MULTIMODAL SPECTROSCOPY AS A TRIAGE TEST FOR WOMEN AT RISK FOR CERVICAL NEOPLASIA:

RESULTS OF A 1,607 SUBJECT PIVOTAL TRIAL

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Disclosure

Advisory Boards
Merck GSK Lily
Guided Therapeutics Study support

Pivotal Trial Clinical Sites

University of Texas Southwest – Dallas, Texas

Principal Investigator – Claudia Werner, MD

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Principal Investigator – Lisa C. Flowers, MD

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Principal Investigator – Leo B. Twiggs, MD / Co PI – Nahida Chakhtoura, MD

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Principal Investigator – Manocher Lashgari, MD

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Orange Coast/SaddleBack Women's Medical Group

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Multimodal Spectroscopy as a Triage Test For Women at Risk For Cervical Neoplasia: Results of a 1,607 Subject Pivotal Trial

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The Georgia Research Alliance

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Edward Wilkinson	*University of Florida*
Stephen Raab	*University of Colorado*

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Clinical Rationale
Cervical Cancer Screening

Current screening and triage methods cause

- Delays in diagnosing significant disease
- Excessive false positive rate

Expensive billions of dollars of unnecessary cost

LightTouch -Technology Advancement

- Advances in the electro-optics, illumination sources and sensors

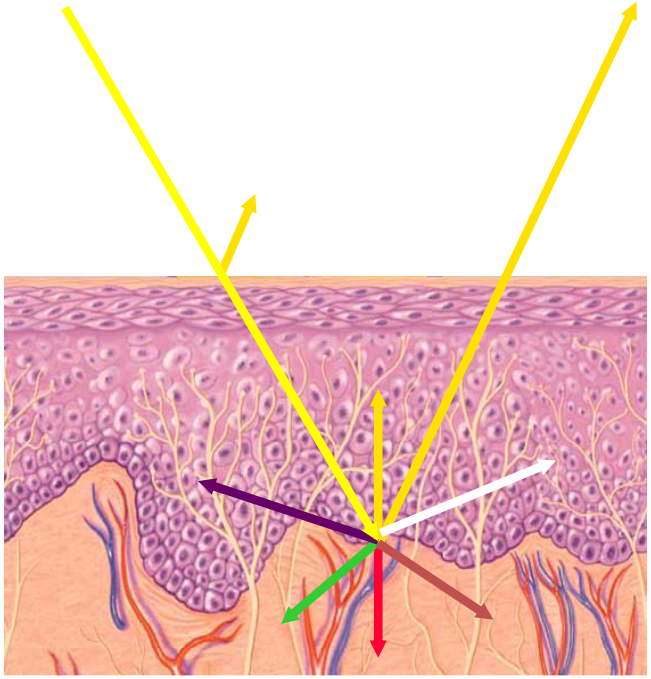
- Efficiencies in performance and cost of multimodal hyperspectroscopy (MHS)

Development of clinically relevant and convenient devices for the detection of cervical neoplasia

Potential Solution: Better Technology

Light In –

Multiple wavelengths used to penetrate different tissue depths



1. *Fluorescence Spectra -*

   Reveal metabolic changes associated with neoplasia

2. *Reflectance Spectra –*

   Reveal morphological changes associated with neoplasia

LightTouch Cervical Spectroscopy

Cervical Neoplasia Detection System

- Measures fluorescence and reflectance spectra at multiple points on the cervix in one minute
- Immediate, objective result
- Low cost device and single patient use disposable
- Built in video colposcope – permits visualization and treatment in the same visit and reimbursable in US using colposcopy CPT 57452
- LightTouch Manufactured by Guided Therapeutics, Inc. / Norcross, Georgia, USA

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LightTouch Study Design

- Each subject served as own control
- Referral Pap/HPV or other risk factor to qualify for study
- On day of study, each subject had endocervical samples taken for Pap and HPV, followed by colposcopy and biopsy
- Histology QA procedure used to reach diagnosis for each subject
- Follow up data (two year) collected if available

Subject Accountability Tree

2079 (Total number of subjects enrolled) – 70 withdrawn

2009

"Spectroscopic Evaluation of Cervical Neoplasia"

2004 - 2008

418 enrolled – 16 withdrawn

402

Beta Interim and Threshold (BIT) arm

Alpha Device 2 April 2007 – 25 Sep 2007

Beta Device 2 May 2006 – 25 Sep 2007
(Included Equivalence Testing
Sep 2006 – Mar 2007)

