A smart fiber optic sensor for detection of oral and cervical cancer in developing world

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Abstract

We report the development of a portable, easy-to-use and low cost, yet accurate and reliable optical spectroscopy device that can aid in the screening and diagnosis of oral and cervical cancer at an early stage. The device uses an innovative smart fiber-optic probe to eliminate operator bias, state-of-the-art photonics components to reduce power consumption, and automated software to reduce the need of operator training, and therefore is well suited for use in low-resource setting.

Introduction

Oral and Cervical Cancers in Developing World

- Each year, over 481,000 new cases of oral cancer are diagnosed worldwide, with a 5-year mortality of ~50% and nearly two-thirds of which occurs in developing world.
- Cervical cancer is the 3rd most common cancer in women with an incidence and death rate of 16 and 9 per 100,000 women, respectively, and 80% of cases occur in the developing world.
- The high death rate is largely due to the fact that developing countries do not have the appropriate infrastructure and resources to support the organized screening and diagnostic programs.

Optical Spectroscopy Can Help Cancer Screening and Diagnosis?

- The optical absorption and scattering properties of epithelial tissues reflect their underlying physiological and morphological properties.
- Optical spectroscopy, particularly quantitative diffuse reflectance spectroscopy (Q-DRS) with a fiber optic probe, can noninvasively quantify these tissue properties.
- Q-DRS has shown promise for diagnosis of early precancerous changes in the cervix and oral cavity by us as well as others [1-7].
- Q-DRS has the potential to provide an effective, low cost, and portable solution for cervical and oral pre-cancer screening in resource-limited countries, such as Haiti.

Challenges for Performing Optical Spectroscopy in Developing World

- There are limited resources, unreliable power supply and not enough trained pathologists and engineers or technicians in developing countries.
- Current optical spectroscopy techniques are susceptible to several sources of systematic and random errors, such as uncontrolled probe-to-tissue interface and lack of a real-time calibration.
- Previous studies indicated that probe pressure could significantly perturb the tissue physiological and morphological parameters [8-17].
- We have shown that non-real-time instrument calibration could cause significant errors in extraction tissue optical properties, particularly scattering coefficient [18].
- Current systems also use bulky, high power and expensive optical components, such as thermal light sources, spectrographs, and cooled CCD cameras, which need a stable power supply.

Here we report the experience we have learned in performing Q-DRS study with a self-calibration probe in Haiti and the development of a portable and robust smart fiber optic sensor system that can be used for the screening and diagnosis of oral and cervical cancer in developing countries.

Optical Spectroscopy Experience in Haiti

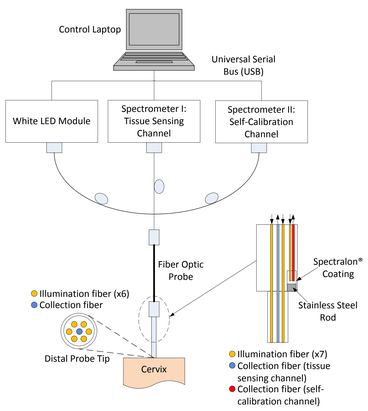


Fig. 1. (a) The portable Q-DRS system consists of a white LED, a spectrometer for tissue sensing, a spectrometer for self-calibration (SC), and a fiber optic probe to deliver and collect diffuse reflectance from 450 – 600 nm from the cervix *in vivo.* All fibers are 200/220 μm in core/cladding diameter with a NA of 0.22. (b) The distal end in contact with tissue consists of a central collection fiber encircled by a ring of 6 illumination fibers with a center-to-center separation of 622 μm. (c) Light delivered to Spectralon® coating and collected via self-calibration collection fiber is used to account for drifts in system throughput in real time. [18, 19]

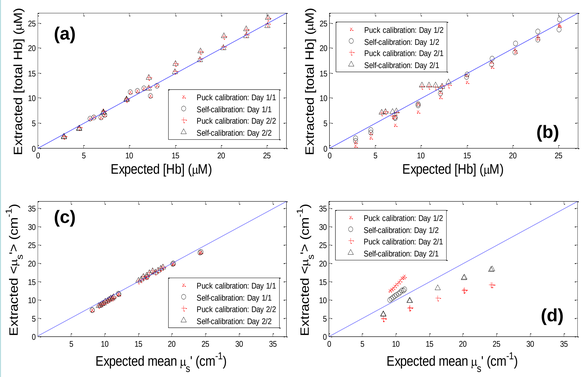


Fig. 2. Phantom experiment: extracted vs. expected [Total Hb] and <μ_s'> when target and reference phantoms are from the same day (a & c), and when target and reference phantoms are from different days (b & d). Either calibration method yielded similar errors for [Total Hb] and <μ_s'> when same-day reference is used. Error for [Total Hb] was similar even when a different-day reference phantom was used. However, extraction error was substantially higher for <μ_s'> when puck-calibration was used in lieu of self-calibration.

