Detection and Characterization of Abnormal Vascular Patterns in Automated Cervical Image Analysis

Wenjing Li and Allen Poirson

STI Medical Systems, 733 Bishop St. Honolulu, Hawaii, 96813, USA
wli@sti-hawaii.com, apoirson@sti-hawaii.com

Abstract. In colposcopy, mosaic and punctation are two major abnormal vessels associated with cervical intraepithelial neoplasia (CIN). Detection and characterization of mosaic and punctation in digital cervical images is a crucial step towards developing a computer-aided diagnosis (CAD) system for cervical cancer screening and diagnosis. This paper presents automated techniques for detection and characterization of mosaic and punctation vessels in cervical images. The techniques are based on iterative morphological operations with various sizes of structural elements, in combination with adaptive thresholding. Information about color, region, and shape properties is used to refine the detection results. The techniques have been applied to clinical data with promising results.

1 Introduction

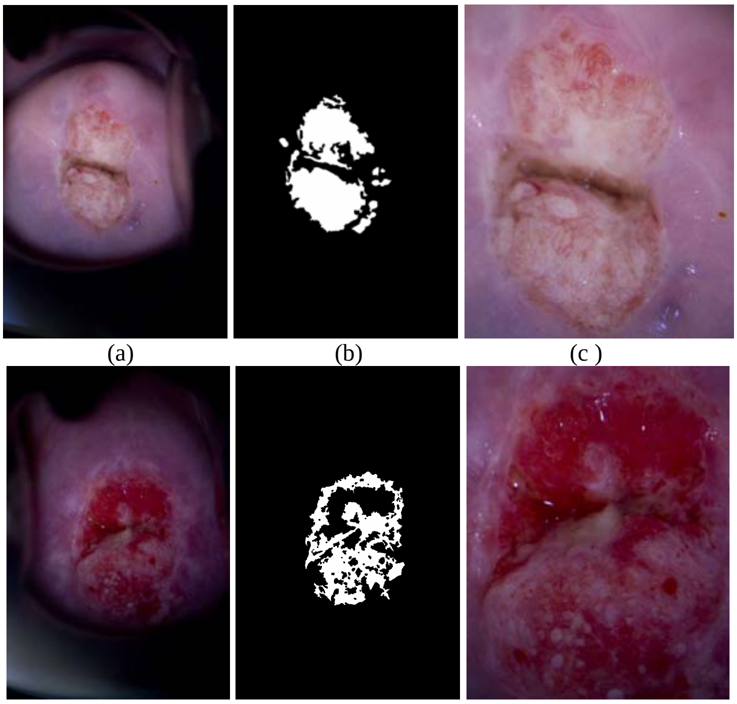
Cervical cancer is the second most common cancer in women worldwide, with nearly a half-million new cases and over 270,000 deaths annually. Because invasive disease is preceded by pre-malignant cervical intraepithelial neoplasia (CIN), if detected early and treated adequately, cervical cancer can be universally prevented. The atypical epithelium is usually categorized as CIN grades 1, 2, and 3 histologically or low-grade and high-grade squamous intraepithelial lesions (LSIL and HSIL), depending on the severity of the lesions.

Colposcopy is the primary diagnostic method used in the US to detect CIN and cancer, following an abnormal cytological screening (Papanicolaou smear). The purpose of a colposcopic examination is to identify and rank the severity of lesions, so that biopsies representing the highest-grade abnormality can be taken, if necessary. A colposcopic examination involves a systematic visual evaluation of the lower genital tract (cervix, vulva and vagina), with special emphasis on the subjective appearance of metaplastic epithelium comprising the transformation zone on the cervix. To visualize the cervix, a colposcope is used which is a binocular microscope with a built-in white light source. During the exam, a 3-5% acetic acid solution (vinegar) is applied to the cervix, causing abnormal and metaplastic epithelia to turn white (acetowhitening effect). Cervical cancer precursor lesions and invasive cancer exhibit certain distinctly abnormal morphologic features that can be identified by colposcopic examination. Lesion characteristics such as color and opacity, margin demarcation and shape, and vascular patterns are considered by physicians (colposcopists) to derive a clinical diagnosis. Due to the subjective nature of the examination, the accuracy of colposcopy is highly dependent upon physician experience and expertise. Colposcopy suffers from low specificity leading to many unnecessary biopsies.

