Measuring blood content, oxygen saturation, and scattering in cervical tissues using multi-spectral imaging

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Objective: Optical detection systems have potential to address challenges in cervical cancer care. Compact, inexpensive light sources, sensors, and wireless internet connectivity are ubiquitous. It is possible to build mobile multi-spectral imaging systems that acquire data at the point of care, and perform computations in the cloud to estimate blood content, oxygen saturation, and light scattering in the cervix. Over time, this additional information would enable better triage at the point of care. Methods: A novel mobile multi-spectral imaging system was built around a tablet form factor, with a 3-LED illumination board and an area-scan camera. Image frames corresponding to each wavelength were recorded. Each multi-spectral cervical data set was captured in under five seconds and uploaded to the cloud for computational analysis. Pixel-wise calculations of blood content, oxygen saturation, and scattering were made in the cloud and returned to the clinician. Sites of cervical biopsy were tracked in software; spectral output was compared to histopathology. The protocol was for this pilot study was approved by the institutional review board. Results: Images of blood content, oxygen saturation, and scattering were obtained. The estimated values were within the range expected for epithelial tissues. Aberrant measurements of blood content and scattering corresponded with biopsy sites. Analyses were done in near real-time. Conclusions: Full-resolution images of blood content and oxygen saturation of cervical tissues hold great potential to supplement current cervical cancer screening methods. Future upgrades will reduce the device size and analysis time.

Abstract

Introduction

Need
There have been few improvements in colposcopy and treatment of cervical lesions in recent years. Taking more biopsies at colposcopy has increased the sensitivity for CIN2, CIN3, and AIS, but has not reduced cancer risk. Colposcopy in particular is limited by the absence of a specific, sensitive stain for cervical abnormalities. Currently colposcopy relies on visual methods based on acetowhenising, a process which occurs after dilute acetic acid applied to the cervix, turning abnormal areas within which in 1-2 minutes. However, not all cervical abnormalities become visually obvious and not all aceto-wetish tissues represent pathology. Similarly, a better visual test could more accurately visualize the cervix prior to CIN1 or CIN2 and ensure the entire lesion is removed (clear margins) in order to lower risk of cervical cancer.

Technology
Multi-spectral imaging has been proposed as a non-invasive method with potential to improve detection of cervical pathologies. The method involves imaging the tissue at selected wavelengths, yielding a 3D-dataset that contains a discrete spectrum at each (x, y) position. By fitting this spectrum to a theoretical model, it is possible to quantify absorption and scattering in the imaged tissue, as well as their respective components. This information contains not only concentrations of oxy- and deoxy-hemoglobin, but also water content and relative amounts of large and small scattering particles, all at the pixel level. Multi-spectral imaging can thus visualize patients non-invasive, label-free, localized at the pixel level. Multi-spectral imaging can thus give new physiological information which has never been so readily available.

The novelty in our system is as follows:
1. It captures an entire image worth of data, whereas previous systems made only point measurements
2. Multi-spectral hardware is integrated into the colposcope, streamlining data acquisition and analysis
3. The system was optimized for mobility and portability, with a coil of materials of 510D03

Clinical potential
Imaging devices can potentially play several roles in cervical cancer care. These include (1) triaging patients who screened positive for HPV and/or cytology tests; (2) guiding biopsies during colposcopy; or (3) assessing margins of LEEP and other excisional therapies. Clinical testing is needed to establish where the technology can best improve care.

Methods

Device
The setup consists of a multi-spectral LED board that was integrated into an optical head (functionally a setup (LEDs + camera) to white light spectrometer on phantoms. The protocol was for this pilot study was approved by the institutional review board. Results: Images of blood content, oxygen saturation, and scattering were obtained. The estimated values were within the range expected for epithelial tissues. Aberrant measurements of blood content and scattering corresponded with biopsy sites. Analyses were done in near real-time. Conclusions: Full-resolution images of blood content and oxygen saturation of cervical tissues hold great potential to supplement current cervical cancer screening methods. Future upgrades will reduce the device size and analysis time.

Screening: HPV × Pap

Coapsy

Biopsy

LEEP

Monitoring + progress

Fig. 2: (A) Optical head of multi-spectral device, with camera on light and LED board on left. (B) As a test, has less experienced clinicians (nurse, GP) directly for biopsy. Capture takes ~20 sec.

Device

Reconstructed RGB Image with ROIs labeled

Multi-spectral image set

Spectral fits transform image data at the pixel level to tissue properties: blood content, oxygen saturation, water content, and scattering parameters

Oximetry imaging of a normal cervix

Fig. 3: (A) Comparison of multi-spectral setup (LEDs + camera) to white light spectrometer (Ocean Optics). Measurements were made on both spectrally reflectance standards (LabSphere) and the skin of healthy volunteers.

Fig. 4: (A) Comparison of multi-spectral setup (LEDs + camera) to white light spectrometer on phantoms. Data from LEDs × spectrometer served as a control. (B) Representative spectrum of skin (forearm) of a healthy volunteer from all 3 methods. (C) Comparison of skin reflectance measured by multi-spectral setup to a spectrometer for 4 volunteers.

Discussion and Conclusion

The above results show preliminary analysis of patients imaged with our multi-spectral system characterized by our algorithm. The image data allows for comparing tissue properties from different regions in the same image, which is advantageous in procedures like colposcopy in which the sensitivity increases with the number of biopsies a provider takes. Moreover, comparing different regions from the same patient controls for effects like the menstrual cycle and local microflora that could also affect the tissue properties.

In looking at the data, it can be seen that the spectral response from normal tissue above and below the excised tissue is consistent with one another. Relative to normal tissue, the averaged spectrum from the acetowhitenise lesion at the center shows that a much higher reflectance at blue and green wavelengths, but not as much at red and near infrared wavelengths. The increased reflectance corresponds to a higher scattering to absorption ratio there than in the normal regions. All these results are consistent with theory – in normal tissue, there is less scattering so that the light can penetrate into the stroma where it is absorbed by the microvascularity, whereas in the acetowhitenise areas the additional scattering of green and blue light increases the amount of light that diffusely reflects from the tissue, while preventing it from reaching the deeper tissue and getting absorbed. Consequently, the increased levels of green and blue reflected light is what gives the tissue its white appearance.

The theoretical model used in the fitting in the above analyses was derived from diffusion theory. One of its key assumptions is that the tissue is a semi-infinite, homogenous medium. However, the cervix has geometrical complexity in 3 dimensions, and is organized by histological layers. Moreover, the blood supply in the tissue is not uniform, as is presumed by the model. As such, the measurements presented here can be considered a first approximation to the true tissue properties. Numerical simulations of light transport in tissue which can easily vary the geometrical properties of the tissue [2, 3] are needed in order to elucidate how different layers with different properties affect the spectral reflectance. Any refined algorithm will need to be validated through experimentation with tissue samples.

Further studies are needed to determine the potential of multi-spectral imaging for cervical cancer care. Specifically, there is a need to better understand the relationship between the menstrual cycle and menopause to the tissue properties, to systematically study a larger cohort of patients with different demographics, as well as better understanding the role acetowhitenising has water content in the cervix, in a quantitative manner.

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References