Training/Hardware/Software de-bugging	55
No or insufficient Histology (follow-up pending)	18
Histopathology Discordance	32
Device did not produce spectra	17
> ¼ cervix covered w/blood or mucus	36
USED FOR THRESHOLD VALIDATION	**244**

1661 enrolled – 54 withdrawn

1607

Primary Efficacy and Performance (PEP) arm

8 June 2004 – 2 April 2007

25 Sep 2007 – 25 Sep 2008
(Pathology embargo until February 2009)
(Included Repeatability Testing Feb 2008 – Sept 2008)

Alpha and Repeatability Training	54
Referral Pap Test Result Unavailable	1
No or insufficient Histology (Follow up Pending)	31
Histology Discordance	37
Device did not produce spectra	24
User Error	17
> ¼ cervix covered w/blood or mucus	36
USED FOR EFFICACY ANALYSIS	**1407**

Pivotal Trial Study Accrual Targets

Estimated Prevalence of CIN 2+ (%)	Number of CIN2+ Cases Required	Number of Benign Cases Required	Total Cases
20.0	165 - 213	414 - 1031	1600-1650

- Enrollment from June 2004 to September 2008 at seven diverse clinical sites
- Follow up data integration starting June 2009

LightTouch Condensed Procedure

- Prep subject per gynecological exam; remove any excessive blood or mucus
- Calibrate LightTouch (20 seconds)
- Using live video feed, insert hollow sight tube through speculum into vaginal canal until tube makes contact with cervix, cervix is in focus and cervical os is centered as well as possible (15-20 seconds)
- Capture video image (<1 second)
- Collect LightTouch spectral data (1 minute)
- Capture second video image to make sure os is still visible (<1 second)
- Withdraw and dispose sight tube
- Test complete

Definitions

- *Final histology – Gold Standard*
  - Pathology QA review involved blinded review by two independent expert pathologists
  - Up to two year histopathology follow-up after LightTouch study

- *Standard of Care*
  - Includes Pap cytology, HPV testing and colposcopic impression

Study Group

- 1607 total
- 1407 analyzed
- Excluded women with discordant or insufficient histopathology, training cases (200)
- **801 with two year follow up**

Up to Two Year Follow Up Results

Clinical Site	Enrolled	Follow up Data Not Yet Made Available	Lost to Follow Up	Follow up Data
University of Texas Southwest	234	64	125	45
Emory University/Grady Hospital	348	48	81	219
University of Miami	313	0	116	197
University of Connecticut Saint Francis Hospital	394	0	164	230
University of Arkansas	48	48	0	0
Medical College of Georgia	130	126	3	1
Orange County California	140	11	20	109
Total	**1,607**	**297**	**509**	**801**

LightTouch vs. Standard of Care

Detection of CIN2+ Using Gold Standard
QA Histopathology, follow-up

- *Standard of care*
  - *Includes Pap cytology, HPV and colposcopy impression*
- *CIN2+*

  - Identified 202
- *76% (202/266)*

- *LightTouch*
  - *Multimodal spectroscopy*
- *CIN2+*

  -Identified 242
- *91% (242/266)*
  - *40 more identified*
  - *40/202*

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LightTouch vs. Standard of Care

Detection of CIN2+ Using Gold Standard
QA Histopathology, follow-up

20% Increase in identification of CIN2+

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LightTouch Triage Tool

Using the result of LightTouch

- Normals-217/556 (39%) would not need further evaluation
- **CIN1**- 176/585 (30%) would not need further evaluation

Significant cost savings

Study Conclusions

- Abnormal cytology had little value as a triage tool unless it was HSIL (high grade)
- LightTouch detected 91% of CIN2+ compared with 76% sensitivity for the current standard of care consisting of Pap, HPV and colposcopically directed biopsy
- LightTouch would have reduced the number of false positives by 39% for women with normal histology and by 30% for women with low grade dysplasia (CIN1 histology)
- Test is relatively simple to perform
  - No safety issues; less discomfort
  - Well accepted by subject
- Provides immediate and more accurate results
- Opportunity to reduce cost to patients and healthcare system

Thank You

Study Results

Modality	% Sensitivity CIN2+ (n = 266)	% Specificity CIN1 (n = 585)	% Specificity Normal (556)
Standard of Care for referral*	76**	N/A (all referred to biopsy)	N/A (all referred to biopsy)
LightTouch	91	30	39

* Includes Pap cytology, HPV and colposcopy impression

** As determined by up to two year follow up