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ORIGINAL ARTICLE

Optical Imaging: Future Tool in Detection of Pre-cancerous and Cancerous Lesions of Cervix and Its Comparison to Colposcopy

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About the Author

Dr Kiran Pandey is working as a professor and Head of the Department of Obstetrics & Gynaecology in GSVM Medical College, Kanpur. She has organized about 66 CMEs as a secretory of KOGS and President Clinical Society. She has attended 97 conferences as a guest speaker, panelist, and chairperson. She has published a total of 109 papers. In the last 6 years, she has published 5 international, 15 national, and 10 state journals. She also contributed a chapter "Current trends in gestational diabetes mellitus" in a book in Obstet & Gynae in FOSGI, Calcutta. Her thesis paper "Optical spectroscopy—a tool for diagnosis of cervical precancerous & cancerous lesion" received Dr. Chittathara & Dr. Gangadharan award.

Abstract

Objectives To study the diagnostic potential of optical imaging and its comparison with colposcopy, in detecting early cervical dysplasia

Methods The study was conducted on 200 patients attending the outdoor of UISE maternity hospital with symptoms suspicious of cervical lesions. All patients were subjected to colposcopy, followed by histo-pathological examination. Out of all HPE, 18 samples each from normal and dysplastic histology were sent to IIT Physics lab, Kanpur for optical imaging. Statistical analysis was done using sensitivity, specificity, PPV, and NPV. Chi square test was applied to calculate p value

Results In optical imaging, depolarization images had shown significant changes in the epithelium region of the dysplastic tissue as compared to normal one. It is found that the mean value of depolarization power for normal cervix tissues is less than 0.32, while for dysplastic tissues it is greater than 0.32

Conclusion Optical imaging is fast, non-invasive tool with high sensitivity and specificity, comparable to colposcopy (sensitivity 88.9 vs 100 %, specificity 83.3 vs 86.6 %) and thus is useful in both for screening and diagnosis of cervical dysplasia

Keywords Optical imaging · Depolarization power · Cancer cervix · Colposcopy

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Introduction

Carcinoma cervix is the second most common cancer among women globally affecting an estimated 490,000

women each year, and causing 270,000 deaths annually [1]. The reported incidence of pre-clinical invasive carcinoma in India is around 1.5/1000 [2]. Developing countries like India account for roughly 80 % of these cases with India contributing to 18 % of total cases [3].

The accessibility of uterine cervix, propensity of cells to exfoliate from pre-cancerous lesions, the evidence from pathological studies of existence of histological changes from mild atypias through pre-malignancy to frank malignancy, the apparently prolonged natural history, the long pre-malignant phase, and the ability for detecting changes, using various screening techniques, provide perhaps the best potential for control of cervical cancer by mass population screening. The mean time interval for progression of cervical pre-cancer to invasive cancer is 10 years [3]. This period can be effectively used for screening to decrease the incidence of invasive cervical cancer.

American Cancer Society recommends that screening should begin 3 years after the onset of vaginal intercourse and not more than 21 years of age [4]. Over 6 billion dollar is spent annually in the evaluation and treatment of low grade lesion suggesting that there is a significant need for new technologies which will improve the detection process and reduce the cost and ease of use in the field setting, as per need of our country. In most of the presently used screening methods, the patient has to come to hospital for screening and with about 80 % of the population living in rural areas in our country, it becomes a difficult preposition and it is, therefore, necessary to develop screening methods which can be carried to the doorstep of the patients, to make mass screening programs successful, especially in rural areas where it is very much needed [5]. Optical imaging (high resolution) technique can image tissue with sub-cellular resolution to probe changes in epithelial cell morphology and epithelial architecture without the need for biopsy, sectioning, and staining [6].

Aims of the Study

The aim of the study is to compare the efficacy of optical imaging with that of colposcopy using histopathology as gold standard in detection of early cervical neoplasia in its pre-invasive stage. If results were promising, to develop, in future, a non-invasive in vivo probe for carcinoma cervix detection.

Materials and Methods

The study was conducted on ($n = 200$) patients attending the outdoor of UISE Maternity Hospital, GSVM Medical College, Kanpur between January 2010 and September 2011 with symptoms suspicious of cervical lesions like persistent abnormal vaginal discharge, low backache, contact bleeding, postmenopausal bleeding, menstrual disorder, and pain in abdomen. The entire procedure was explained to patients and their informed consent was taken. All patients were subjected to colposcopy and histo-pathological examination (HPE). Out of all HPE, $n = 18$ samples each from normal and dysplastic histology were sent to IIT Physics lab, Kanpur for optical imaging (OI). Results of optical imaging were compared with that of colposcopy using statistical analysis sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Chi square test was applied to calculate p value.

Colposcopic evaluation was done between 8th and 12th day of menstrual cycle and it provided the study of surface epithelium and underlying connective tissue along with its vascular network. Change in color, lesion margin, and surface configuration, vessels and iodine staining were noted after application of acetic acid and lugol's iodine. We used Reid colposcopic index (RCI) [7] for scoring lesions.

