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Polarized Light Colposcopy Compared with Standard Colposcopy

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Abstract

Objective—The objective of this study was to determine the potential benefits of polarized light colposcopy compared with standard colposcopy examinations in the evaluation of women with abnormal cervical cytology.

Materials and Methods—Polarized and standard colposcopy examinations were performed on 330 subjects. Respective images and biopsy annotations were obtained. Sensitivity and specificity; differences in the severity of cervical neoplasia; agreement of colposcopy impression, biopsy intent and biopsy site; and differences in the number of biopsies were determined using the ROC, Bowker's test of symmetry, kappa statistic and paired t-test, respectively.

Results—The sensitivity and specificity for a lesion being seen with non-polarized light and polarized light colposcopy were 96.8% and 64.5%; and 96.8% and 64.9%, respectively. There was no statistically significant difference in the ROC of the lesion being seen between non-polarized (80.7) and polarized (80.9) colposcopy. Likewise, there was no statistically significant difference in the ROC of intent to biopsy between non-polarized (80.2) and polarized colposcopy (78.8). The agreement of cervical histopathology and colposcopy impression for non-polarized and polarized colposcopy were 0.986 and 0.952, respectively. There was no significant difference between non-polarized and polarized colposcopy in the mean number of lesions seen or number of sites intended to biopsy.

Conclusions—Polarized light colposcopy was not useful as an adjunct to conventional colposcopy in this study. Further research needs to be performed to determine the overall utility of polarized light colposcopy in clinical practice.

Keywords

Cross polarization; colposcopy; cervical neoplasia; colposcopy adjunct

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Conflicts of interest: None

Introduction

Colposcopy is a challenging clinical procedure and the suboptimal accuracy of colposcopy has been demonstrated.¹⁻⁹ Optimizing the accuracy of colposcopy is now one of the leading concerns in the entire cervical cancer prevention process.¹⁰ One recommendation has been to collect multiple cervical biopsies to improve the sensitivity of colposcopy.¹¹ However, such an approach increases cost, discomfort, bleeding, anxiety and procedural time. Although colposcopy is the diagnostic standard of care, there may be a need to improve the detection of cervical neoplasia by augmenting the technique of colposcopy.¹²

Polarized light colposcopy could be used for evaluating the epidermis and initial papillary dermis, the areas from which most lower genital tract neoplasias arise.^{13, 14} The dermatologic use of polarized light allows the identification, evaluation and discrimination of neoplastic skin lesions.¹⁵⁻¹⁸ Polarized light enables deeper interrogation of the cervical microvasculature and gland clefts. Our preliminary work, based on analysis of digitized cervical images, demonstrated the ability of polarized light colposcopy to better discriminate cervical intraepithelial neoplasia (CIN) 2/3 from CIN 1 when compared with non-polarized light colposcopy.¹⁹ However, no clinical trials have prospectively evaluated the use of polarized light during colposcopy.

The goals of this project were to test the hypothesis that polarized light colposcopy will enhance and increase the detection of cervical cancer precursors and improve the discrimination of cervical neoplasias.

Methods

Subject population

Women 21 years of age living in or near Augusta, Georgia or in Cusco, Peru with a recently abnormal cervical cytology result and scheduled for a colposcopy examination were asked to enroll in the study. Subjects were enrolled at the GRU Cancer Center and CerviCusco Clinic in Cusco, Peru. All subjects read and signed an institutional review board-approved informed consent document before participating. Exclusion criteria included acute cervical hemorrhage, severe cervicitis, excessive menses, hemorrhagic diatheses, pregnancy, and unwillingness to participate. Peruvian subjects whom were unable to read or write were included, and they received assistance from trained bilingual CerviCusco staff. The Peruvian National Institutes of Health (INS) and the Georgia Regents University Institutional Review Boards approved the study. Pertinent disease specific demographic information was collected from each patient.

