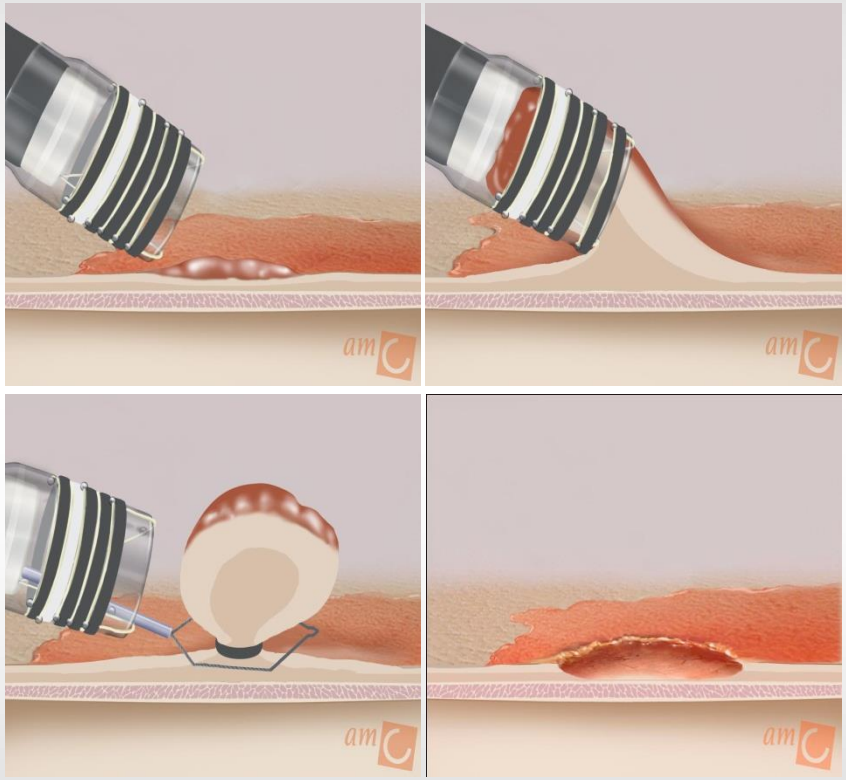
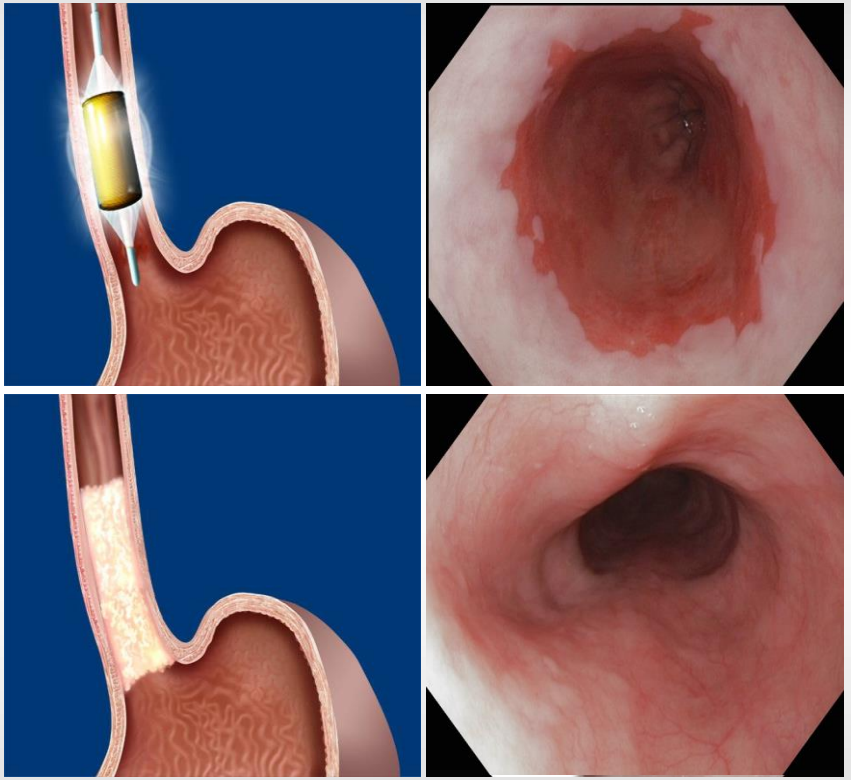
Managing early esophageal dysplasia





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Disclosures Jacques Bergman

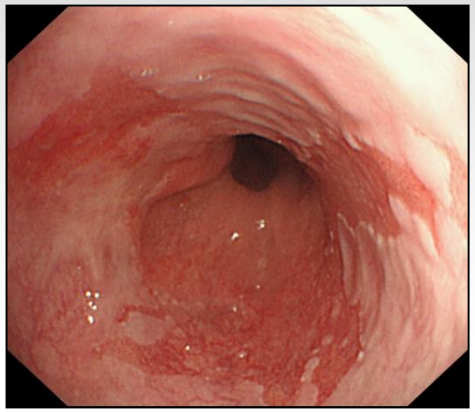
• Research support for IRB approved studies	• Olympus Endoscopy • Fuji-film • Cook Medical • Boston Scientific • GI Solutions Medtronic • Erbe • Ninepoint Medical • C2 therapeutics • Cernostics • Interpace
• Financial support for training programs	• GI Solutions Medtronic • Boston Scientific
• Honorarium-consultancy-speakers fee	• Cook Medical • Boston Scientific • GI Solutions Medtronic

10 years ago:

