

Optical Imaging: Which Modalities Should Every Endoscopist Know and Love?

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Disclosures

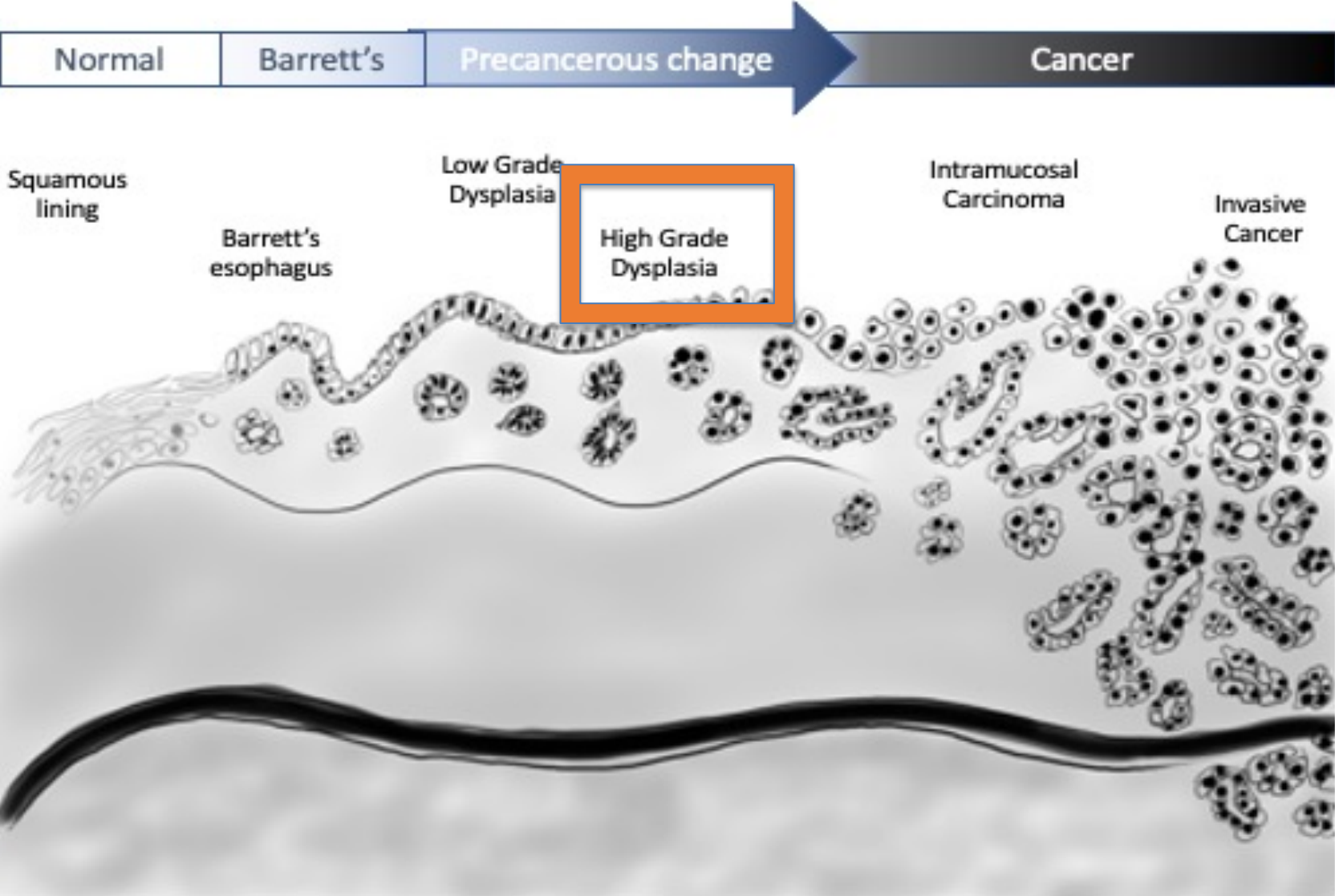
Current

- Exact Sciences (Advisory Board)
- Lucid (Research)
- Cernostics (Consulting)
- Medtronic (Consulting)
- Ambu (Consulting)

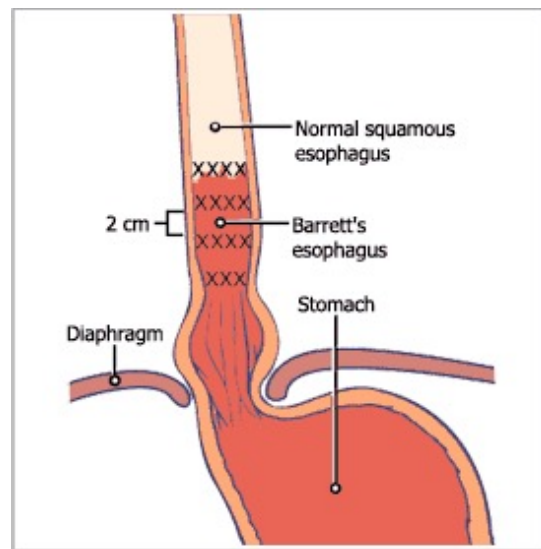
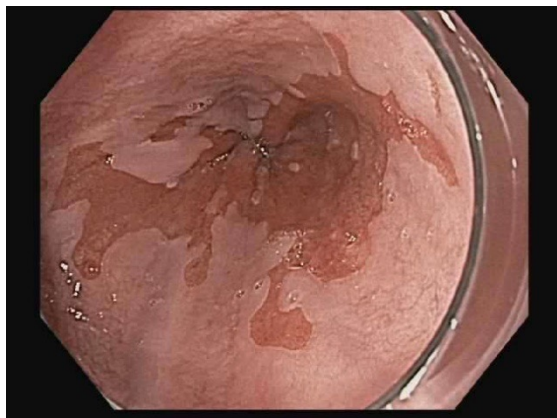
Past

- Olympus (Research)
- Pentax (Research)
- Mauna Kea Technologies (Speaking, Consulting)

Histology in Barrett's Esophagus



Standard Surveillance for Detection of Dysplasia



- **Endoscopic documentation**

- Longer segments are at higher risk of neoplasia than short segments.
- Suboptimal documentation of length and biopsy protocol

- **Visible lesions**

- Higher risk for harboring neoplasia
- Can be subtle and challenging to detect
- Variable detection of lesions
 - Community vs expert (60% v 87%)