Among the colposcopic signs that identify pre-cancerous regions, the abnormal vascular patterns called punctation and mosaic are major diagnostic features [1]. Punctation is a colposcopic finding reflecting the capillaries in the stromal papillae that are seen end-on and penetrate the epithelium. When the stroma and accompanying capillaries are "pressed" between islands of squamous epithelium in a continuous fashion, a honeycomb or chicken-wire pattern called mosaic is produced. Punctation and mosaic can be seen in both normal and abnormal cervical epithelium. Abnormal vessels can be enhanced during a colposcopic exam by using green-filtered light. If the punctation or mosaic is not located in a field of acetowhite epithelium, it is unlikely to be associated with CIN. The punctation or mosaic pattern is described as fine or coarse. If the vessels are fine in caliber, regular, and located close together, it is more likely that the patterns represents a benign process or low-grade CIN. If the intercapillary distance of the vessels is increased and the vessels are coarser in appearance, the grade of the lesion is usually more severe.

Digital imaging is revolutionizing medical imaging and enabling sophisticated computer programs to assist the physicians with Computer-Aided Diagnosis (CAD). Detection of abnormal vascular patterns has been a very challenging task due to several factors such as lack of good quality, high resolution images, glare and mucus effects, non-uniform illumination, large intra-patient variation, and other artifacts on the surface of a cervix. One pilot study [2] uses a generalized statistical texture analysis technique to characterize six types of cervical vascular patterns. The approach in this study represents the vascular structure using line segments and constructs the statistical distribution of the line segments. First and second order statistics derived from the joint and/or marginal distribution are used as textural measures for cervical lesion classification. However, in the experiments, the region of interest is pre-marked and automatic detection of vessels is not addressed. In [3], preliminary results are presented on detecting mosaic patterns using both color and geometric features. The method used seems to over-detect the vascular structure on both normal cervix region, and in the acetowhite regions. Besides, punctation vessel detection has not been addressed. To our knowledge, a robust method to detect the abnormal vascular patterns in cervical images automatically and effectively has not been achieved.

In this paper, we present our work on automatically detecting and characterizing mosaic and punctation vessels in digital cervical images. First, the abnormal region is detected by locating the acetowhite region (the area turning white after application of acetic acid) of the image. Second, a novel mosaic detection technique is presented, which includes mathematical morphology with a rotating line structure element of multiple sizes, branching point detection, and a vascular structure tracing. Third, the punctation detection technique is introduced by applying a "hole" enhancement procedure, morphological transforms with a multiple-size disk structure element, followed by a refinement procedure using gradient and shape information. The properties of the mosaic and punctation are also analyzed based on the clinical phenomenology. Experimental results demonstrate the effectiveness of the techniques. Discussions and conclusions are given finally.



(a) (b) (c)

(d) (e) (f)

Fig. 1. Preprocessing steps to find the region of interest for vascular detection, (a), (d) Original images, (b), (e) Abnormal regions detected, (c), (f) The regions of interest for vessel detection.

2 Abnormal Region Detection

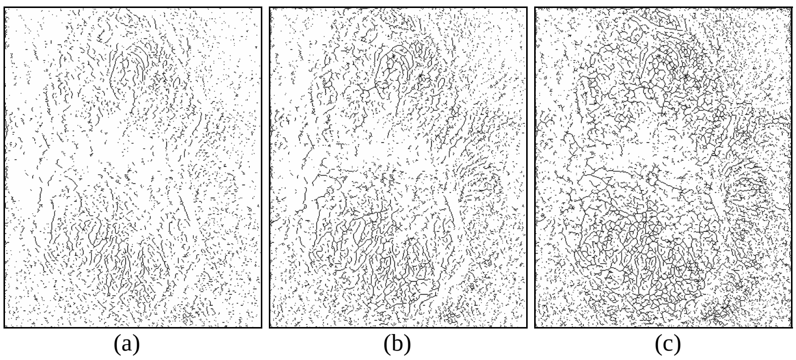
According to colposcopy, acetowhite epithelium refers to epithelium that transiently changes color from pink or red to white after application of 3% to 5% acetic acid. It is the most common colposcopic feature observed when cervical intraepithelial neoplasia is present. We have developed an automatic segmentation of acetowhite region detection algorithm based on color and texture information. The algorithms use multiple unsupervised segmentation techniques to address different anatomic features and different levels of acetowhite lesions. The details can be found in [4]. When mosaic and punctation are not located in the acetowhite epithelium, they are unlikely to associate with CIN. Therefore, we focus on the detection and characterization of the mosaic and punctation within the acetowhite epithelium. Fig. 1 (a) and (d) shows the original cervical images. Fig. 1 (b) and (e) shows the corresponding acetowhite regions. The region of interest for abnormal vessel detection is the rectangular region for the maximal area of the acetowhite lesion, as shown in Fig. 1(c) and (f).