Formalin fixed cervical tissue samples of all 200 patients were sent to Department of pathology, GSVM Medical College for histopathology.

For optical imaging, $n = 18$ samples each from normal and dysplastic histology were sent to Department of Physics, Indian Institute of Technology (IIT) Kanpur. The samples were pathologically characterized, containing both epithelial and stromal regions on glass slides. The lateral dimension of tissue sample was 4×6 mm having thickness of 5 μm. These samples were illuminated with He–Ne laser, and Mueller images of these tissue slides were recorded on a charged couple device (CCD) camera (KAF-0401LE, Eastman Kodak, Rochester, 130 NY, USA) having resolution of 786×512 pixel. Mueller decomposition images were used to discriminate between normal and dysplastic tissue.

Scheme 1 shows the study design.

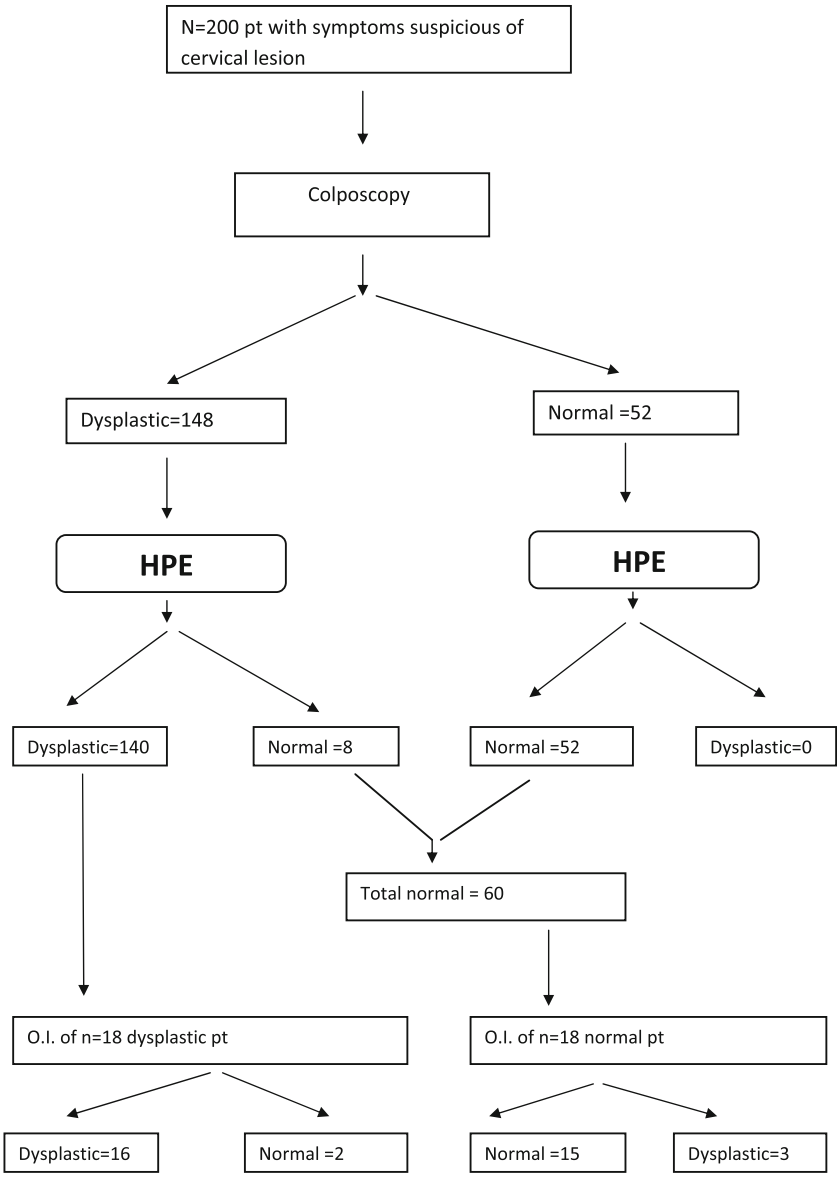
Results

Table 1 shows correlation of pt with dysplastic colposcopic finding i.e., 148 pt with that of HPE. A total of 8 pt (RCI 1 = 6 pt+RCI 2 = 2 pt) were false positive on colposcopy though HPE shown them as inflammatory.

Table 2 shows that 52 pt that was normal on colposcopy was also found to be normal on HPE, thus false negative pts were zero with colposcopic examination.

Table 3 shows that 2 dysplastic pt (FN) and 3 normal pt (FP) were shown as normal and dysplastic, respectively, on optical imaging.

Table 4 shows comparable sensitivity and specificity of colposcopy to OI (sensitivity 100 vs 88.89 %, specificity 86.6 vs 83.3 %).



