Esophageal Cancer Screening

exact sciences

MAYO CLINIC

Esophageal cancer:
One of most lethal cancers in US

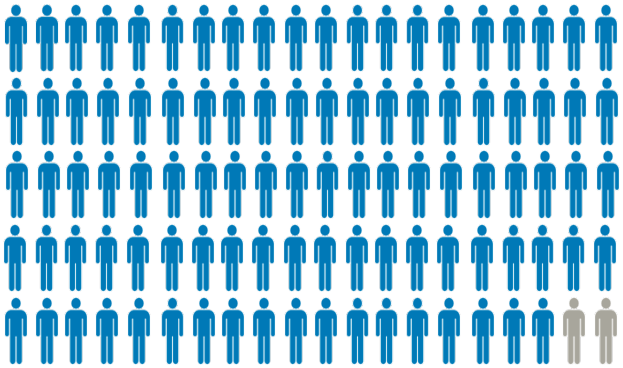
16,980
new cases per year

15,590
deaths per year

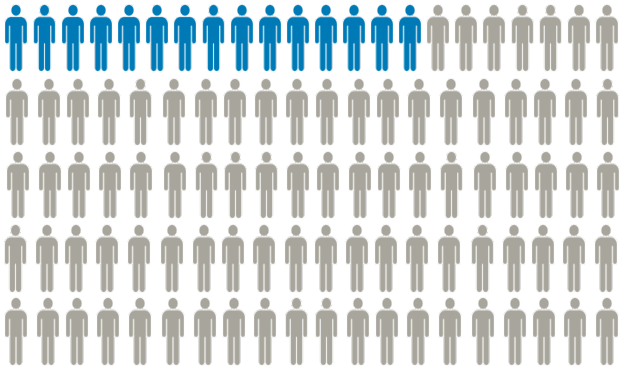
exact sciences

Source: Am Cancer Soc. *Cancer Facts & Figures* 2015. Atlanta: American Cancer Society; 2015.

Urgency to detect esophageal cancer before symptoms develop



98 out of 100
survive 5 years if
diagnosed asymptomatic in
Stage I



<15 out of 100
survive 5 years if
diagnosed after symptoms in
Stages I, II, III or IV

Pech et al. Gastroenterology 2014;14:652

exact sciences

Source: SEER 18 2004-2010

Collaborating to detect pancreatic cancer early

- Leveraging long-standing relationship and building on success of Cologuard®
- Significant intellectual property portfolio
- Proprietary know-how and biospecimens
- World leadership in cancer care through early detection

MAYO CLINIC

exact sciences

Pancreatic Cancer Screening

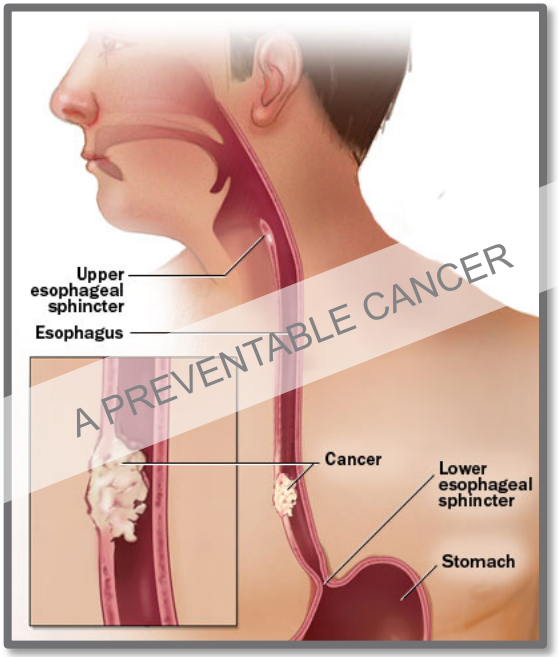
David A. Ahlquist, MD
Gastroenterologist,
Gatton Professor of
Digestive Diseases Research,
Mayo Clinic

exact sciences

MAYO CLINIC

Opportunities for early detection of esophageal cancer

- Recognizable pre-malignant condition: Barrett's esophagus
- Effective endoscopic treatment for Barrett's esophagus and earliest stage esophageal cancer
- Molecular tools offer potential to improve effectiveness of early detection