Low grade dysplasia

High grade dysplasia

Mucosal cancer

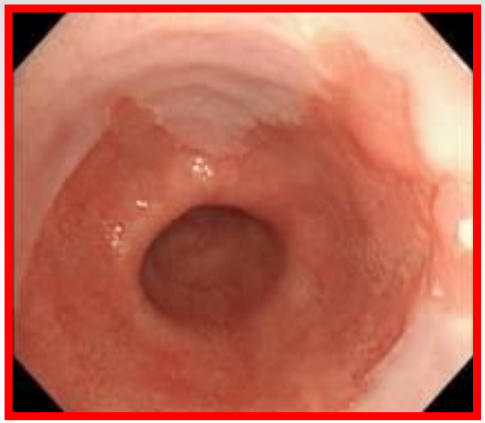


Submucosal cancer

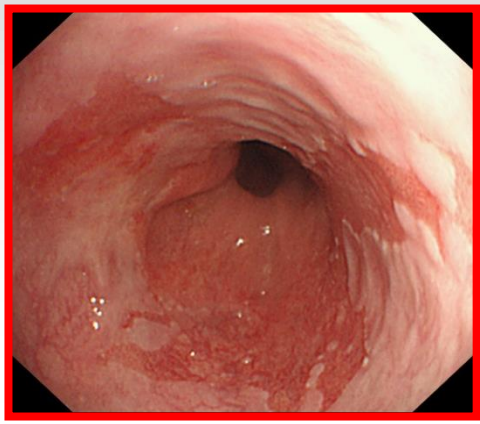
10 years ago:

Low grade dysplasia

High grade dysplasia



Mucosal cancer



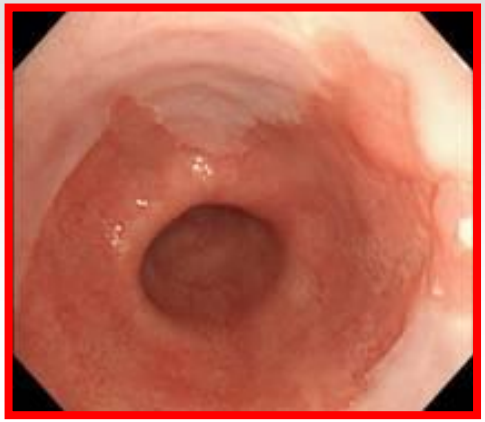
Submucosal cancer

- Early cancer: esophagectomy.

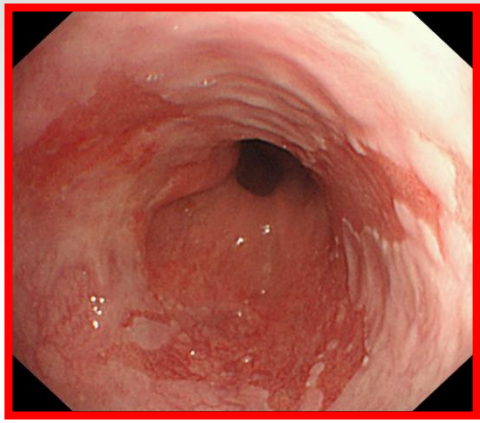
10 years ago:

Low grade dysplasia

High grade dysplasia



Mucosal cancer



Submucosal cancer

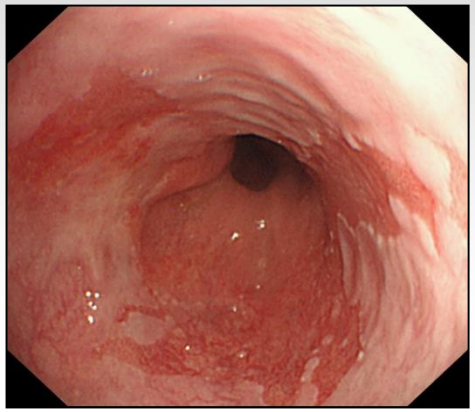
- Early cancer: esophagectomy.
- Endoscopic Tx for LGD or HGD only in clinical trials

Candidates for treatment in 2017

Low grade dysplasia

High grade dysplasia

Mucosal cancer

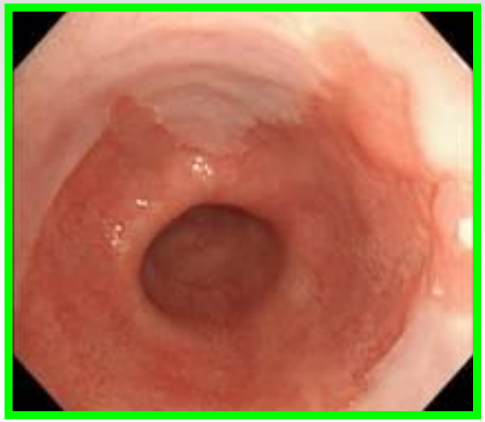


Submucosal cancer

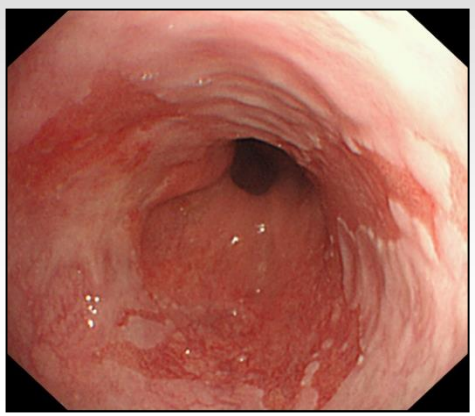
Candidates for treatment in 2017

Low grade dysplasia

High grade dysplasia



Mucosal cancer



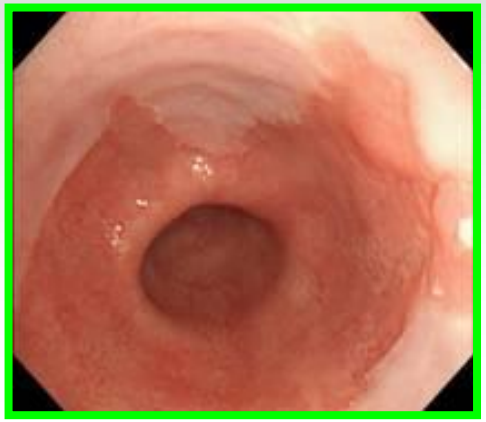
Submucosal cancer

- HGD and mucosal cancer: endoscopy first choice.

