty Gynaeco-Oncologists to diagnose and treat these women in India. Screening for cervical neoplasia using the Papanicolaou (Pap) smear, followed by colposcopy, biopsy, and treatment of neoplastic lesions has reduced the incidence and mortality of cervical cancer in countries with organized programs. However due to lack of resources and infrastructure, enforcing such organized programs in developing countries like India is difficult. One of the ways for identification of abnormal area of the cervix, after a positive screening test for cervical cancer is the colposcopic examinations routinely performed by GynecoOncologists. A colposcope is a low-power, stereoscopic, binocular field microscope with a powerful light source used for magnified visual examination of the uterine cervix to help in the diagnosis of cervical cancer. Alternatives to colposcopy examinations are being explored in developing countries like the direct visual inspection (DVI), visual inspection with acetic acid (VIA), visual inspection with acetic acid under magnification (VIAM), visual inspection with Lugol's Iodine (VIL) and cervicography which is a diagnostic medical procedure in which a non physician takes pictures of the cervix and sends it to the experts for interpretation. Recent reviews have shown that the performances of these methods have sufficient sensitivity and specificity when performed by trained professionals as an alternative to Pap smear screening in low resource settings.

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We propose screening/diagnosis of cervical cancer through development of an image analysis algorithm that automatically identifies the abnormal/ affected zone in the cervix collected from a sequence of cervical images and provides objective assessment of the severity of the cancer. This would provide confidence to a non expert in referring positive cases to an expert and reduce the rate of false positives of the existing cervicography and visual inspection techniques.

Uterine cervical image analysis has been widely researched. Yang et al. [1] developed a sophisticated technique for precise detection of the acetowhite regions using deterministic annealing technique. Automated glare removal techniques have been explored by Lange et al [2]. Juan et al. proposed a method to do image registration for colposcopic data [3]. However very few systems [4], [5], [6] have been reported in the literature for automated analysis of colposcopic images to provide objective assessment of the severity of the cancer. Li e al. [4] propose a method to score aceto white regions in post acetic acid applied cervical images by segmenting the aceto white regions. They use a GMM based approach to segment the aceto-white regions. In [5], the authors discuss a method to identify neoplastic tissues from pre and post acetic acid digital images captured from a multi spectral colposcope. They use a supervised classification method to identify the neoplastic/ aceto white regions in post acetic acid images and generate a disease probability map. In continuation of their work in [4], Li et al present another method where they use spectral features to grade the severity of cancer.

In our paper we propose to objectively quantify the severity of cancer in digital cervical images obtained after the application of acetic acid and Lugol's iodine. Unlike the methods discussed above, we segment the Lugol's iodine image to identify the abnormal tissues and map them to acetic acid images to accurately identify the abnormal tissues in post acetic acid images as well. To the best of our knowledge we have not come across any prior art that involves segmentation of post Lugol's Iodine images to identify the transformation zone.

The rest of the paper is follows. In section II we discuss the overall approach of the proposed method. Section III discusses the results and finally we conclude in Section IV.

II. Proposed Method

A. Clinical Background

Cervix is the lower most part of the uterus which extends into the vaginal canal. Ectocervix is the portion of cervix

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visible through the vaginal canal and is lined by the squamous epithelium. Endocervix is the portion extending from the external Os which is the external orifice of the cervix. This is lined by columnar epithelium. The junction of these two types of epithelium is called the transformation zone. The transformation zone lies between the new squamocolumnar junction (New SCJ) and the original squamocolumnar junction (Original SCJ). The transformation zone is the most common area for cervical cancer to occur. Figure 1 shows the schematic diagram of a cervix region and its constituents. During VIA, on application of acetic acid areas of the cervix which have abnormal vascular pattern turn white and are often considered for biopsy. VIA is followed by VIL which is the application of Lugol's iodine solution to help highlight areas of abnormality.

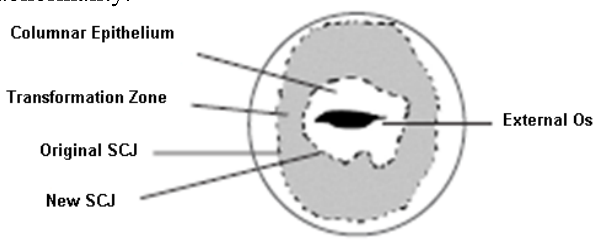

Figure 1: Schematic diagram of a cervix region

B. *Proposed Solution*

Sequences of images consisting of pre acetic acid (I_{PA}), post acetic acid (I_A) and post Lugol's Iodine (I_L) cervical images which are used to examine a patient under colposcope are employed for developing the algorithms. A block diagram of the proposed approach is shown in Figure 2.

