



CLINICAL ARTICLE

Digital camera assessment for detection of cervical intraepithelial neoplasia in rural El Salvador

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Abstract

Objective: To explore the feasibility of digital photography for primary cervical cancer screening in a low-resource setting in El Salvador. **Methods:** Three independent examiners performed Pap test, visual inspection, digital camera assessment and colposcopy on each subject. **Results:** Lesions were detected in 99 of 504 patients (20%) by visual inspection, 72/504 (14%) by DART and 90/504 (18%) by colposcopic impression. Seven of 504 patients (1.3%) had CIN on histology. Pap detected 2 of 7 subjects (29% sensitivity) (C.I. 4%, 56%), visual inspection detected 5 of 7 (71% sensitivity, C.I. 34%, 95%), digital assessment detected 6 of 7 (86% sensitivity C. I. 45%, 99%), and colposcopic impression detected 5 of 7 (71% sensitivity, C.I. 34%, 95%). **Conclusion:** This small pilot trial demonstrates the potential value and feasibility of performing digital camera assessment of the reproductive tract on women in a developing country setting.

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1. Introduction

Cervical cancer is the leading cause of cancer mortality among women in developing countries [1]. Many of these countries lack the resources to establish traditional, cytology-based cervical cancer prevention programs. Unfortunately, the Pap

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smear has a low sensitivity estimated at about 50% [2] and requires a level of infrastructure that is unsustainable in most developing countries. As a result cytology-based screening is largely unavailable and therefore likely to have little impact on the disease. Even when cytologic screening is available a limitation is that Pap smears often have unsatisfactory predictive value especially in populations with a high prevalence of inflammation [3].

In order to address these concerns, less expensive, more practical alternatives have been explored. One method that has gained popularity in

developing countries is visual inspection with acetic acid (VIA). This method uses acetic acid to detect white changes on the cervix that are associated with cervical cancer precursor lesions. One recent review estimates that the sensitivity of this method is 66–99% and the specificity is 64–98% [4]. Another well-known study states that it is more sensitive but less specific than the conventional Pap smear [5]. In many nascent “see and treat” programs, women with lesions that are detected with VIA are offered immediate treatment with cryotherapy [6]. Despite excellent sensitivity with VIA, the relative lack of specificity of this technique is thought to be responsible for treating women without cervical cancer precursors with ablative therapy. Clearly, new visual inspection modalities with improved specificity and equal or better sensitivity would result in less over-treatment of women screened with these visual modalities.

Cervicography is a form of magnified photographic inspection of the cervix that has been shown in the past to be a reliable method of detecting cervical cancer precursor lesions. [7–10]. Cervicography, however, is cumbersome, as analogue photography does not allow for real-time inspection. The concept of magnified photography in a real-time scenario gave rise to digital photography with magnification onto a video screen. A few studies show that the technique shows promise for cervical cancer screening [11,12]. Digital camera assessment of the reproductive tract (DART) employs the use of an ordinary digital camera attached to a television monitor and has the capability of providing real-time magnified images of the cervix (Fig. 1). Photographs can be obtained from these images and can thus provide a permanent record of the assessment. Because of the complimentary nature of visual inspection and DART, we hypothesized that digital DART can augment visual inspection as a means of primary screening.

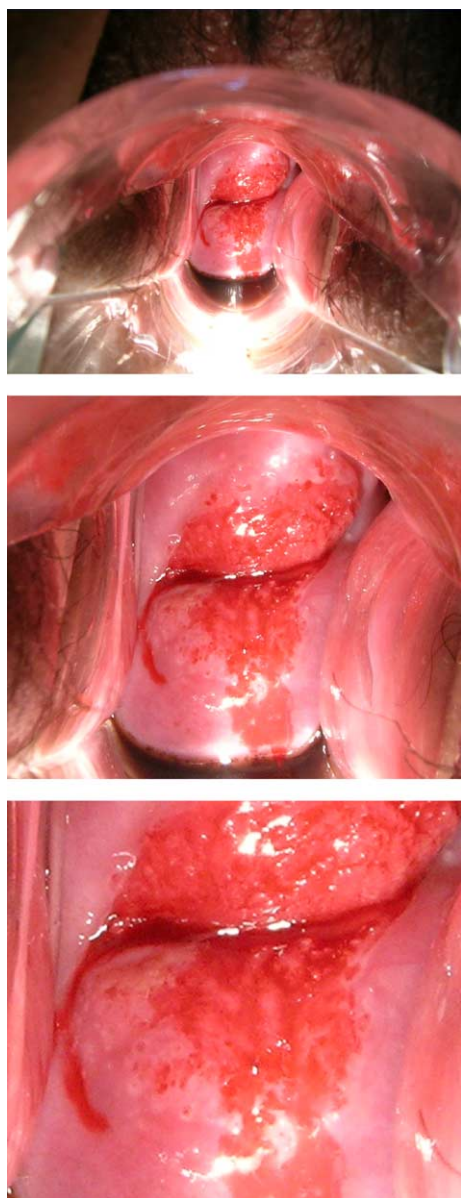


Figure 1 DART photograph at low, medium and high magnification. This patient had CIN III on biopsy.

