



UC Irvine Health



# *Contemporary Management of Barrett's Esophagus*

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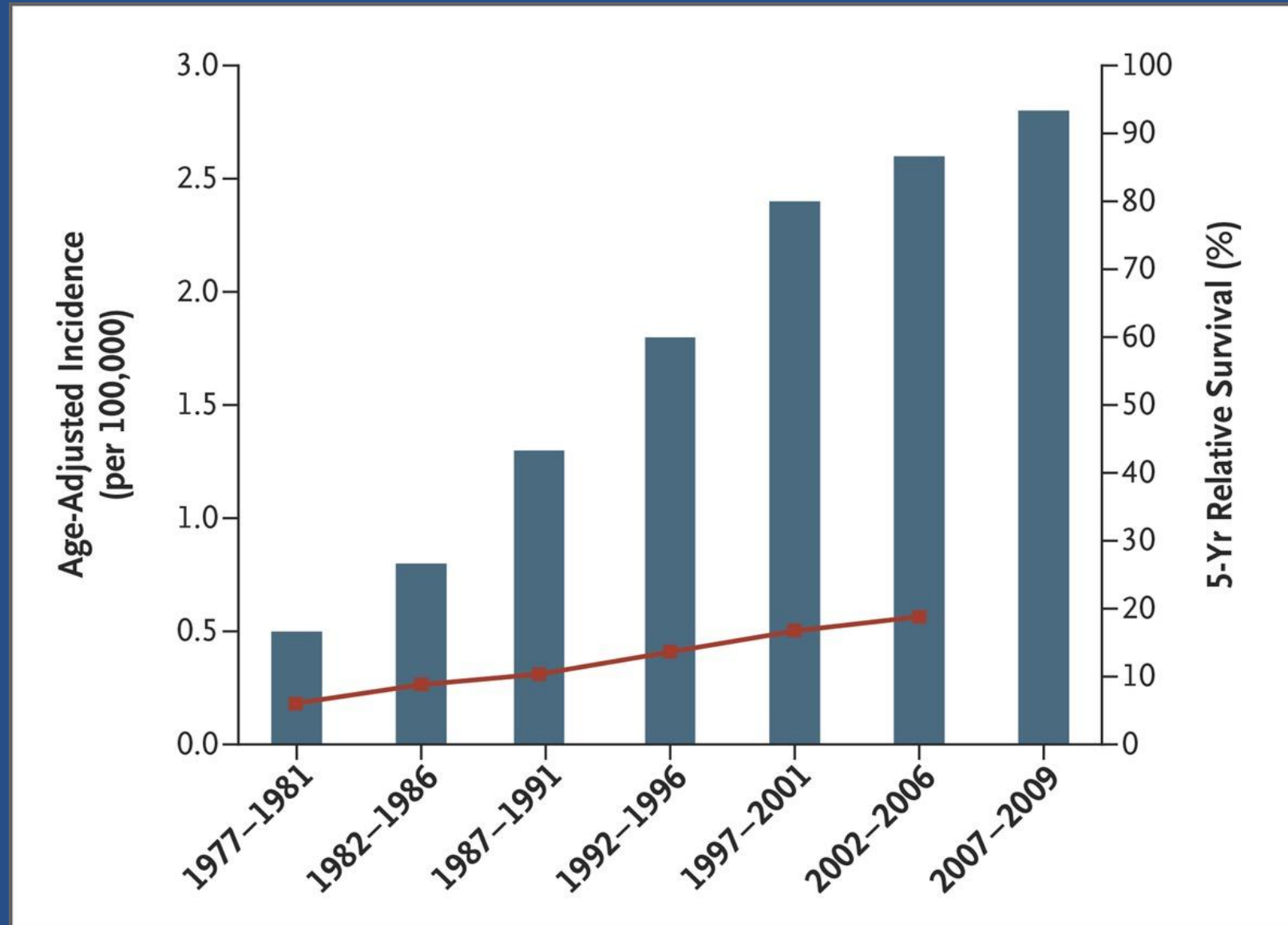
# Outline

- Background
- High level Imaging tools in 2026
- Surveillance
- Treatment
- Takeaways

# Disclosures

No Disclosures

# Esophageal Adenocarcinoma an extremely poor prognosis



# Framing the problem

600%

- Rise in EAC incidence since the 1970s

5%

- BE that progresses to cancer

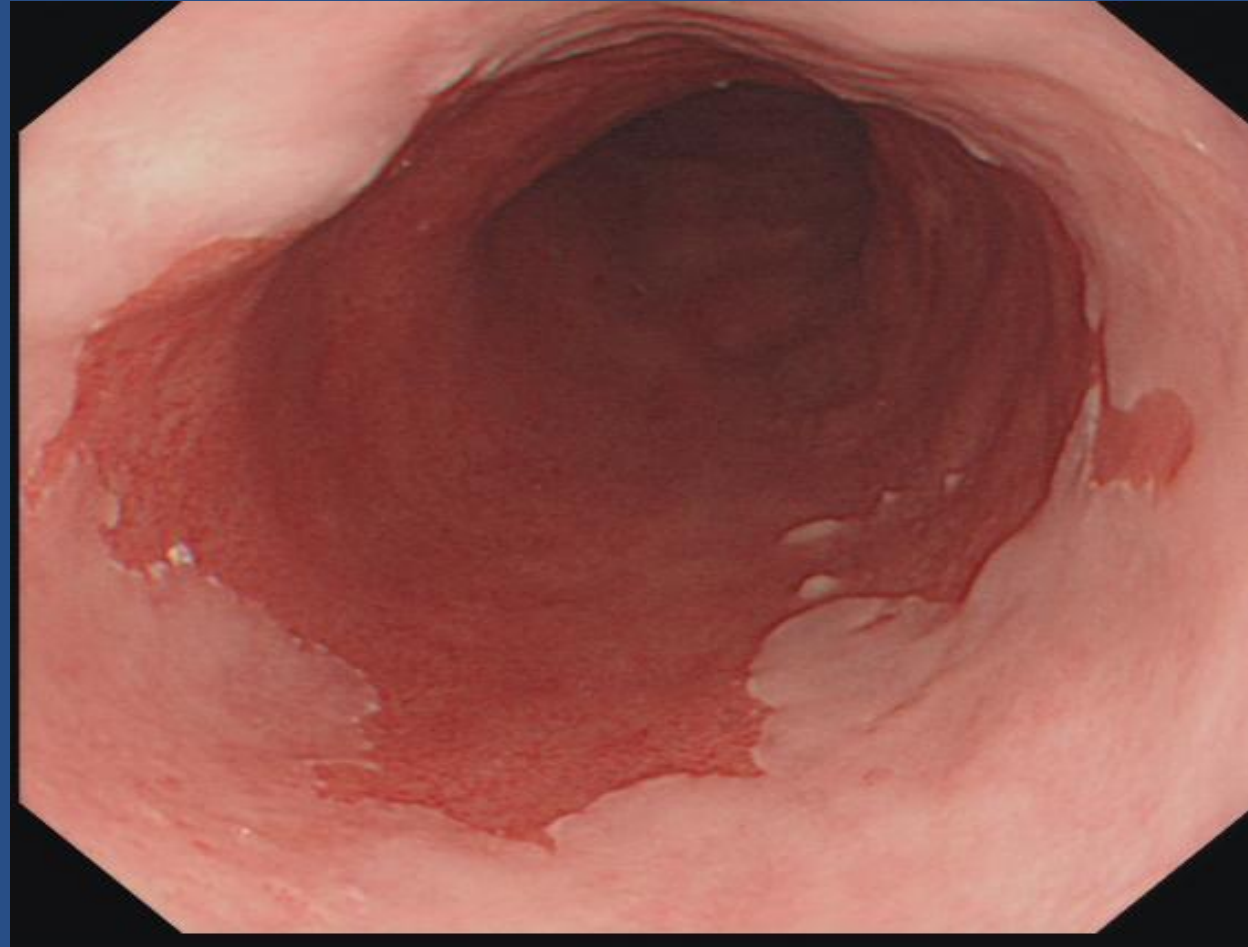
~85%

- Community LGD downgraded by expert pathology

The paradigm has shifted: **Surveillance-dominant** → **Treatment-dominant**

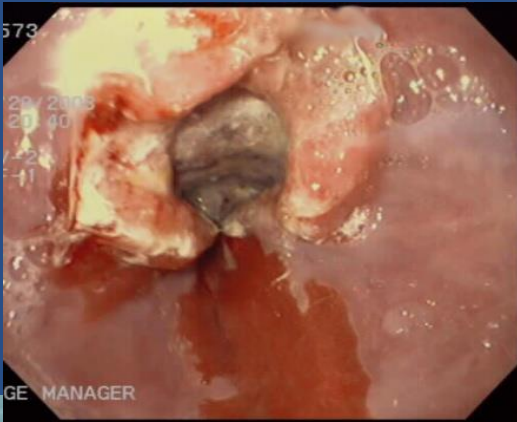
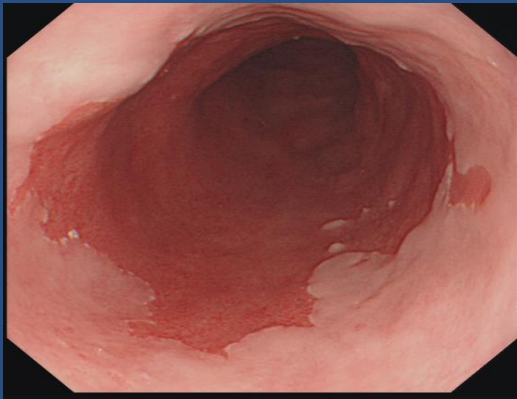
Key tension: Who truly needs EET vs. who are we overtreating?

# Barrett's Esophagus



*..the condition in which metaplastic columnar epithelium that predisposes to cancer development replaces the stratified squamous epithelium*

# Evolution of Barrett's



Squamous esophagus

Chronic inflammation

Barrett's metaplasia

Low-grade dysplasia

High-grade dysplasia

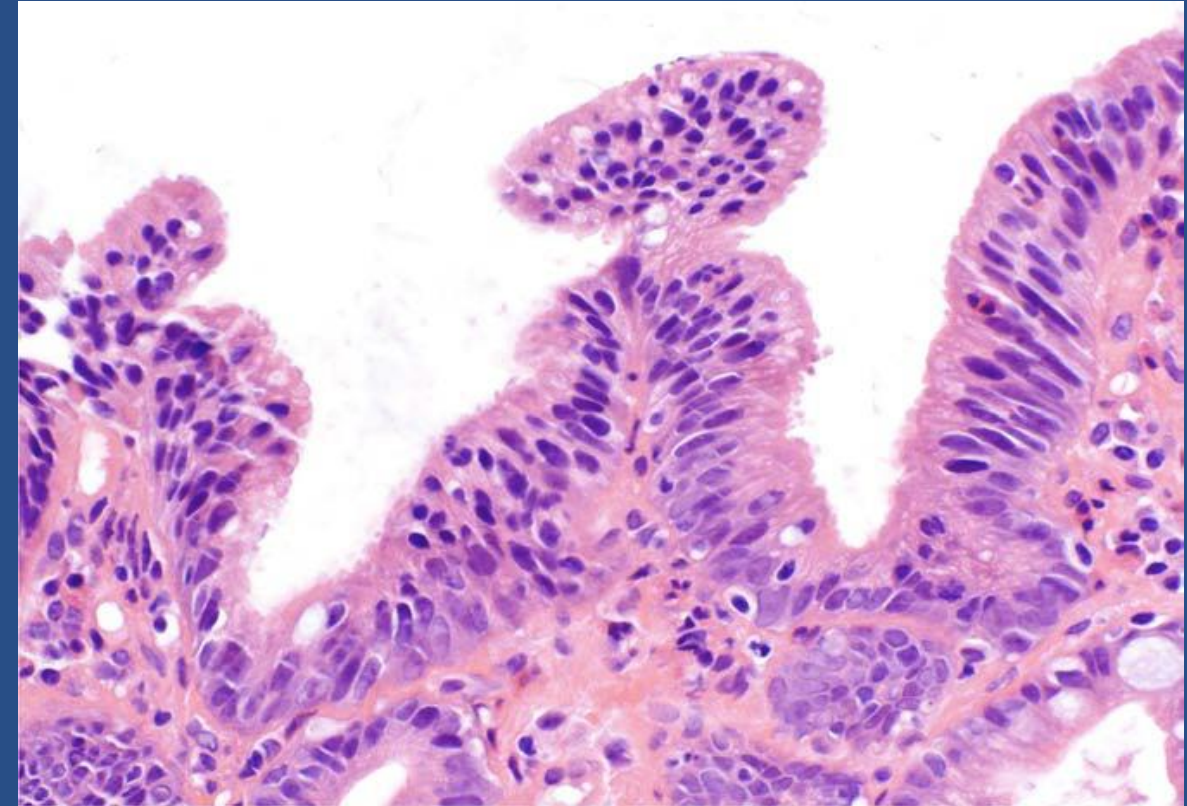
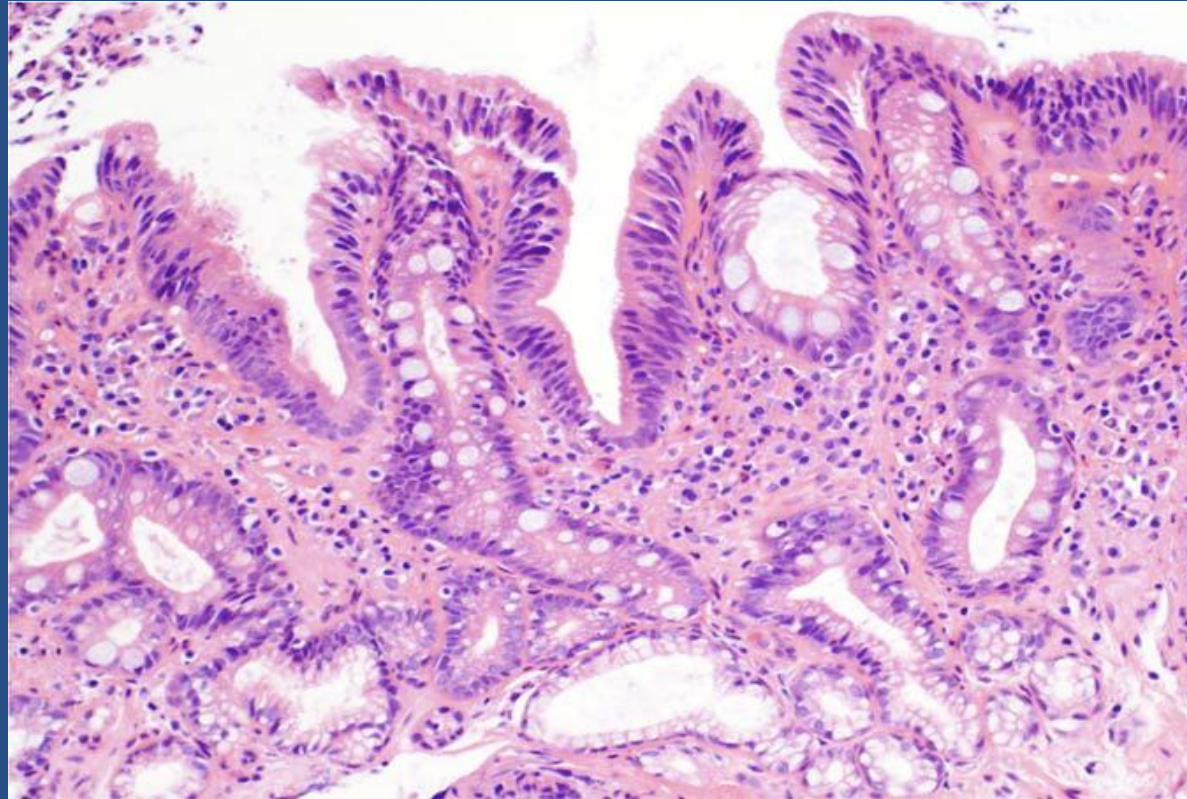
Adenocarcinoma