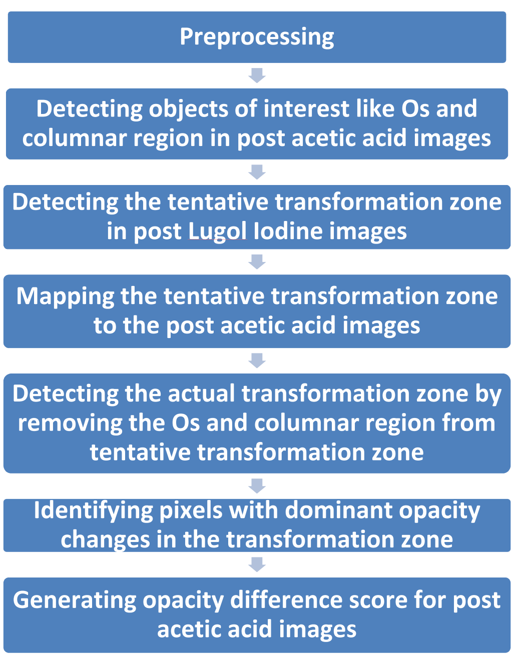

Figure 2: Block diagram of the proposed solution

The quality of cervical images is attributed to many factors including glare/ glint/ specular reflection. Glare eliminates the color information in affected pixels and thus makes image analysis algorithms unreliable. So the first step in preprocessing is removing glare pixels from the sequence of colposcope images. This is followed by segmenting pre and post acetic colposcope images to detect Os and columnar epithelium region. This step is followed by detecting tentative transformation zone in post Lugol's Iodine images based on the color changes that the effected cervical zone depicts on the application of Lugol's Iodine. This is followed by identifying the actual effected zone in post acetic acid images. Next we identify those pixels in the effected zone that show dominant opacity changes. Finally each post acetic acid image is given an opacity difference score with respect to the pre acetic acid image which can be used to objectively quantify the severity of cancer.

C. *Preprocessing*

Glare regions are detected as small, saturated and high contrast regions. We open an image, I_{PA}/ I_A/ I_L, in RGB color space. G component of the RGB color space is used as the feature space as it provides good glare to background ratio. A local maximum for histogram generated by G component is identified that represents saturated values. A mask for the glare pixels is generated and applied on the image 'I' to remove glare pixels from it.

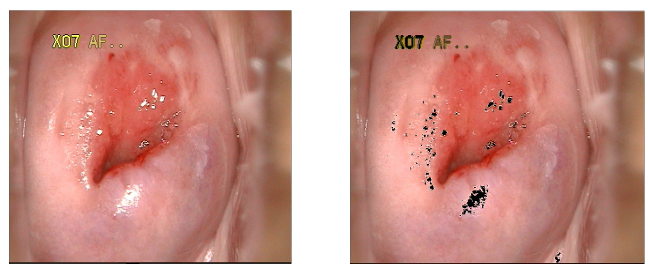

Figure 3: (a) Image with glare (b) Image after removing glare

D. *Detecting anatomical regions like Os and columnar epithelium regions in acetic acid images*

We identify the anatomical regions, i.e. the Os and columnar epithelium regions in I_{PA} and I_A in a fully automated way using an unsupervised two class classification technique based on K-means clustering. The I_{PA} and I_A are segmented using K-means clustering of pixels based on their color into 2 clusters in the RGB color space. The cluster centers are initialized randomly and Euclidean distance metric is used to assign a pixel to its nearest cluster center. The smaller of the two clusters is labeled as Os along with columnar epithelium region. It is now required to separate the Os from the columnar epithelium region. We separate Os and columnar epithelium using minimum variance quantization. Minimum variance quantization works by associating RGB values of pixels in the Os and columnar regions to a number of smaller cubes that an RGB color cube is subdivided into based on the variance between the pixel values. This is followed by mapping all colors that fall within each cube to the color value at the center of the cube. Thus the Os and columnar epithelium regions are separated. We then iteratively remove small and disjoint clusters which are the outliers within both Os and columnar epithelium regions. Figures below show the identification of Os and columnar epithelium regions.