2. Materials and methods

The project was approved by the Institutional Review Board of the University of Southern California in conjunction with approval letters from local government and health officials. This study was designed to assess the feasibility of a larger trial comparing the sensitivity and specificity of the conventional Pap smear, visual inspection, and DART to the gold standard, colposcopy. The study was also designed to see if this technology was appropriate in a resource-poor setting.

2.1. Personnel

Examiners were U.S.-based physicians associated with university-based OB/GYN programs including 5 OB/GYN generalists, 2 OB/GYN residents, 1 GYN oncologist and 1 GYN pathologist. All participants completed a brief training program in visual inspection where an experienced colposcopist (JCF) reviewed multiple color images of cervical lesions with instruction. Subsequently JHPIEGO visual inspection of the cervix flash card sets was available for review.

2.2. Equipment

A Nikon Coopix 5400 digital camera (NikonUSA, Melville, NY) was chosen because of its 5-mega-pixel capacity and its economic feasibility. The camera retails for under US\$300. It also had capability for manual area or spot focus and manual spot metering. It had timed-shutter release and we were able to connect it to a video display and zoom on the stored image.

A Welch Allyn (Skanenteles Falls, NY) speculum with an attached halogen lighting system was used for cervical illumination, as camera-supported flashes or external illumination were not adequate, producing poor quality images. The cost of the light is less than US\$200.

A Leica colposcope (Heerbrugg, Switzerland) was used for colposcopic evaluation. This colposcope was chosen because of its quality and relative portability. The retail cost of the colposcope is US\$7300.

2.3. Methods

This research was completed by participants in a medical delegation with a non-governmental U.S.-based organization called BasicHealth: El Salvador. One of the missions of BasicHealth is to conduct public health research in conjunction with local health workers. Prior to this delegation, physicians and volunteers from the Salvadoran Red Cross informed women in the community that they were invited to receive health care at a health fair in the center of the town that lasted for 3 weeks. A temporary clinic was constructed by the Red Cross volunteers at a local church.

Women presented for primary screening at a health fair and were invited to participate in the study. Informed consent was obtained by Spanish-speaking health professionals. Patients were included if they were aged 18–75, had an intact uterus, and were able to give voluntary written

consent. Patients were excluded if they had surgical removal of the cervix, history of cervical, endometrial, vulvar or ovarian cancer, had a Pap smear in the past six months, or were pregnant. Demographic information and reproductive history were collected.

After a brief targeted physical exam, a conventional Pap smear was taken, 5% acetic acid solution was placed on the cervix and VIA was performed with the naked eye. The first examiner recorded the result of VIA as positive or negative consistent with previously published criteria [6]. A positive result was any aceto-white lesion. DART was performed by a second examiner who was unaware of the results of VIA or the Pap. Using the same criteria, a positive result was recorded upon identification of an aceto-white area.

Colposcopic examination and ECC was then performed by a third, independent, examiner who was also unaware of the previous results. Colpo-

Table 1 Demographics

	Number	Percent
<i>Age</i>		
<35	159	32%
36–50	170	34%
>50	175	35%
Median (range)	42	(18–75)
<i>Gravida</i>		
0	14	3%
1–3	194	39%
4–6	142	28%
>6	153	30%
Median (range)	4	(0–16)
<i>Smoking status</i>		
Yes	22	4%
No	477	96%
Missing	5	
<i>Previous Pap smear</i>		
Yes	454	90%
No	48	10%
Missing	2	
<i>Age at first intercourse</i>		
<18	173	33%
18–20	160	32%
21–25	127	25%
>25	42	8%
Missing	2	
Median (range)	19	(9–39)
<i>Number of lifetime partners</i>		
1	282	56%
2	110	22%
>3	110	22%
Missing	2	
Median (range)	1	(1–11)

Table 2 Histology results

	Number	Percent (%)
Normal	496	99
CIN I	1	0.2
CIN II	1	0.2
CIN III	1	0.2
In situ	4	0.8

scopic impression was recorded as positive or negative using standard colposcopic criteria. Biopsies were taken of any suspicious lesion. In the absence of a visually detected lesion, an anterior cervical biopsy was obtained. The anterior cervix was chosen for biopsy as it is more commonly involved by cervical cancer precursors [13].

All specimens, including Pap smears and cervical biopsies, were shipped to Pathnet Laboratories (Van Nuys, CA), a pathology laboratory specializing in women's healthcare, and read by a gynecologic pathologist who was blinded to all previous results. Pathnet was selected for its focus on women's health and its quality assurance program. All pathology services were donated for the purposes of this study.

The number of patients enrolled was based on the number that could be seen in a 3-week period of time designated as a "health fair". These health fairs are organized by a non-governmental organization called BasicHealth: El Salvador. The mission of the organization is to provide primary health care and perform public health research.

The results obtained from this pilot study will be used to determine the scope of a larger, more definitive trial. Data were summarized and the sensitivity, specificity, and the predictive value were calculated. Statistical software SAS, version 9.0 was used for all analyses [14].