- **Seattle Protocol**

- Visible lesions
- Multiple levels for occult disease
 - random 4QB q1-2 cm
 - q1 cm if history of dysplasia
- Limitations
 - Sampling error
 - Lag time in diagnosis
 - Poor adherence with protocol is associated with increased risk of missed neoplasia.
 - Longer segments are associated with poor adherence

Reid BJ et al. Am J Gastroenterol. 2000

Peters et al. Dis Eso 2008

Wani et al. GIE 2019

Scholvinck et al. Endoscopy 2017

Boys et al J Gastrointest Surg 2020

Curvers et al Eur J Gastro Hep 2008

High Quality Endoscopic Assessment: “5 L’s”

5L's	Assessment	Tools & Tips
Landmarks	Endoscopic Landmarks <ul style="list-style-type: none"> - Diaphragmatic Impression - Top of Gastric folds - Squamocolumnar Junction 	
Length	Length of Barrett’s segment Length and Extent of esophagitis	Prague Classification (C and M) Los Angeles grading system
Look	Take time to inspect and evaluate for subtle lesions	High resolution endoscope Distal attachment cap Chromoendoscopy and virtual chromoendoscopy Inspection Technique Recognition of Subtle Lesions
Lesions	Identify, Document, and Target Visible lesions which have high risk of harboring neoplasia	Paris Classification Tissue acquisition with EMR or targeted biopsies
Levels	Assess multiple levels for occult dysplasia	Seattle Protocol Additional Tissue Acquisition techniques

Foundation for Better Detection

Tools

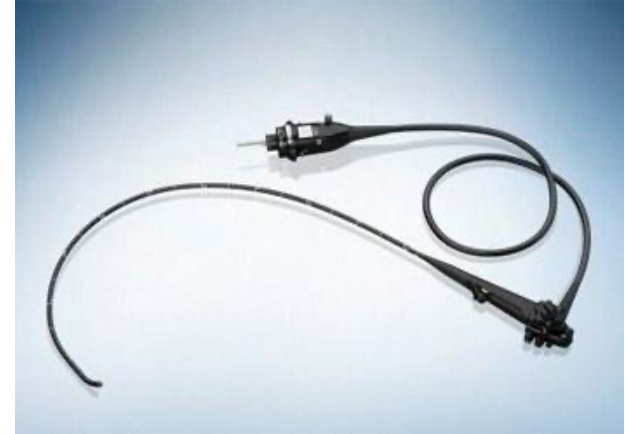
- High resolution endoscopy
- Soft distal attachment cap
- Enhanced endoscopic imaging

Techniques

- Suction, Irrigation & Mucolytics
- Insufflation and Deflation
- Tip deflection
- Retroflexion

Recognition

- Inspect
 - Longer Inspection time is associated with higher rates of detection
 - Suspicious lesions (p=0.0001)
 - HGD/EAC (p=0.001)
 - >1 min / centimeter BIT
- Train to recognize subtle, flat lesions