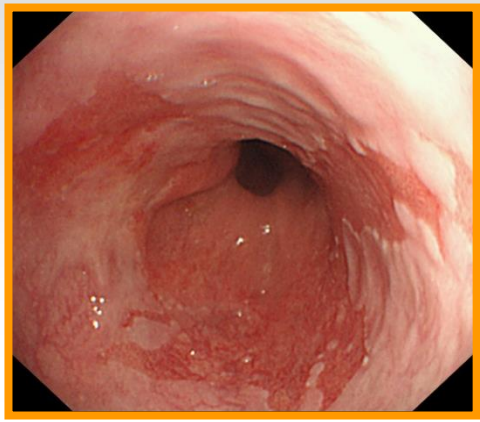
Candidates for treatment in 2017

Low grade dysplasia

High grade dysplasia



Mucosal cancer



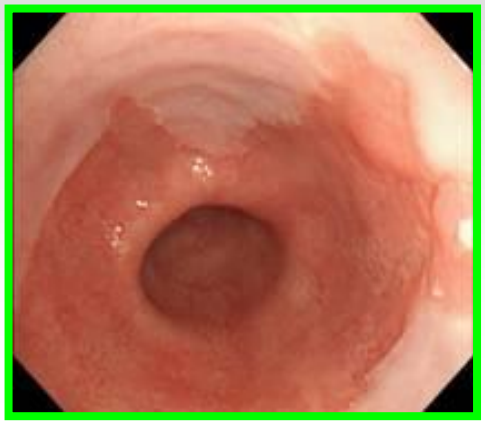
Submucosal cancer

- HGD and mucosal cancer: endoscopy first choice.
- Sm-ca: esophageal preservation a realistic goal.

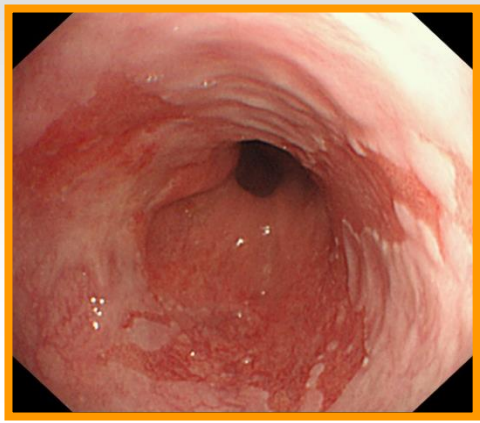
Candidates for treatment in 2017

Low grade dysplasia

High grade dysplasia



Mucosal cancer



Submucosal cancer

- HGD and mucosal cancer: endoscopy first choice.
- Sm-ca: esophageal preservation a realistic goal.
- LGD (histological confirmation): ablation therapy.

Just because you can doesn't mean you should

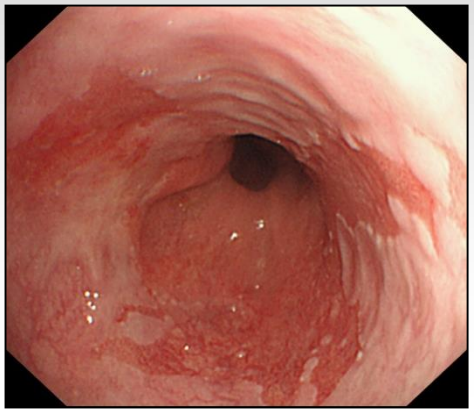
Non-dysplastic BE

- Outside the focus of my presentation.
- Few data to justify treatment for NDBE.
- I treated 5 non-dysplastics over the last 10 years…

Low grade dysplasia

High grade dysplasia

Mucosal cancer



Submucosal cancer

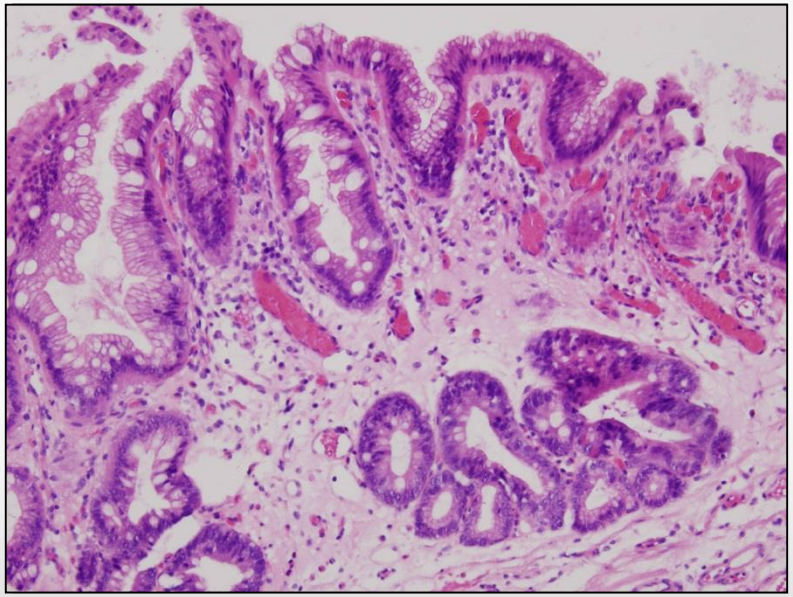
Two pitfalls in treating HGD

- Are you sure that the patient has high-grade dysplasia?
- Are you sure that the patient does *NOT* have invasive cancer?

The over- and under-diagnosis dilemma's of HGD

“Over-diagnosis dilemma” of managing HGD

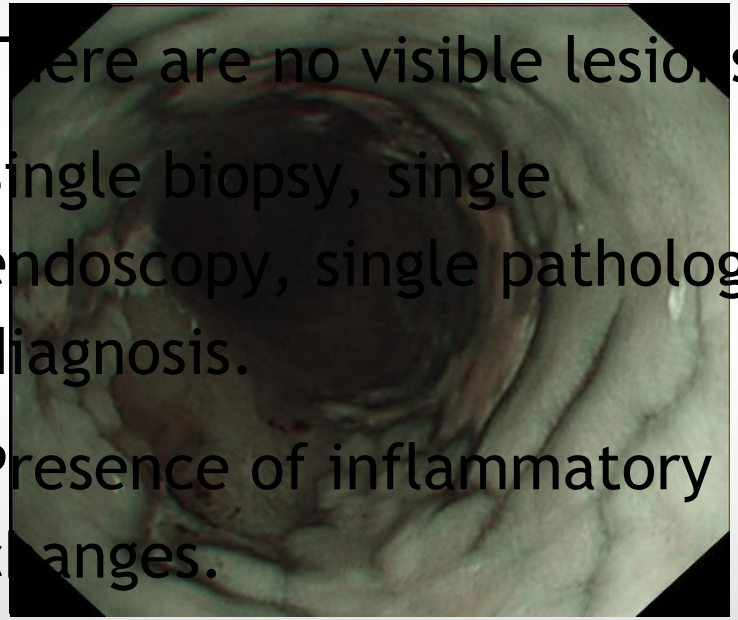
Reactive changes or HGD?



