High Resolution Microendoscopy (HRME): A Low-Cost Point-of-Care Diagnostic for Cervical Cancer Prevention

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Cervical Cancer is Preventable

- **Known Etiology:**
  - Human Papillomavirus (HPV)

- **Prevention:**
  - HPV Vaccination

- **Screening:**
  - Pap Test, HPV DNA Testing, VIA

- **Treatable Pre-Invasive Phase:**
  - Cervical Cone/LEEP/Cryotherapy
  - Takes ~10y to progress from pre-invasive disease to cancer

Dr. Harald zur Hausen
Nobel Prize, 2008
Inequity of Cervical Cancer

85% of cervical cancer cases occur in the developing world.
Cervical Cancer Prevention in USA

Three Clinical Visits:
1. Pap test +/- HPV testing
2. Colposcopy with cervical biopsies if abnormal Pap
3. If significant precancerous lesions (<5%) - conization/LEEP/cryotherapy - Removal or ablation of precancerous lesion

** Pathology/lab services required at each step
** Not feasible in low resource settings
Availability of Pathologist

Number of People per Pathologist:
• UK: 15,108*
• US: 19,232**

*Royal College of Pathologists, 2012
**Anatomic and Clinical Pathologists, AAMC, 2007

Adesina et al., Lancet Oncology, 2012
High-Resolution Microendoscope (HRME)

• Novel cervical visualization technique
• Developed by Dr. Rebecca Richards-Kortum and team at Rice University
• Assesses morphologic features typically evaluated by pathologists in-vivo in real-time:
  – N/C ratio, nuclear size, atypia, pleomorphism
• Eliminates the need for colposcopy, cervical biopsies and pathology services
HRME

- Proflavine (topical contrast agent that stains nuclei) is placed on cervix
- A fiber-optic probe is applied
- Fluorescence from the proflavine-stained epithelium is transmitted back to the HRME
- Image is displayed on a computer screen in real-time allowing for “See & Treat”
HRME - Normal vs. CIN2/3
Reducing Size and Cost

$500 $1500 $2500
Pilot Study – Barretos, Brazil

• Prospective study of 59 consecutive patients undergoing colposcopy for an abnormal Pap test
• HRME images obtained for all lesions noted on colposcopy and normal appearing areas
• Abnormal appearing areas were biopsied and reviewed by two independent, blinded pathologists as well as a US-based study pathologist
Barretos Cancer Hospital; 59 women referred for abnormal Pap
Pilot Study – Barretos, Brazil

• The N/C ratio, mean nuclear area and eccentricity were calculated from HRME images

• A diagnostic algorithm was developed to distinguish high-grade lesions (CIN2/3 and cancer) from less severe lesions (CIN1/benign)

• Performance was compared to histologic diagnosis
HRME - Objective Interpretation
HRME - Objective Interpretation
Pilot Study – Barretos, Brazil

• A total of 79 acetowhite lesions were noted in 46 patients
• Biopsies were performed of all lesions
• Adequate HRME images were obtained in 59 of these lesions (75%)
### Pilot Study – Barretos, Brazil

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Histology</th>
<th>HRME = CIN 2+</th>
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<tbody>
<tr>
<td>Normal</td>
<td>9 (15%)</td>
<td>22%</td>
</tr>
<tr>
<td>CIN 1</td>
<td>16 (27%)</td>
<td>31%</td>
</tr>
<tr>
<td>CIN 2</td>
<td>12 (20%)</td>
<td>83%</td>
</tr>
<tr>
<td>CIN 3</td>
<td>19 (32%)</td>
<td>95%</td>
</tr>
<tr>
<td>Cancer</td>
<td>3 (5%)</td>
<td>100%</td>
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Conclusions

• Pilot study demonstrated HRME accurately diagnose of CIN2+
• HRME imaging may provide a low-cost, accurate, point-of-care alternative to colposcopy and directed cervical biopsies
• Further evaluation in large prospective studies:
  – Houston, Texas-Mexico border, El Salvador, mobile units in rural Brazil
UH2 – Low Cost Technology Program

• Incorporate HRME in a mobile diagnostic and treatment unit

• Pilot study of 200 women

• Compare rates of treatment completion for screen+ women (mobile unit in their local area vs. traveling to a central facility)
Colposcopy/HRME/Cryo Unit
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