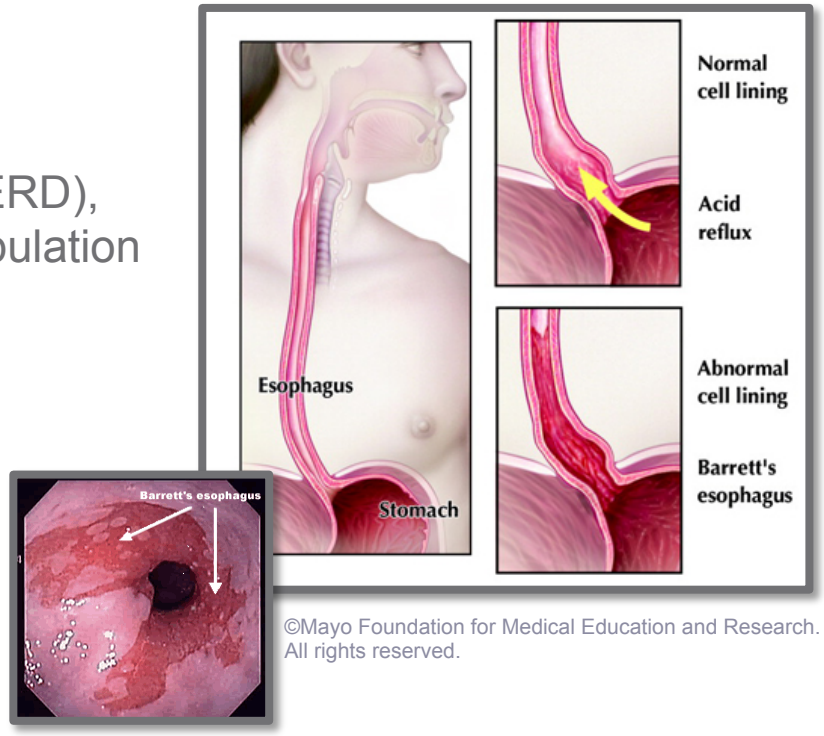
Source: *Pech et al. Gastroenterology 2014;146:652

What is Barrett's esophagus?

- A premalignant change in lining of lower esophagus
- Linked to gastro-esophageal reflux (GERD), which occurs in 40% of general US population
- Broad prevalence*

General population	3-15%
Patients with GERD	8-25%

- Readily recognized by endoscopy

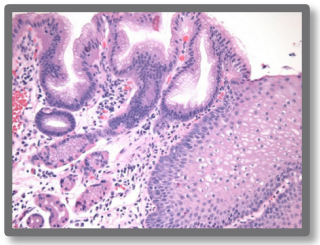


exact sciences

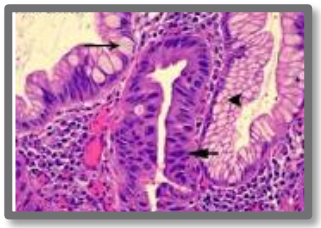
Source: *Ther Clin Risk Manag 2007 ;3:1035

Progression from Barrett's esophagus to cancer

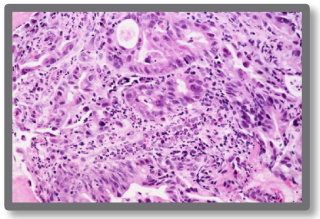
- Histological progression
  - Long pre-symptomatic window
  - Barrett's esophagus → low grade dysplasia → high grade dysplasia → cancer
- Increased cancer risk with Barrett's esophagus **11-50x**
- Lifetime cancer risk with Barrett's esophagus **5-20%**