**Injury:**  
Acid & bile reflux

**Genetics:**  
Gender, race,  
?other factors (cox-2)

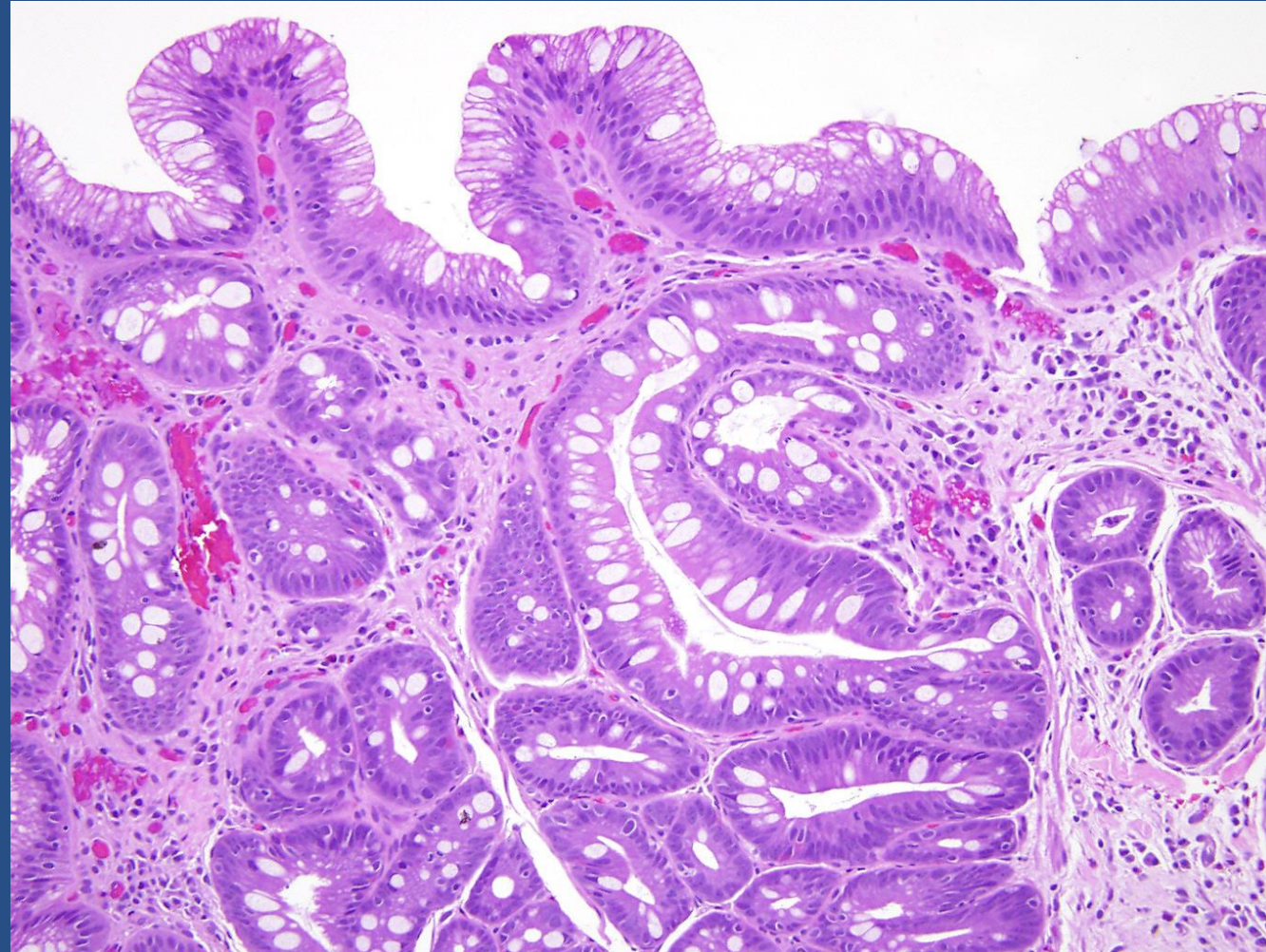
**Accumulate Genetic Changes**

# Grade: Low Grade Dysplasia



- **Cytologic changes:** Nuclear hyperchromasia, stratification, increased nuclear:cytoplasmic ratio and increased abnormal mitoses
- **Architectural changes:** None

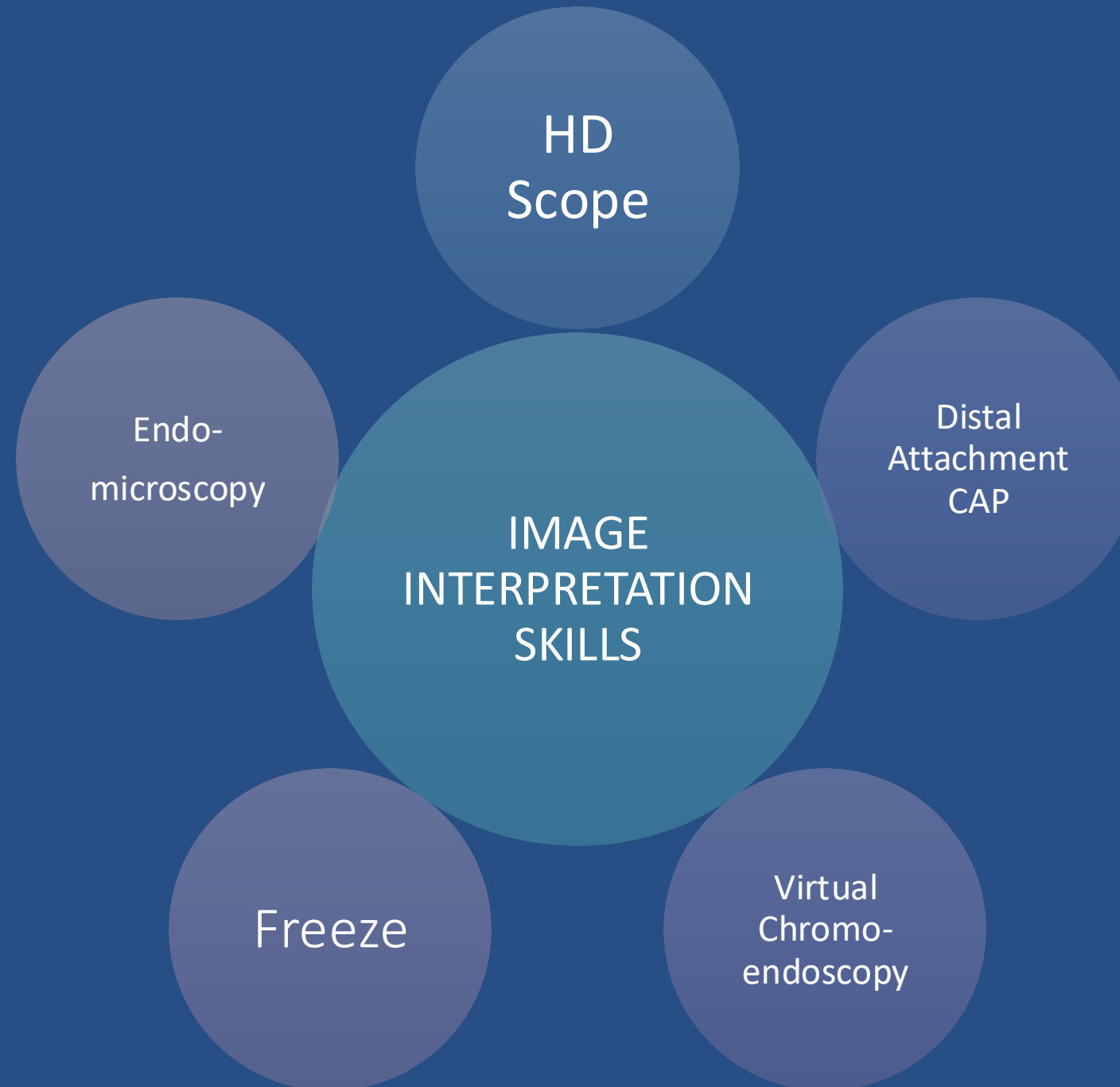
# Grade: High Grade Dysplasia



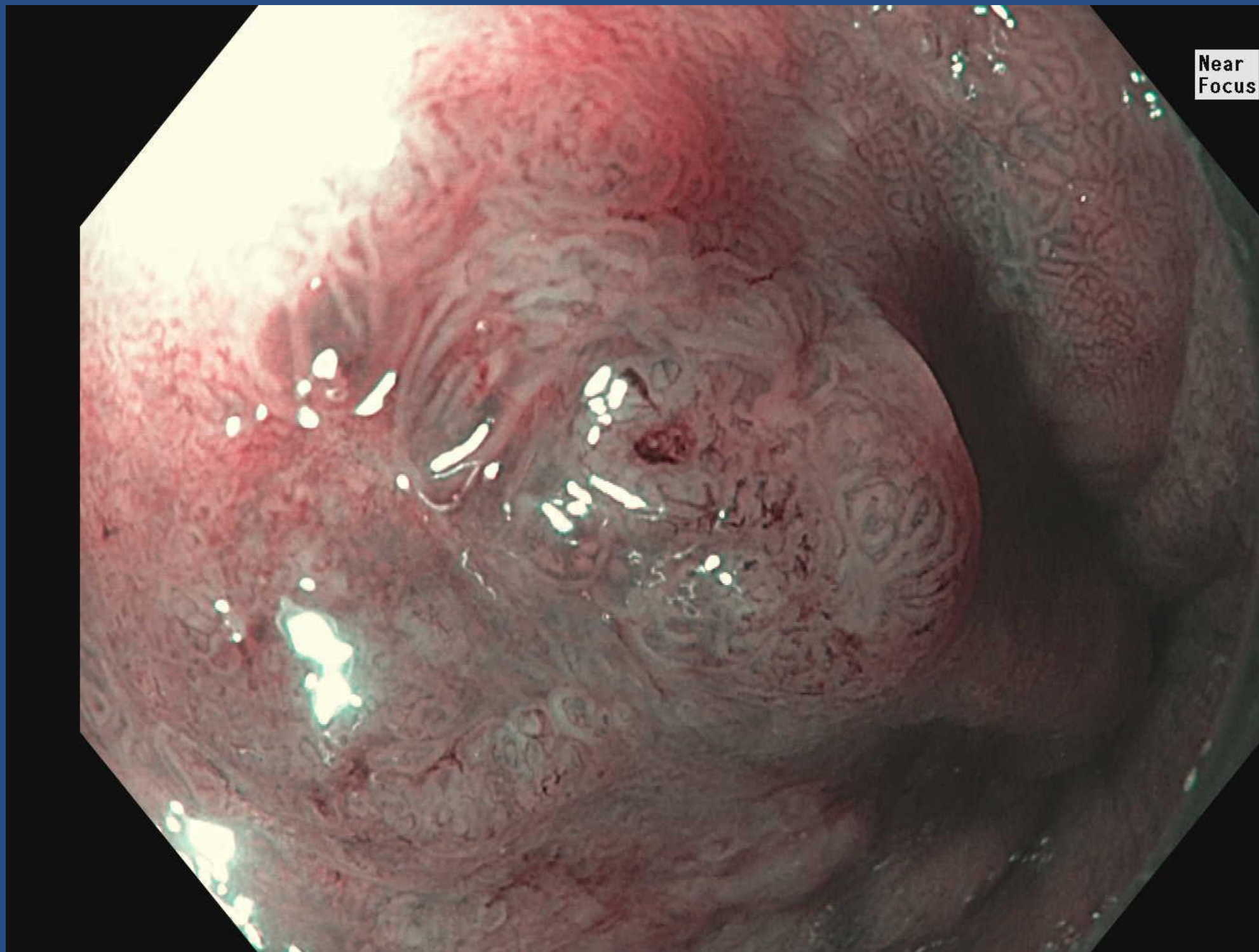
- **Cytologic changes:** Nuclear hyperchromasia, stratification, increased nuclear:cytoplasmic ratio and increased abnormal mitoses (more pronounced than LGD)
- **Architectural changes:** Glandular distortion, branching and crowding

# How do we see dysplasia in Barrett's Esophagus?

# High Level Imaging Tools in 2026







Endoscopy has reached the limits of human visual capacity

Endo-  
microscopy

HD Scope

IMAGE  
INTERPRETATION  
SKILLS

Distal  
Attachment  
CAP

Freeze

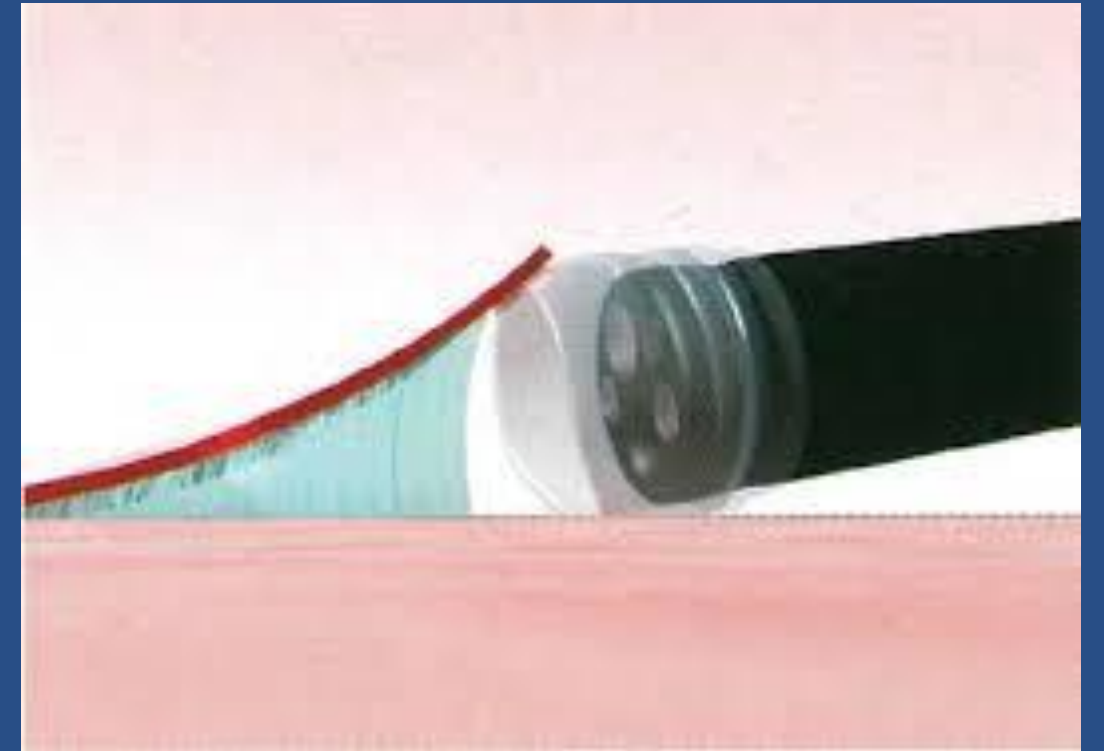
Virtual  
Chromo-  
endoscopy

# Use a Distal Attachment Cap



# Distal Attachment Caps

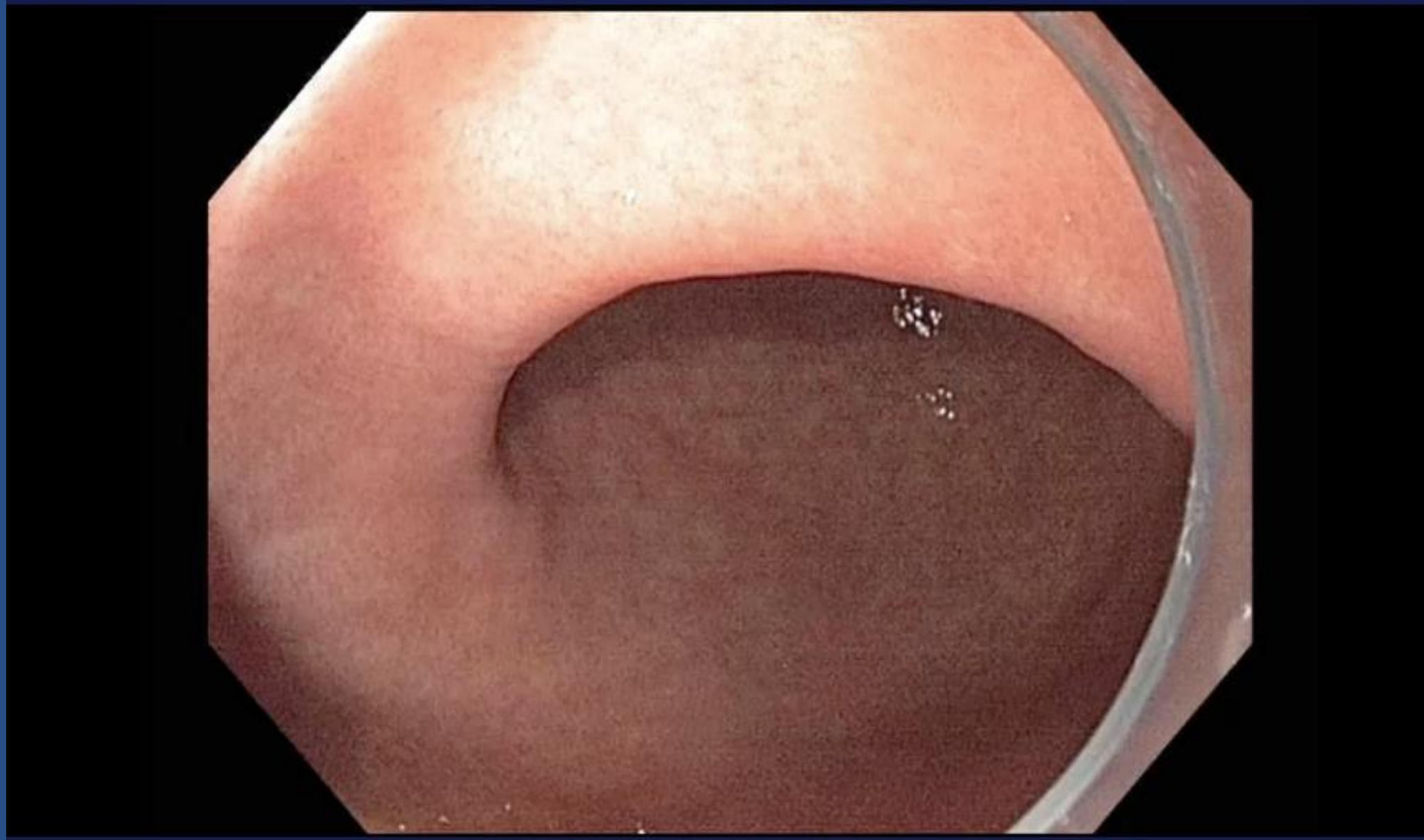
- Traditionally used for Endoscopic Submucosal Dissection (ESD) procedures to assist with traction
- Now being used in more endoscopic procedures including colonoscopy to improve polyp detection

