

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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OBJECTIVE: Recent advances in the electro-optics, illumination sources and sensors integral to multimodal hyperspectroscopy (MHS) have led to efficiencies in performance and cost, enabling the development of clinically relevant and convenient devices for the detection of cervical neoplasia. To date, however, convincing prospective clinical evidence of efficacy has yet to emerge. We report here the first such pivotal clinical study that combines a completely prospective evaluation of MHS (LightTouch, Guided Therapeutics, Inc. Norcross, GA) with a comprehensive histopathology review and up to two year follow up of women to maximize the validity of the gold standard comparison of colposcopically-directed biopsies.

METHODS: In this seven-center study, 1,607 women at risk for cervical neoplasia were tested using MHS, including 125 with high-grade squamous intraepithelial lesion (HSIL) papanicolaou tests (Paps), 71 with atypical squamous cells-cannot exclude high-grade squamous intraepithelial lesion (ASC-H) Paps, 737 with low-grade squamous intraepithelial lesion (LSIL) Paps, 523 with atypical squamous cells of undetermined significance (ASC-US)/atypical glandular cells of undetermined significance (AGC-US) Paps, one with no Pap results and 150 with normal or benign cytology but were at risk for other reasons including positive human papillomavirus (HPV) results, previous dysplasia and recurrent benign findings. All 1,607 women in the study were used to evaluate safety and acceptability of the procedure while 200 were excluded from efficacy analysis for the following reasons: 54 women were used for training each of the 19 physicians and seven nurses that conducted the tests, 69 either had no or discordant histopathology/referral cytology results and are pending follow up, 36 did not conform to the protocol because blood and/or mucus covered more than 25% of the cervix, 17 because of user errors and 24 because the device malfunctioned and did not produce coherent spectroscopic data. A histopathology review procedure of the 1,407 evaluable women involving two independent pathologists in addition to each site pathologist rendered diagnoses that included 266 women with cervical intraepithelial neoplasia (CIN) 2+, 585 with CIN1 and 556 with no CIN (yield of positive biopsies = 19%). The final diagnoses included data on 801 women who returned for follow up visits based on American Society For Colposcopy and Cervical Pathology (ASCCP) guidelines.

RESULTS: Histopathology review and follow up data revealed that the current standard of care consisting of Pap screening results, HPV testing and colposcopically-directed biopsy identified 202 of 266 cervical intraepithelial neoplasia (CIN) 2+ lesions at the time of study enrollment for a sensitivity of 76%. MHS identified 243 of the 266 CIN2+ lesions as positive for a sensitivity of 91%, a 20% increase in detection rate ($p < 0.0001$, McNemar's Test). In addition, MHS would have reduced by 39% the number of non-CIN cases and by 30% the number of CIN1 cases referred to colposcopy and biopsy. There were no adverse events reported from the study and women accepted the procedure without issue.

CONCLUSIONS: Multimodal Hyperspectroscopy offers the potential of a cost effective test that provides an immediate result at the point of care while detecting significantly more moderate and high-grade dysplasia and significantly reducing the need for additional testing for benign and CIN1 lesions.

KEY WORDS: cervical cancer screening, spectroscopy, cervical cytology