Barrett's esophagus without dysplasia



Barrett's esophagus with dysplasia (high grade)



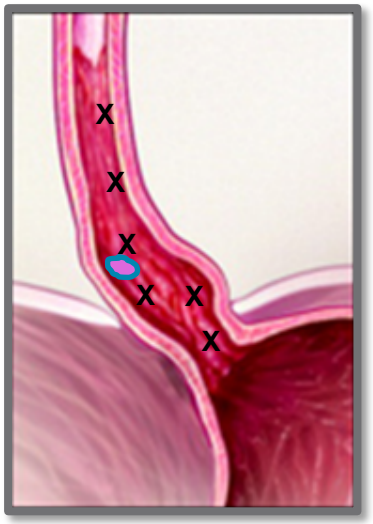
Mucosal cancer

exact sciences

Current approaches for early detection face multiple challenges

	Barrett's Esophagus Screening	Barrett's Esophagus Dysplasia Surveillance
	Endoscopy	Endoscopy
Status	Guideline recommended in patients with GERD	Guideline recommended periodic surveillance in patients with BE (random biopsies)
Challenges	Poor adherence	50% miss rate for cancer and focal high grade dysplasia by conventional (every 2cm) random biopsies*

Barrett's Esophagus
Random biopsies frequently miss focal dysplasia



Focal dysplasia
X Random biopsies

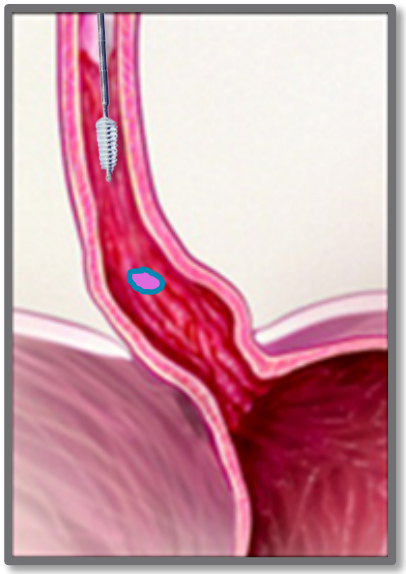
exact sciences

Sources: Sharma P et al. Clin Gastroenterol Hepatol 2006;4:566.
Reid B et al. Am J Gastroenterol 2000; 95: 3089
Falk GW et al. Gastrointest Endosc 1999;49:170–6.
Thomas T et al. Aliment Pharmacol Ther 2005;21:747–55.

Our solution:
A clinical application of esophageal brushing

- Evaluate and monitor Barrett's esophagus
- Endoscopic brushing of Barrett's segment
- More representative and accurate than random biopsies
- Assay of methylated DNA markers to determine presence of dysplasia or cancer

Esophageal brushing to detect Barrett's dysplasia



Focal dysplasia

exact sciences

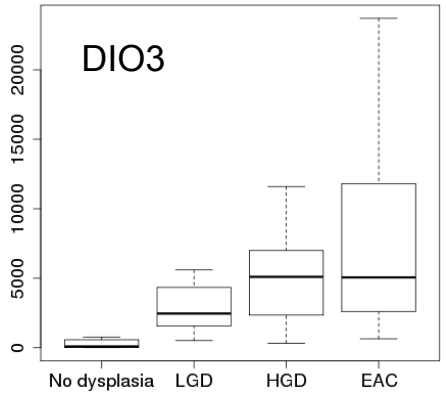
Using endoscopic brushing to detect Barrett's esophagus-related dysplasia and cancer