Foundation for Better Detection

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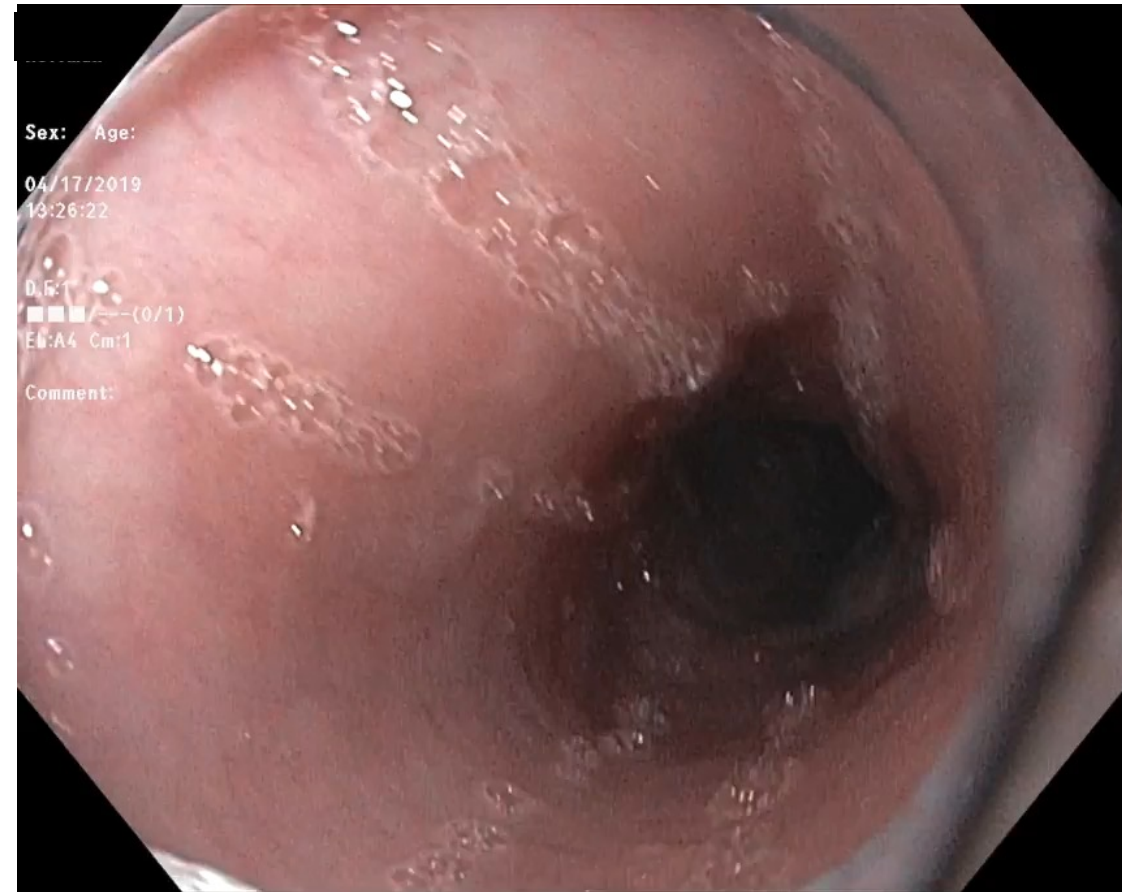
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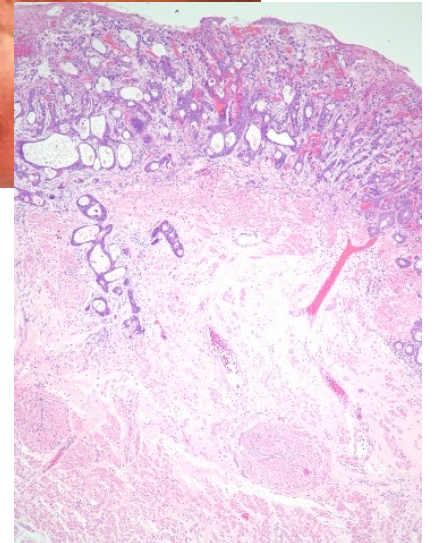
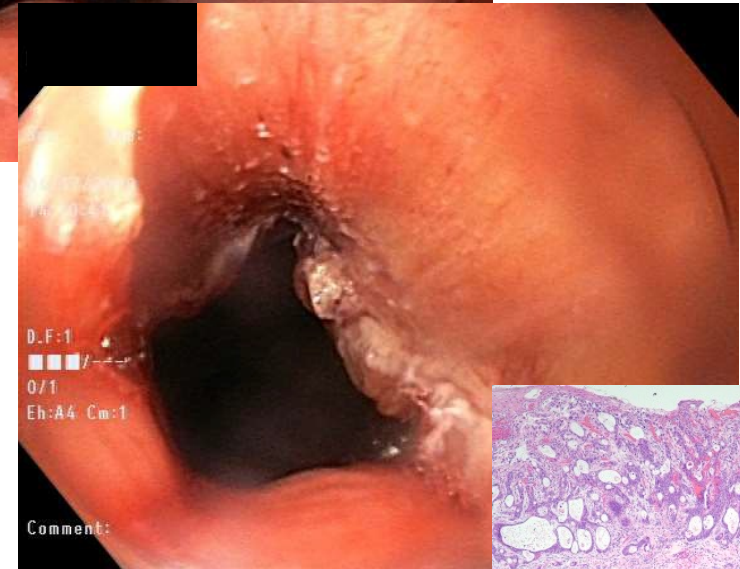
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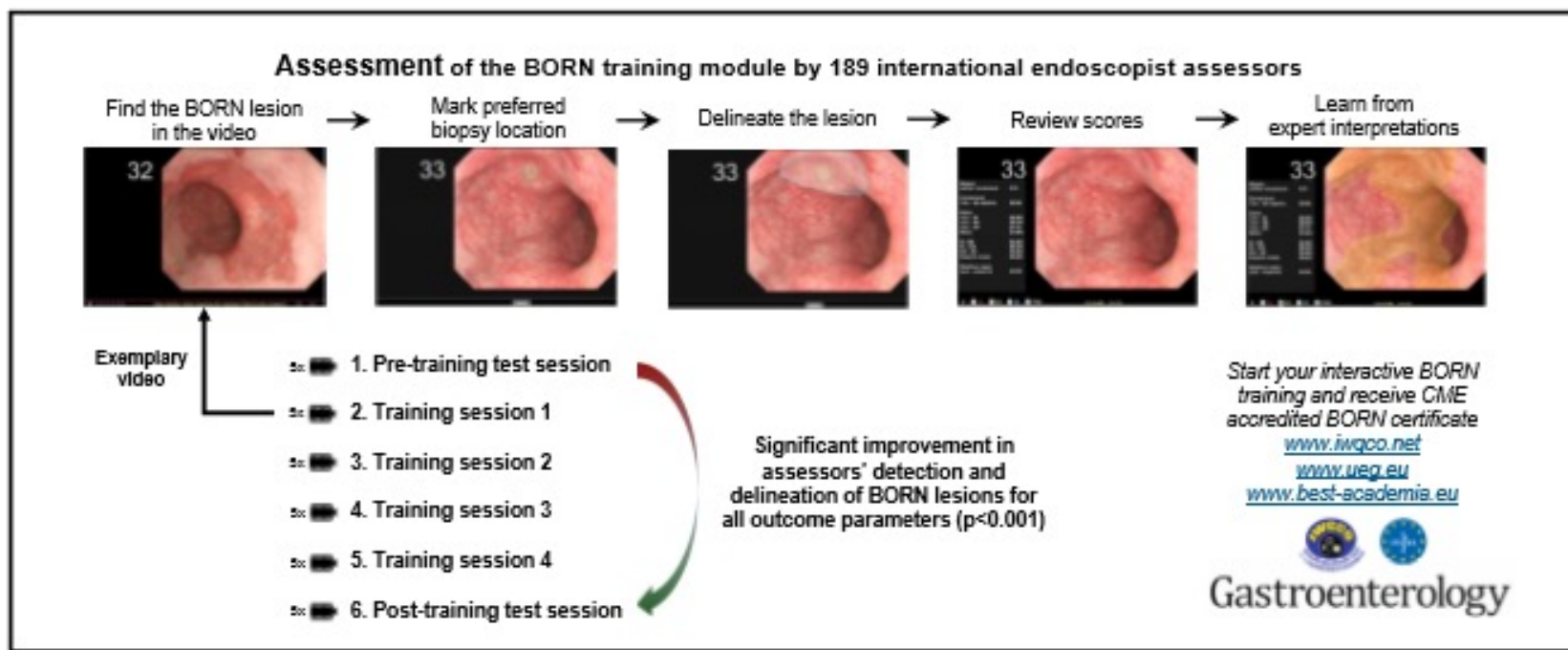
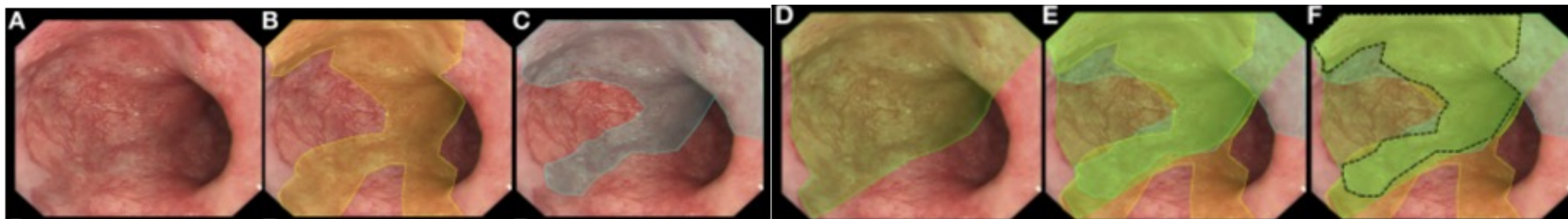
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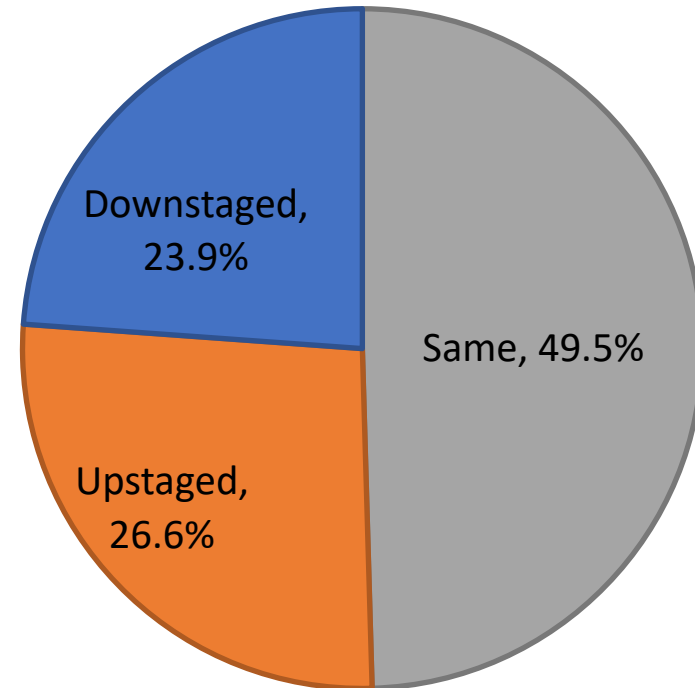
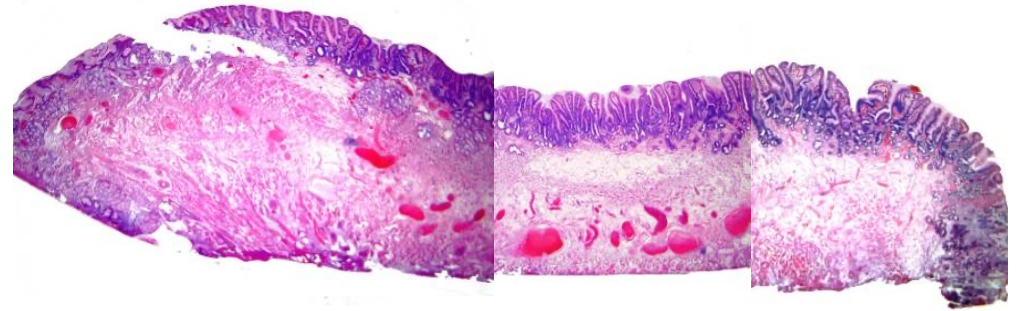
Recognition Training Module



