Quantitative Optical Spectroscopy Offers a Cost Effective Method for Diagnosing Cervical Cancer

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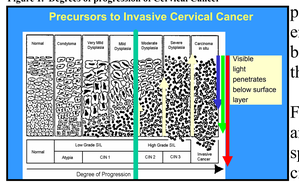
Introduction/Objectives

Current methods for detection and management of cervical pre-cancers may miss significant disease and generate false positives.[1,2] The result can be a delay in diagnosis or over-treatment. The Guided Therapeutics' LightTouch™ device was developed to address this need in a cost-effective manner. Through early detection and an increase in the yield of positive biopsies, the LightTouch device is designed to reduce the number of false positives with a concomitant high negative predictive value.

The LightTouch is designed to change the current methodology used to detect cervical cancers and pre-cancers. The LightTouch uses biophotonic technology to scan the cervix and detect morphological and biochemical abnormalities that indicate cervical pre-cancer and cancer. Using reflectance and fluorescence spectroscopy in a hyperspectral arrangement, the LightTouch is able to measure the entire cervix in less than one minute. Visible light can penetrate tissue below the surface cell layers up to and beyond the basement membrane allowing diagnosis of precancers in the cervix (Figure 1).

Figure 1. Degrees of progression of Cervical Cancer



Fluorescence spectra reveal biochemical and metabolic changes while reflectance spectra reveal morphological changes associated with pre-cancer (Figure 2). For reflectance measurements light from a xenon arc lamp was directed under software control to the cervix. For fluorescence measurements, light from the arc lamp is band pass filtered to select spectral bands known to excite fluorophores associated with neoplastic processes. Each of the fluorescence wavelengths are applied automatically under software control in a predetermined order and scan pattern. The resultant fluorescent spectral output of the cervical tissue is imaged onto a charge coupled device (CCD) camera and stored for processing and analysis.

The system consists of two main physical components, the hand held unit and the base unit. The handheld unit is connected to the base unit via an electrical, data and fiberoptic cable. The fiber optic cable transmits light from the base unit, which contains the xenon arc lamp to the hand held unit which contains the optical processing elements (e.g., filters and lenses) and the CCD camera. (Figure 3). The base unit also houses a computer for control and data processing. This includes the capability for a diagnostic algorithm based on spectroscopic information measured from the cervix, calibration data and other patient data, such as Pap results or patient demographic data.

Figure 2. Spectroscopy Measurement

What do we measure?

- Biochemistry: Fluorescence 300-500 nm excitation
  - NADH, FAD, Tryptophan
  - Collagen, Elastin
  - Porphyrin
- Morphology: Reflectance 350-900 nm
  - Increase in Nuclear/Cytoplasmic ratio
  - Hyperchromasia
  - Loss of cellular differentiation
  - Angiogenesis

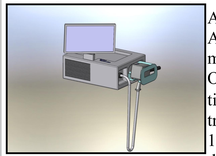
The LightTouch® has been engineered for cost effectiveness. For example the device uses an arc lamp instead of high power lasers and has been designed to use consumer grade optical and electronic components. The clinical device (Figure 3) is a cost, size and complexity reduced version of a predecessor research device (not pictured). The same engineering methods have been used to develop the commercial version (Figure 4). The commercial version is a table top, portable design that is equivalent in performance to the present clinical device.

Figure 3. LightTouch Clinical device

Clinical Need

Approximately 55 million women, in the United States, are screened annually for cervical cancer using the Pap test.[3] Of that 55 million, it is estimated that approximately 84% have no apparent abnormalities and return to a normal screening schedule.[4,5] The remaining 16% of women are shown to have an abnormality detected in their results and are required to go through follow up care. The Pap test misses 40% and 50% of disease due primarily to sampling and reading errors.[6] For example, of the approximate one million cells collected as little as 5% may actually make it onto the slide; even fewer cells if using liquid cytology.[7]

Figure 4. LightTouch table-top device (concept)



An estimated 90% of abnormalities found by Pap are ASC-US, ASC-H, L-SIL or greater. Approximately 6 million women are referred to biopsy on a yearly basis. Of that 6 million, the vast majority of biopsies are negative for significant disease.[8] For example, the ALTS trial showed that only about 5% of ASCUS Pap tests and 10% of LSIL Pap tests will result in a histopathalogical diagnosis of CIN3.