Scheme 1 Typical depolarization power images of **a** normal and **b** dysplastic state in the epithelium region of the cervical tissue section

Table 1 Correlation of dysplastic colposcopic findings with histopathological diagnosis (using RCI)

Colposcopic index	Histological diagnosis				
	Inflammatory	CIN I	CIN II	CIN III	Carcinoma
0	–	–	–	–	–
1	6	21	–	–	–
2	2	25	–	–	–
3	–	21	12	–	–
4	–	19	10	9	–
5	–	–	9	6	–
6	–	–	3	4	–
7	–	–	–	–	–
8	–	–	–	–	1
Total = 148	8	86	34	19	1

Discussion

Prevention and control of cancer are a burgeoning field because of advance in understanding the biology of carcinogenesis. Aim of our study was to emphasize on early detection of cervical dysplasia lesions by OI technique.

Tables 1 and 2 show the correlation of colposcopic findings to histology. The sensitivity was calculated to be 100 % and specificity 86.6 % with PPV 100 % and NPV 94.5 %. In a study done by Mojgan et al. [8] found sensitivity and specificity of colposcopy to be 80 and 80 %, respectively.

Figure 1 shows the 2D Mueller decomposition images in terms of depolarization power for epithelium region. In the depolarization images, significant changes were

Table 2 Correlation of colposcopic finding with histopathological diagnosis

Histopathology colposcopy	Normal	Dysplastic	Total
Normal	52 (TN)	00 (FN)	52
Dysplastic	08 (FP)	140 (TP)	148
Total	60	140	200

TP True positive, *FP* false positive, *TN* true negative, *FN* false negative

p value is <0.05 = Association is statistically significant

Table 3 Correlation of optical imaging with histopathological diagnosis

Histopathology optical imaging	Normal	Dysplastic	Total
Normal	15 (TN)	02 (FN)	17
Dysplastic	03 (FP)	16 (TP)	19
Total	18	18	36

p value is <0.05 = Association is statistically significant

Table 4 Comparison of screening methods (colposcopy and optical imaging) for cervical cancer

Screening method	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Colposcopy	100	86.6	94.59	100
Optical imaging	88.89	83.33	84.21	88.24

observed in the epithelium region of the dysplastic tissue as compared to normal one. It is found that the mean value of depolarization power for normal tissues is generally less than 0.32, while for dysplastic tissues it is greater than 0.32 as shown in Fig. 2. The large value of depolarization power in dysplastic tissue indicates an increase in the value of scattering coefficient.

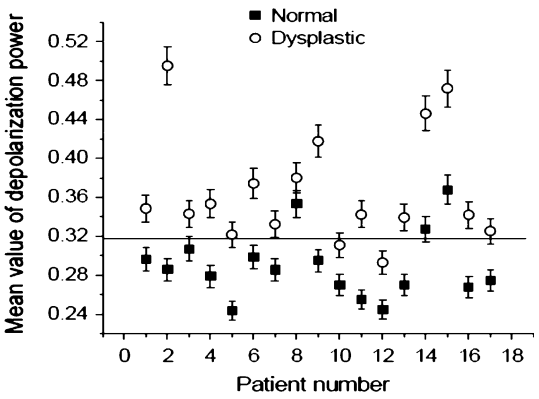


Fig. 2 Mean values of depolarization power in epithelium side in normal and dysplastic tissue sample ($n = 18$ each)

Conclusions

The results of our investigations on human cervical tissue slides are very promising. We have obtained a clear demarcation between normal and dysplastic tissue through depolarization power images. To make this approach amenable for clinical purpose as a supplement technique, a careful statistical analysis is required on a large number of in vitro samples and optical imaging will be next step toward the in vivo studies in detection of cervical cancer in future.

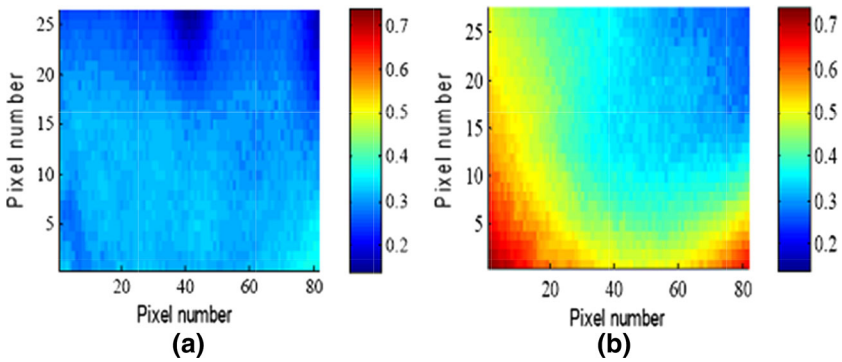


Fig. 1 Typical depolarization power images of **a** normal and **b** dysplastic state in the epithelium region of the cervical tissue section

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Compliance with ethical requirements and Conflict of interest Ethical clearance taken in the form of informed consent from all the patient in the study. Kiran Pandey, Sonal Jain, Ajay Bhagoliwal declare that they have no conflict of interest.

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