Diagnosis by EMR

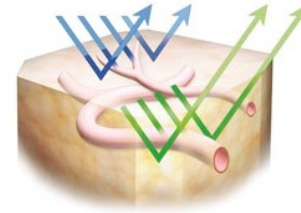


- Endoscopic mucosal resection (EMR) should be done to stage any visible lesion in the setting of dysplasia.
- EMR more accurate than biopsies for assessing neoplasia in BE.
 - 1/3 – 1/2 of DX by biopsy up-staged or down-staged p/ EMR
 - Higher IOA among pathologists with EMR than with biopsy
- EUS not recommended for early T staging
 - Meta-analysis (n=895, 11 studies) 75% accuracy
 - Overstaging and understaging of early T lesions
 - Appropriate for N staging

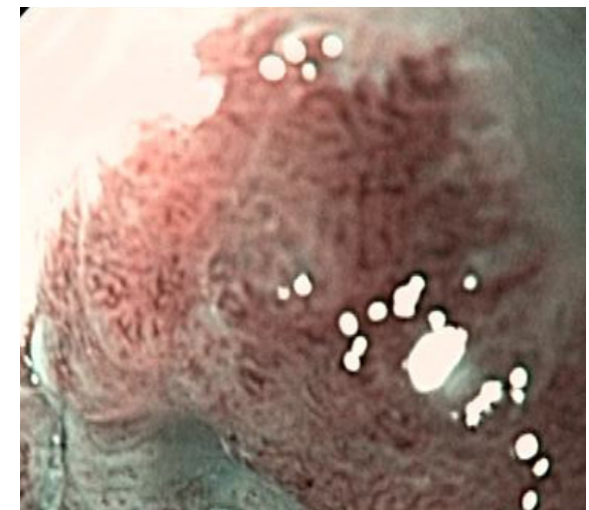
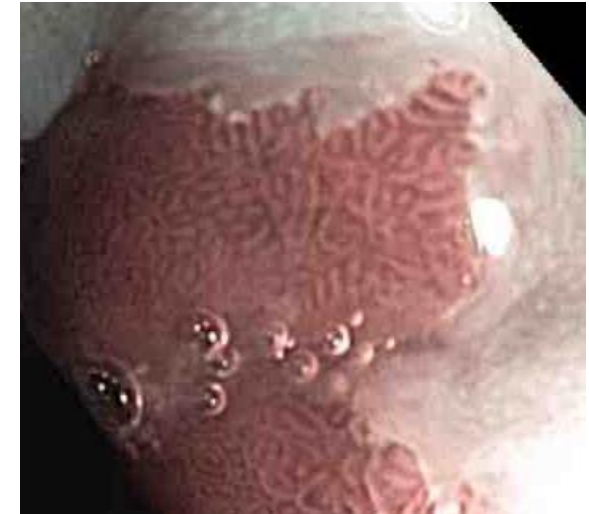


*Konda et al. CGH 2014; Chennat, Konda et al. AJG 2009;
Thota et al. DDW 2014; Wani et al. CGH 2010; Wani et al. DDS
2013; Qumesya et al Dig Liver Dis 2018; Qumseya et al. GIE 2019*

Digital Chromoendoscopy



- Narrow band imaging (NBI)
 - Filtered Blue Light
 - Enhances Mucosal pattern and Vascular Pattern
 - Most studied