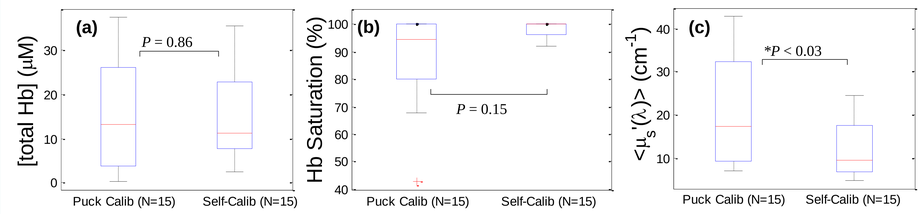


Fig.3. (a) [Total Hb] extracted from colposcopically normal sites in patients was not significantly associated with the calibration method. (b) Hemoglobin saturation (HbSat) extracted from the same tissue sites was also not significantly associated with the calibration method. (c) The extracted <μ_s'> from same tissue sites was significantly associated with the calibration method.

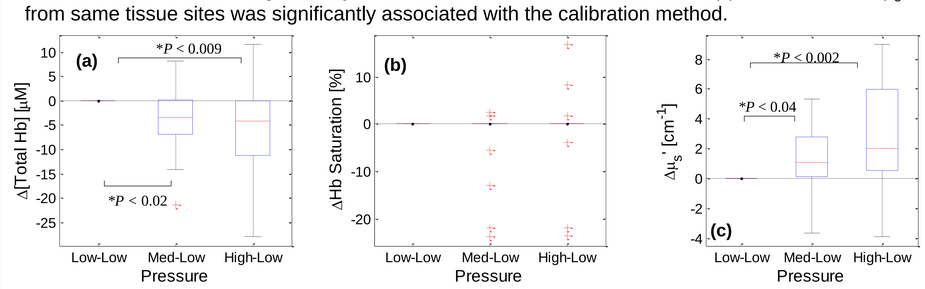


Fig.4. Diffuse reflectance spectra were acquired with the SC probe from 19 colposcopically normal sites in 19 patients with low, medium, and high contact pressures. Extracted (a) [total Hb], (b) HbSat, and (c) <μ_s'> at medium and high probe pressures were subtracted from those extracted at low pressure. Significant differences in extracted optical properties were observed in Δ[total Hb] and <μ_s'> (medium and high versus low pressure over 450-600 nm. Dashed lines represent no change from values extracted using diffuse reflectance obtained at low applied probe contact pressure.

Smart Fiber Optic Sensor

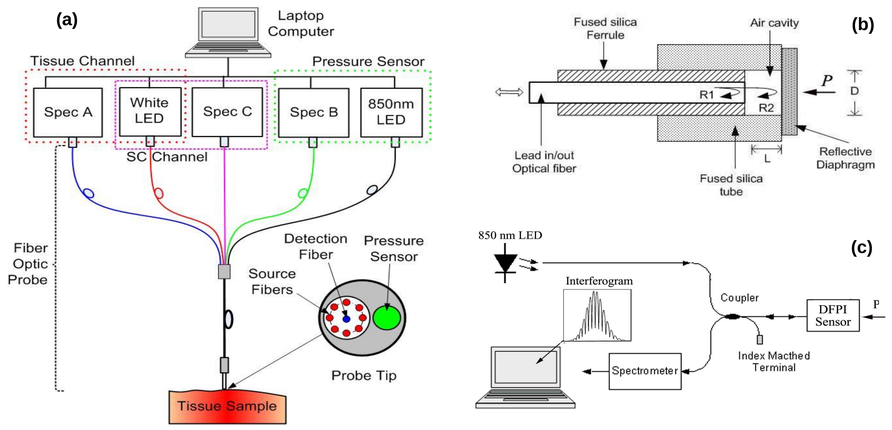
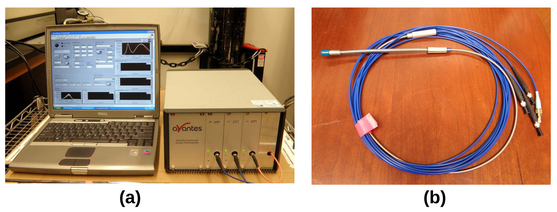


Fig.5. (a) Schematic of a smart optic sensor system; (b) diagram of a diaphragm-based F-P interferometric (DFPI) pressure sensor.; and (c) schematic of a DFPI sensor system.



(a) (b)

Fig.6. Photograph of (a) the portable smart fiber optic sensor system and (b) smart fiber-optic probe.

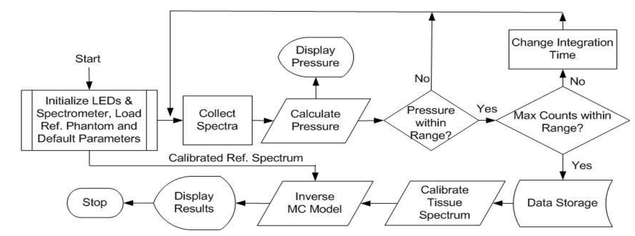


Fig. 7 Flow chart of the LabVIEW® software for instrument control, data acquisition and real-time analysis.