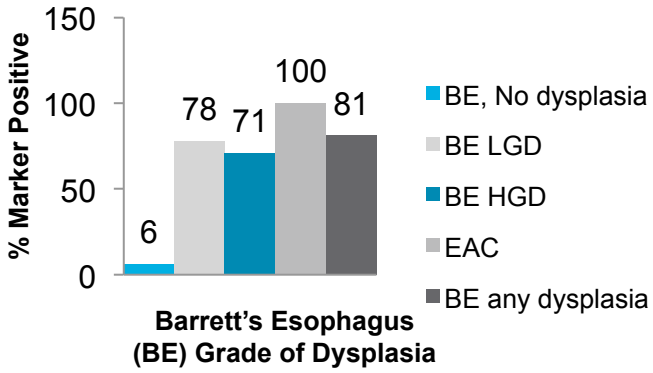
- Addresses clinical need to increase sensitivity
- Potential to improve surveillance outcomes
  - Better cancer prevention by improved dysplasia detection
  - Reduced cancer mortality by improved early stage detection
  - Lower treatment-related morbidity as early detection allows endoscopic Rx
- Health economics are driven by enhanced detection over biopsy alone

exact sciences

Our approach to successful early detection in Barrett's esophagus

- Identified and secured best-in-class markers
  - Whole methylome discovery
  - On tissue validation, best markers highly discriminant (AUC ~1)*
- Demonstrated feasibility
  - BE dysplasia and early-stage EAC detection from whole esophageal brushing
  - 3-marker panel: sensitivity 81% any dysplasia, 100% early EAC**
- Optimize marker combinations and assay methods
- Validate in clinical case-control study





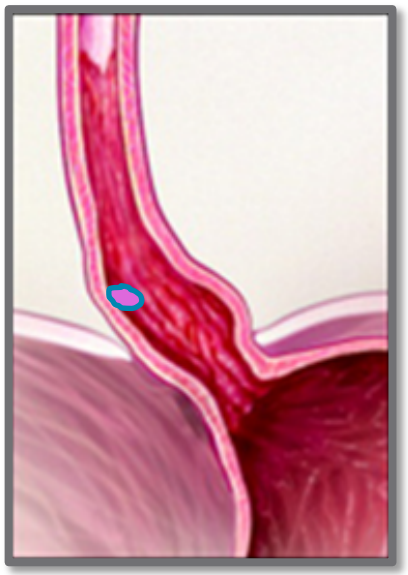
exact sciences

Source: *Taylor et al. DDW 2015, **Iyer et al. DDW 2015

Mayo Clinic's prospective esophageal brushing study

Primary Aim

Assess accuracy of methylated DNA markers in esophageal brushings to detect BE-related esophageal cancer and dysplasia



N=300

Normal esophagus (100)

BE without dysplasia (100)

BE with dysplasia: LG, HG, or mucosal EAC (100)

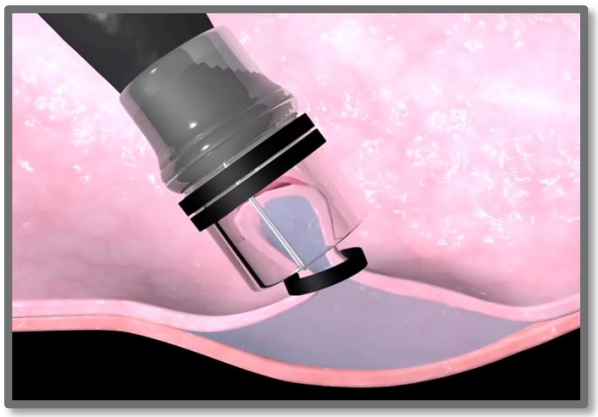
Biospecimens Collected

esophageal brushings, sponge-on-string

exact sciences

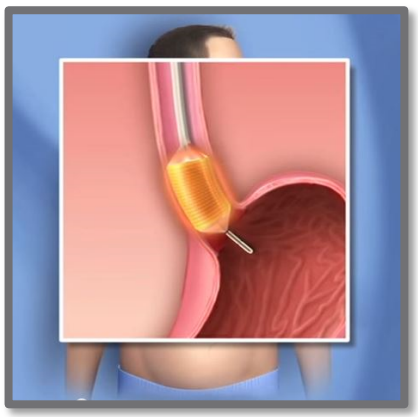
Effective endoscopic options to treat and prevent esophageal cancer