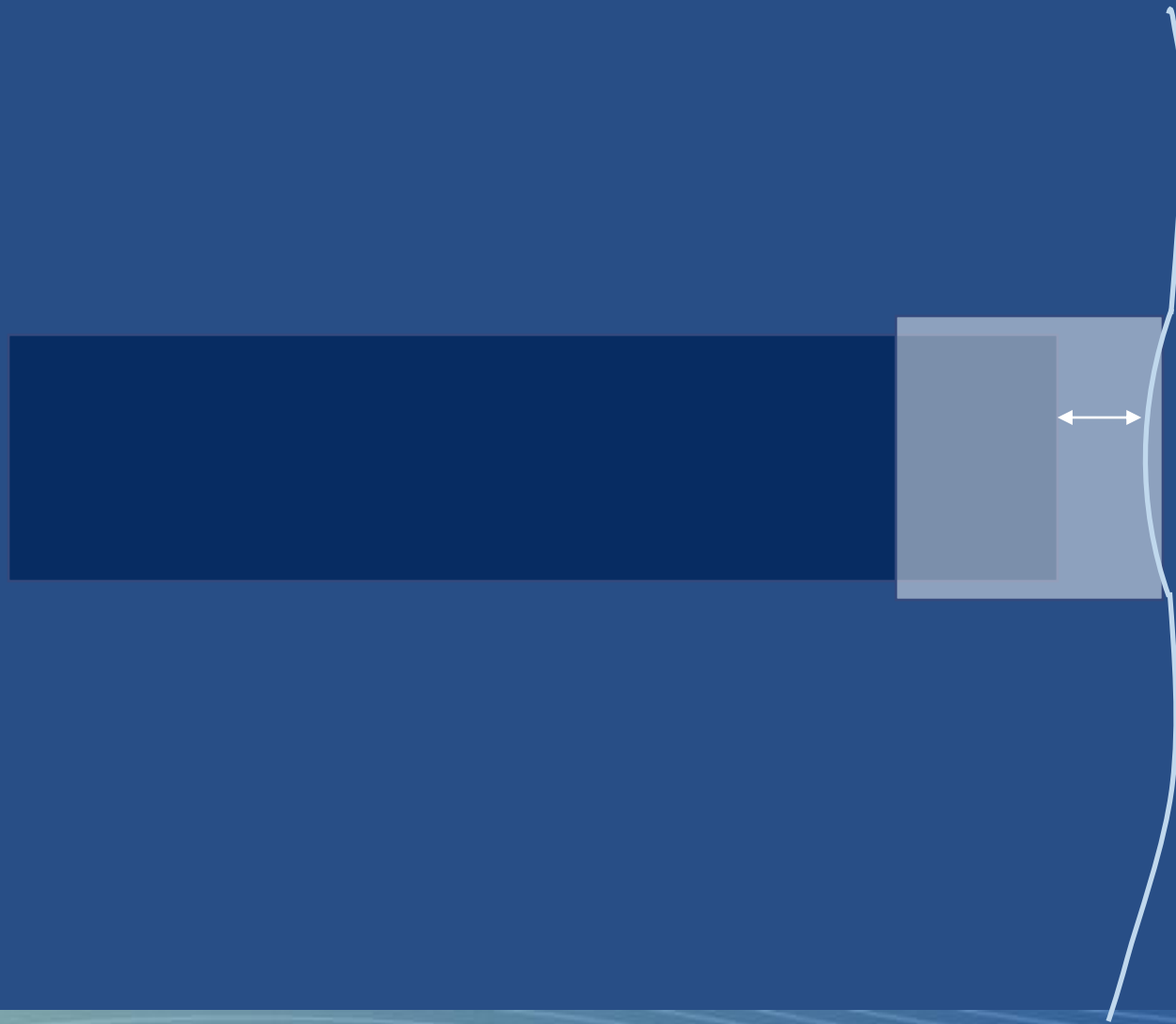


# Cap Position for ESD Procedure

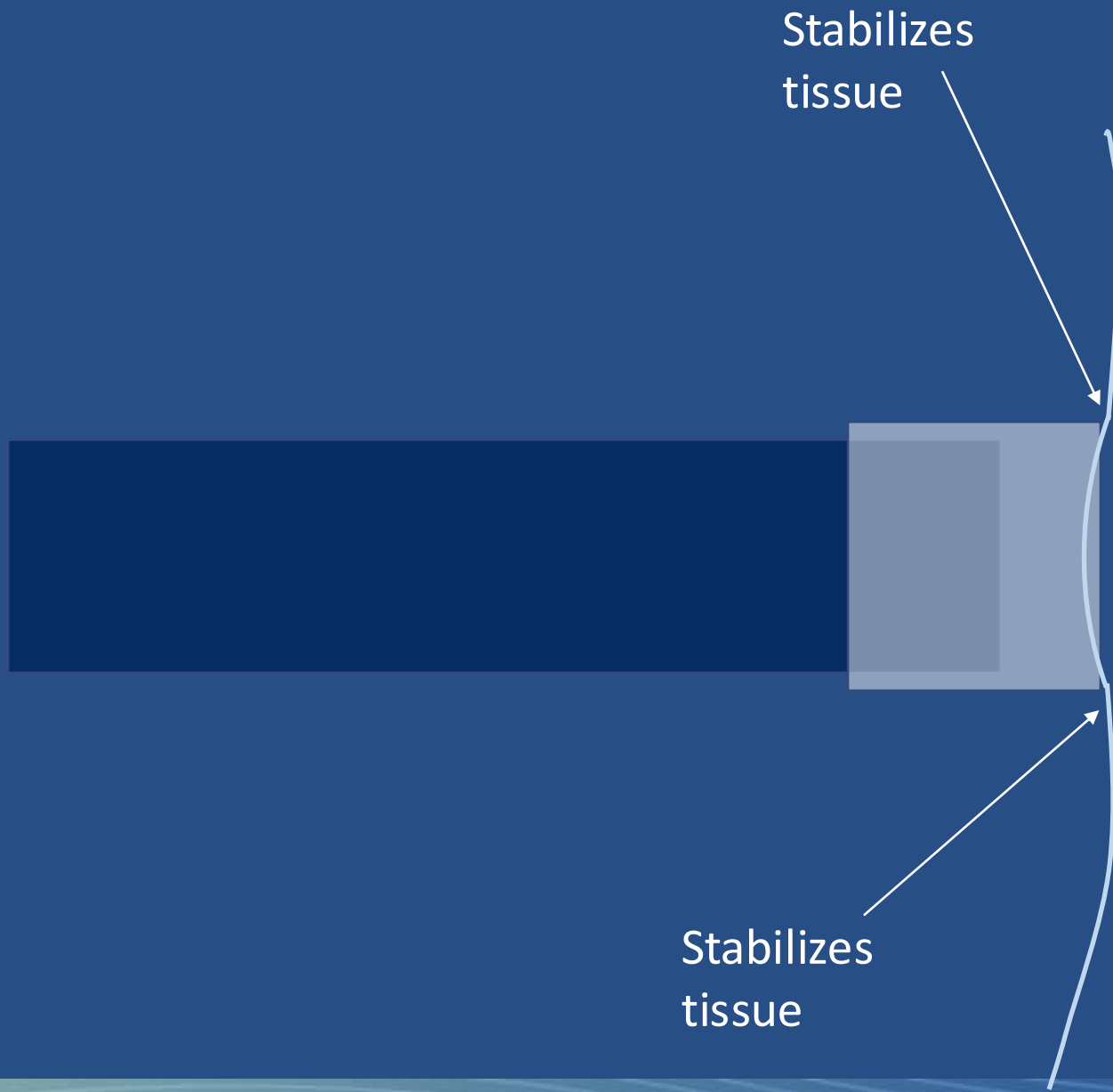


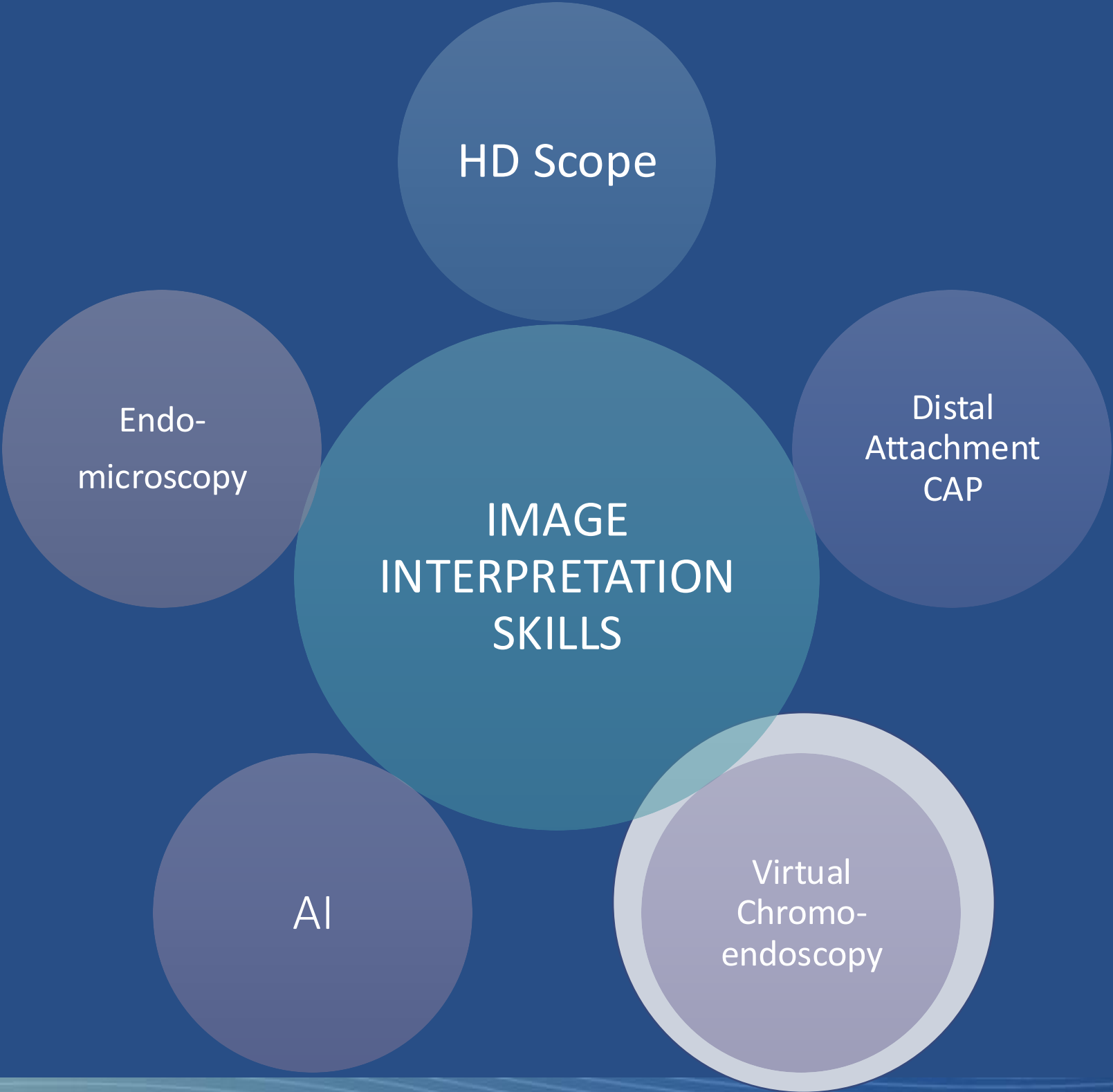
# Cap Position for Imaging Procedure





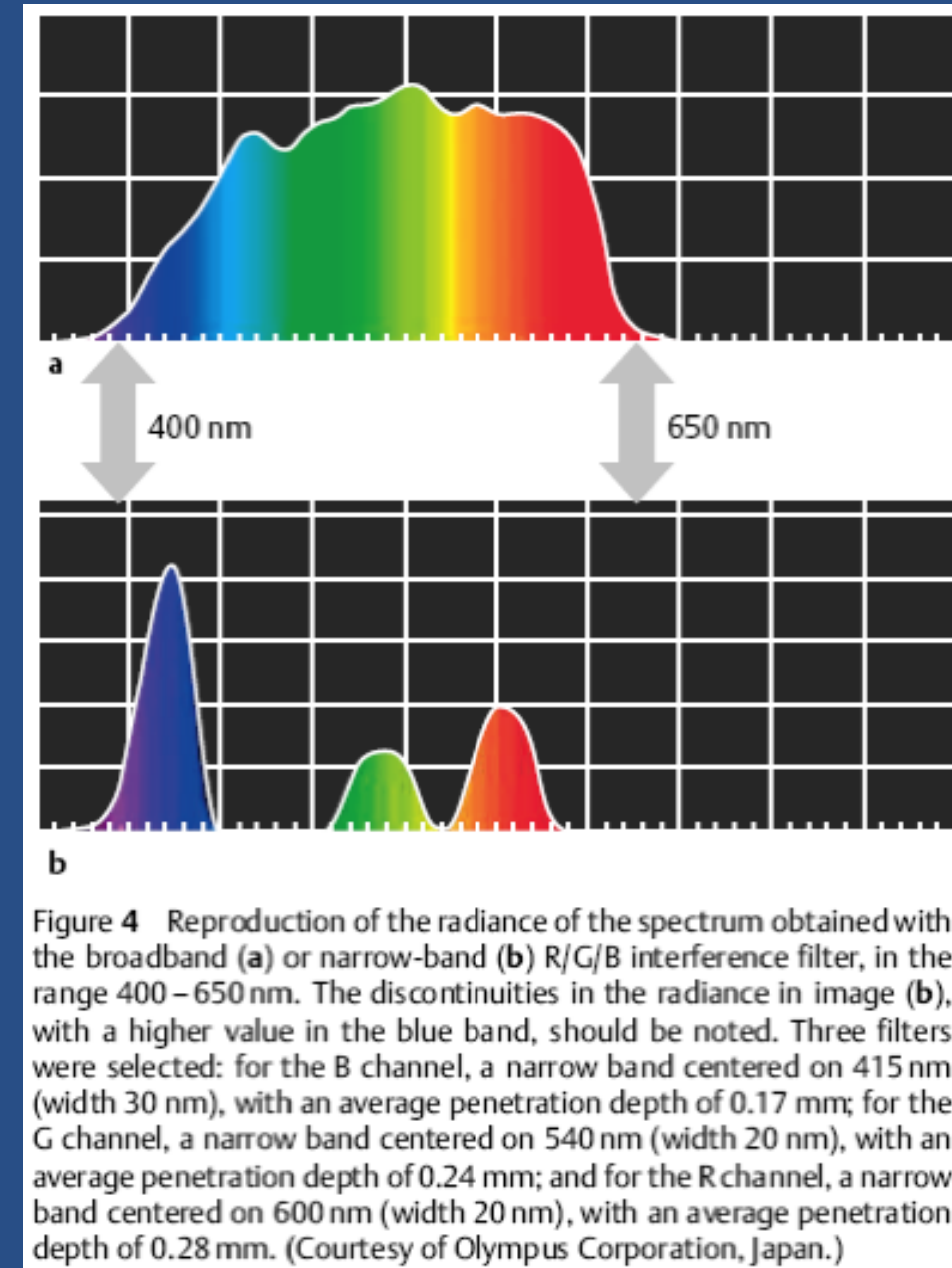
Maintaining a set distance  
away from the tissue  
(No red out)