Review pathology by expert in this field

Erosive esophagitis?

- There are no visible lesions
- Single biopsy, single endoscopy, single pathologist diagnosis.
- Presence of inflammatory changes.

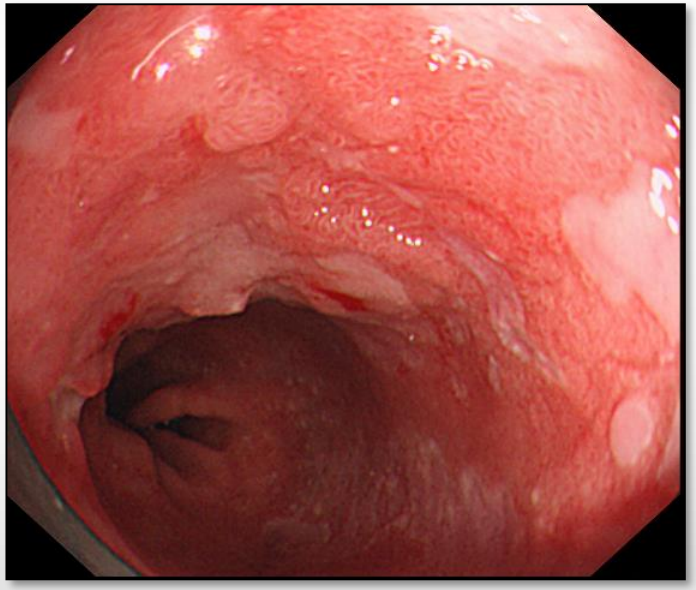


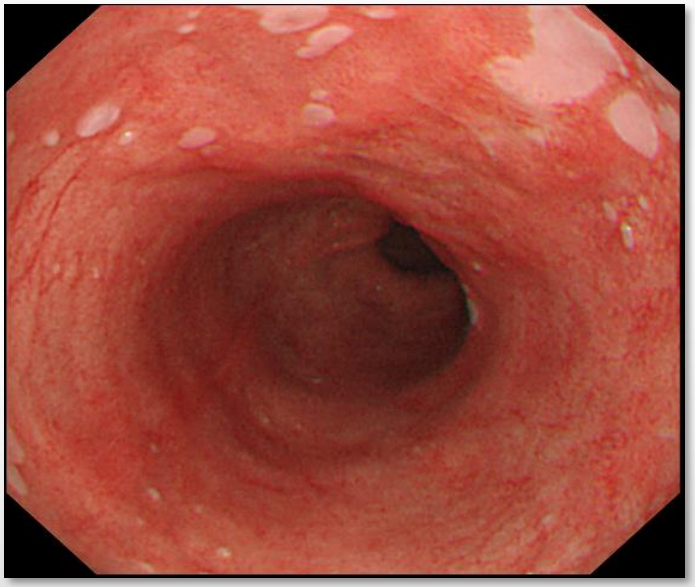
Repeat biopsies after high-dose PPI

“Under-diagnosis dilemma” of managing HGD

“Under-diagnosis dilemma” of managing HGD

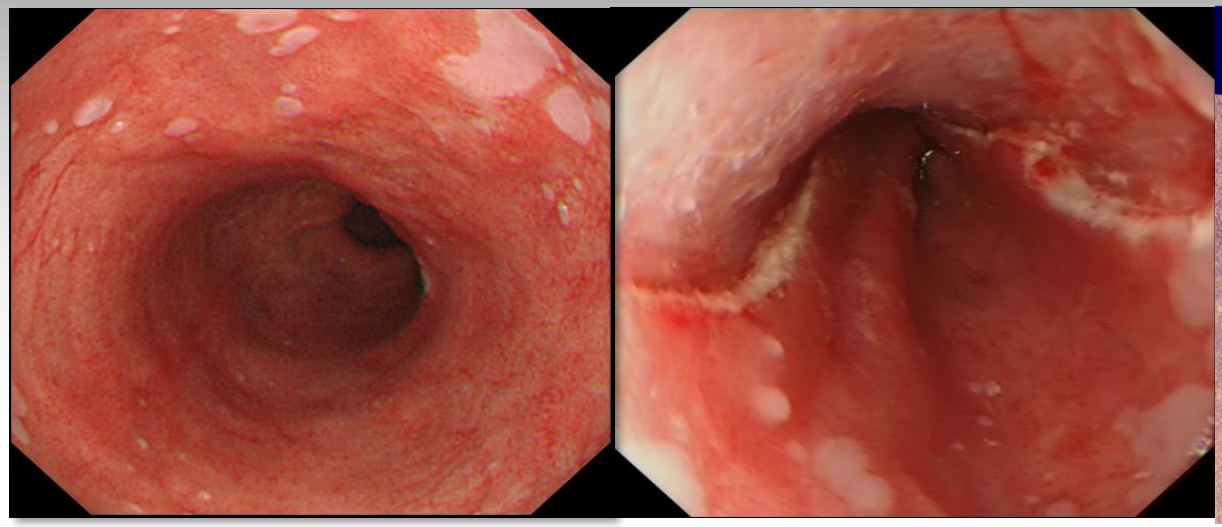
Don’t trust the pathologist more than your own eyes!