Laboratory Test Results:

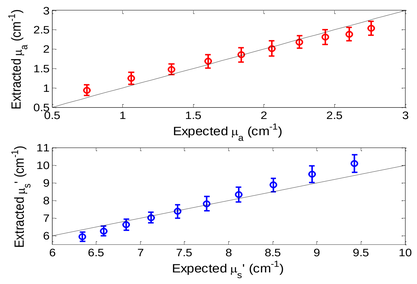


Fig.8. Phantom experiment: extracted v.s. expected phantom <μ_a> and <μ_s'> between 420-630nm. The phantoms were created by using 1.0 μm polystyrene microspheres as scatterer and metHb as absorber.

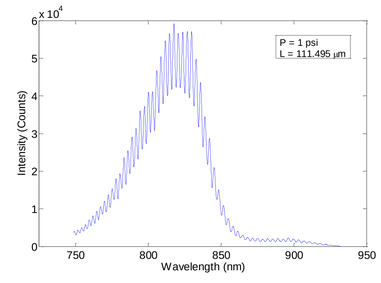


Fig.9. A typical interferogram measured with smart probe under a nitrogen pressure of 1.0psi.

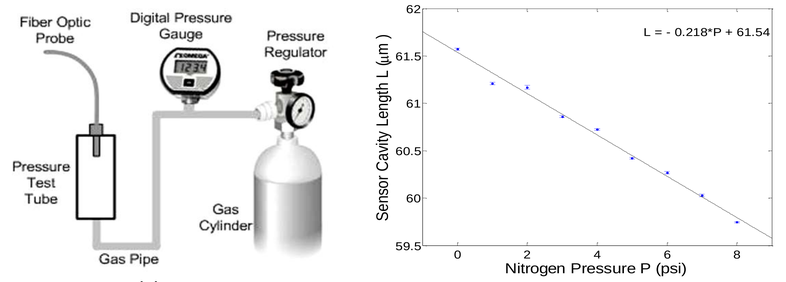


Fig.10. (a) Schematic of experimental setup for pressure sensor test. (b) Measured air cavity length of smart sensor 1 as a function of the applied nitrogen pressure P.

Future Work

- To estimate how well the probe pressure can be manually controlled with the smart sensor on oral mucosa from 10 healthy volunteers. (Funded by NIH/NIBIB R03)
- To establish probe pressure range $P_{set}\pm\Delta P$ and recovery time point for both oral and cervical tissues (Funded by the R03 & NIH/NCI R21).
- To conduct a clinical study in Haiti to acquire quantitative and operator bias free measurements of tissue absorption and scattering, and to determine those sources of intrinsic optical contrast that best differentiate high grade lesions (CIN 2+ and invasive cancer) from their benign counterparts (CIN 1 and normal). (Funded by NIH/NCI R21)

References

1) M.C. Skala, et al, Opt Exp, 2007. 15(12): p. 7863-7875
2) V.T. Chang, et al, Neoplasia, 2009. 11(4): p. 325-32.
3) M.G. Muller, et al., Cancer, 2003. 97(7): p. 1681-92.
4) A.W. Sharwani, et al, Oral Oncol, 2006. 42(4): p. 343-9.
5) Y.N. Mirabal, et al, J Biomed Opt, 2002. 7(4): p. 587-94.
6) N.M. Marin, et al., Gynecol Oncol, 2005, 99(3 Suppl 1): p. S116-20.
7) D.C. Arifler, et al, J Biomed Opt, 2006. 11(6): p. 064027.
8) E.K. Chan, et al, IEEE Selected Top. in Quantum Electronics, 1996. 2(4): p. 943 – 950
9) R. Reif, et al, J Biomed Opt, 2008. 13(1): p. 010502.
10) Y. Ti and W.C. Lin, Opt Exp., 2008. 16(6): p. 4250-62
11) Chan, E.K., et al, IEEE J. Selected Topics in Quantum Electronics, 1996. 2(4): p. 943 - 950
12) Nath, A., et al, J Biomed Opt, 2004. 9(3): p. 523-33.
13) Rivoire, K., et al, Am J Obstet Gynecol, 2004. 191(5): p. 1606-17
14) Shangguan, H., et al, Proc SPIE. on *Laser-Tissue Interaction IX*. 1998.
15) Atencio, J.A.D., et al, Optical Memory & Neural Networks, 2009. 18: p. 6-14.
16) Chen, W., et al, J. Phys. D: Appl. Phys., 2005. 38: p. 2691–95.
17) S. Ruderman, et al, Biomed. Opt. Express 1, 489-499 (2010).
18) B. Yu, et al, J Biomed Opt, 2011: 16(1): p. 011010
19) V.T. Chang, et al, Opt Exp.., in press.

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