Abstract

In developed countries, cervical cancer screening programs have been highly successful. In the United States a 70% decrease in the mortality of cervical cancer has occurred since the 1960's largely due to the Papanicolaou test. However, it is not clear how best to translate these advances to developing countries, where cervical cancer remains the leading cause of cancer death for women. Cytology-based screening, followed by colposcopic detection is expensive and requires extensive laboratory infrastructure and trained personnel, which are often unavailable in low resource settings. Techniques such as visual inspection with acetic acid (VIA) and visual inspection with Lugol’s Iodine (VILI) are less expensive and require minimal supplies and infrastructure; however there are concerns that these approaches do not have adequate specificity without extensive provider training and experience. Objective cervical cancer screening techniques which are easy to interpret, provide rapid results, and have both high sensitivity and specificity would be highly beneficial in developing countries. We have developed a multispectral digital colposcope (MDC) which is designed to rapidly image the cervix and is used with automated image analysis algorithms that provide objective delineation of neoplastic areas. In this paper we describe an effort to implement this device in Ibadan, Nigeria, to determine the feasibility of conducting clinical trials using the MDC as an experimental screening device. Our aim was to test the device in a location where it might be most beneficial and to collect data useful for developing new, low-cost, low-maintenance devices. Multiple obstacles limited the success of imaging using the MDC in Nigeria including an unstable supply of electricity and a lack of available spare parts and tools. We conclude that these obstacles must be overcome by robust and simple device designs in order to successfully test an imaging-based screening device in Nigeria or other developing countries.

Introduction

Cervical cancer remains the leading cause of cancer mortality among women in the developing world [1]. Screening programs have been shown to be highly effective in developed countries, helping to reduce death due to cervical cancer in the United States by 74% between 1955 and 1992 [2]. These programs rely on cytological techniques such as the Papanicolaou smear often followed by magnified visual inspection with a colposcope and biopsy of abnormal appearing areas. Cytologic screening and colposcopy are often ill suited for developing countries, however, because of their relatively high cost, substantial need for infrastructure, trained personnel, and the long time between when testing occurs and when results are available [3]. With this in mind, new approaches to screening in developing countries have focused on technologies with minimal resource needs such as visual inspection with application of acetic acid (VIA) and visual inspection with Lugol’s Iodine (VILI) [3–6]. It has been projected that screening even once in a lifetime with VIA can lead to a 25% reduction in the lifetime risk of cervical cancer in developing nations [7].

In low-resource settings, estimates of the accuracy of VIA vary widely, with reported sensitivity ranging from 90.1% to 55% and specificity from 92.2% to 65% [4]. In a study in Kinshasa, Congo of 1528 woman, it was found that physicians using VIA achieved both a higher sensitivity and specificity for detection of disease as compared to nurses [4], highlighting the importance of provider experience and training. Additionally, it is generally agreed that VIA has a higher sensitivity than cytology for detecting high grade lesions but a lower specificity. The variations in accuracy of VIA lead to concerns about its reproducibility. The potential for a high number of false-positive results raises concerns about over treatment in resource-poor environments. Magnified visual inspection with colposcopy and application of acetic acid can improve specificity, but its use is limited by the cost of a colposcope.

A low-cost device that provides easy to interpret images of the cervix with a higher specificity than VIA may lead to more effective cervical cancer screening in low-resource settings. Several groups have developed magnified optical imaging devices which mimic the operation of the colposcope at a reduced cost and in some instances with the added ability to capture and save images. Cremer et al. used a simple commercially available digital camera in El Salvador and noted higher sensitivity than with VIA [8]. Walmer et al. developed a battery powered colposcope suitable for low-resource settings [9]. The Program for Appropriate Technology in Health (PATH) has developed the AviScope™ which uses LED illumination
and provides 4× magnification [10,11]. These devices are promising, but need further development and testing in larger clinical trials to compare their effectiveness to colposcopy, VIA, and VILI.