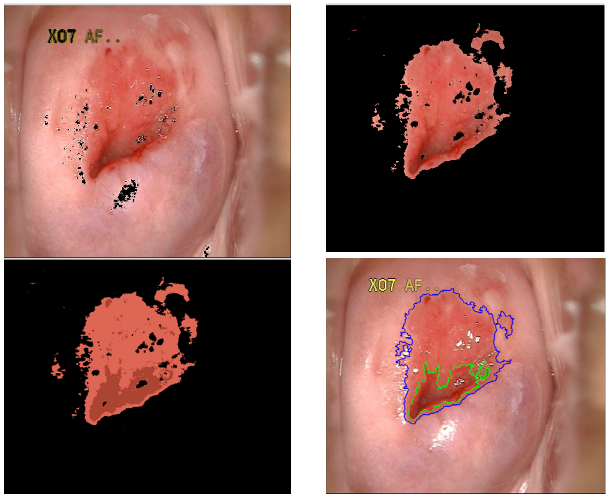

Figure 4 : (a) Original glare free image (b) Os and columnar region identified (c) Os and columnar regions seperated by minumum variance quantization. (d) Os and columnar regions demarked after removing outliers

E. Identification of Transformation Zone

Detecting transformation zone in the I_{PA} and I_A is a two step approach. In the first step post Lugol's Iodine images are processed to tentatively detect the transformation zone based on the color changes that it depicts on the application of Lugol Iodine. The post Lugol's Iodine image, I_L is segmented using color based K-means clustering into two clusters, I_{L1} and I_{L2}. It is observed that the histogram of the red component ($I_{L1}(R)$) of the cluster containing the transformation zone follows a normal distribution while it is not true for the other cluster. In order to automatically identify the cluster that contains the transformation zone, we model the normal distribution. Let the histogram for the red component of both the clusters be represented as $H(I_{L1}(R))$

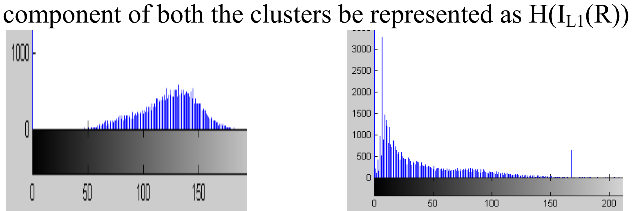

Figure 5 (a) Normal distribution of red values in cluster representing transformation zone (b) Random distribution of red values that do not contain transformation zone

and $H(I_{L2}(R))$. Both the histograms are smoothed using a gaussian kernal and the number of peaks in $H(I_{L1}(R))$ and $H(I_{L2}(R))$ are identified. The histogram containing only one peak is considered to belong to the cluster that contains the transformation zone. We then iteratively remove small and disjoint regions in this cluster. The convex hull of this cluster is defined as the tentative transformation zone in I_L.

In the second step, the tentative transformation zone identified in I_L is mapped to I_{PA} and I_A. The Os and the columnar epithelium regions detected in I_{PA} and I_A are subtracted from the tentative transformation zone to obtain the actual transformation zone.

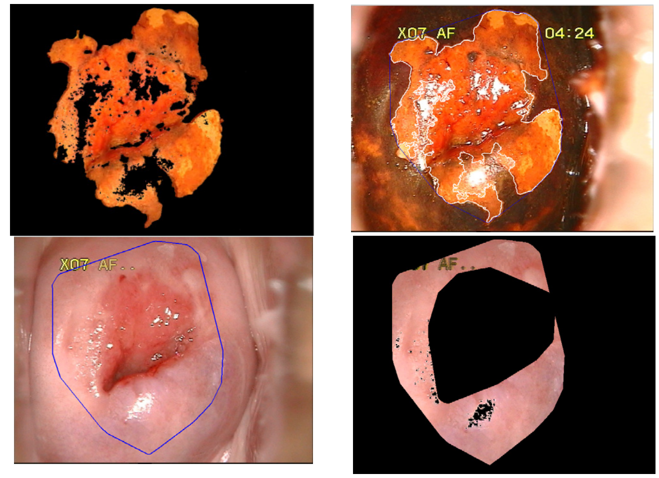

Figure 6: (a) Tentative transformation zone identified in post Lugol's Iodine image (b) Convex hull of the tentative transformation zone (c) Tentative transformation zone mapped to pre acetic acid image (d) Actual transformation zone identified in pre acetic acid image