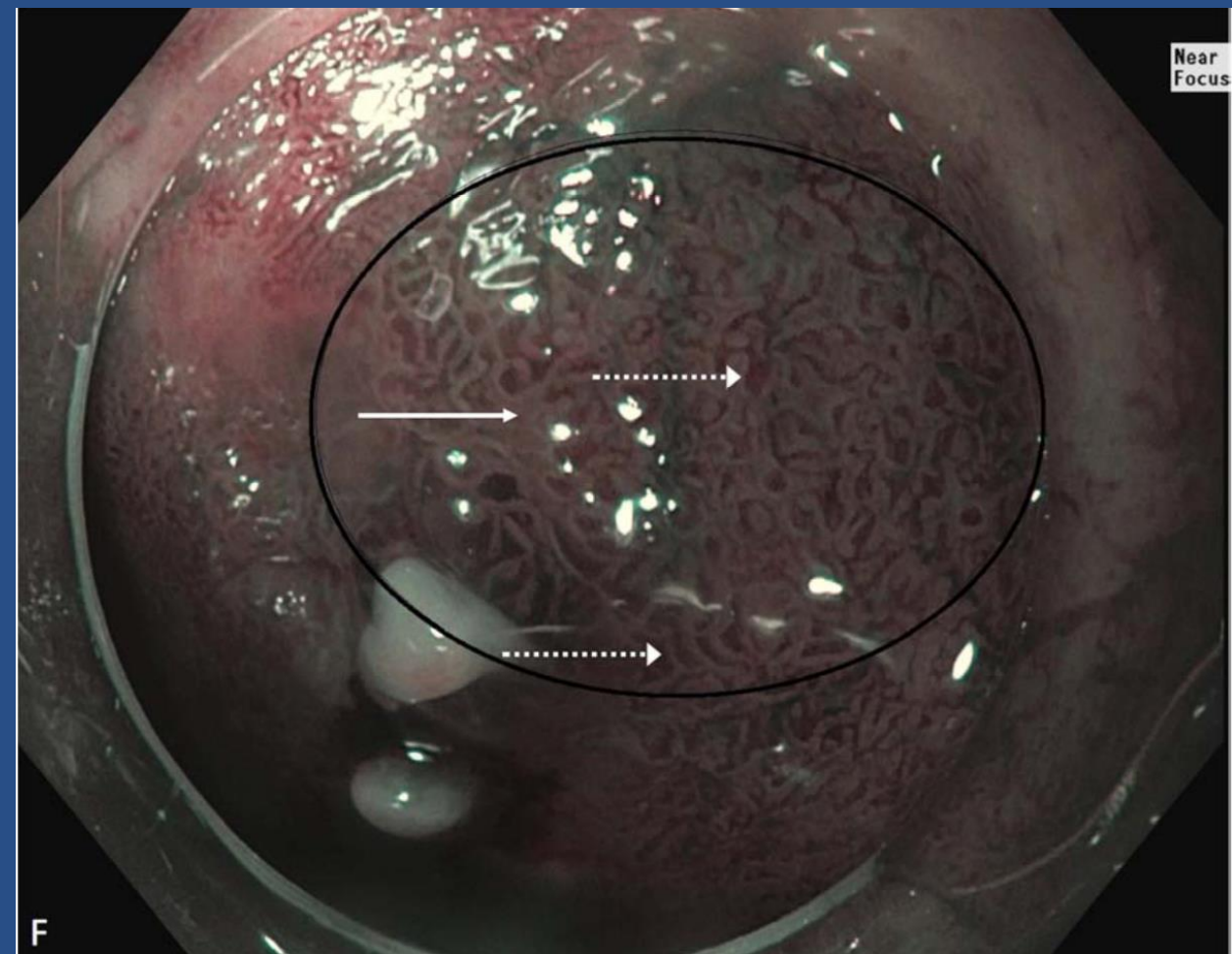
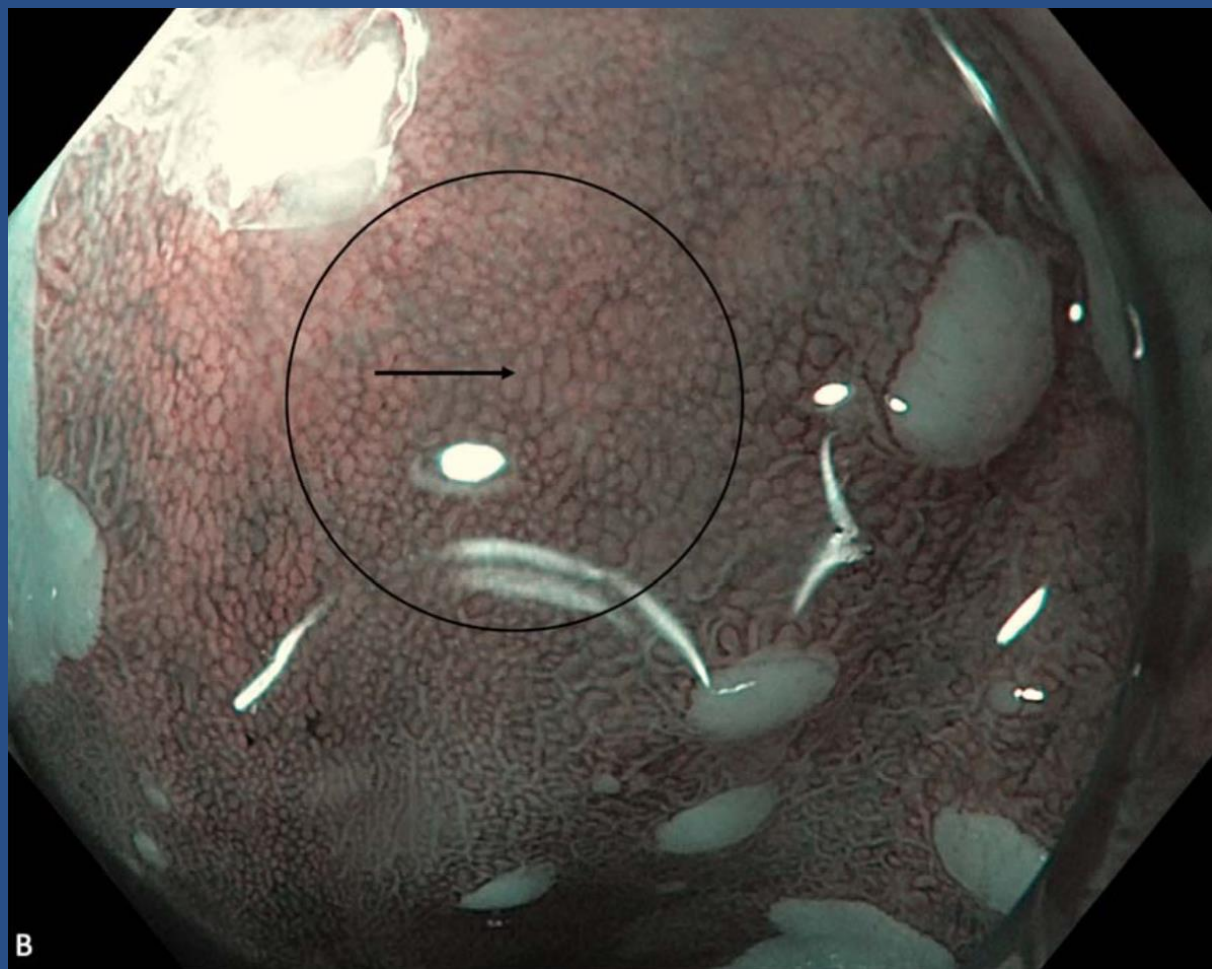




# Narrow Band Imaging

- Improves the visibility of capillaries, veins and other subtle tissue structures
- NBI uses two discrete bands of light when combined offer an extremely high contrast image of the tissue surface.

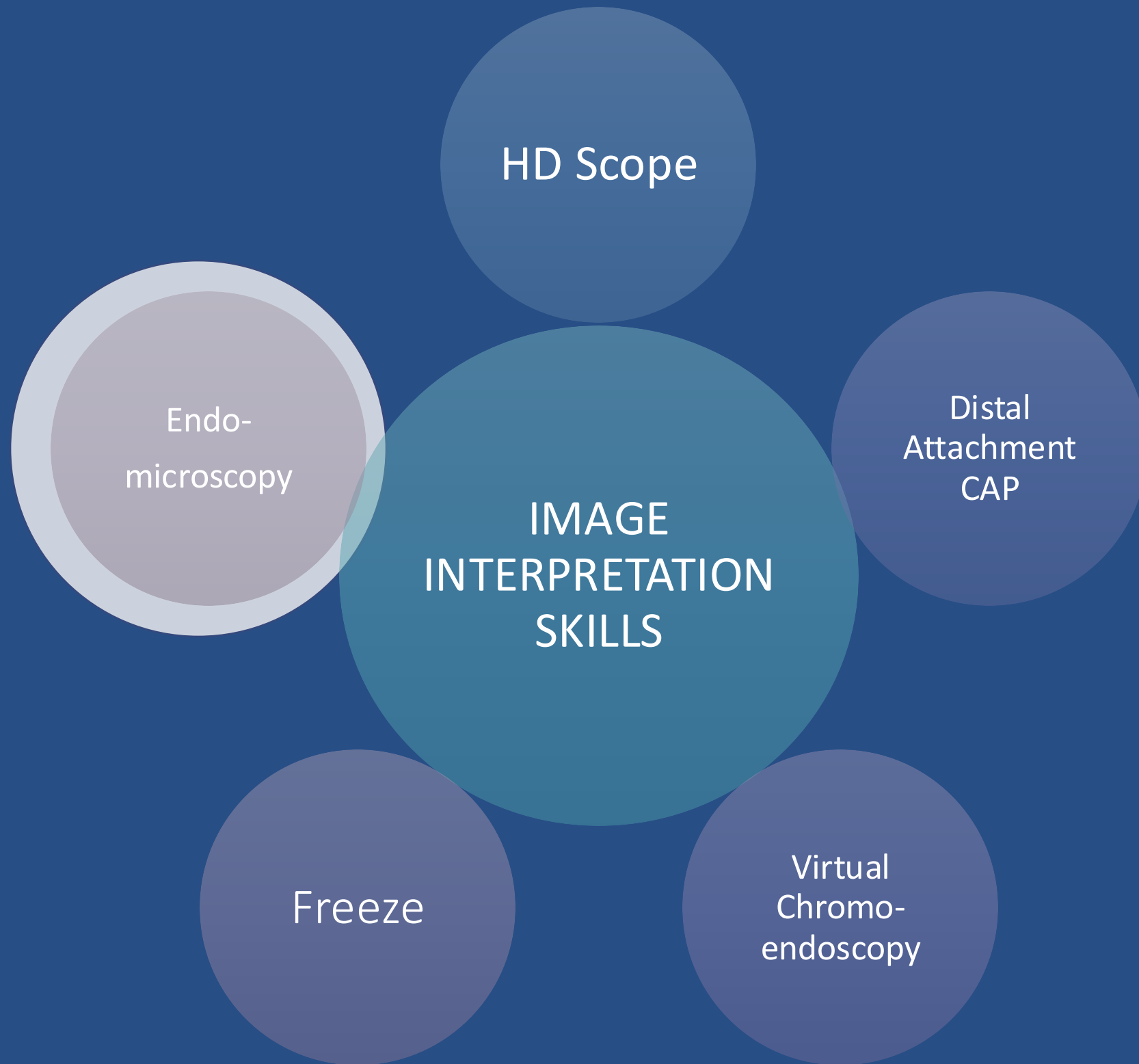




Morphologic Characteristics		Classification
Mucosal Pattern	Circular, Ridged, Villous, Tubular	Regular
	Absent or Irregular	Irregular
Vascular Pattern	Regularly situated along or between ridges Normal, long, branching patterns	Regular
	Focally or diffusely distributed vessels not following normal architecture	Irregular

# NBI for Detecting Dysplasia within Barrett's

- Barrett's International NBI Group (BING)
- The BING criteria identified patients with dysplasia.
- Achieved **85% overall accuracy**, with **80% sensitivity** and **88% specificity**; in high-confidence cases, accuracy exceeded **92%** with strong inter-observer agreement ( $\kappa = 0.68$ ).
- Offers a reliable, visual NBI classification to enhance detection of dysplasia/EAC, supporting more targeted biopsies and early diagnosis across clinical settings.

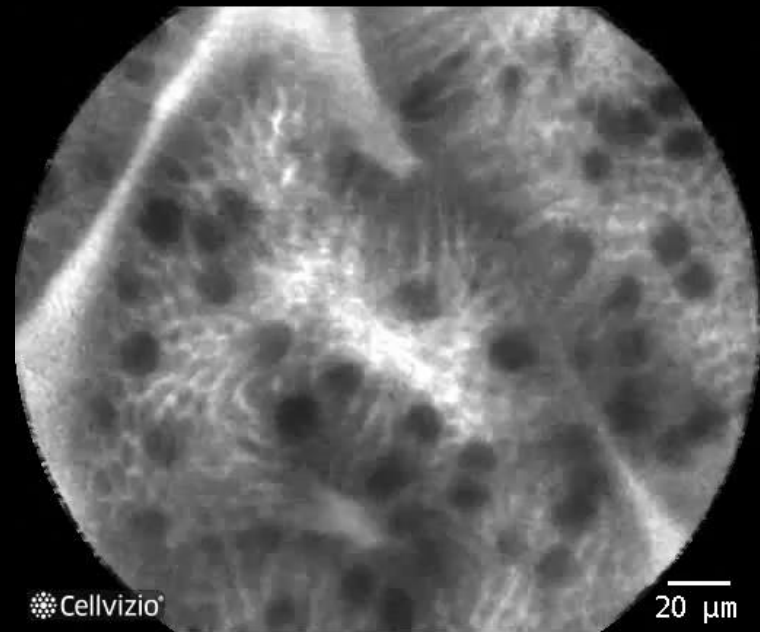




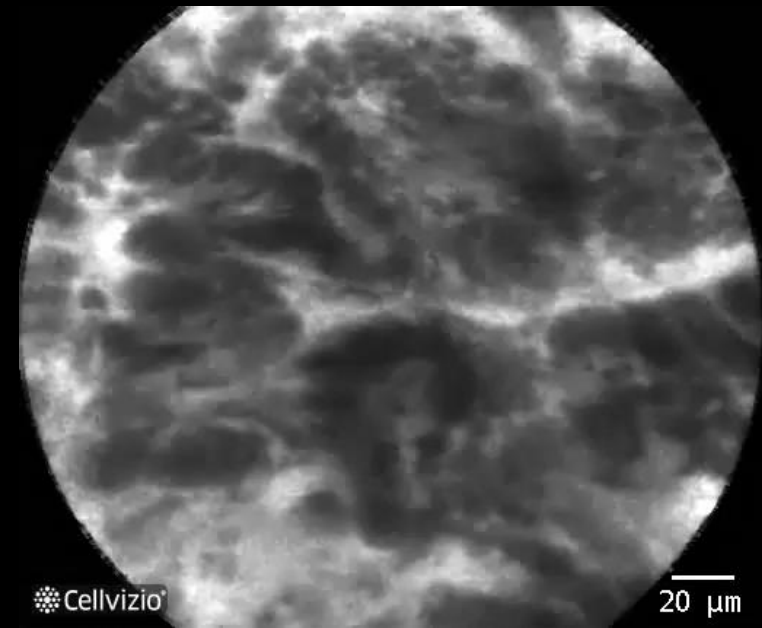
Probe Based

\*Pooled sensitivity and specificity of this technology exceeds 80% for the diagnosis of HGD and EAC