	Sensitivity	NPV	Specificity
PIVI Threshold	90%	98%	80%
Overall Performance	94.2%	97.5%	94.4%

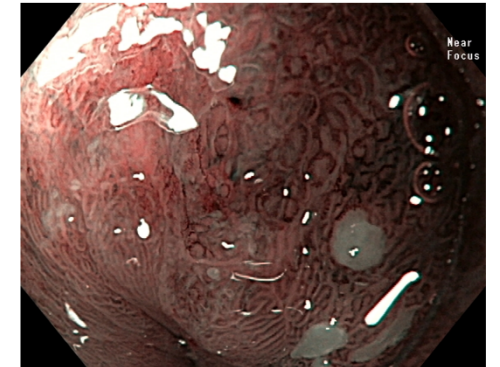
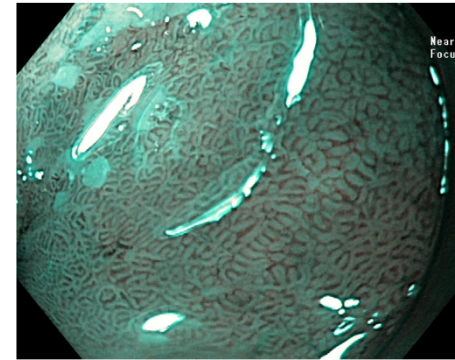
BING Criteria: Consensus Development

Morphologic characteristics	Classification
Mucosal pattern	
Circular, ridged/villous, or tubular patterns	Regular
Absent or irregular patterns	Irregular
Vascular pattern	
Blood vessels situated regularly along or between mucosal ridges and/or those showing normal, long, branching patterns	Regular
Focally or diffusely distributed vessels not following normal architecture of the mucosa	Irregular

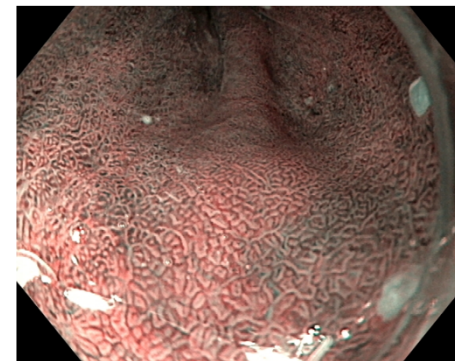
Regular

Irregular

Mucosal



Vascular



NBI with Near Focus

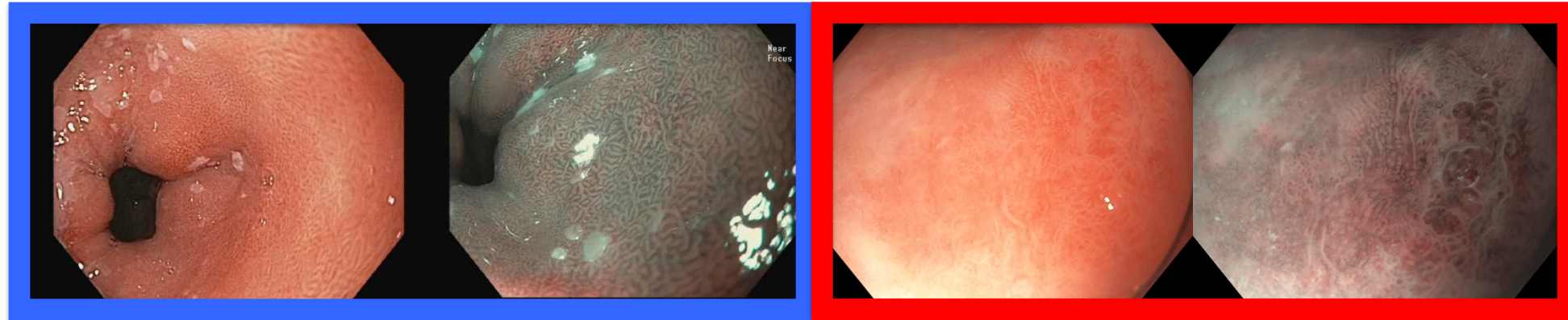


Table 4. Accuracy and Sensitivity Analysis of the BING Criteria for the Prediction of Dysplasia in Barrett's Esophagus

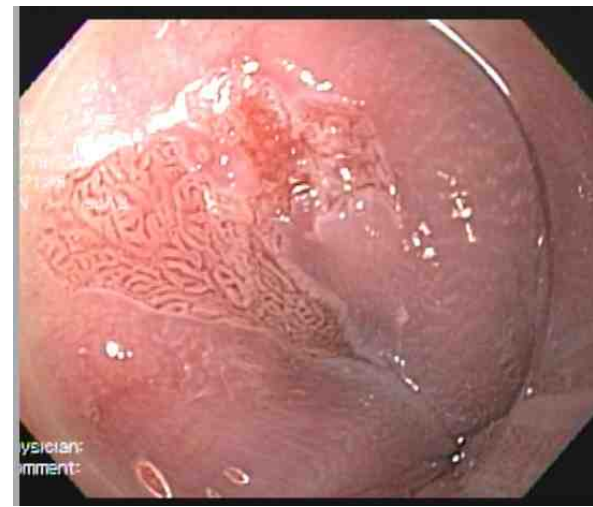
Predictions	Accuracy, % (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
Overall	85.4 (82.6–87.9)	80.4 (75.6–85.1)	88.4 (85.4–91.4)	80.7 (75.9–85.4)	88.3 (85.2–91.2)
High-confidence	92.2 (89.3–94.5)	91.1 (86.8–95.4)	92.9 (89.8–95.9)	88.5 (83.7–93.2)	94.6 (91.8–97.2)
Low-confidence	74.1 (68.4–79.2)	62.4 (52.9–71.8)	81.1 (75.1–87.0)	66.3 (56.8–75.8)	78.3 (72.1–84.4)

CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

* Confidence in NBI with near focus 92% versus 74.1% $p < 0.001$

Acetic Acid (AA)

- Acetic acid
 - Chromoendoscopy
 - Contrast agent
 - Enhances mucosal pit pattern temporarily with a whitish effect
- Proposed Portsmouth Criteria
 - Focal loss of acetowhitening & surface patterns
 - Endoscopists performance improved using criteria to aid in recognition
 - Sensitivity 98.1% (from 79.3%)
 - NPV 97.4% (from 80.2%)