In order to investigate improvements to traditional colposcopy by adding additional imaging modalities, our group developed the Multispectral Digital Colposcope (MDC) which is currently involved in clinical trials in the United States and Canada. The design is described elsewhere [12] but, briefly, it adds the capability to measure fluorescence and polarized reflectance images as part of a commercially available colposcope. Images are captured using a CCD camera connected to a desktop computer. Automated image analysis algorithms provide real-time delineation of precancerous areas. Clinical trials using the MDC may lead to future low-cost devices targeted to the developing world utilizing its most useful characteristics. Recently our group had the opportunity to test the MDC at the University of Texas M.D. Anderson Cancer Center and Rice University both in Houston, Texas, and by UCH Ibadan, Nigeria.

Obstacles to pilot clinical trials in Nigeria

Nigeria is home to one quarter of Africa’s population and cervical cancer accounts for the deaths of over 8000 women in Nigeria each year [13]. Screening programs in Nigeria are in their infancy and face many challenges. Papanicolaou smears cost $6 USD at UCH while the average Nigerian’s yearly income is $1040 (PPP international dollars) and 70% of the population live below the poverty line [14]. There is a significant shortage of laboratory infrastructure and currently only 690 laboratory health workers are available to read cytology slides for the entire country [14]. Skepticism, poverty and some mistrust of screening programs further hinder patients participation.

We traveled to the UCH in Ibadan, Nigeria, in February and July 2006 as part of a new collaboration to assess the feasibility of conducting clinical trials using the MDC. The need for low-cost screening tools is great in Nigeria, and it was felt to be an ideal location in which to determine unanticipated obstacles to screening in a developing country. UCH Ibadan is the largest hospital in the country with well-trained physicians and was selected as an initial screening location for these reasons. Pilot clinical trial protocols to test the MDC in this setting were reviewed and approved by the Institutional Review Boards at the University of Texas M.D. Anderson Cancer Center and Rice University both in Houston, Texas, and by UCH Ibadan, Nigeria.

On the first trip, all equipment that was brought from the United States was taken as checked luggage which places limitations on the number and size. We were forced to forgo bringing bulky equipment such as an uninterruptible power supply (UPS). Volunteer participants were inspected by both US and Nigerian physicians using standard colposcopy with the addition of acetic acid. A Papanicolaou smear was obtained. Suspicious lesions were treated with the loop electrosurgical excision procedure and excised tissue was preserved in paraffin blocks. Images were obtained from ten patients over 2 days with a simplified version of the MDC controlled by laptop computer.

Frequent and sometimes lengthy power outages (often lasting from a few minutes to an hour) were perhaps the most significant obstacle to screening with the MDC. We often found ourselves working in the dark attempting to switch to the hospital’s diesel power generators. Although backup generators were often engaged during power outages, there was not an integrated transfer of power in the clinic, so it was necessary to plug equipment into a separate outlet to utilize generator power. Although the laptop could easily run on batteries during power outages, power fluctuation between outages caused the CCD camera, powered through a standard outlet, to incorrectly communicate with the laptop. This forced us to restart the MDC computer tens of times during the 2 days, often during screening, causing significant delays which interrupted patient care.

The MDC light source, a xenon arc lamp, eventually failed to ignite; the cause of this failure was likely due to power fluctuations. Recurrent problems such as overheating of the laptop due to high ambient temperatures and heat output from the light source caused us to lose at least some data from two patients. We discovered the importance of bringing our own basic hand tools because the hospital had a very limited supply available consisting primarily of several screwdrivers. Adequate training of hospital staff to use the MDC sometimes proved difficult during our several day stay at the hospital. These difficulties often stemmed from a lack of experience with some of our technologies. One particularly talented technician responsible for most instrumentation maintenance of the hospital had not previously used a computer before. This trip had made us understand the significant barriers of using a device such as the MDC even in what can be assumed the most favorable of conditions in Nigeria.