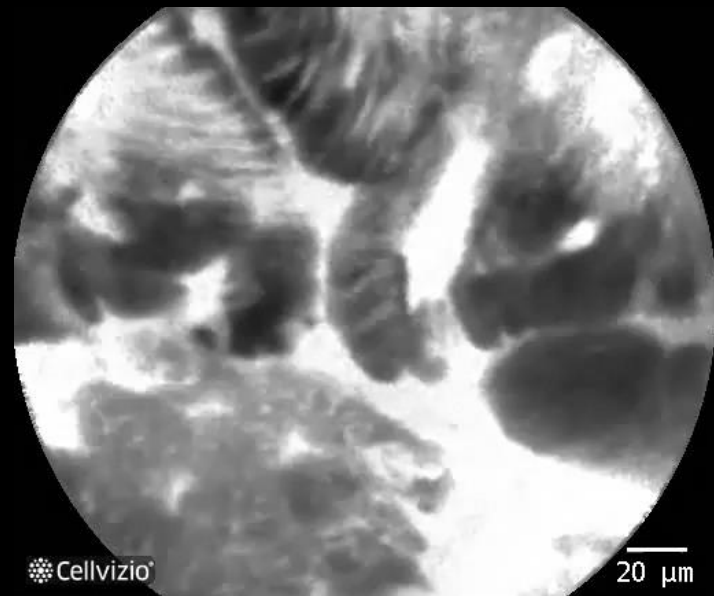
Barrett's Esophagus > Image pattern recognition



intestinal metaplasia



adenocarcinoma



high grade dysplasia

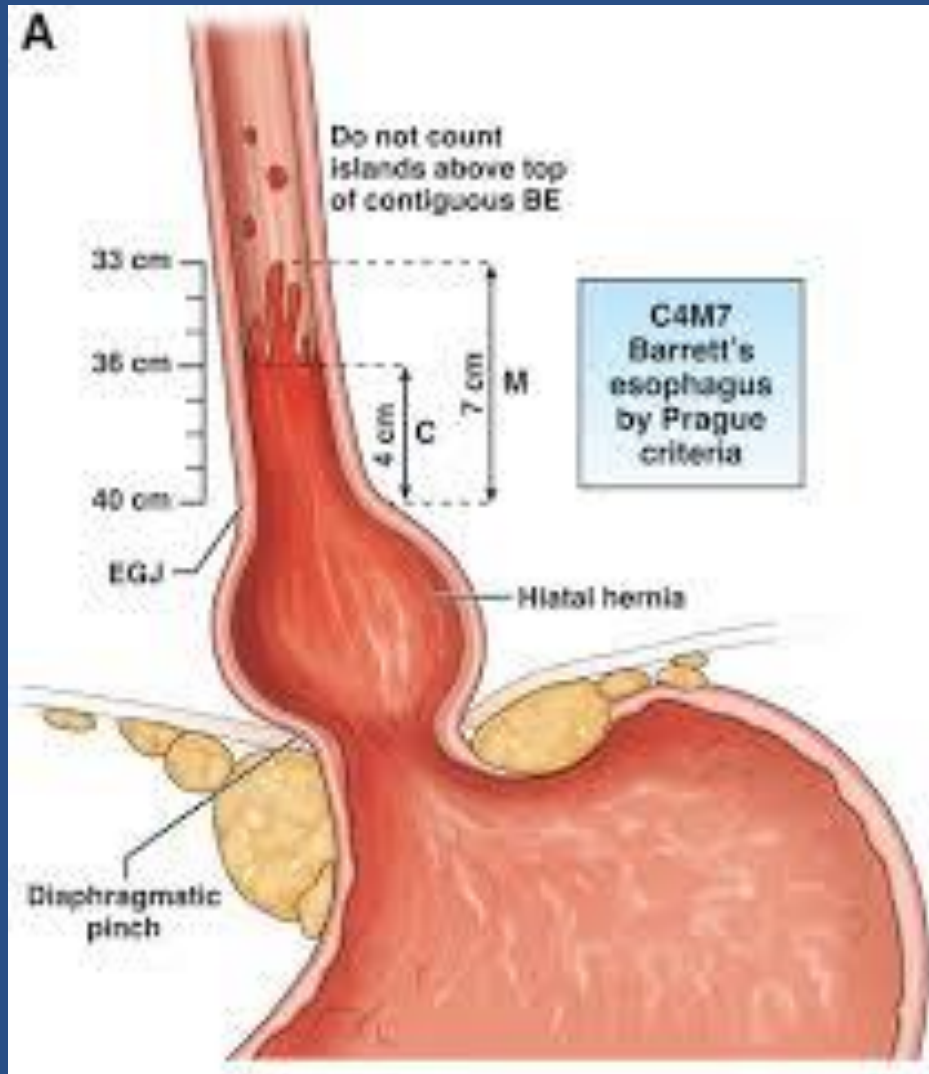
# Innovations in Surveillance

Imaging

**Tissue Sampling**

Biomarker Analysis

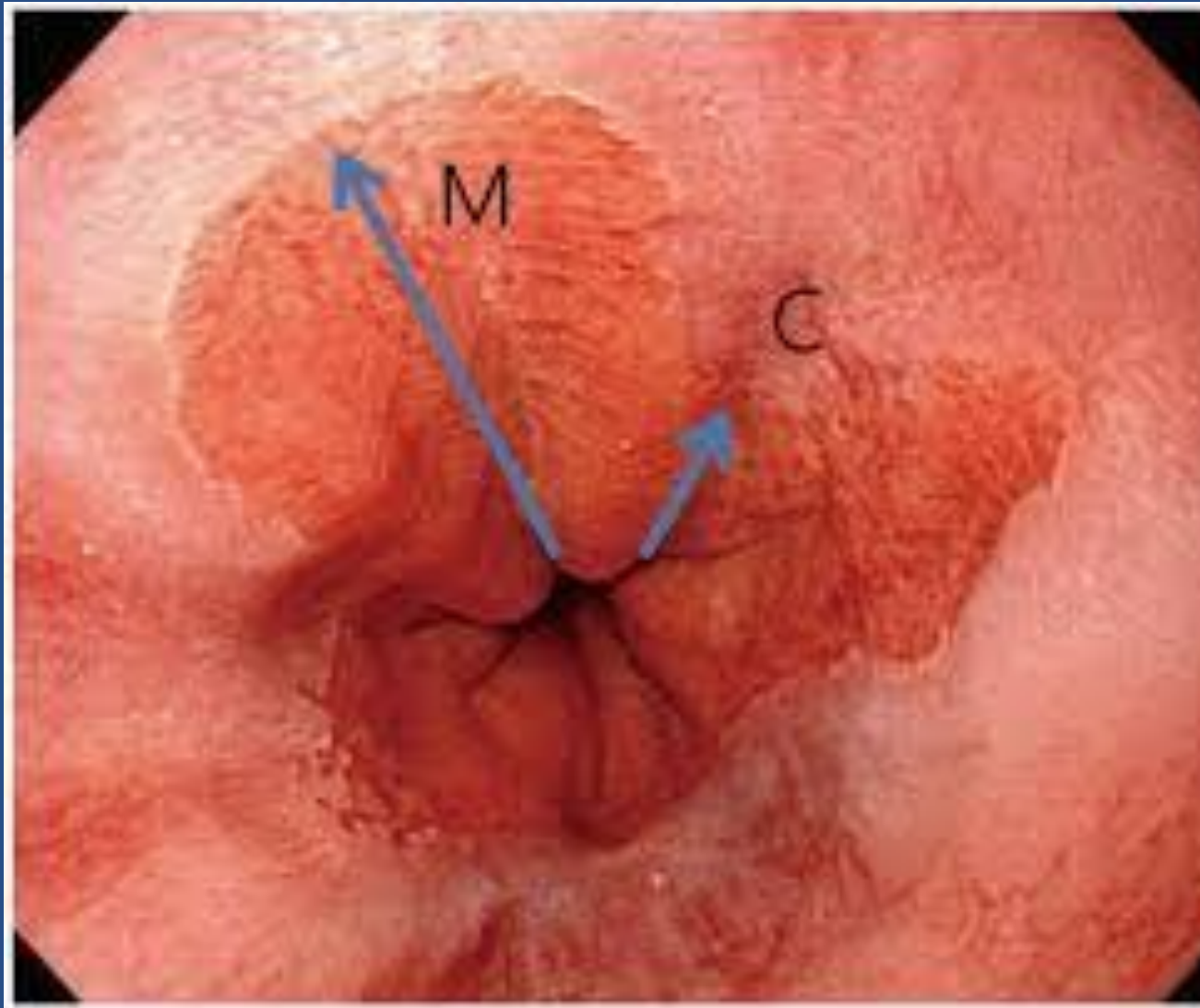
# Endoscopic Surveillance



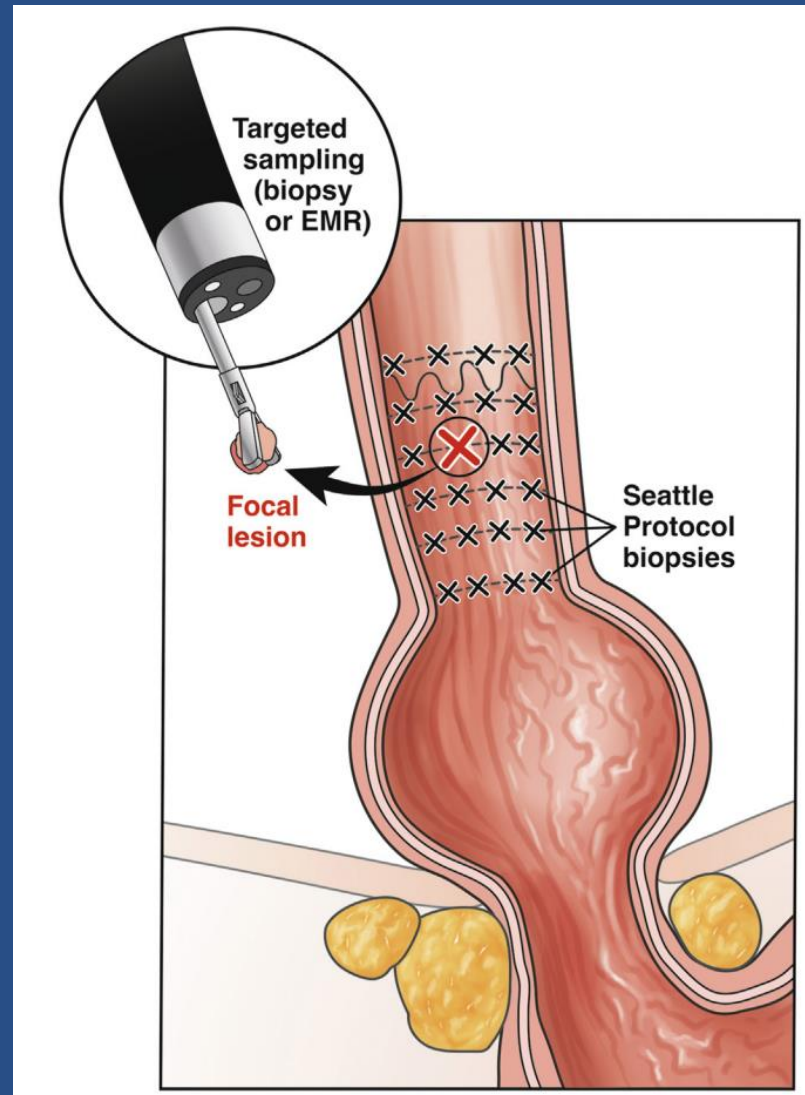
## Prague classification

- **Landmarks:** Measure from the gastroesophageal junction (GEJ) to squamo-columnar junction (SCJ)
- **Reproducible and reliable**, even across observers

Shaheen, N Am J Gastroenterol. 2022 Apr 1;117(4):559–587



# Structured Biopsy Protocol



## Seattle Protocol

- **4-quadrant biopsies every 1–2 cm along the Barrett's segment**
- **Targeted biopsies of any visible lesions**
- **For short segment a minimum of 8 biopsies**

Iyer, P , Chak, A. *Gastroenterology* 2023;  
*Abela J et al. American Journal of Gastroenterology, April 2008.*

# Surveillance may not prevent cancer

## Magnitude and Time-Trends of Post-Endoscopy Esophageal Adenocarcinoma and Post-Endoscopy Esophageal Neoplasia in a Population-Based Cohort Study: The Nordic Barrett's Esophagus Study

Sachin Wani<sup>1</sup>, Dag Holmberg<sup>2</sup>, Giola Santoni<sup>2</sup>, Joonas H Kauppila<sup>3</sup>, Martti Farkkila<sup>4</sup>,  
My von Euler-Chelpin<sup>5</sup>, Nicholas J Shaheen<sup>6</sup>, Jesper Lagergren<sup>7</sup>

## Post-endoscopy Barrett's neoplasia after a negative index endoscopy: a systematic review and proposal for definitions and performance measures in endoscopy

David Lieberman<sup>3</sup>, Sachin Srinivasan<sup>2</sup>, Venkat Nutalapati<sup>2</sup>,  
Anush Kalgotra<sup>4</sup>, Suneha Sundaram<sup>1 5</sup>, Alessandro Repici<sup>6 7</sup>,  
Michael F Kaminski<sup>8 9</sup>, Prateek Sharma<sup>1 2</sup>

## The Effect of Endoscopic Surveillance in Patients with Barrett's Esophagus: A Systematic Review and Meta-analysis

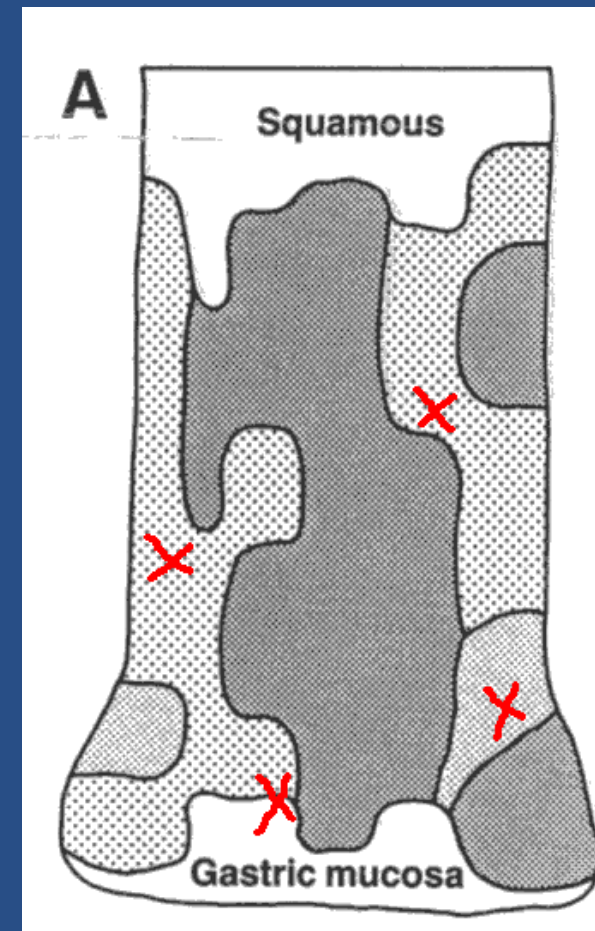
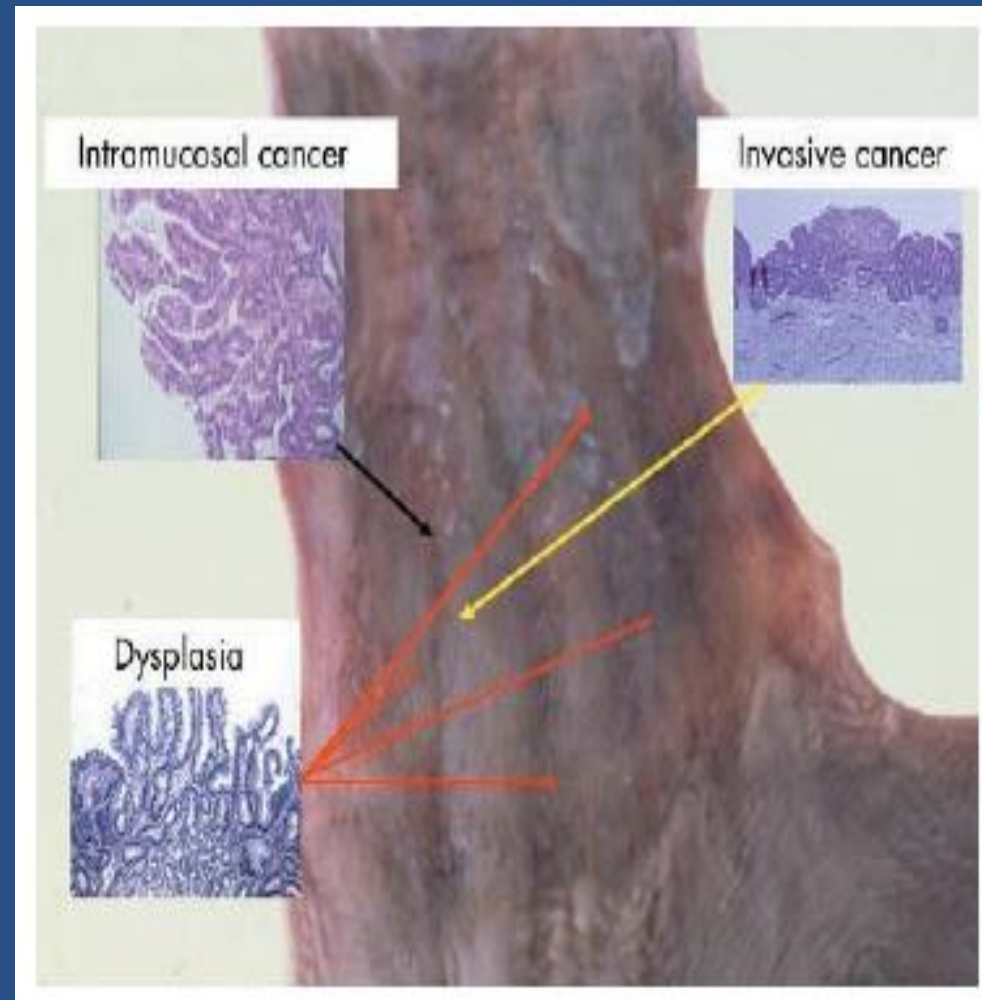
Don Chamil Codipilly<sup>1,\*</sup>, Apoorva Krishna Chandar<sup>2,\*</sup>, Siddharth Singh<sup>3</sup>, Sachin Wani<sup>4</sup>, Nicholas J Shaheen<sup>5</sup>,  
John M Inadomi<sup>6</sup>, Amitabh Chak<sup>2</sup>, Prasad G Iyer<sup>7</sup>