ASGE PIVI Meta-analysis (4 studies)

	Sensitivity	NPV	Specificity
PIVI Threshold	90%	98%	80%
Overall Performance	97%	99%	85%

Chromoendoscopy and Virtual Chromoendoscopy

TABLE 4. Summary of recommendations and quality of evidence

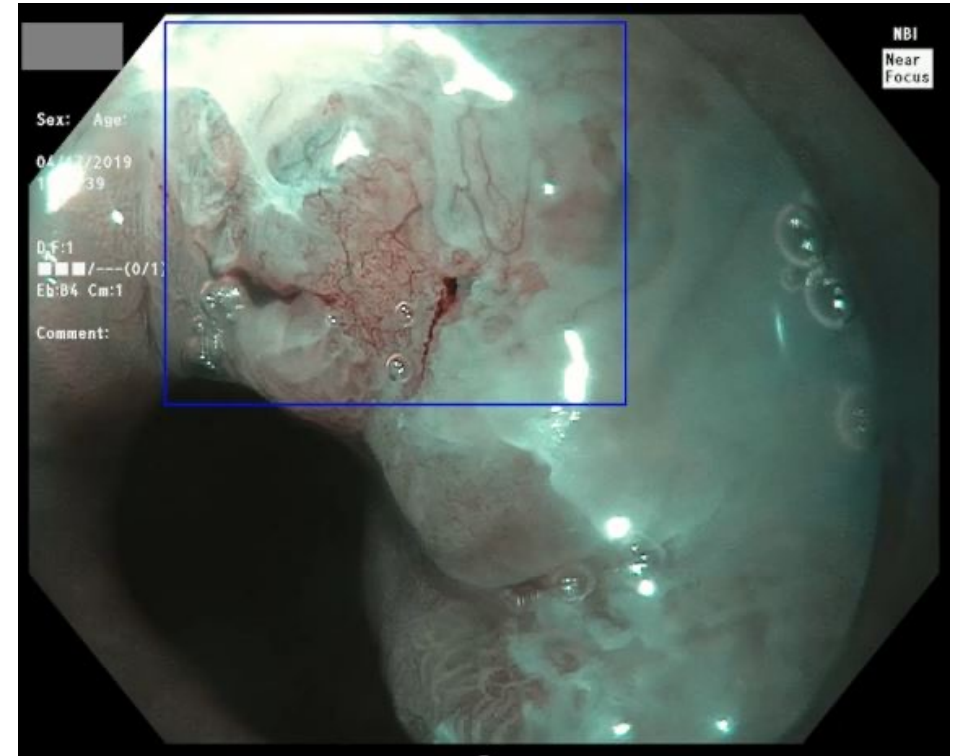
Statement	Strength of recommendation	Quality of evidence
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In patients with BE undergoing surveillance, we recommend using chromoendoscopy, including virtual chromoendoscopy and Seattle protocol biopsy sampling, compared with white-light endoscopy with Seattle protocol biopsy sampling.

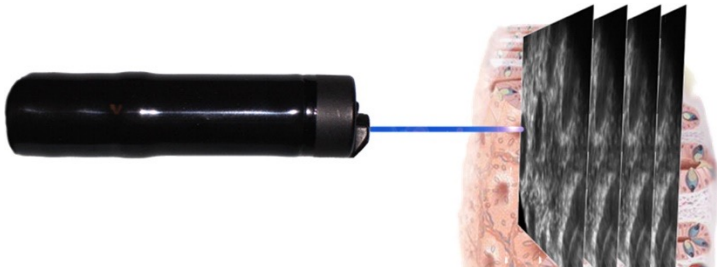

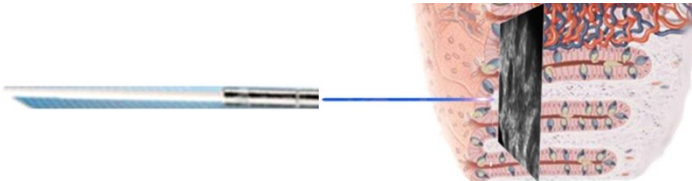
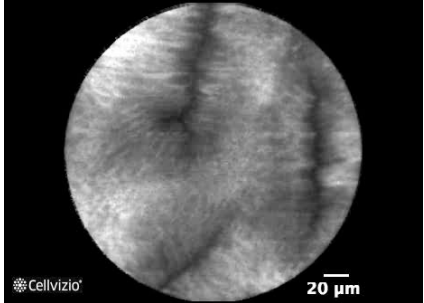
RF, Barrett's esophagus; NA, not applicable; EAC, esophageal adenocarcinoma; IMC, intramucosal cancer; VLE, volumetric laser endomicroscopy; WATS-3D, wide-area scanning with computer-assisted 3-dimensional analysis.

Artificial Intelligence : Computer aided detection1

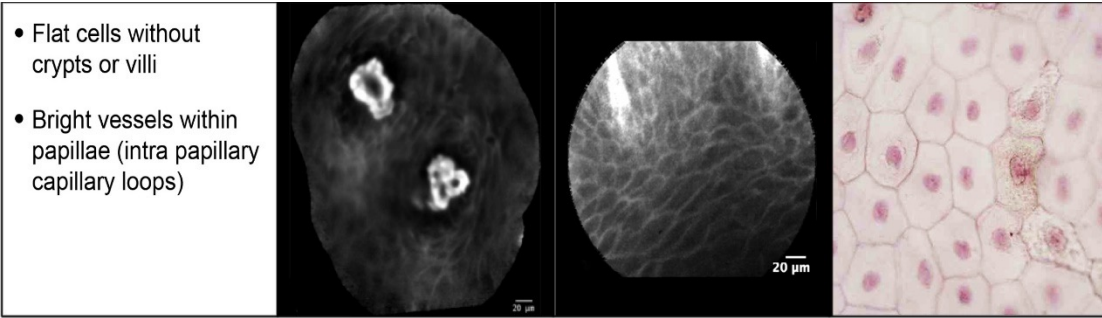
- ARGOS project
 - 494,364 still images
 - accuracy of 92% for detection dysplasia
 - sensitivity of 95% & specificity of 85%
- CAD with convolutional neural networks
 - Still images
 - accuracy 93.7%
 - sensitivity 95.6% & specificity 91.8%
 - AUC 0.94
 - 30 pre-recorded video clips
 - per-lesion sensitivity of 95%
 - per-patient negative predictive value of 100%



