

DEPARTMENT OF BIOMEDICAL ENGINEERING

MARQUETTE UNIVERSITY

MEDICAL COLLEGE OF WISCONSIN

*Creating a Better Diagnosis:*  
**Can we improve cervical cancer screening with Limited resources?**

Bing Yu, PhD  
 Assistant Professor

Conversations with Scientists

MCW ADVANCING A HEALTHIER WISCONSIN ENDOWMENT

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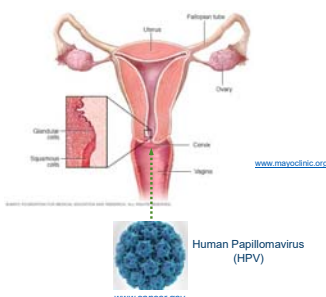
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What's Cervical Cancer?



www.mayoclinic.org

www.cancer.gov

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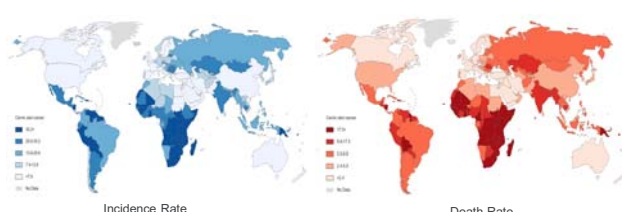
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Global Statistics

- 570,000 new cases and 311,000 death in 2018



Global Cancer Statistics 2012 & 2018

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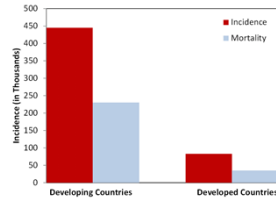
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## The Disparity of Cervical Cancer



~90% in low- and middle-income countries



Global Cancer Statistics 2012




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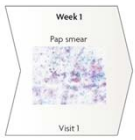
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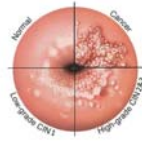
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## Screening, Diagnosis and Treatment



If test is positive

If high-grade or cancer is found



www.cervivor.org

- Very treatable if diagnosed early
  - 5-year survival rate: ~100% at pre-cancerous stage, 12% at invasive stage



Thekkek, N. et al., *Nat Rev Cancer*, 2008, 8(9); Goldie et al., *N Engl J Med*, 2005.




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## Screening Performances

|           | Sensitivity | Specificity                  |
|-----------|-------------|------------------------------|
| Pap smear | 44 – 78%    | 90-99%                       |
| HPV test  | 34-100%     | 31-94%<br>(no location info) |

- HPV vaccination, screening, and treatment reduced the incidence and death rates in developed countries.



Sankaranarayanan, R. et al., *N Engl J Med*, 2009, 360(14); Denny, L. et al., *Cancer*, 2000, 89(4)  
 Shalini I. Kulasingam, et al., *Evidence Syntheses*, No. 86, 2011  
 JA Tidy, et al., *BMC*, 2013 Mar;12(4):400-10; discussion 410-1




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## In Developing Countries

### Low vaccination rate

- HPV vaccination: \$390 to \$450

### Low screening rate (<5%) & High death rate

- Dedicated clinic visits for specimen collection
- Follow-up and treatment
- A pathology lab
- Skilled staffs
- Expensive



(Photo courtesy of CerviCusco, Cusco, Peru)



B Yu, et al., *Austin J. Biomed. Eng* 1 (2), 1007 (2014)




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## Screen-and-Treat Strategy

- ACCP screen-and-treat strategy in the developing world:
  - Visual inspection with acetic acid (VIA), or
  - VIA with low power magnification (VIAM)
  - Combined with cryotherapy
- VIA sensitivity as good as Pap smear
- Significantly low specificity (40-60%)
  - high false positive
  - unnecessary follow-up and treatment.
- Urgent to improve the specificity of VIA/VIAM.

### VIA tests results



Negative



Positive

Photo source: JHPiEGO



R. Sankaranarayanan, et al., *N Engl J Med*, 2009, **360**(14); L. Denny, et al., *Cancer*, 2000, **89**(4); J. Jeronimo, et al., *Int J Gynecol Cancer*, 2014, **24**(3).