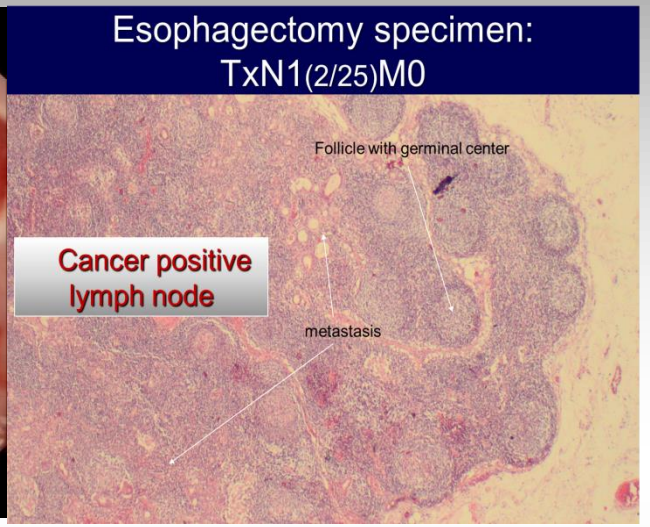




This is not HGD: this is cancer!

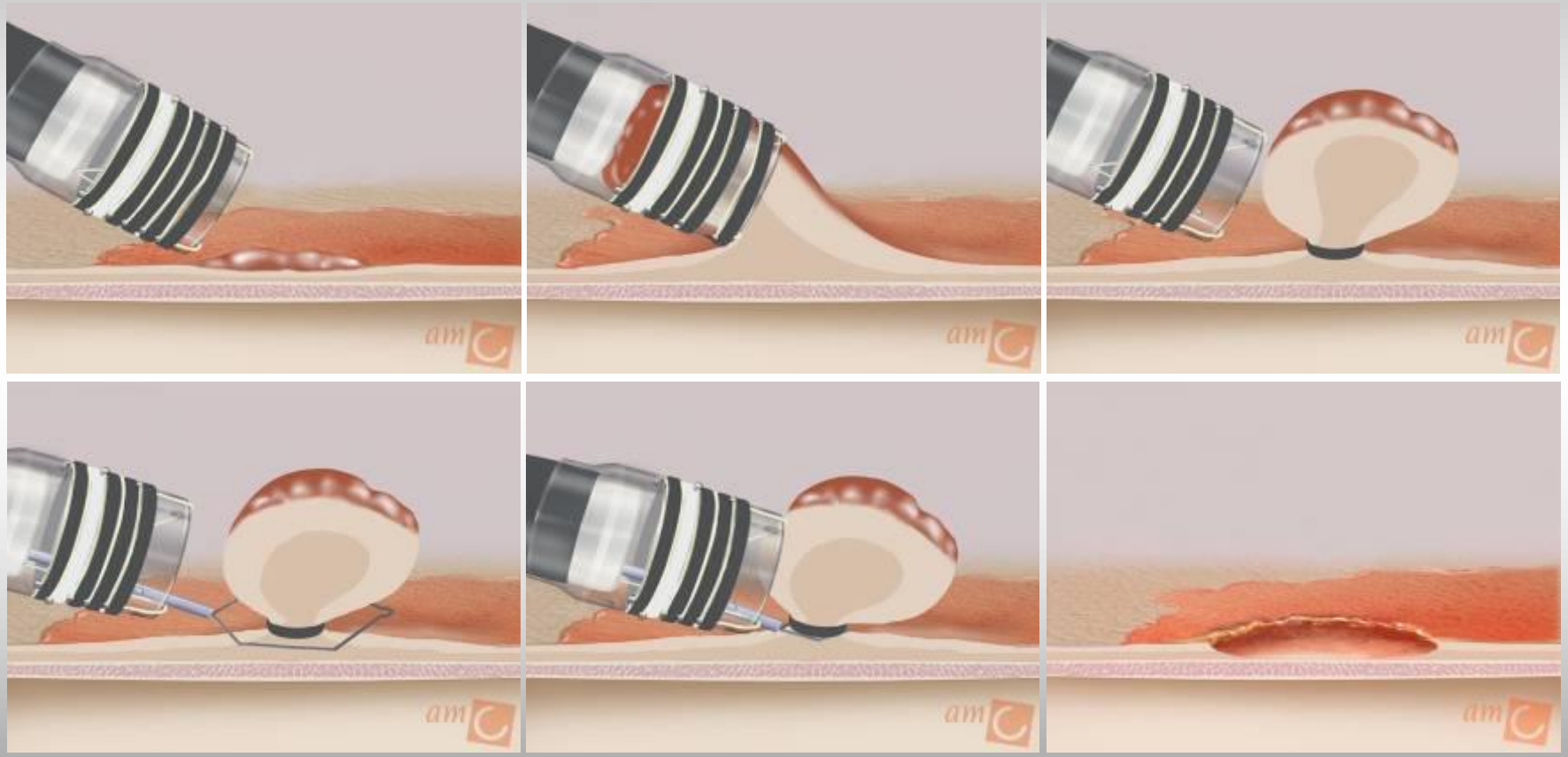
Endoscopic Resection (ER)





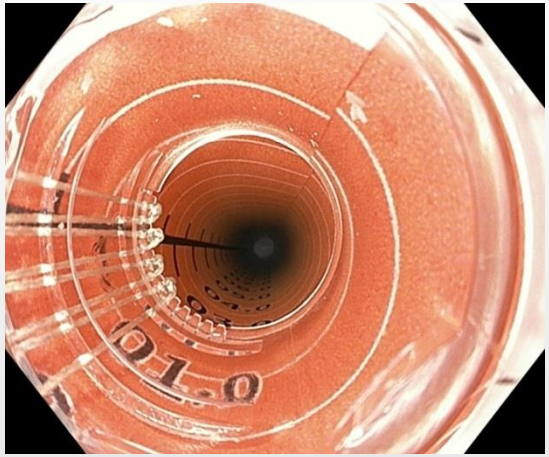
- The *ONLY* reliable way to distinguish mucosal from submucosal cancers.
- The *ONLY* way to diagnose poorly differentiated cancers or lymfovascular invasion.