Study Design

Following insertion of a vaginal speculum and application of 5% acetic acid, polarized and non-polarized high-resolution digital RGB images (at 7.5×) were taken of the ectocervix (Figure 1). Thereafter, non-polarized light colposcopy was performed as standard of care. The colposcopist derived a colposcopic impression and indicated whether a biopsy was necessary. So as to not compromise the next examination, Lugol's Iodine solution was not applied. Then, a polarized colposcopy exam was performed. As before, the colposcopist

derived a colposcopic impression, indicated whether a biopsy was necessary and annotated the site of pending biopsy. Then, if indicated, cervical biopsies were obtained from colposcopic changes as seen during the non-polarized light colposcopy exam. The exact site of the biopsy was annotated on the non-polarized digital image. Thereafter, if indicated, a cervical biopsy was obtained based upon the polarized light colposcopy exam. The exact site of the biopsy was then annotated on the polarized digital image. Endocervical sampling and endometrial biopsies were obtained as clinically indicated. A “safety exam” was conducted after certain difficult videocolposcopy cases when evaluation using an optical colposcope was deemed necessary. Findings based on this exam were used only to help define the final diagnosis. All histopathologic specimens were analyzed and adjudicated by a three-member pathology panel.

Instruments

Two colposcopes were used during the trial; the UltraSight™ HD colposcope (STI, Honolulu, HI) and the Welch-Allyn video colposcope (Welch-Allyn, Skaneateles Falls, NY).²⁰ Each of the colposcopes contained cross polarization filters. Both colposcopes and associated hardware permitted digital video interface to capture, store and annotate digital colposcopic images. An optical colposcope was used for “safety” examinations to provide an additional appraisal and guide histopathologic sampling.

Statistical Analysis

All statistical analysis was performed using SAS 9.4 (SAS Institute, Inc., 2013, Cary, NC, USA). Descriptive statistics were calculated for all variables. We determined the sensitivity and specificity of polarized compared with non-polarized light colposcopy for detection of cervical neoplasia and area under a receiver operating characteristic curve (ROC) using logistic regression. The outcome variables were the biopsy result for a specific biopsy site and the most severe histopathology of all sites biopsied when multiple biopsies were obtained. The independent variables were whether a lesion was seen during the colposcopic examination or whether a biopsy was intended using non-polarized or polarized colposcopy. If a lesion wasn't seen using a colposcope then the biopsy intent, histopathology, and colposcopic impression of the site were indicated as no intent, normal or not done histopathology, and normal impression. Agreement of colposcopic impression, lesion visibility, cervical biopsy histopathology, and biopsy intent between polarized and non-polarized colposcopy was determined using kappa statistics and McNemar's test. Differences in the number of lesions seen and the number of biopsies taken based on whether the lesion was seen with non-polarized compared with polarized light colposcopy were determined using a paired t-test.

Results

Data were available for 330 subjects enrolled in the US (175) and Peru (155) and are seen in Table 1.

The sensitivity, specificity, odds ratio and the area under a receiver operating characteristics curve (ROC) for polarized and non-polarized colposcopy examinations are seen in Table 2.

The sensitivity and specificity for a lesion being detected with non-polarized light and polarized light colposcopy were 96.8% and 64.5%; and 96.8% and 64.9%, respectively. There was no statistically significant difference in the ROC of the lesion being seen between non-polarized (80.7) and polarized (80.9) colposcopy ($p=0.85$). Likewise, there was no statistically significant difference in the ROC of intent to biopsy between non-polarized (80.2) and polarized colposcopy (78.8) ($p=0.29$). The odds ratios for detecting a lesion were of similar magnitude for non-polarized (55.9) and polarized colposcopy (56.8). However, the odds ratios for intending to biopsy lesions were 41.5 for non-polarized and 23.3 for polarized colposcopy.

The agreement of lesion seen and biopsy intent for non-polarized and polarized colposcopy are seen in Table 3. Table 4 displays the agreement of cervical histopathology and colposcopic impression for non-polarized and polarized colposcopy. Agreement between the two types of colposcopy was high ($\kappa > .90$) for all the variables and there were no differences in the direction of disagreement between polarized and non-polarized colposcopy.