3 Mosaic Analysis

3.1 Mosaic Detection

Mosaic vasculature appears colposcopically as a red tile-like polygonal grid viewed within an area of acetowhite epithelium. The small blocks of epithelium, encompassed by the mosaic vessels vary in size, shape, and uniformity. The intercapillary distances between mosaic vessels vary depending on the severity of neoplasia. In general, as vessel caliber and intercapillary distance increase, the severity of neoplasia also increases. Based on the phenomenology of the mosaic pattern, we propose a robust abnormal mosaic detection algorithm for cervical images. Taking the acetowhite area of the cervical image as input, the method consists of the steps outlined below.

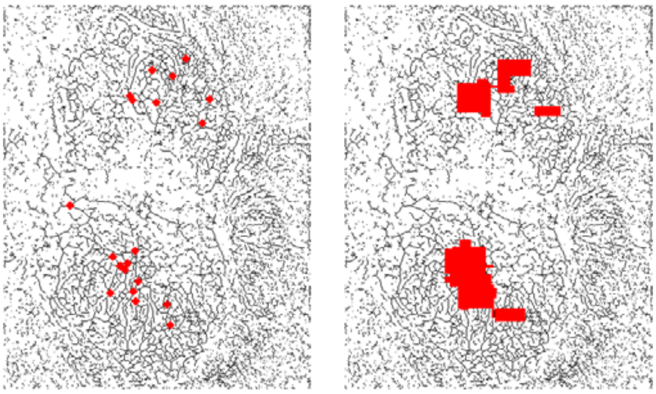
a. Iterative detection of vascular structure. In 1993, Thackray **[5]** presented a semi-automatic segmentation method for vascular network images using a combination of mathematical morphological opening with a linear rotating structuring element (ROSE). The method has proved to be effective on initial segmentation of dominant vascular networks containing vessels of different size and orientations. However, in cervical images, the mosaic pattern is only a subset of vascular structures. The dominant texture region also covers anatomy of the cervix and artifacts on the surface. Therefore, we adapted this theory in combination with an adaptive thresholding and a thinning procedure to do the initial segmentation. In each iteration, a top hat transform is performed using the line structure element at one particular direction. An average spatial distance metric is computed each time until it reaches a pre-defined threshold. The resulting images are thresholded using an adaptive parameter and then combined with results from the previous iteration. Fig. 2 shows the intermediate results at different iteration steps. It can be seen that after a certain number of iterations, all the fine vascular structures in the image are well captured. However, some short noisy line segments are also included. They will be removed in the next step.



(a) (b) (c)

Fig. 2. Vascular Pattern detection (a) 1st iteration, (b) 3rd iteration, (c) final iteration.

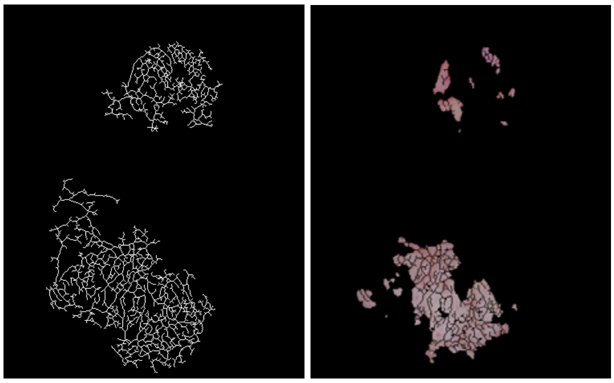
b. Detection of branching points and high probability mosaic regions. The mask image with initial detection results is scanned with a 3 by 3 square window. The positions where the number of white pixels within the square is greater then 3 are marked as initially branching points. The branch points are further refined to remove the false detected ones. Regions with more than two branch points within a window indicate an area with high probability of having a true mosaic vessel pattern. The branching points are used as seeds for vessel tracing the thinned enhanced vessel structure. Fig. 3 shows the branch points and the results of high probability region detection.