*3% and 13% of Barrett's-related high-grade dysplasia or cancer is diagnosed within one year of the initial endoscopy*

**Why are patients in surveillance programs still ending up with advanced cancer?**

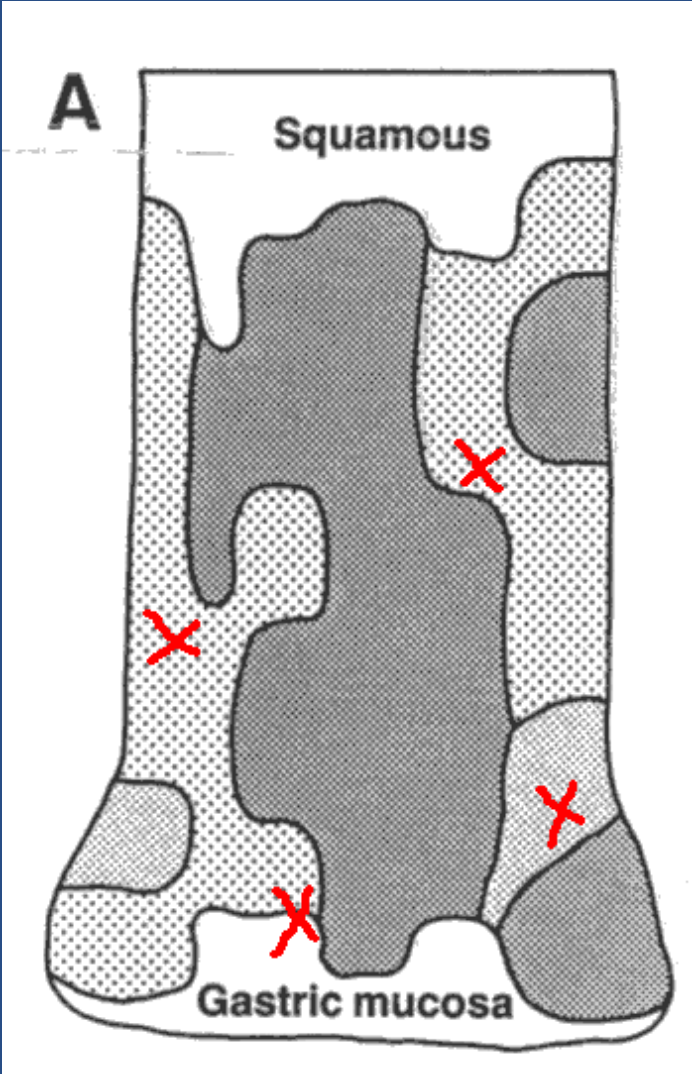
# Sampling Error

*Traditional histology limitations: sampling error (4Q biopsies cover <5% of BE surface), significant interobserver variability, binary staging misses molecular heterogeneity*



- Metaplasia ("specialized")
- Indefinite for Dysplasia/  
Low Grade Dysplasia
- High Grade Dysplasia
- Cancer

# Theoretical advantage to brush sampling

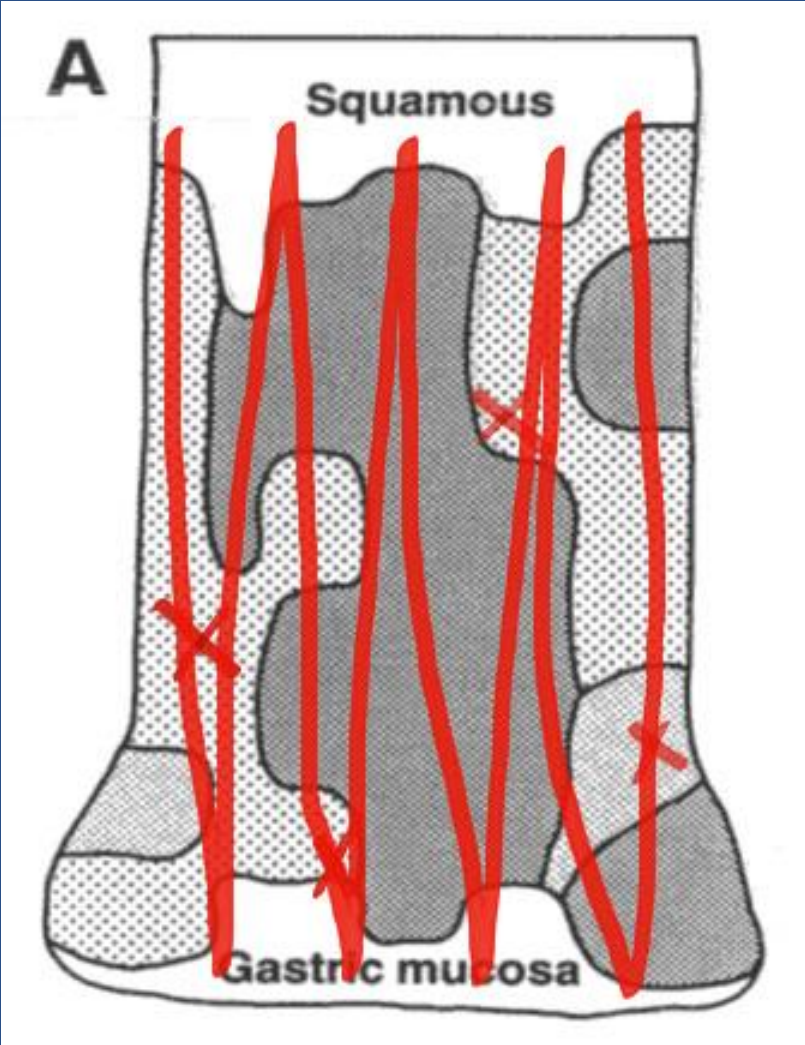


Forceps biopsy has significant potential for sampling error

The brush biopsy samples a much larger area

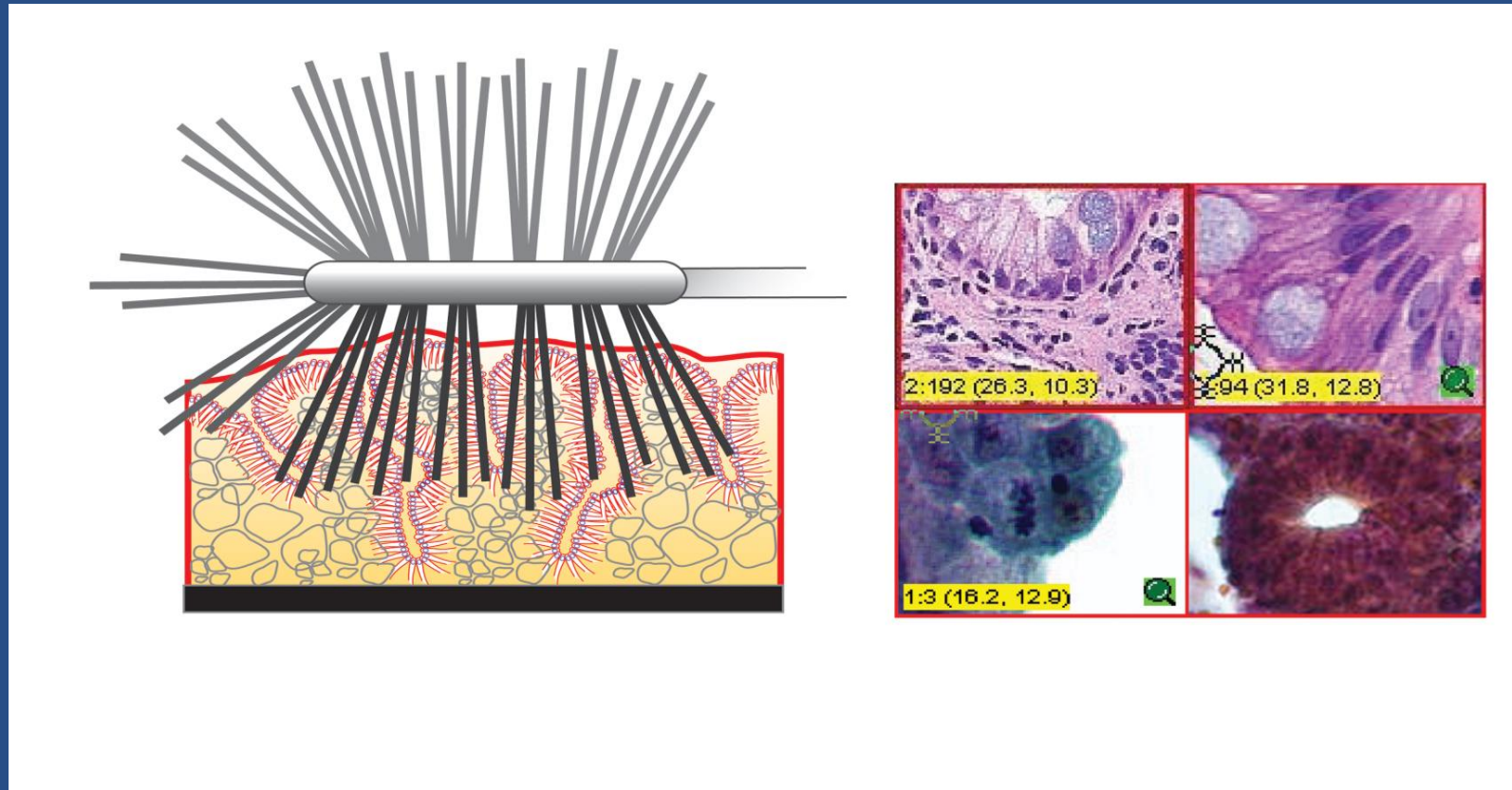


- Metaplasia ("specialized")
- Indefinite for Dysplasia/ Low Grade Dysplasia
- High Grade Dysplasia
- Cancer



# Biopsy Brush

- EndoCDx WATS<sup>3D</sup> Brush
  - Obtains transepithelial biopsy



# WATS<sup>3D</sup> Society Guidelines/Recommendations



August 2019

WATS<sup>3D</sup> was included in ASGE Guidelines for the screening and surveillance of Barrett's esophagus



January 2020

The American Foregut Society (AFS) published a white paper supporting the routine use of WATS<sup>3D</sup> for the evaluation of BE

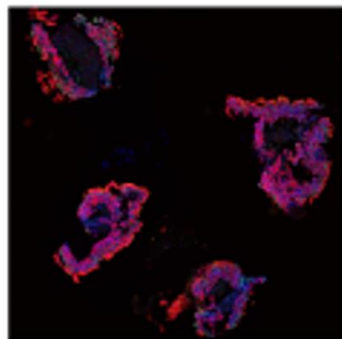


June 2020

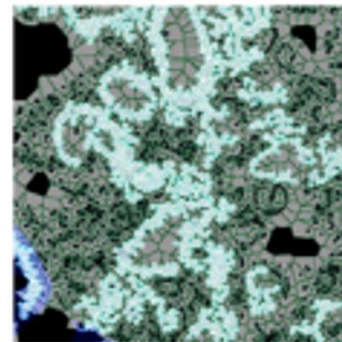
The SAGES Technology and Value Assessment Committee (TAVAC) concluded that “WATS<sup>3D</sup> is a safe and effective adjunctive to forceps biopsies in the evaluation of BE, low-grade dysplasia, and high-grade dysplasia.”

# TissueCypher

**Multiplexed Fluorescence  
Labeling & Imaging of 9  
Biomarkers & Nuclei**



**Quantitative  
Image Analysis <sup>1</sup>**



15 Features  
automatically  
extracted by  
image  
analysis  
software

**Risk  
Classification <sup>2</sup>**

15 Features  
Scaled & Weighted\*



Risk Score\*

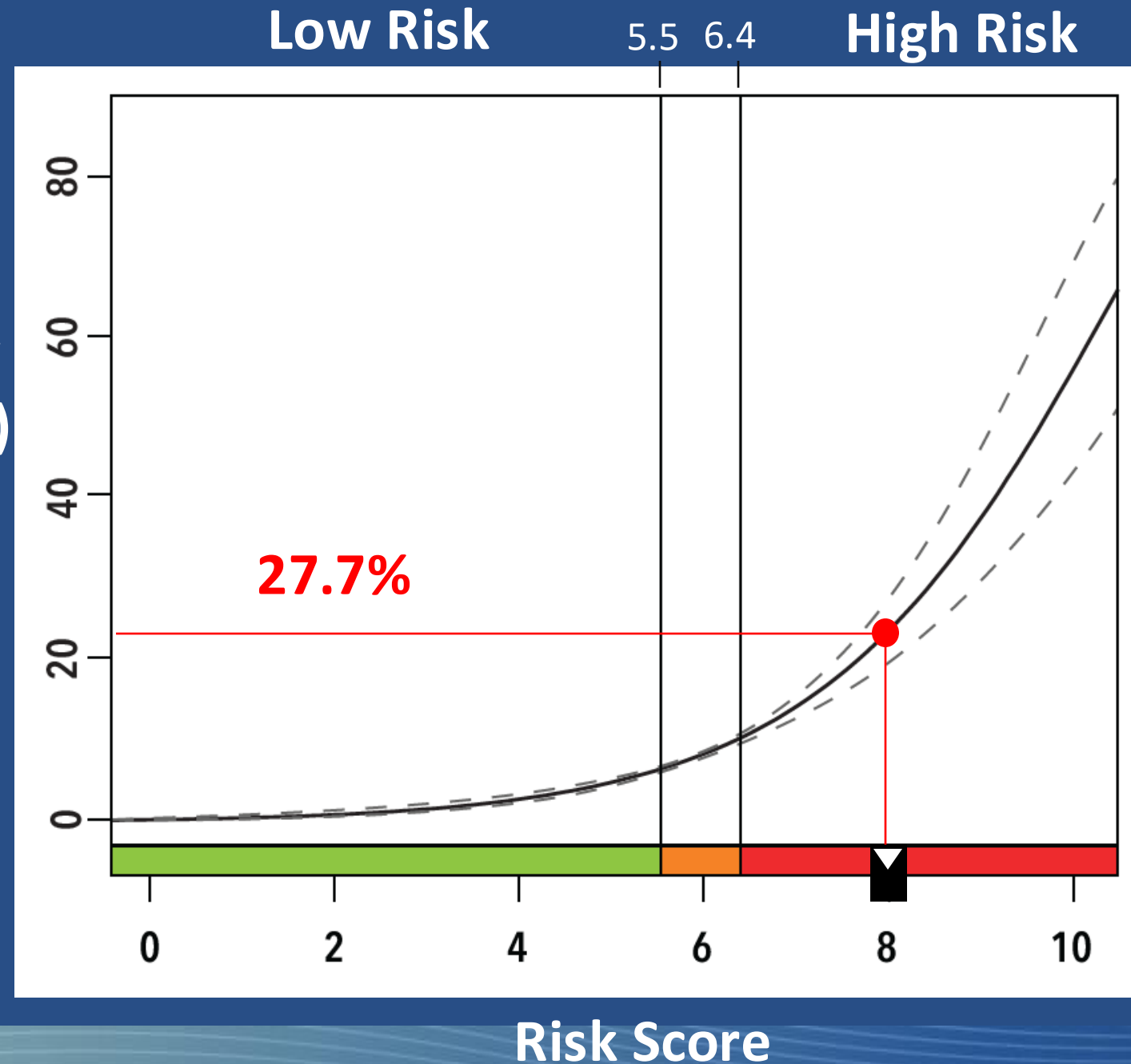


Low Risk    Inter Risk    High Risk  
(0 - <5.5)    (5.5 - <6.4)    (6.4 - 10)

<sup>1</sup>J Pathol Inform. 2015 Aug 31;6:48. <sup>2</sup>Critchley-Thorne et al., Cancer Epidemiol Biomarkers Prev. 2016 Jun;25(6):958-68.