There was no significant difference between non-polarized and polarized colposcopy in the mean number of lesions seen or number of sites intended to biopsy based on the lesion being seen overall or among those with at least one biopsy (Table 5).

Discussion

In our previous laboratory-based study, we were better able to detect CIN 2 using polarized light colposcopy digital images compared with non-polarized light colposcopy images.¹⁹ Polarized light colposcopy also helped to better discriminate cervical normal and abnormal epithelium in addition to different levels of cervical neoplasia.¹⁹ However, in this clinical trial, polarized light colposcopy demonstrated the same sensitivity and specificity to detect cervical lesions as non-polarized light colposcopy. Moreover, the agreement of non-polarized and polarized colposcopy for cervical histopathology and colposcopy impression were quite high ($\kappa > 0.90$). Histopathology and colposcopy agreement levels were also similar. The conflicting findings noted between the two studies may be explained by the differences observed between static and dynamic examination of the cervix. A real-time appraisal is considered more comprehensive based on the additional information gained, particularly the epithelial response to 5% acetic acid over time. In addition, the removal of glare from colposcopy images in the laboratory-based study may have contributed more than initially expected with respect to the diagnostic differences noted between light sources. The use of a green filter and changes in the levels of magnification may have provided added value during live examinations. Use of polarized light involves only a portion of the complete examination. While polarized light colposcopy may be useful as an adjunct to standard colposcopy, a dynamic, comprehensive examination provides the critical information for accurately detecting and diagnosing cervical neoplasia.

Similar equivalency was noted when we compared the use of each type of light source to determine whether cervical biopsy was necessary or not. A reduction of the number of unnecessary cervical biopsies during colposcopy would be of clinical benefit. Because few

discordant cases between non-polarized and polarized light colposcopy were encountered in this trial, we were unable to determine if polarized light colposcopy can significantly reduce the number of unnecessary cervical biopsies.

Our study was limited by several factors. Firstly, all of the examinations were conducted by experienced colposcopists, which may have biased our appraisal with respect to polarized light colposcopy reducing the number of cervical biopsies. Secondly, because of recommendations to delay cervical cancer screening until age 21, we enrolled fewer young women in the study than originally anticipated. In these young women, immature metaplasia is frequently noted on the ectocervix. But it can be difficult to discriminate immature metaplasia from cervical neoplasias (CIN1) because of the presence of acetowhite epithelium, mosaic and punctation vascular findings observed in both scenarios. Use of polarized light permits interrogation of features found about 1mm beneath the surface of the epithelium. Therefore, in many cases, the acetowhite color noted in immature metaplasia disappears with the use of polarized light. In contrast, high grade lesions may extend approximately 5mm beneath the surface of the epithelium and polarized light does not alter the acetowhite response. Polarized light then should help to discriminate more superficial (benign to severe) from deeper (severe) acetowhite lesions. Consequently, the actual attributes of polarized light colposcopy may have been underestimated in this study. Given these limitations, further research needs to be performed to determine the diagnostic utility of polarized light colposcopy in clinical practice.

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Figure 1. Non-polarized (left) and Polarized (right) Digital Cervical Images

A large low grade and smaller high grade cervical lesion are seen in the non-polarized image. The margin of the low grade lesion can be seen extending to the limits of the ectocervix at 10 o'clock. The polarized image only depicts the more severe neoplasia located near the cervical os.

Study Procedures**Endpoint Analyses**

Figure 2.
Polarized Colposcopy Study Design

Table 1

Demographic results for all subjects (n=330 subjects)

Variable	Level	Number	Percent
Ethnicity	Hispanic	127	38.6
	Non-Hispanic	202	61.4
Race	Black	2	0.6
	White	208	63.0
	Asian	1	0.3
	American Indian	118	35.8
	Multiracial	1	0.3
Previous Pap Test Result	Other	13	6.7
	ASCUS	30	15.5
	ASC-H	27	13.9
	LSIL	91	46.9
	HSIL	20	10.3
	AGC	13	6.7
Age (Mean, SD)		34.9	11.2
Cervical Histology	Normal	179	54.2
	CIN1	76	23.0
	CIN2	35	10.6
	CIN3	37	11.2
	Cancer	3	0.9
Colposcopy Impression	Normal	141	42.7
	Low Grade	107	32.4
	High Grade	77	23.3
	Cancer	5	1.5