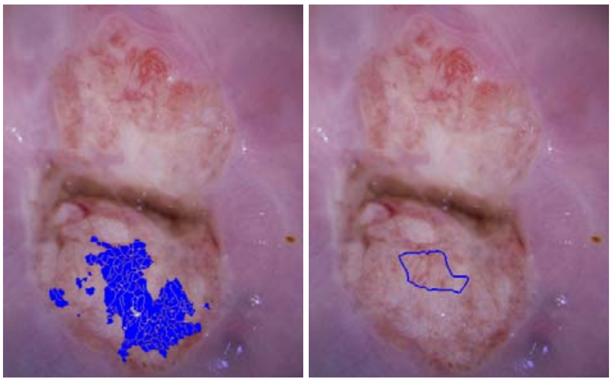
(a) (b)

Fig. 3. Detection of (a) branching points and (b) high probability of mosaic regions

c. Tracing of mosaic structures. All branching points within a high probability region in the original vessel structure are used as seeds for tracing and identifying the mosaic patterns. The tracing procedure starts at a branching point and then detects it connected points (vessels) in eight possible directions one by one to locate complete vessel structure. Fig. 4 (a) shows the results for the traced mosaic vessel structure.



(a) (b)



(c) (d)

Fig. 4. (a) The traced vessel structures (b) the detected mosaic patterns, (c), the refined mosaic patterns, (d) colposcopic annotation.

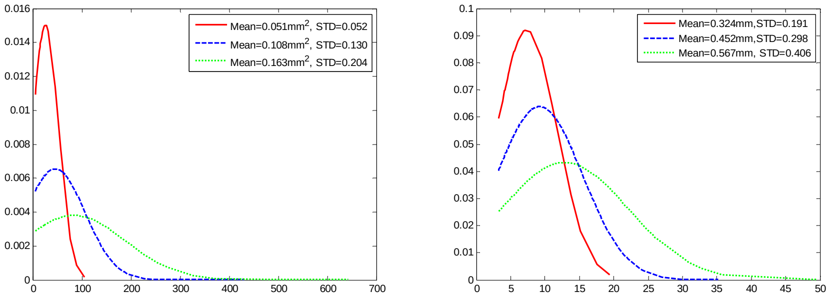
d. Mosaic region identification. According to the phenomenology of mosaic vessels in colposcopy, the mosaic regions are extracted as the closed region from the traced vascular structure. Those regions are further refined based on its color properties, surface area, and its intercapillary distance. Since we are only interested in the abnormal area related to the disease severity, the area outside the acetowhite epithelium is eliminated. Fig. 4 (b) shows the detected mosaics and (c) shows the final mosaic vessels after refinement.

3.2 Mosaic Characterization

Mosaic are categorized colposcopically as fine or coarse, based on their diameter. A fine mosaic pattern is a closely interwoven, lacy, delicate network of capillaries of nearly normal caliber, dispersed perpendicularly in stromal ridges resembling red grouting between small white ceramic tiles. A uniformly consistent small intercapillary distance may be seen with immature metaplasia, a congenital transformation zone, and CIN 1 lesions.

A coarse mosaic pattern is characterized by dilated varicose vessels that enclose larger diameter, irregularly shaped mosaic epithelial blocks. The abnormal coarse vascular pattern is also confined invariably to a well-demarcated, dense acetowhite lesion. The epithelial pegs between the vessels are larger and more varied in shape, reflecting irregularity and an increase in intercapillary distance. A wide, irregular, non-uniform intercapillary distance and coarse-caliber vessels would be typical of a mosaic pattern seen with CIN3. The analyzed mosaic provides insight into the nature of the epithelium being inspected [6]. The mean intercapillary distance between mosaic vessels in CIN2 is significantly less than seen in CIN3. Consideration of the distribution of a mosaic vessel further helps to determine the type of epithelium observed.

All the properties of the mosaic patterns are recorded including intensity, color, surface area, perimeter, the shortest axis length and the longest axis length. Their distribution is modeled as Gaussian. The standard deviations of the size of the mosaics and their intercapillary distances represent the irregularity of the mosaic patterns. Fig. 5 (a) shows the distributions of surface area for different mosaic regions and (b) shows the corresponding distributions of the intercapillary distances. The intercapillary distance of a mosaic is defined as the distance between the farthest two points in the mosaic. The solid-line curve in the figures is more likely to be fine mosaic since both of the mean and standard deviation are smaller and the dot-line curve in the figure is more likely to be coarse mosaic region. The decision boundary between coarse and fine mosaics is computed from a representative training set with 19 subjects.



(a) (b)

Fig. 5. Characterization of mosaics (a) Surface area distributions of different mosaic regions (b) Intercapillary distance distributions of different mosaic regions.