Multiband Mucosectomy

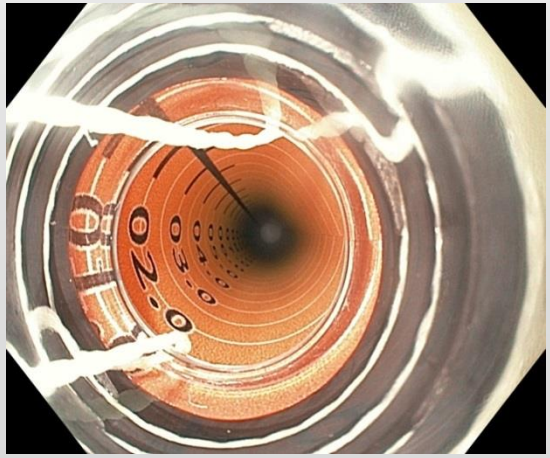


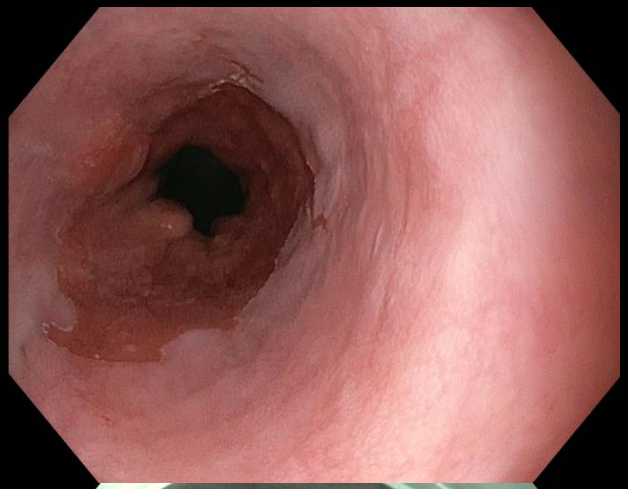
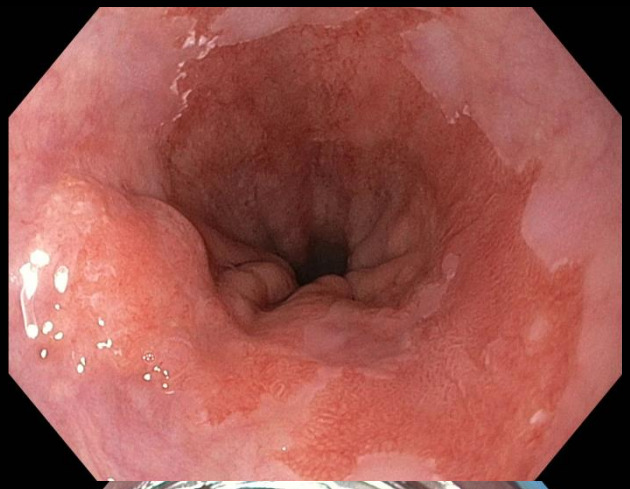
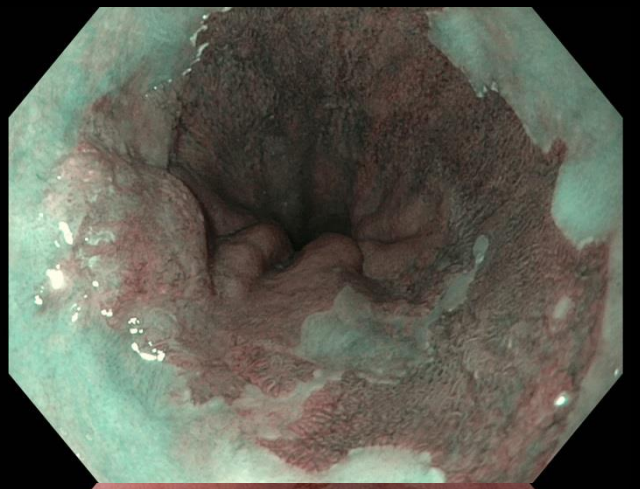
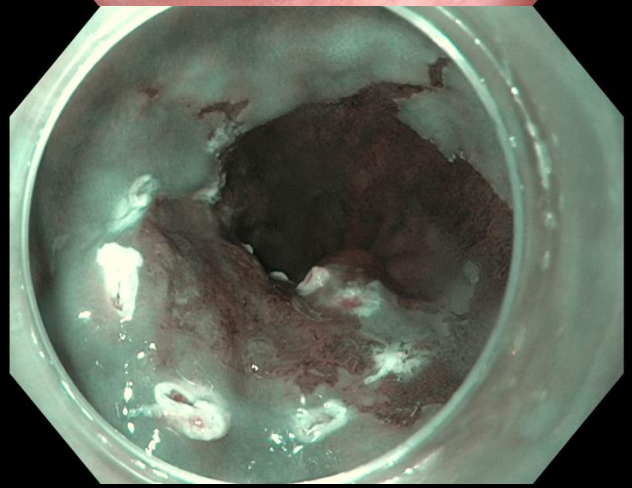
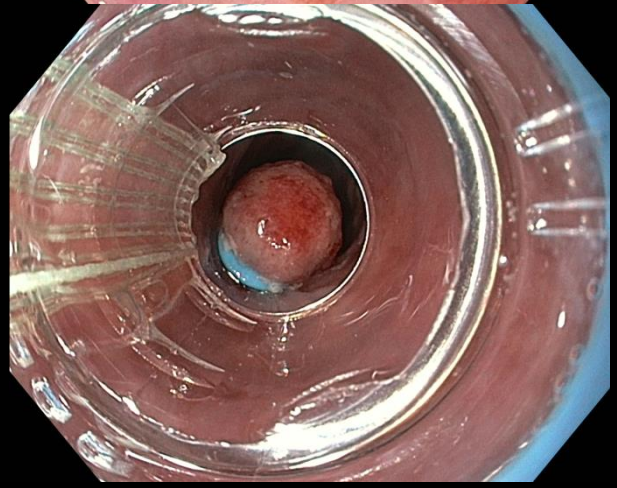
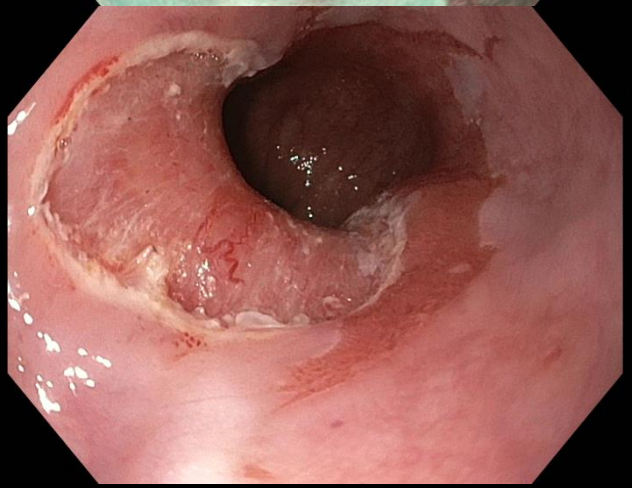
New: Captivator EMR device