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## Our Solution: SmartME

### Locate lesions with VIA

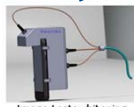
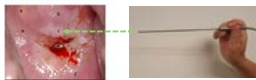


Image Acetowhitening with a SmartME



Remote Server for Diagnosis




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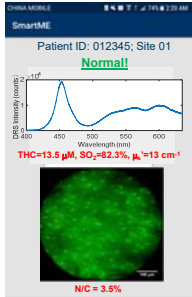
### SmartME Device



- Low-resolution video camera :**
  - Large coverage
  - Replace colonoscope
  - Guide optical spectroscopy and imaging
- Optical spectroscopy :**
  - Diffuse reflectance
  - Measures tissue total hemoglobin contents (THC), Saturation (SO<sub>2</sub>), and scattering property (μ<sub>s</sub>)
- Fiber-bundle imaging :**
  - High-resolution fluorescence imaging
  - 3 micrometer resolution
  - Nucleus-to-cytoplasm ratio (N/C)

SmartME Patient ID: 012345; Site 01

**Normal!**



THC=13.5 μM, SO<sub>2</sub>=82.3%, μ<sub>s</sub>=13 cm<sup>-1</sup>

N/C = 3.5%

2017 Marquette University Biophotonics Lab

X. Hong, et al. J. of Biophotonics, under review.

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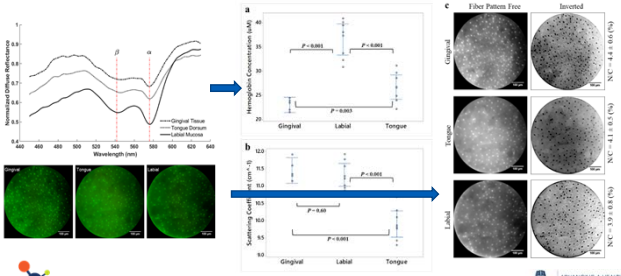
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### Prelim Results from Normal Oral Tissues



**a** Hemoglobin (μM)

| Tissue   | Mean  | SD   | P-value |
|----------|-------|------|---------|
| Gingival | ~13.5 | ~2.5 | P=0.003 |
| Labial   | ~13.5 | ~2.5 | P=0.003 |
| Tongue   | ~13.5 | ~2.5 | P=0.003 |

**b** Scatter Coefficient (cm<sup>-1</sup>)

| Tissue   | Mean | SD | P-value |
|----------|------|----|---------|
| Gingival | ~13  | ~2 | P=0.003 |
| Labial   | ~13  | ~2 | P=0.003 |
| Tongue   | ~13  | ~2 | P=0.003 |

**c** Fiber Probe Free vs Inserted

| Location | Mean | SD   | P-value        |
|----------|------|------|----------------|
| Gingival | ~4.5 | ~1.5 | N/C=4.1 (0.0%) |
| Tongue   | ~4.5 | ~1.5 | N/C=4.1 (0.0%) |
| Labial   | ~4.5 | ~1.5 | N/C=3.9 (0.0%) |

X. Hong, et al. J. of Biophotonics, under review.

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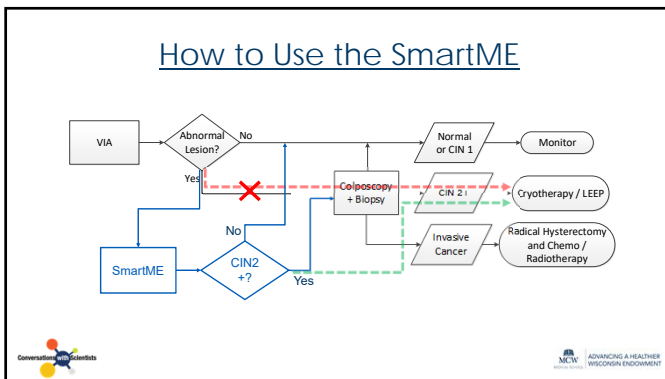
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## How Can We Improve Screening Rate?



Modified from:  
[www.indsurpatrifour.com/treatments/cancer/india-cervical-cancer.html](http://www.indsurpatrifour.com/treatments/cancer/india-cervical-cancer.html)

- VIA: 40-60% Sp, >40% unnecessary biopsies
- VIA + SmartME: 85% Sp, <15% unnecessary biopsies
- Additional cost: \$2.50/procedure
- 240 unnecessary biopsies prevented in 1,000 patients
- \$72,500 saved, screen another 1,000 patients



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## What's Next?

- 300 patients study
- Determining the sensitivity and specificity
- Algorithm training
- FDA approval



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## Summary

- Cervical cancer disproportionately affects women in poor areas and current screening methods are inaccurate, unaffordable, and inaccessible.
- We are using multiple engineering tools to create a SmartME that is portable, affordable and globally connected.
- The SmartME may improve the screening rate and accuracy in resource-poor areas.
- Things you can do to help:
  - Raising awareness of cervical cancer
  - Participating in research
  - Support NGOs, e.g., ACCP, WHO, Bill & Melinda Gates Foundation, etc.



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## Acknowledgement & Disclosure

**YU Lab members:**

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Xiangqian Hong  
Tongtong Lu  
Renee Fisher  
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**Collaborators:**

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THANK YOU!



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