Endoscopic curative removal of early cancer



endoscopic mucosal resection

Endoscopic ablation



radio frequency

Endoscopic ablation

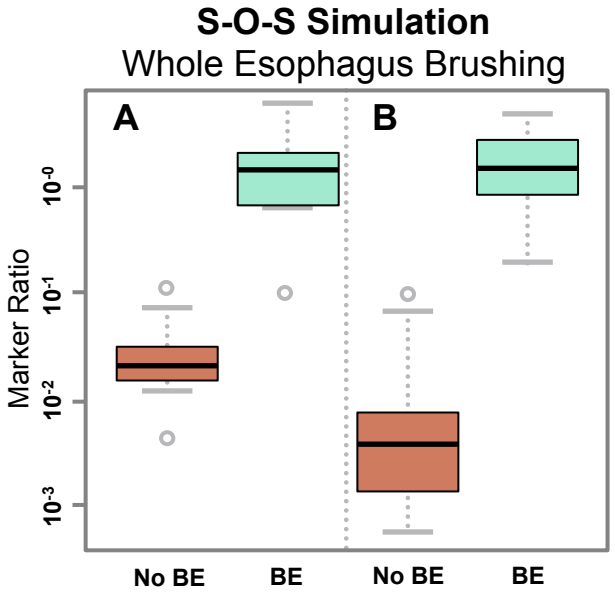
cryotherapy

exact sciences

Source: Images courtesy of Mayo Foundation for Medical Education and Research

Opportunities for early detection in Barrett's esophagus with new molecular tools

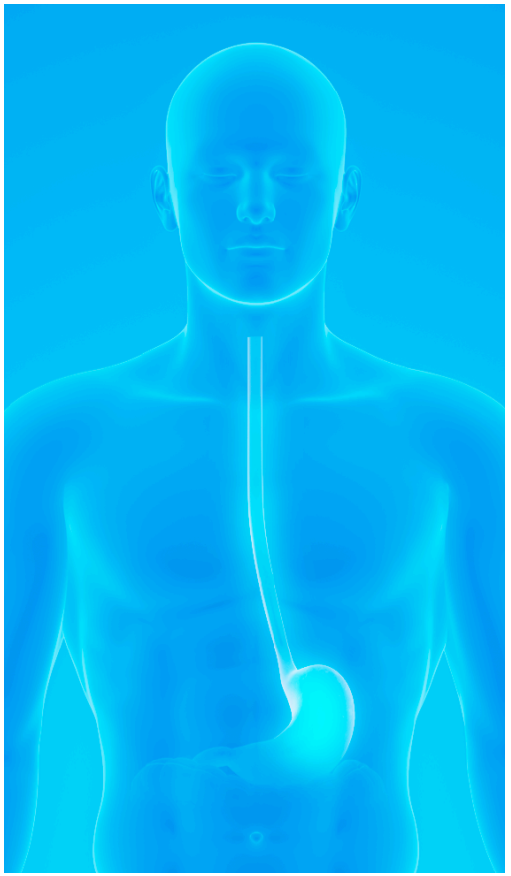
- Endoscopic brushing (near-term)
  - Dysplasia surveillance
- Sponge-on-string (longer-term)
  - Population screening
    - Early studies suggest feasibility*
    - Optimal markers and methods needed
  - Dysplasia surveillance
    - Early studies suggest feasibility
    - Optimal markers and methods needed



Source: *Iyer et al. DDW 2014

Paving the way to esophageal cancer screening in patients

- Initiating clinical trial with Mayo Clinic
- Evaluating regulatory pathway
- Building powerful economic story for Medicare and commercial payers



exact sciences

US market opportunity for esophageal cancer early detection

	Total Number of Patients in Addressable Population Per Year	US Market Opportunity
Dysplasia surveillance (every 2 years for diagnosed Barrett's patients)	1M+	$500M+

exact sciences

exact sciences