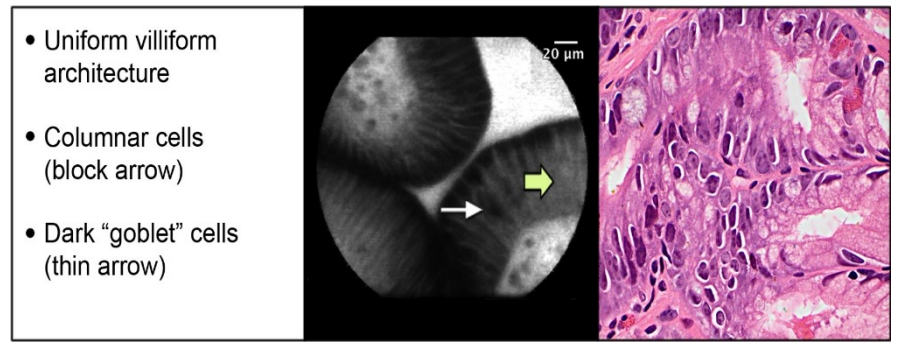
Confocal Laser Endomicroscopy

	Technology	System	Depth	Resolution	Span
Endoscope based CLE (eCLE) (not available)	Confocal Laser Endomicroscopy (CLE)	Scope & processor	0 – 250 microns	0.7 micron	550 microns
					
Probe Based CLE (pCLE) (commercially available)	Confocal Laser Endomicroscopy (CLE)	Probe	65 microns	1 micron	240 microns Video
					

Confocal Laser Endomicroscopy

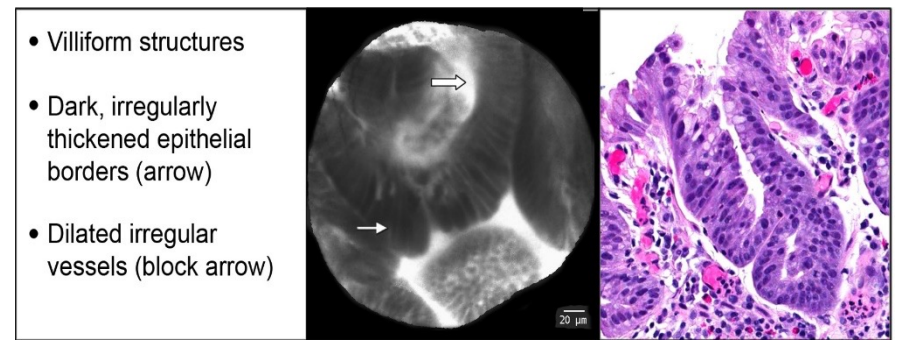


Normal Squamous Epithelium

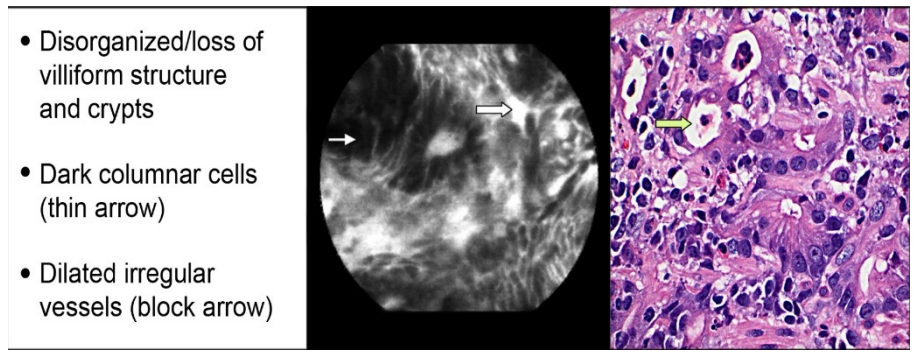


Non-dysplastic Barrett's Esophagus

1. Epithelial surface appears saw-toothed
2. Goblet cells not easily identified
3. Glands are not equidistant
4. Glands are unequal in size and shape
5. Cells are enlarged
6. Cells are irregular and not equidistant from one another.



High-grade Dysplasia



Adenocarcinoma

Wallace et al. Endoscopy 2011

Gaddam et al. AJG 2011

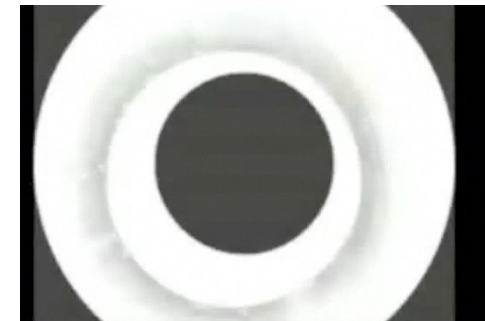
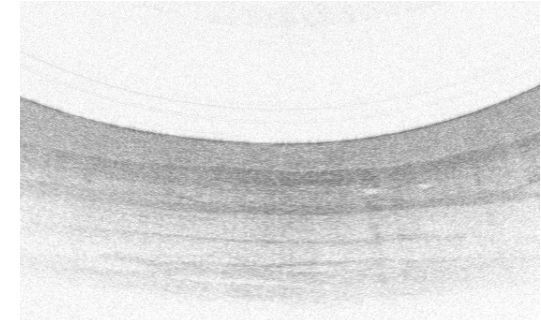
CLE and PIVI Thresholds

	Sensitivity	NPV	Specificity
PIVI Threshold	90%	98%	80%
Overall Performance	90.4%	96.2%	89.9%

- Not recommended for widespread use in general surveillance
- Role in referral centers with high cases of dysplasia & expertise in CLE

Volumetric Laser Endomicroscopy

- Optical coherence tomography based technology
- Laser probe in balloon catheter
- Enables micro architectural imaging down to 7 micron resolution and 3 mm deep
- Offers a cross sectional span of 6 cm
- Histologic correlation feasible with laser marking
- Not currently commercially available



