

MULTIMODAL SPECTROSCOPY AS A TRIAGE TEST FOR WOMEN AT RISK FOR CERVICAL NEOPLASIA: EXPERIENCE WITH A LOW COST COMMERCIAL PROTOTYPE
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OBJECTIVE: We evaluated multimodal hyperspectroscopy (MHS) in a busy private practice setting in Orange County, California. Women enrolled at our clinic and two others were tested with a cost and size reduced version of the MHS device using a single-use patient interface. In addition, our population consisted mainly of women who are most at need for effective triaging to biopsy, i.e., those with atypical cells of undetermined significance (ASC-US), atypical squamous cells, cannot rule out a high grade lesion (ASC-H) and low grade squamous intraepithelial lesion (LSIL) Papanicolaou (Pap) results and mostly positive human papilloma virus (HPV) results. The objective of the study was to compare the results of MHS with the current standard of care for triage in general and with the Pap test in particular.

METHODS: After initial training and debugging, (n = 61) 444 women were tested at three clinical centers using preproduction prototypes of the MHS device (Guided Therapeutics, Inc. Norcross, GA). A histopathology quality assurance review procedure was used for all subjects in the study along with two year follow up when available to determine histological diagnoses. Data analyses included receiver operating characteristic (ROC) curves along with estimates of sensitivity, specificity and predictive values.

RESULTS: Accounting for protocol deviations, user/device errors and no or discordant histology results, data from a total of 320 women were available for analysis, including 14 with normal referral cytology, 153 with atypical squamous or glandular referral cytology, 148 with LSIL referral cytology and five with high grade squamous intraepithelial lesion (HSIL) or malignant referral cytology. Histologically, 41 women were diagnosed with cervical intraepithelial neoplasia (CIN2+), 145 with CIN1 and 134 with benign or normal cervixes. Using a prospectively set threshold, sensitivity for CIN2+ disease and specificity of normal and benign cervixes for MHS alone were 88% and 44% respectively, as compared with 56% and 44% for cytology alone, an improvement of 56% for MHS over Pap cytology. MHS was positive for 69% of CIN1 lesions. Integrating cytology results for each subject with the MHS result did not improve performance, as specificity remained at 44%, but sensitivity of MHS and Pap combined fell to 85%. In both cases, however, the improved sensitivity of MHS compared with the Pap test was statistically significant ($p < 0.01$, Fisher's Exact Test). Positive and negative predictive values (excluding CIN1 lesions) for MHS alone were 32% and 92% respectively, as compared with 23% and 77% for cytology. Triage value, reflected by area under the ROC curve was 0.54 for cytology, 0.64 for MHS alone and 0.68 for MHS combined with cytology, although the value added by combining cytology with MHS occurred at the low sensitivity end of the ROC curve and thus would have minimal clinical significance. There were no adverse events and, similar to its predecessor prototype, women found the procedure with the new device acceptable.

CONCLUSIONS: In the first clinical evaluation of a lower cost commercial prototype, MHS increased detection of CIN2+ by 56% over the Pap test when both tests were equalized for specificity at 44%, the specificity for MHS using a prospectively determined threshold. The population studied had insignificant numbers of HSIL cytology and thus Pap cytology essentially had negligible triage value when compared with MHS. MHS offers the potential of a cost effective and efficient modality for earlier detection of CIN2+ disease in women at risk for cervical disease, while at the same time reducing the number of colposcopies and biopsies currently performed on normal and benign cervixes.

KEY WORDS: cervical intraepithelial neoplasia (CIN), early detection, cost effective spectroscopy