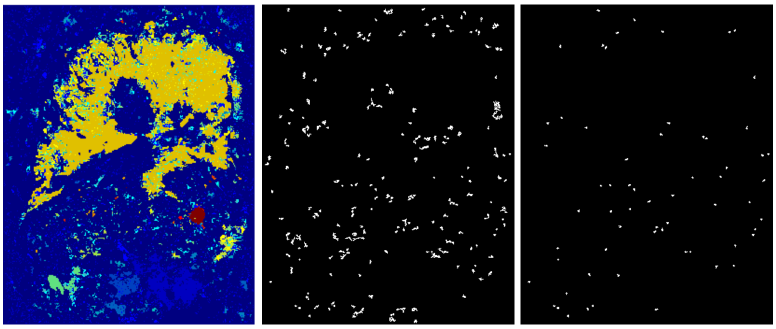
4 Punctation Analysis

4.1 Punctation Detection

Punctation appears as tiny red dots of variable dimensions usually present within an area of acetowhite epithelium. Both the size or diameter of punctation (caliber of the loop vessels) and the distance between punctation (intercapillary distance) vary depending on the severity of the underlying disease. Punctation detection has not yet been addressed in the literature. Since the punctation patterns appear very small in the cervical images, the quality of the image has a major impact on the detection of the punctation vessels. Poor focus, narrow depth of field, and non-uniform illumination are all obstacles to an effective detection.

Our initial punctation detection technique employs the same strategy as the mosaic detection. Instead of rotating line structure elements, disk structure elements with various sizes have been used for the top hat transforms. Due to insufficient image quality, we designed a pre-processing procedure to enhance the punctation structure.

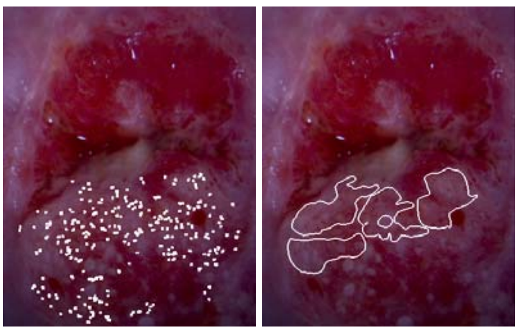
The enhancement procedure consists of a series of morphological operations, including extraction of a green band image, a “hole” closing operation, and a contrast enhancement technique with a toggle operator. The technique highlights the hole-like vascular structures in the image, which is a crucial pre-processing step for the punctation detection. An example of the “hole” enhancement image can be seen in Fig. 6(a).



(a) (b) (c)

Fig. 6. (a) Enhancement of “holes” in the image (b) the punctation mask before the refinement (third iteration) (c) the punctation mask after the refinement (third iteration)

The initial result of punctation detection is usually noisy and has many false positives. A post-process procedure is required to refine the results. Various region properties are computed, including the local gradient information, region area, and the eccentricity of the regions. Gradients and region area use heuristic rules based on the imaging distance and clinical prior knowledge. The eccentricity of the region has a high impact removing the false detected regions. Fig. 6 (b) shows the punctation mask before the refinement in a single iteration, and Fig. 6 (c) shows the corresponding punctation mask after the refinement procedure. Finally, the detected region is further refined by excluding the non-acetowhite regions, glint regions, and other anatomic regions (Os, and columnar epithelium), as seen in Fig. 7(a).



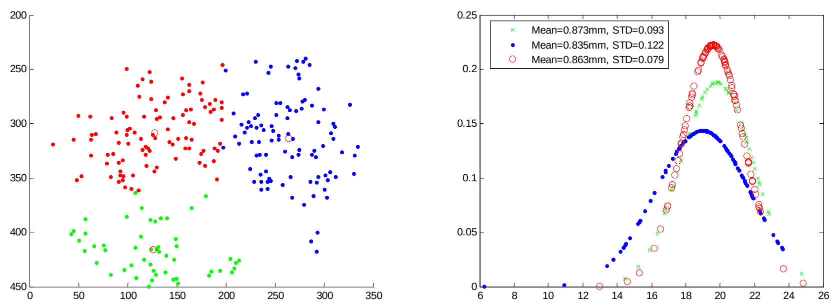
(a) (b)

Fig. 7. Final Punctation detection and it colposcopic annotation (a) the punctation detection results, (b) colposcopic annotation.