# TissueCypher Results

5-year Probability  
of Progression (%)



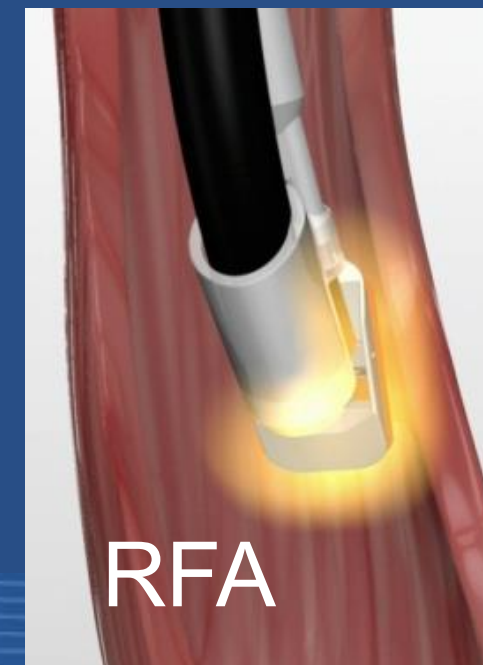
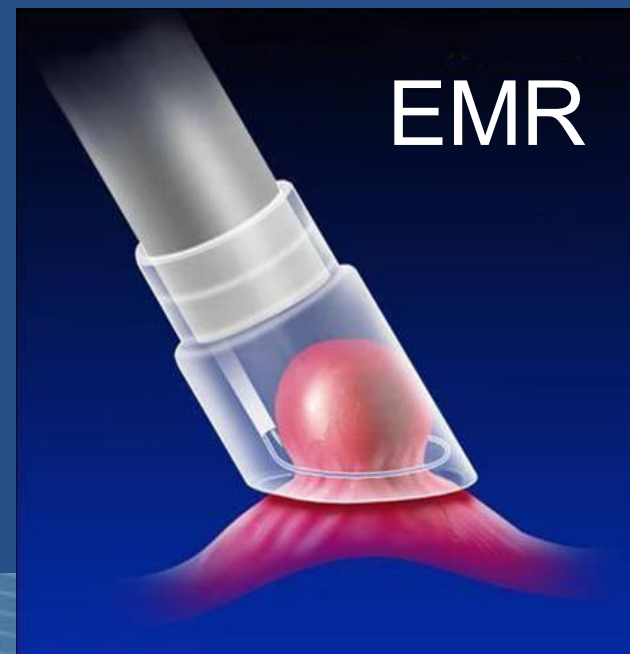
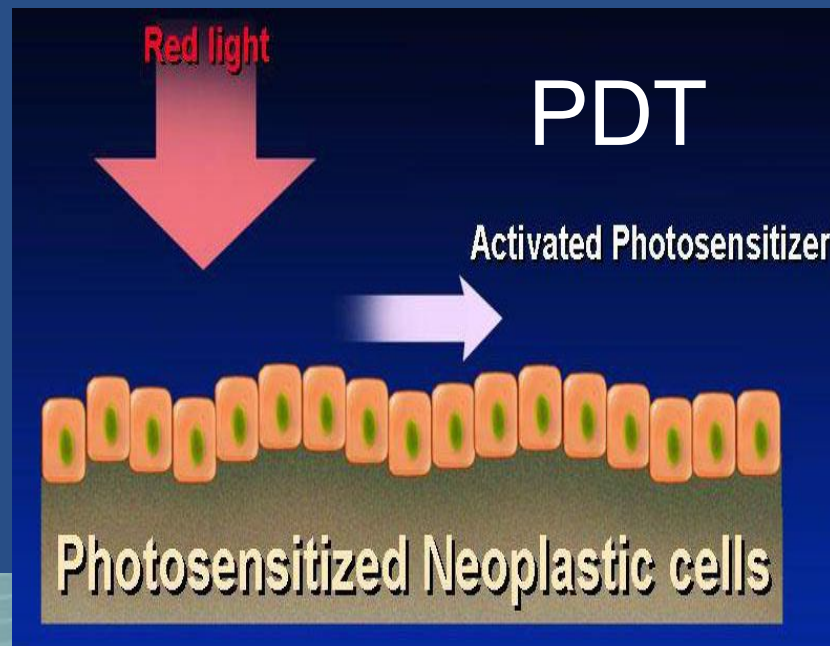
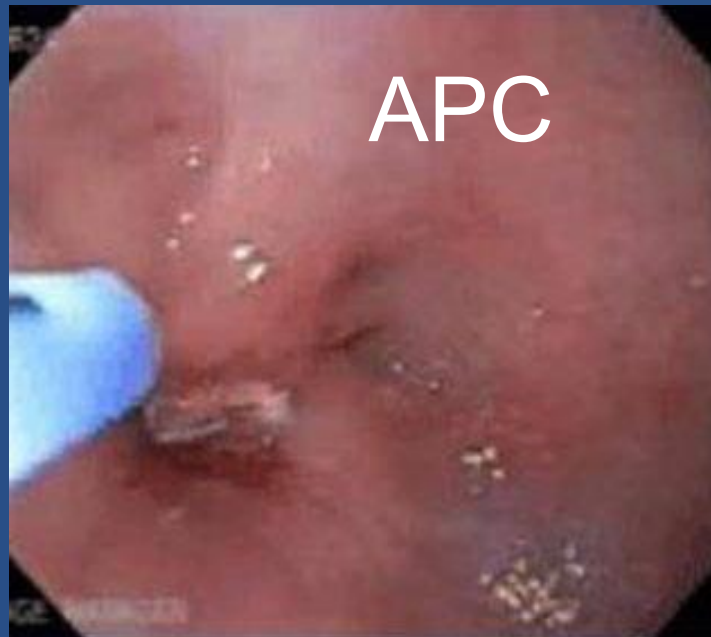
Risk CATEGORY
5 year progression risk
HIGH
INTERMEDIATE
LOW

# Endoscopic Eradication Therapy

# An ideal therapy would ...

- Completely eradicate the lesion
- Be safe & well-tolerated
- Prevent neoplastic progression
- Alter life-long surveillance

# Mucosal Ablation

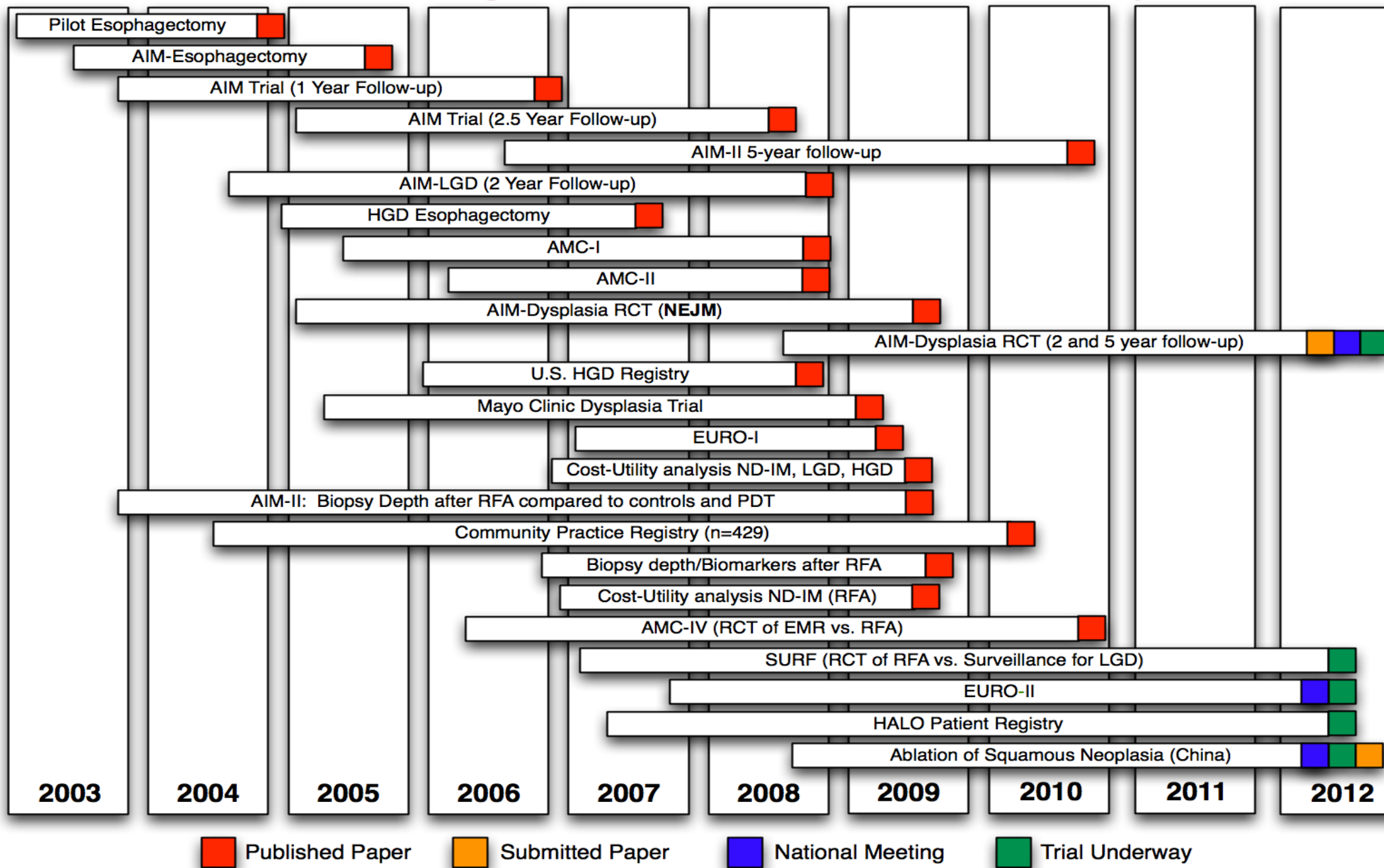


# Radiofrequency Ablation



## Clinical Trial Timeline

### Studies Assessing the HALO<sup>90</sup> and HALO<sup>360</sup> Ablation Systems

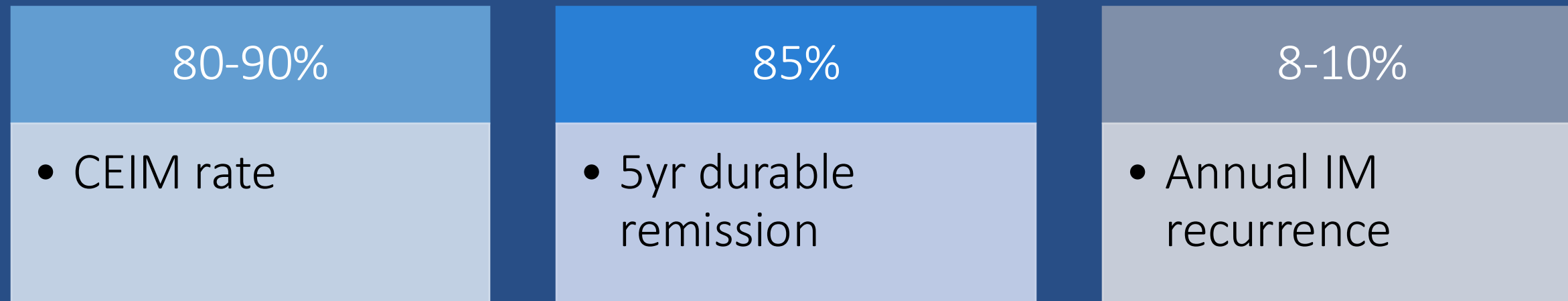


# Ablation Device Family



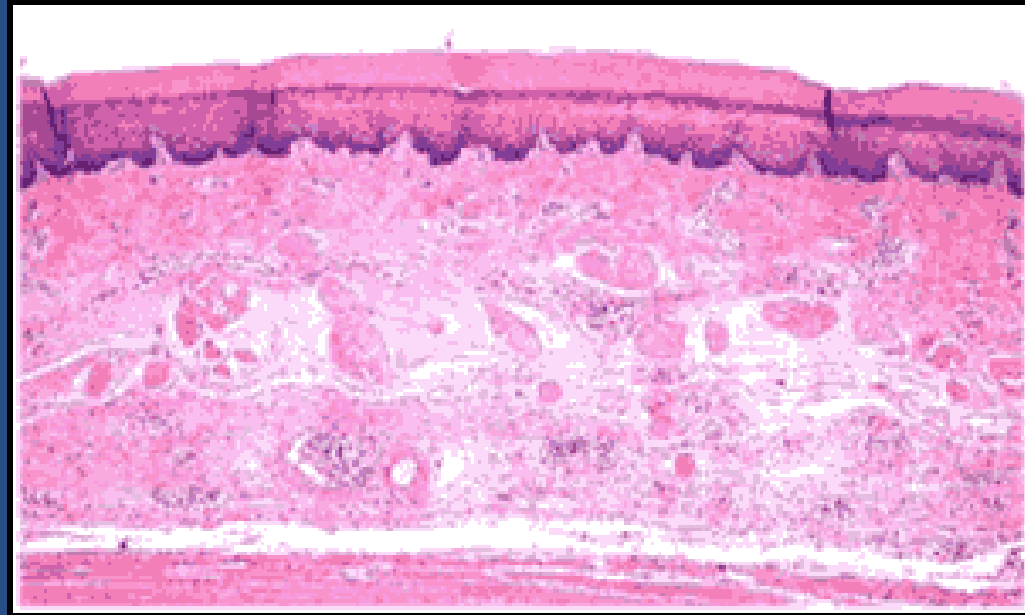
# Ablation: RFA

- RFA is the gold standard for flat dysplasia in BE

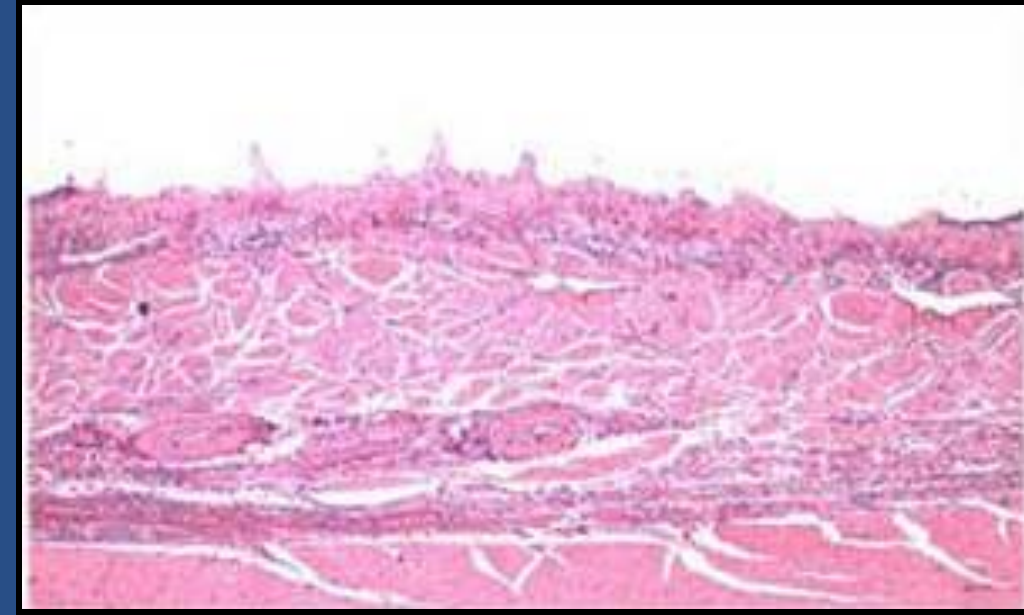


*Predictors for treatment failure: long segment BE, large hiatal hernia, inadequate acid suppression, prior EMR scarring, incomplete ablation on initial treatment*