The ALTS Trial also showed that current pre-colposcopy triage after referral for ASC-US/HPV+ and LSIL patients would still miss between 30% to 40% of CIN3 disease. Colposcopy, as determined by the ALTS trial has difficulty in determining the need for and in locating biopsy sites. For example no significant disease difference was found between the "worst appearing" site biopsied and the next site.[9]

The LightTouch device, unlike colposcopically directed biopsy, is objective and does not require extensive training. The entire cervix is scanned and information is acquired down to the depth of the stroma. This is expected to increase the yield of positive biopsies through early detection of any abnormalities. Since early disease (pre-cancers) originate predominantly in the layers of cells adjacent to the basement membrane; disease can be identified earlier with the LightTouch than with existing methods. Additionally, the built in high definition video colposcope allows better identification of potential biopsy locations. This combination of spectroscopic information and improved high definition video colposcopy can assist physicians in deciding where to biopsy and/or deciding treatment options (Figure 6).

Figure 5. Spectral Output of Cervical Tissue

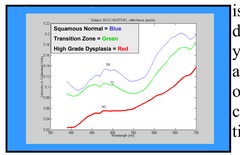
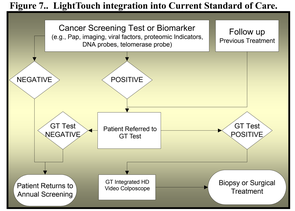


Figure 6. Dr. Lisa Flowers using the LightTouch Beta hand-held device at our Grady Memorial Hospital clinical site.

Point of Care

The LightTouch device allows for immediate consultation based on the results of the test. With the LightTouch, results are provided in minutes as compared with weeks for current methods. The LightTouch is intended to be used as a triage device prior to colposcopy (Figure 7). The ability to provide immediate results will increase patient follow through and treatment compliance. The integrated high-definition colposcope can be used for follow up work including colposcopy and biopsy.

Figure 7.. LightTouch integration into Current Standard of Care.



Physician Benefits

The LightTouch offers a variety of benefits to the doctor.

- Low Cost System
- High Negative Predictive Value Test[10,11]
- Immediate Results/Higher Patient Compliance
- Built in High Definition Colposcope for immediate reimbursement
- Technician Operated/Frees up Physicians time

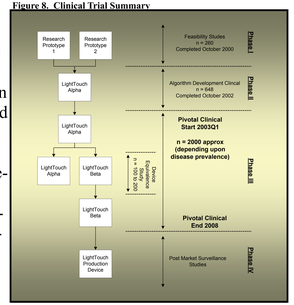
Patient Acceptance

The LightTouch offers a variety of benefits to the patient. In a patient acceptance survey[12] we have found that:

- 85% of the patients want their doctor to have the LightTouch.
- 81% of those women would like for the LightTouch to replace the Pap test
- 91% would want insurance to cover the LightTouch exam.
- 87% of those patients surveyed would recommend the LightTouch to a friend.

The use of the LightTouch device as a colposcopic adjunct was supported very favorably by women in this study.

Figure 8. Clinical Trial Summary



Summary

The LightTouch device has the potential to significantly improve the detection and management of cervical disease. It has been shown in previous studies to accurately, and non-invasively, detect moderate and high-grade cervical dysplasia while simultaneously reducing the false positive rate for benign cervices. The device provides immediate results and is designed to free up physician time as it may be operated by a technician.

Clinical/Evaluation Summary

We completed a Phase 1 feasibility study with 260 subjects enrolled. The feasibility study in conjunction with marketing data helped optimize and select device features as well as establish safety for the purpose of obtaining a non-significant risk designation from all IRB's. Our NCI supported Phase 2 multicenter trial consisted of 648 subjects and the data was used to train and validate our algorithm. Currently we are in the process of completing Phase 3 of our plan, the FDA pivotal trial. The intended population is all women 16 years or older who have been found to have ASC-US, ASC-H or L-SIL.

References

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CAUTION - Investigational device. Limited by federal law to investigational use. The availability of any product in the U.S. developed from these technologies is dependent on FDA marketing approval.