ASCUS- Atypical Squamous Cells of Undetermined

Significance ASC-H- Atypical Squamous Cells, Can't

Exclude High Grade LSIL- Low Grade Squamous

Intraepithelial Lesion

HSIL- High Grade Squamous Intraepithelial Lesion

AGC- Atypical Glandular Cells

CIN- Cervical Intraepithelial Neoplasia

Table 2 Sensitivity, specificity, odds ratio and AROC for polarized and non-polarized colposcopy examinations

Colposcope	Odds Ratio (95% CI)	p-value for OR	Sensitivity	Specificity	AROC (95% CI)
Lesion Seen					
Non-Polarized	55.9 (17.2 – 181.2)	<0.01	0.97	0.65	0.81 (0.77 – 0.84)
Polarized	56.8 (17.5 – 184.1)	<0.01	0.97	0.65	0.81 (0.78 – 0.84)
Biopsy Intent					
Non-Polarized	41.5 (14.8 – 116.4)	<0.01	0.96	0.65	0.80 (0.77 – 0.84)
Polarized	23.3 (10.4 – 52.3)	<0.01	0.93	0.65	0.79 (0.75 – 0.83)

Logistic Regression

CI = Confidence Interval

Table 3

Agreement of lesion seen and biopsy intent for non-polarized and polarized colposcopy

Polarized	Variable	Level	Non-Polarized				Kappa (95% CI)	McNemar's Test p-value
			Yes		No			
			N	%	N	%		
Lesion Seen	Yes	181	49.5	6	1.6	0.93 (0.89 – 0.97)	0.75	
	No	7	1.9	172	47.0			
Polarized	Variable	Level	Non-Polarized				Kappa (95% CI)	McNemar's Test p-value
			Biopsy		Do Not Biopsy			
			N	%	N	%		
Biopsy Intent	Biopsy	177	48.4	6	1.6	0.91 (0.87 – 0.95)	0.31	
	Do Not Biopsy	10	2.7	173	47.3			

CI = Confidence Interval

Table 4
Agreement of cervical histology and colposcopic impression for non-polarized and polarized colposcopy

Polarized		Non-Polarized						Kappa (95% CI)	McNemar's Test p-value
Variable	Level	CIN2, CIN3, or Cancer		Normal or CIN1					
Cervical Histology	CIN2/3, Cancer	N	%	N	%			0.99 (0.97 – 1.00)	1.00
	Normal or CIN1	91	24.9	1	0.3				
Polarized		Non-Polarized						Kappa (95% CI)	McNemar's Test p-value
		Normal	Low Grade	High Grade	Cancer				
Variable	Level	N (%)	N (%)	N (%)	N (%)			0.95 (0.93 – 0.98)	0.91
Colposcopic Impression	Normal	181 (49.5)	7 (1.9)	1 (0.3)	0 (0.0)				
	Low Grade	6 (1.6)	80 (21.9)	0 (0.0)	0 (0.0)				
	High Grade	0 (0.0)	1 (0.3)	82 (22.4)	0 (0.0)				
	Cancer	0 (0.0)	0 (0.0)	0 (0.0)	8 (2.2)				

CI = Confidence Interval

CIN- Cervical Intraepithelial Neoplasia

Differences in the number of lesions seen and number of biopsies obtained for non-polarized and polarized colposcopy

Table 5

Variable	Non-Polarized		Polarized		p-value
	Mean	SD	Mean	SD	
Number of Lesions Seen	0.57	0.68	0.57	0.68	0.76
Number of Biopsies	0.57	0.68	0.56	0.68	0.29
Using only subjects when at least 1 biopsy was indicated (n=160)					
Number of Lesions Seen	1.18	0.48	1.17	0.49	0.76
Number of Biopsies	1.17	0.49	0.14	0.52	0.29

Paired t-test

SD- Standard Deviation