The second trip, several months later, was coordinated with the difficulties of the first trip in mind. We shipped a great deal of equipment several weeks beforehand and we were able to bring a newer version of the MDC, shown in Fig. 1, to Ibadan with medical grade backup batteries capable of powering the system during power outages for up to an hour. Seventeen patients were imaged on this trip with much more success than

Fig. 1. The MDC in Nigeria on the second trip. The modified colposcope is shown in the center and the laptop with light source and controller are shown to the left. The UPS is shown on the bottom right.
the first trip. Fig. 2 shows an example of images taken in Nigeria of a lesion on the cervix in white light and fluorescence modes. No patient data were lost due to system failure or power fluctuations. These improvements came at a high price however. A certified electrician was brought on the trip to monitor power levels and to work with the technical staff at the hospital to provide more reliable power. The cost of additional equipment such as power regulators and UPS systems was substantial. Image data from both trips are currently being analyzed and compared with pathology to determine the effectiveness of detecting lesions in the first pilot trials.

Lessons learned and future directions

It was ultimately decided that conducting larger, long-term clinical trials at the UCH Ibadan, with the current MDC device was both unfeasible and undesirable to our African collaborators. The amount and expense of equipment needed to run the MDC combined with the additional training times of an already overextended hospital staff was unrealistic. Equipment would be exceedingly difficult to repair considering the amount of time and effort needed to obtain replacement parts such as lamps for the light source. We were told that obtaining common replacement fuses for equipment in the hospital often involved a several hour trip to another city, Lagos. Providing technical support from our laboratory in the U.S. would be an additional challenge.

A step forward is needed from the relatively complex, experimental device to a screening tool which is not entirely dependent on wall power and needs little maintenance. Similar conclusions by other researchers have been reached regarding medical equipment in low-resource settings. In a study of medical equipment failures in 10 developing countries, the most common cause of device failure was inadequate power supply. In the same study, the authors note that although initial cost can be a barrier, medical devices do not always need to be simple or cheap to work in the developing world. Training was often not the cause of equipment failure, but rather was due to an inability to maintain the equipment resulting from a lack of spare parts [15]. The MDC for example would needed regular lamp replacements from a specific vendor in the U.S. A more robust system might rely on LEDs for illumination because of their long life and low power consumption.

Currently, available data show that the AviScope™ is marginally more sensitive than VIA (60.7% versus 55.7%) while providing similar specificity [11]. Trials using other promising technologies have been too limited by small sample size to produce sensitivities and specificities for comparison to VIA. Devices such as the AviScope™ and the Walmer device are promising due to their low cost and simplicity but are limited by lack of magnification, low illumination intensity, and minimal depth of focus. Improvements in these areas, combined with the possible addition of new imaging modalities identified by the MDC, may increase diagnostic performance to acceptably high rates while maintaining the advantages of device simplicity and low cost.

It was notable that although equipment in general was scare in the hospital, certain high-tech devices such as mobile phones were relatively ubiquitous and many physicians at the hospital owned laptop computers. It might be highly beneficial to develop screening devices that borrow these resources where available. For example, a screening device based around a digital camera might be appropriate even if a computer is needed if the interface with the computer is simple and commonly available (e.g., a USB port). In this case the screening device need not rely on a devoted computer system but could borrow an available laptop.

Concluding remarks

Objective screening techniques may be more beneficial to the developing world than VIA and VILI if lower false-positive rates obtained can be balanced with low-cost and low-maintenance devices. From our experience, even with the most favorable of conditions, testing in developing countries should use devices that do not completely rely on wall power and that will not require replacement parts.

Conflict of interest statement

RR-K has an ownership stake in Remicalm, Inc which is a commercializing technology related to that described in this paper. All other authors declare that they have no conflict of interest.

Acknowledgments

This work was supported by the National Institutes for Health (NIH) grant PO1 CA 82710-04, and the Exxon Mobile Corporation.
References


Darren Roblyer
Rebecca Richards-Kortum
Department of Bioengineering, Rice University, 6100 Main St. Houston, TX 77251-1892, USA

Sun-Young Park
Department of Biomedical Engineering, The University of Texas at Austin, Austin, TX 78712, USA

Isaac Adewole
Department of Ob/Gyn, College of Medicine, University of Ibadan, Nigeria

Michele Follen
Department of Biomedical Engineering, MD Anderson Cancer Center, Houston, TX, 77030, USA
E-mail address: mfollen@mdanderson.org.
Corresponding author.

6 July 2007