OCT-SI

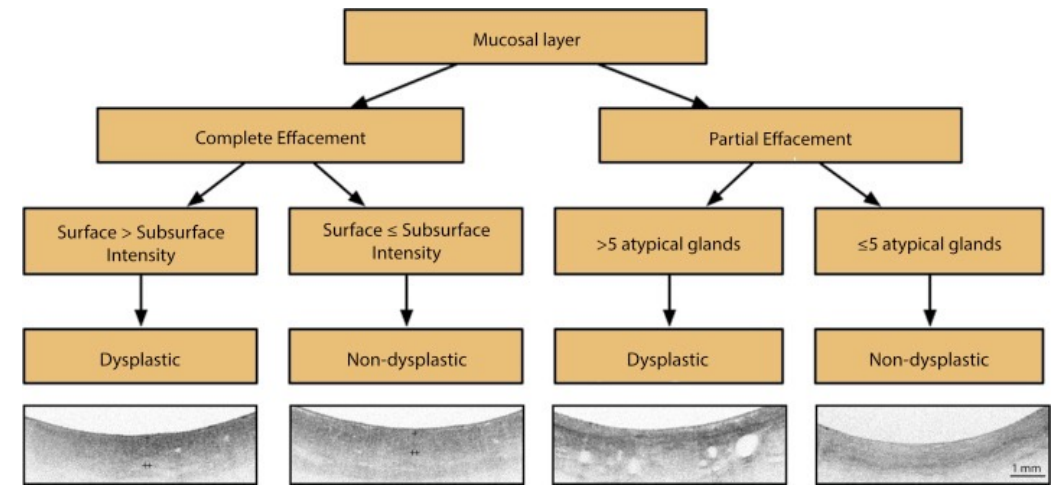
Signal Intensity Score	surface intensity < subsurface intensity = 0	
	surface intensity = subsurface intensity = 1	
	surface intensity > subsurface intensity = 2	
Glandular Architecture Score	no mucosal glands = 0	
	glands or ducts without atypia* = 1	
	glands or ducts with atypia* = 2	

Sensitivity 70%
Specificity 60%
Accuracy 67%

Evans JA et al CGH 2006

VLE

VLE- DA



Sensitivity 86%
Specificity 88%
Accuracy 87%

Leggett et al. GIE 2015

Amsterdam

VLE PREDICTION SCORE	
Layering	
Layering present (> 50%)	0
Lack of layering (< 50%)	6
VLE surface signal	
Surface signal < subsurface	0
Surface signal = subsurface (>50%)	6
Surface signal > subsurface (<50%)	8
Gland architecture	
Irregular glands (0-5 glands)	0
Irregular glands (> 5 glands)	5

- Score of 8
- Sensitivity 83%
- Specificity 71%

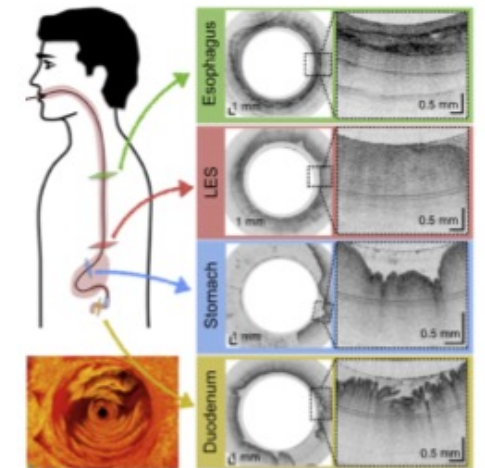
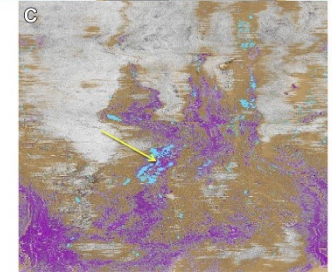
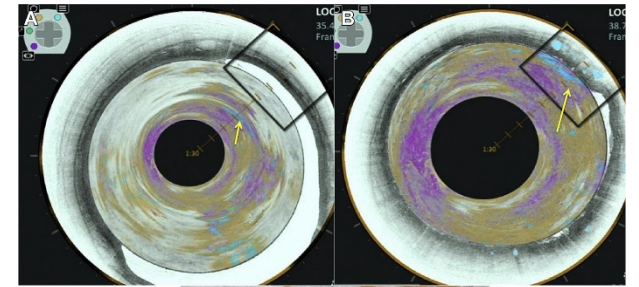
Swager et al. GIE 2017

OCT & VLE performance

OCT HGD/IMC	Studies Patients	Sensitivity	Specificity
OCT Off line Per lesion	4 studies N=170	89%	91%
OCT Real time Per lesion	3 studies n= 138	79%	94%
VLE HGD/IMC	Studies Patients	Sensitivity	Specificity
VLE Per lesion	5 studies N=309	85%	73%
VLE Real time Per patient	3 studies n= 35	100%	55%

Volumetric Laser Endomicroscopy

- Multicenter registry (1000 patients, known or suspected BE)
 - VLE guided tissue acquisition in 71% of cases and treatment in 54%
- Multicenter study, 10 experts, Web based module with VLE videos of Region of Interest
 - High confidence
 - Accuracy 88%
 - Sensitivity 83%
 - Specificity 90%
 - Fair agreement (kappa = 0.29)
- Multicenter study, 12 experts, Web based module with VLE videos of Full Scans
 - High confidence : Correct neoplastic diagnosis (81 %) & Lesion location (73 %)
 - Fair agreement (kappa 0.28)
- Computer aided detection algorithm developed and tested
 - CAD : Accuracy 85%, Sensitivity 91%, and Specificity 82%
 - VLE expert : 77%, 70%, 81% respectively



Smith et al Dis Esophagus 2019
Struyvenberg et al Dis Esophagus 2020
Struyvenberg et al Endoscopy 2021
Struyvenberg et al GIE 2020

Trindade et al. Gastro 2019
Gora et al. GIE 2018
Dong CGH 2021

Tools you should know and love



Tools you should know and love



•Summary

- Remember the 5 L's: Landmarks, Length, Look, Lesions, and Levels for a high-quality endoscopic assessment.
- Look carefully with tools like HRE, NBI, and consider a soft cap. Use good inspection technique, recognize subtle lesions, and spend adequate time.
- Advanced endoscopic imaging may improve detection and localization of neoplasia. These modalities may be more accessible with the help of computer aided detection.
- Visible lesions in the setting of dysplasia should be diagnosed with endoscopic mucosal resection which can have both a role in diagnosis and therapy.