3. Results

Five hundred and four women were enrolled in the study. Patient demographics are listed in Table 1. Lesions were detected in 99 of 504 patients (20%)

by visual inspection, 72/504 (14%) by DART and 90/504 (18%) by colposcopic impression. Cytology was classified according to the Bethesda system. Of the 504 Paps collected, 459 (91%) showed no evidence of intraepithelial lesion or malignancy, 32 (6.3%) were unsatisfactory, 3 (0.6%) had ASC-US, 2 (0.4%) had ASC-H, 1(0.2%) had LGSIL, and 3 (0.6%) had HGSIL.

Seven of the 504 patients had positive histology (Table 2). Ninety-eight percent of the patients (496/504) demonstrated only benign cervical tissue, one (0.2%) had CIN I, one (0.2%) had CIN II, 1 (0.2%) had CIN III, and four subjects (0.8%) had an adenocarcinoma in situ. Severe cervicitis was present in 13% of the biopsies.

Pap detected 2 of 7 subjects (29% sensitivity; C.I. 4%,56%), visual inspection detected 5 of 7 (71% sensitivity; C.I. 34%, 95%), digital assessment detected 6 of 7 (86% sensitivity; C.I. 45%, 99%), and colposcopic impression detected 5 of 7 (71% sensitivity; C.I. 34%, 95%). Positive predictive values of all of the visual inspection techniques were relatively low and similar among the methods (5–8%) compared to the Pap smear (22%) (Table 2). Negative predictive values were high at 99% or greater. Patients with lesions of CIN II or greater were treated with LEEP.

4. Discussion

This pilot study demonstrates that performing DART for primary cervical cancer screening in a developing country is feasible. Despite the low prevalence of disease in the population tested, DART detected a similar number of lesions as VIA and colposcopy and detected more lesions than the Pap smear. In addition, the equipment used to perform DART including the camera, television, and light source cost under US\$1000, are ubiquitous in most developing countries, are portable, and are easily repairable in case of damage. This compares to colposcopy, which is not available in many settings, difficult to repair, and exceeds US\$7000 in cost.

Table 3 Comparison of various modalities

Modality	Sensitivity (%)	95% C.I. of sensitivity (%)	Specificity (%)	95% C.I. of specificity (%)	(+) Predictive value (%)	95% C.I. of (+) PV (%)	(-) Predictive value (%)	95% C.I. of (-) PV (%)
VIA	5/7 (71)	(34, 95)	402/496 (81)	(77, 84)	5/99 (5)	(2, 12)	402/404 (99.5)	(98.0, 99.9)
DART	6/7 (86)	(45, 99)	429/496 (86)	(83, 89)	6/72 (8)	(3, 18)	429/430 (99.8)	(98.5, 100)
Colposcopic impression	5/7 (71)	(34, 95)	412/496 (83)	(79, 86)	5/90 (6)	(2, 13)	412/414 (99.5)	(98.1, 99.9)
Pap smear ^a	2/7 (29)	(5, 66)	453/460 (98)	(97, 99)	2/9 (22)	(4, 56)	453/458 (98.9)	(98.1, 99.9)

^a Thirty two patients had unsatisfactory Pap smear, and four patients had missing data.

One possible advantage of DART suggested by the study is the improvement in the number of women who have false positive exams when compared to VIA (14% vs. 20%). In a “see and treat” setting this would translate into fewer women being treated with ablative therapy for benign conditions. Trials targeting a larger number of women are needed to confirm this initial observation.

The relatively small sample size of our pilot study limits the conclusions that can be made regarding the sensitivity, specificity and positive predictive value, given that the incidence of cervical intraepithelial lesions was only 1–2%. We were surprised by the relatively low incidence of disease in this population. It was our understanding prior to our arrival that the targeted population was a high-risk, unscreened group of women. However, during the health fair we discovered that most women had been screened and treated for cervical cancer precursors in a recent health campaign.

Another limitation of the study was that the light source we used for visualization is not routinely available in El Salvador. The replacement bulbs are also difficult to find in El Salvador. After the trial ended, we identified a fiberoptic speculum that can be used with a hand-held flashlight, is relatively inexpensive (under US\$0.25 per speculum) and is readily available in San Salvador. In a larger trial, it would be more appropriate to use this technology that is easily available within El Salvador.

Apart from the limitations this relatively small trial has numerous strengths. It was conducted in a low-resource setting that is characteristic of high-risk areas in many parts of the world. In addition, several different modalities were directly independently compared (Table 3) and the reference standard (colposcopic biopsy) was applied to all subjects. Since we had tissue samples from all study participants we were able to accurately measure the disease in this population. Finally, all examiners, including the pathologist, were blinded to previous results.

In conclusion, this study suggests that DART is quite promising for primary screening in a low-resource setting. A larger trial, preferably in an unscreened population or with more known positive patients, should be conducted more rigorously to

determine the sensitivity of this modality and better assess its potential as a screening or confirmatory tool.

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