F. Opacity Change Detection

Using the transformation zones identified in pre acetic acid and post acetic acid images, we can generate an opacity difference score [7] for all post acetic acid images acquired for a patient with respect to the pre acetic acid images which would aid in capturing the changes taking place due to the application of acetic acid. Broadly, in the post acetic acid images, pixels in the transformation zone which show dominant opacity changes are identified and they are compared with their corresponding pixels in pre acetic acid image. The steps to generate opacity difference score is as follows:

- Convert the RGB values of the transformation zone in post acetic acid images to Lab color space (L component closely matches human perception of lightness/whiteness)
- Cluster pixels in the transformation zone to two levels of whitish regions, i.e., dominant opacity change and minor opacity change
  (To match opaque white, and translucent white practiced clinically)
- Remove the pixels with minor opacity change
- Identify the corresponding pixels of the dominant opacity change in the pre-acetic acid image
- Compute opacity difference score for a post acetic acid image with respect to its pre acetic acid image

The opacity difference score is computed as follows:

$$OpacityDifferenceScore = \frac{1}{N}\left(\sum (I(i,j) - J(i,j)) \times r(i,j)\right)$$

where,

I = Image with dominant pixels in pre-acetic acid image

J = Image with dominant pixels in post acetic acid image

N = Number of pixels with dominant opacity changes

r = Binary image with dominant opacity changes

(i,j) = A pixel in the spatial domain of image I / J / r

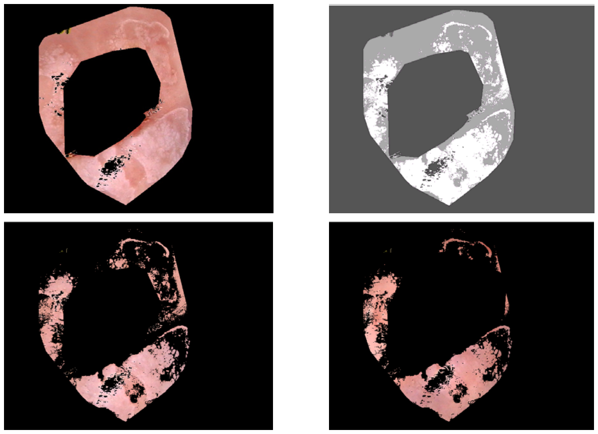

Figure 7: (a) Transformation zone in post acetic acid image (b) Pixels with minor and dominant opacity changes in the transformation zone (c) Pixels with dominant opacity changes in post acetic acid image (d) Corresponding pixels with dominant opacity changes in pre acetic acid image

The opacity difference score is computed for all the post acetic acid images with respect to pre acetic acid images. Figure below shows the variation in opacity for post acetic acid images taken at different time.

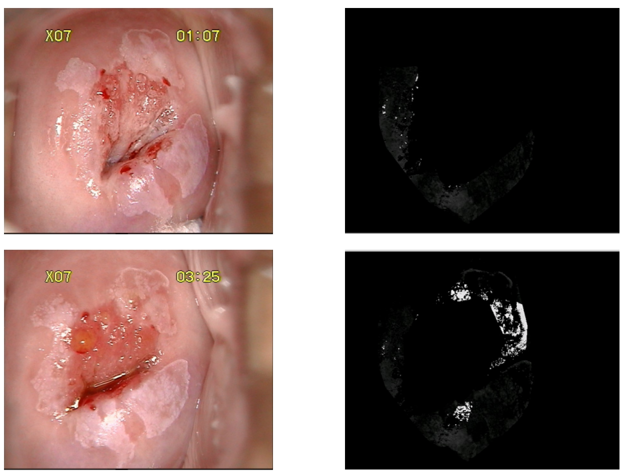

Figure 8: (a) Post acetic acid image taken after 1:07 min of applying acetic acid (b) Opacity image with opacity difference score of 18.46 (c) Post acetic acid image taken after 3:25 min of applying acetic acid (d) Opacity image with opacity difference score of 43.28

It is observed that the opacity difference score for the image taken at 3.25 sec is more than the opacity difference score of the image taken at 1.07 sec. This is in compliance with the clinical know how that the tissues with high nucleus turn white with application of acetic acid with time. This change in color will help to predict the presence of cancer if the opacity difference score appears faster and persists longer.