Captivator



Duette



EURO-II Study

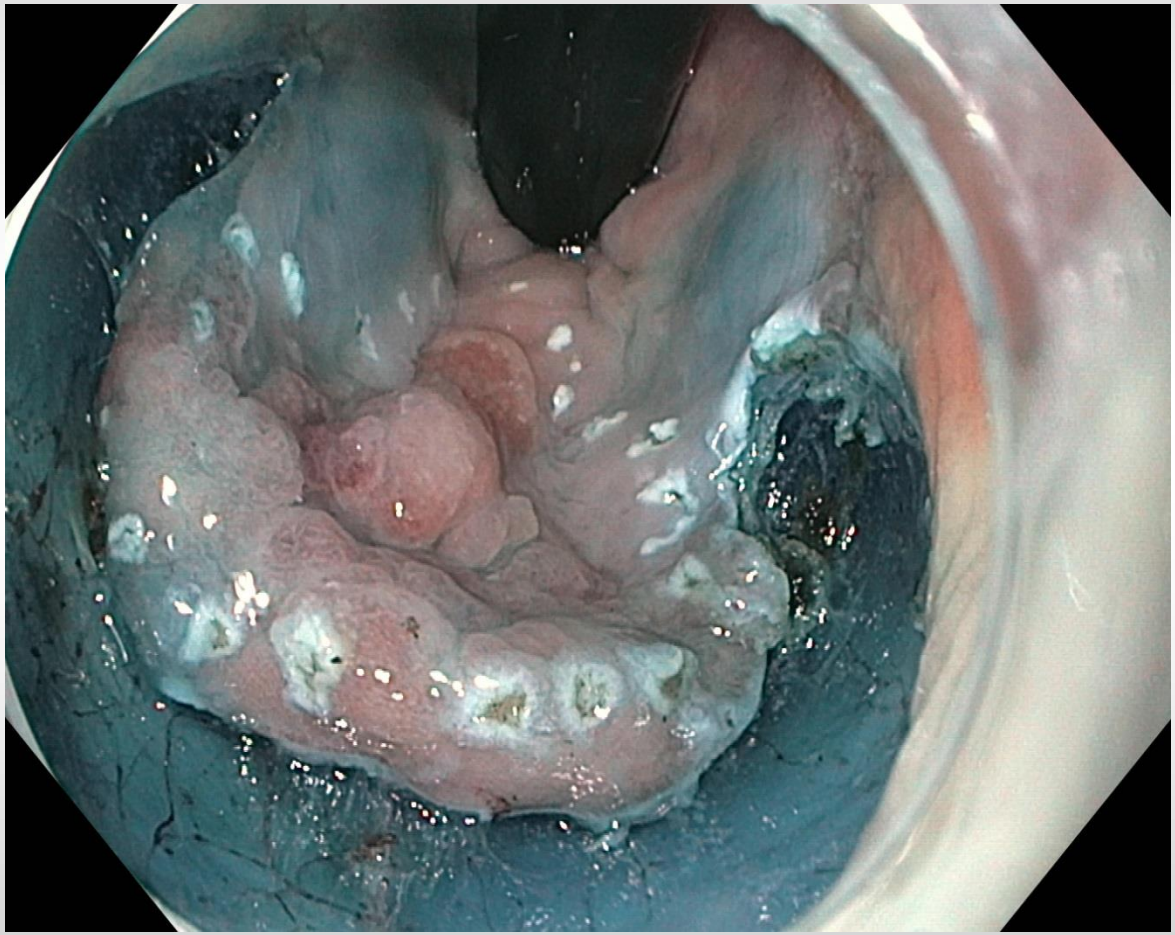
Phoa et al. Gut 2015

EURO-II Study

Phoa et al. Gut 2015

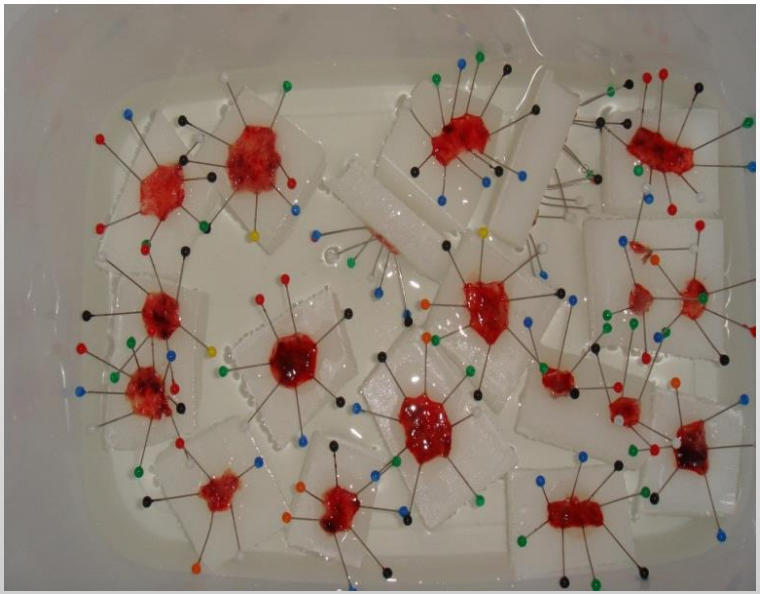
- 13 leading centres in Europe;
- ER+RFA for HGD/EC in Barrett's
- 132 patients
  - Eradication of neoplasia:98%
  - Complete removal of BE: 93%.
- 47 months FU
  - Persistent remission of neoplasia in 96%
  - Persistent remission of IM in 92%