4.2 Punctation Characterization

Fine punctation is a regular pattern of looped capillaries of narrow diameter, usually closely and uniformly spaced. When fine punctation is confined to an abnormal acetowhite lesion within a field of immature metaplasia, it is usually indicative of a low-grade lesion (CIN1). When fine punctation is confined to an abnormal acetowhite lesion on the original squamous epithelium, it may represent either a HPV-induced lesion or a variation of the normal metaplastic process. In coarse punctation, the capillaries appear more pronounced because the loop capillaries are dilated and the intercapillary distance is greater. Furthermore, coarse punctation is more irregularly spaced. In CIN3 lesions, 57% of vessels exhibit intercapillary distance of more than 300um [7]. A vascular pattern of coarse punctation usually indicates a high-grade lesion, or CIN2, 3, and possibly early invasion.

In order to assess the severity of the lesion, the detected punctations are further classified as different clusters according to their spatial distribution using an EM (Expectation Maximization) algorithm. In each cluster, properties such as the local area, local gradient, and distance matrix are recorded. The intercapillary distance of the punctation is calculated as the average distance of the neighboring punctations to the corresponding point. The neighborhood range is based on a pre-defined window. Fig. 8 (a) shows three clusters of the punctation vessel and Fig. 8 (b) shows the distribution of the intercapillary distances. The similarity of distribution of intercapillary distances indicates a similar type of punctation, coarse in this case. As with mosaic characterization, the decision boundary between the coarse and fine punctations is determined from a representative training set with 30 subjects.



(a) (b)

Fig. 8. Clustering the punctation data (a) the three clusters (b) their corresponding distributions of intercapillary distances

5 Discussions and Conclusions

Using our digital colposcope, we acquired 100 high-quality, cross-polarized image sets from hospitals in Peru. The mosaic and punctation detection results are being evaluated by expert colposcopists. Histopathology results from LEEP (Loop Electrosurgical Excision Procedure) are also available to provide "gold standard" for disease severity. Fig. 4 (d) and Fig. 7 (d) show two examples of the colposcopic annotations on mosaic and punctation regions. The subjects shown in this paper have been verified by histopathology as having HSIL. The quantitative analysis of the performance will be done soon using a region based match around the cervical os region.

A CAD system for colposcopy has a direct impact on improving women's health care. Detection and characterization of the abnormal vessels are one crucial step in developing the CAD system. This paper presents a novel application of image processing technique in cervical cancer screening and diagnosis. The vessel detection techniques presented here are fast and robust. The computed features of abnormal vessels will serve as inputs to a tissue classification routine, together with other diagnostic features like color, opacity, shape, and demarcation. The results of the classification routine will provide the physician the suggested diagnosis and biopsy sites.

Acknowledgements

The authors would like to thank Daron Ferris (MD) for the colposcopic annotation, Johan Hakansson for his early development work, and Marcelo Soto-Thompson, John Hargrove, and Ulf Gustafsson for the comments and discussions.

References

1. Reid, R. and Scalzi, P.: Genital warts and cervical cancer. VII. An improved colposcopic index for differentiating benign papillomaviral infections from high-grade cervical intraepithelial neoplasia. Am. J. Obstet. Gynecol. 153 (6) (1985) 611-618
2. Ji, Q., Engel, J., and Craine, E.: Texture analysis for classification of cervix lesions. IEEE Trans. Med. Imaging 19 (11) (2000) 1144-1149
3. Srinivasan, Y., Hernes, D., Tulpule, B., Yang, S. et al.: A probabilistic approach to segmentation and classification of neoplasia in uterine cervix images using color and geometric features, in *Proc.of SPIE Medical Imaging,* **5747**. (2005) 995-1003
4. Li, W.: Automated image analysis of uterine cervical images, in *Proc.of SPIE Medical Imaging, submitted,* (2007)
5. Thackray, B.D. and Nelson, A.C.: Semi-automatic segmentation of vascular network images using a rotating structuring element (ROSE) with mathematical morphology and dual feature thresholding. IEEE Trans. Med. Imaging 12 (3) (1993) 385-392
6. Mikhail, M.S. and Romney, S.L.: Computerized Measurement of Intercapillary Distance using Image Analysis in Women with Cervical Intraepithelial Neoplasia: Correlation with Severity. Obstet. Gynecol. 95 (4 Supplement) (2002) 2S-3S
7. Ferris, D., Cox, J.T., O'Connor, D.M., Wright, V.C., and Foerster, J.: Modern Colposcopy, Textbook and Atlas. Second. American Society for Colposcopy and Cervical Pathology, (2004)