III. Results and Discussions

The proposed algorithm has been tested on RGB images collected from 17 subjects using a Philips Goldway Colposcope. For each subject we have at least three images, ie, one pre acetic acid, one post acetic acid and one post Lugol's Iodine image. In total the algorithms have been tested on 60 images. All the images have been collected using a colposcope with 7-10X zoom. The algorithm's performance was assessed by qualitative subjective inspection by a physician. It has been observed that the algorithm performs significantly well in identifying the cancerous regions. However registering the acetic acid images and Lugol's iodine images are required to get an accurate identification of the transformation zone. Figure 9 (b) shows that the transformation zone identified in Figure 9 (a). It would have been more accurate had the two images been registered. However, image registration is beyond the scope of this paper.

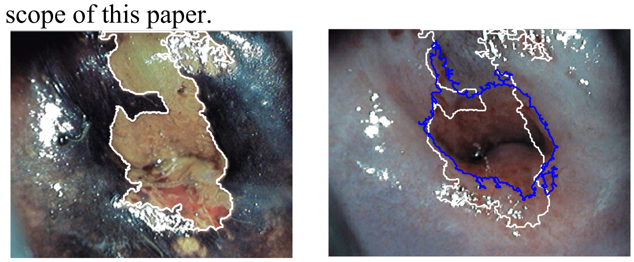

Figure 9: (a) Transformation zone identified in post Lugol's iodine image (b) Transformation zone mapped to the post acetic acid image

IV. Conclusion and Future Work

In this paper we discussed diagnosis of cervical cancer through development of an image analysis algorithm that automatically identifies the transformation zone in the cervix collected from a sequence of cervical images and provides objective assessment of the severity of the cancer. Thus the algorithm could be a part of expert system that could objectively quantify the severity of cancer. Automatic grading of the cancer is beyond the scope of this paper.

The novelty of this paper is in developing a robust algorithm that could identify the transformation zone by using post Lugol's iodine image and pre/post acetic acid images. In future we would like to register the sequence of cervical images before identification of the transformation zone.

References

[1] S. Yang, J. Guo, P. King, Y. Sriraja, S. Mitra, B. Nutter, D. Ferris, M. Schiffman, J. Jeronimo, and R. Long, "A multi-spectral digital cervigram™ analyzer in the wavelet domain for early detection of cervical cancer", *Proc.SPIE,* vol. 5370, pp. 1833-1844, 2004.

[2] H. Lange, "Automatic glare removal in reflectance imagery of the uterine cervix*", Proc SPIE* , vol. 5747, pp. 2183-2192, 2005.

[3] J. D. Garc´ıa-Arteaga and J. Kybic, "Automatic Landmark Detection for Cervical Image Registration Validation", vol. 28, no. 3, pp. 454-68, March 2009.

[4] W. Li, J. Gu, D. Ferris, A. Poirson, "Automated Image Analysis of Uterine Cervical Images", Proc SPIE, 6514, pp. 65142, 2007.

[5] S.Y. Park, M. Follen, A. Milbourne, H. Rhodes, A. Malpica, N. MacKinnon, C. MacAulay, M. K. Markey, R. Richards-Kortum, "Automated image analysis of digital colposcopy for the detection of cervical neoplasia," *Journal of Biomedical Optics*, vol. 13, no. 1, pp 014029.

[6] W. Li, V. Raad, J. Gu, U. Hansson, J. Hakansson, H. Lange, A. Poirson, "CAD for cervical cancer screening and diagnosis A new system design in medical image processing," Computer Vision for biomedical image applications , LNCS Springer, vol.3765/2005, pp. 240-250, 2005.

[7] W. Li, S. Venkataraman, U. Gustafsson, D. Ferris and J. C. Oyama , " Using aceto white opacity index for detecting cervical intraepithelial neoplasia", *Journal of Biomedical Optics*, vol. 14, no. 1, pp 014020, 2009.