# Histological Representation



Normal



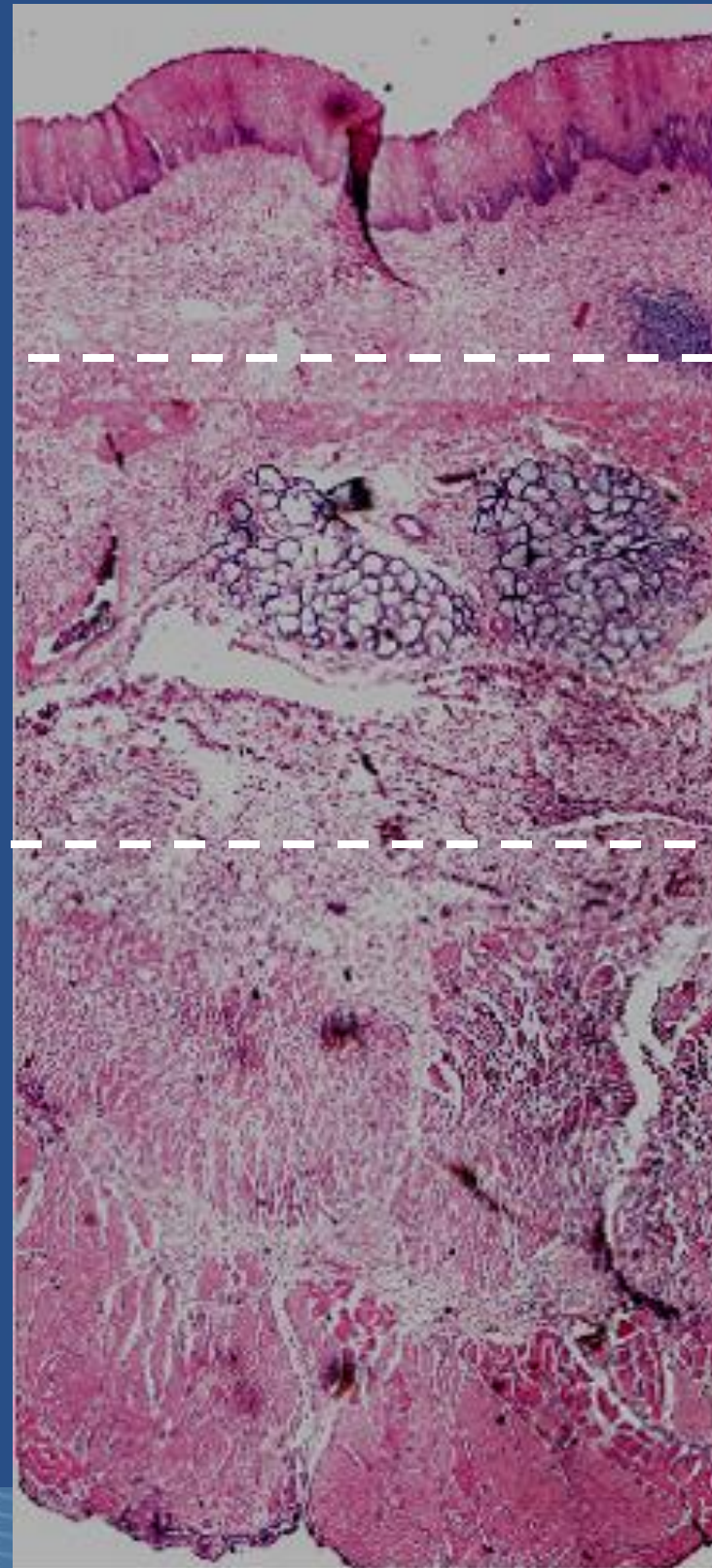
Post RF Ablation

# Human Esophagus

Epithelium  
Lamina Propria  
Muscularis Mucosae

Submucosa

Muscularis Propria



RFA Depth

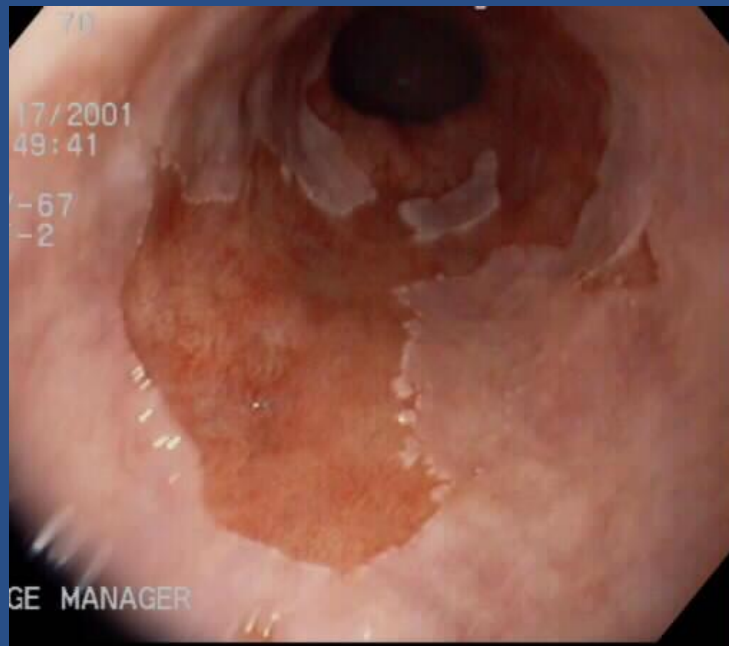
PDT, APC &  
Cryo Depth

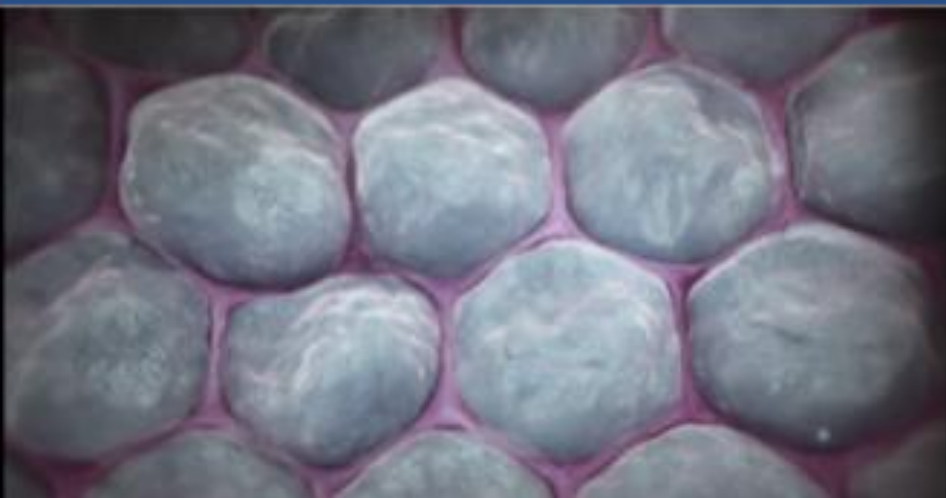
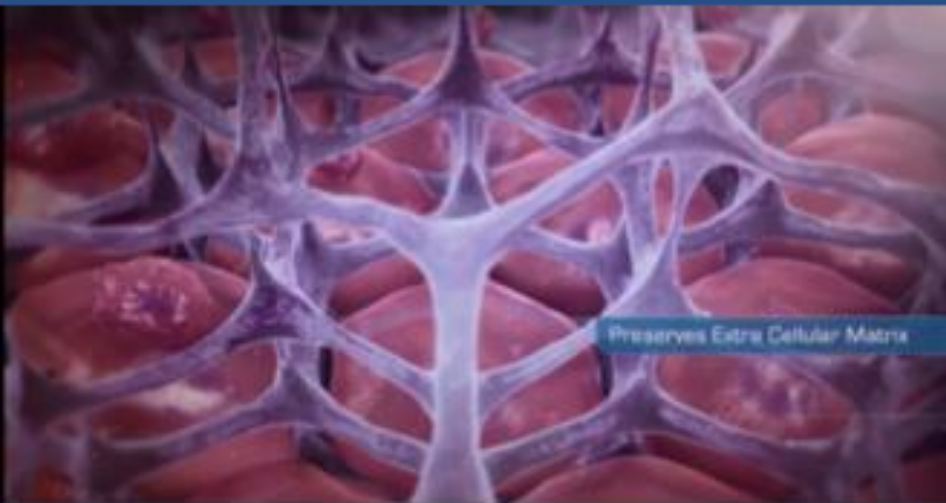
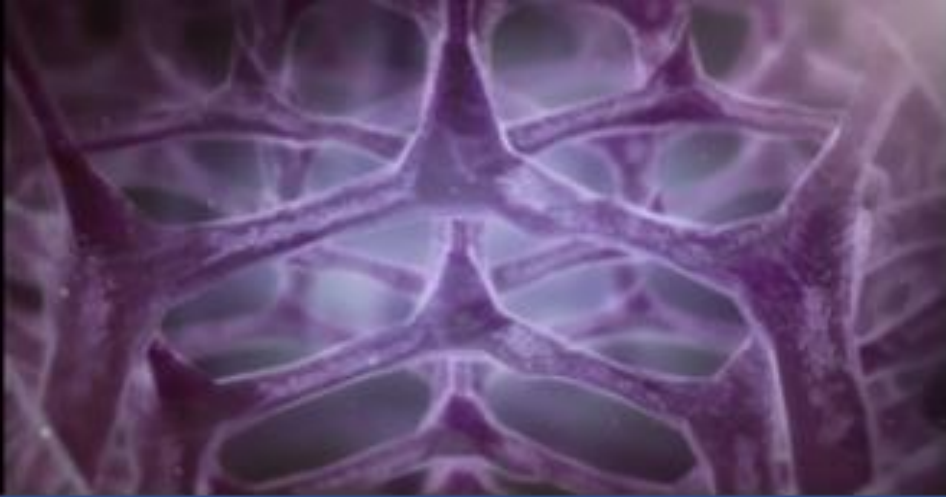
EMR Depth

Surgical  
Depth

# Cryoablation

**Mechanism:** Flash-freezing via rapid freeze–thaw cycles causes cell membrane rupture while preserving submucosal collagen scaffold → promotes favorable wound healing | Two FDA-cleared delivery systems: **Cryoballoon (N<sub>2</sub>O)** • **Spray Cryotherapy (liquid N<sub>2</sub> / CO<sub>2</sub>)**





**Mechanism:** Flash-freezing via rapid freeze–thaw cycles causes cell membrane rupture while preserving submucosal collagen scaffold → promotes favorable wound healing | Two FDA-cleared delivery systems: **Cryoballoon (N<sub>2</sub>O)** • **Spray Cryotherapy (liquid N<sub>2</sub> / CO<sub>2</sub>)**

# Ablation: Cryotherapy

## Cryoballoon (CSA, Merit Endoscopy)

- Prospective data now comparable to RFA for CEIM. (CE-IM 64.1%, Recurrence ~8.3%)
- Simpler setup, good tolerance, FDA-cleared.

## Best Roles Today

- RFA failures (CE-D 76%, CE-IM 46%)
- Patient tolerance/anatomy issues/Post-EMR scarring
- Increasing first line at high volume centers

## Cryo Spray (Steris)

- Longer established, flexible delivery, good for irregular anatomy.
- Malignant & palliative
- Requires CO<sub>2</sub> decompression venting.

**Bottom line:** Cryo = RFA for dysplastic BE in head-to-head data. Role expanding beyond salvage — first-line, post-EMR scar, radiation-altered mucosa, IMC, and palliative.

# Esophageal Cancer Palliation



National  
Comprehensive  
Cancer  
Network®

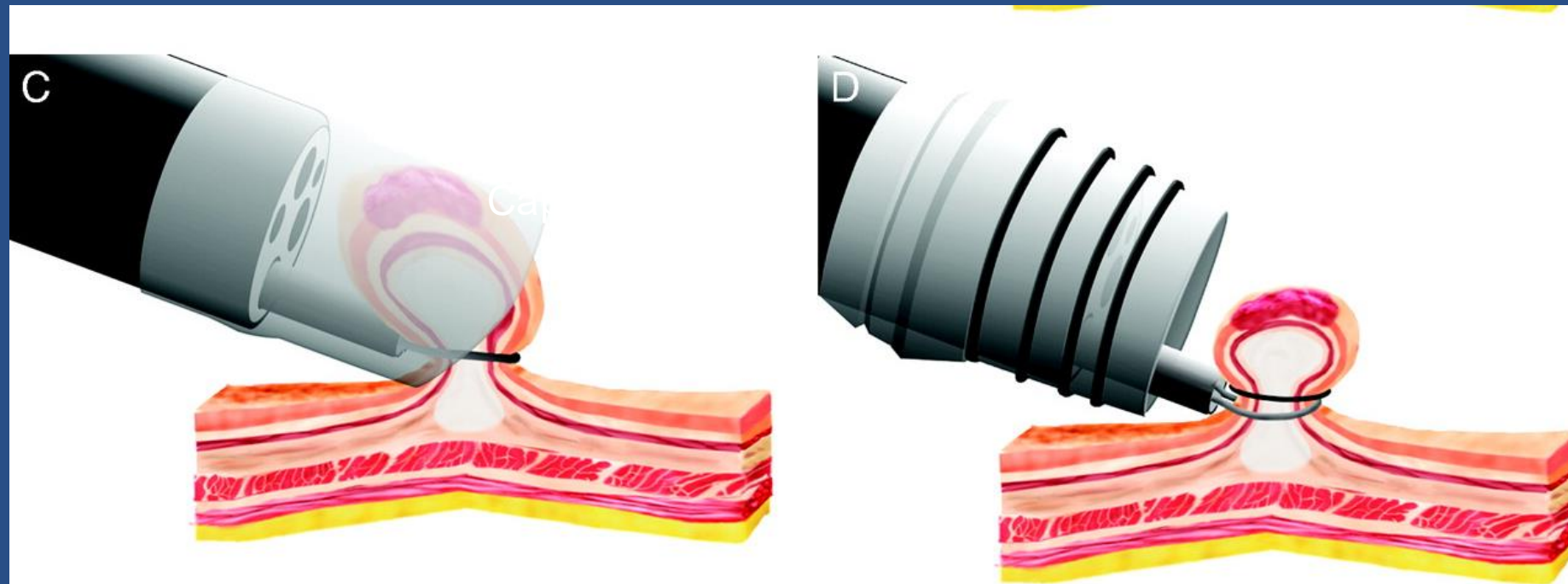
**NCCN Guidelines Version 2.2012**  
**Esophageal and Esophagogastric Junction Cancers**

[NCCN Guidelines Index](#)  
[Esophageal Table of Contents](#)  
[Discussion](#)

- Long term palliation of dysphagia can be achieved with endoscopic tumor ablation by Nd: YAG laser, **Cryotherapy** and insertion of expandable metal or plastic stents

# Endoscopic Management of Early Esophageal Cancer (T1a and T1b)

- Endoscopic Mucosal Resection = Esophagectomy for outcomes in low risk T1aN0MO grade I (stage IA) EAC at high risk centers.
- Overall excellent long term outcomes in stage IA EAC.



# Endoscopic Resection: EMR vs ESD

Always resect visible nodules before ablation – but the technique choice drives staging accuracy and surgical decision making

## EMR – Mucosal Resection

- Cap-assisted or multiband mucosectomy
- Ideal for nodules < 2 cm
- Well-validated, widely available
- Piecemeal resection acceptable for flat lesions
- Upstages pathology in ~30–40% of cases
- Go-to for most visible lesions in BE

## ESD – Submucosal Dissection

- En bloc resection regardless of size
- Required for lesions > 2 cm or when sm invasion suspected
- Allows accurate T-staging (sm1 vs sm2/3)
- Critical for the surgery decision
- US adoption growing but still lags Asia/Europe
- Higher technical difficulty; referral to expert centers

# Key Takeaways

1

- Confirm ALL dysplasia with an expert GI pathologist before any management change

2

- Molecular risk stratification (TissueCypher) is entering mainstream practice — know when and how to use it

3

- Resect visible lesions FIRST — never ablate over a nodule; EMR/ESD drives staging and surgical decision-making

4

- RFA is durable (~85% at 5 years) but not curative — post-EET surveillance is lifelong; recurrence risk never reaches zero



Thank you!

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