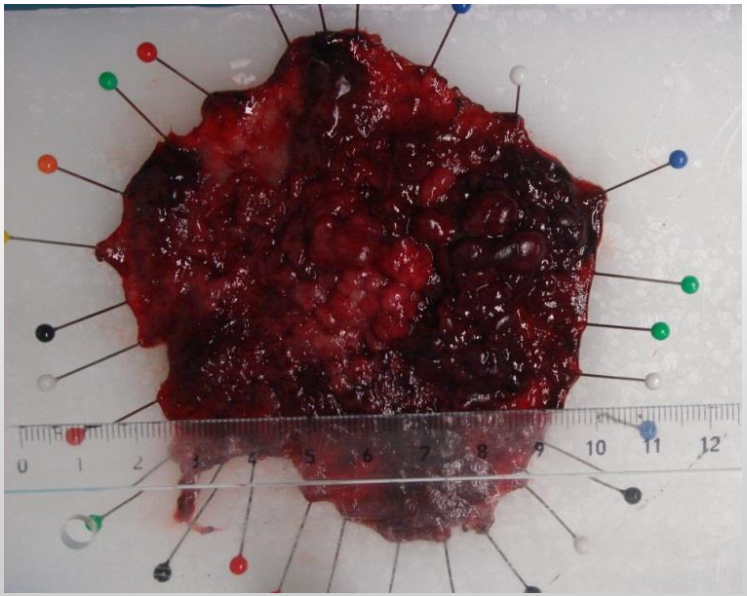
EMR or ESD for Barrett's neoplasia?



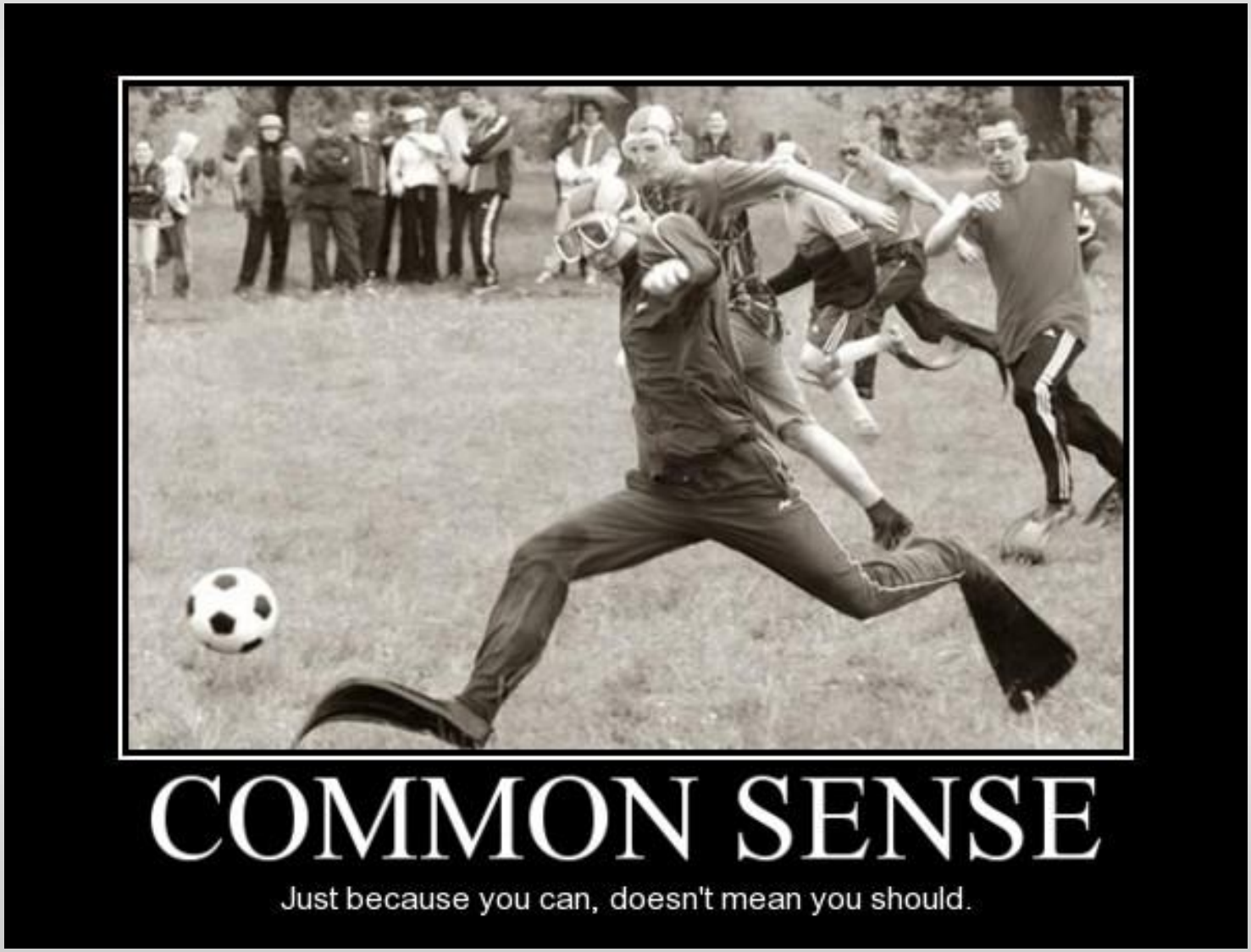
Why is ESD better than EMR?

- En-bloc vs. piecemeal resection
  - ✓ Easier for the pathologist
  - ✓ Less artefacts
  - ✓ Better assessment radicality resection





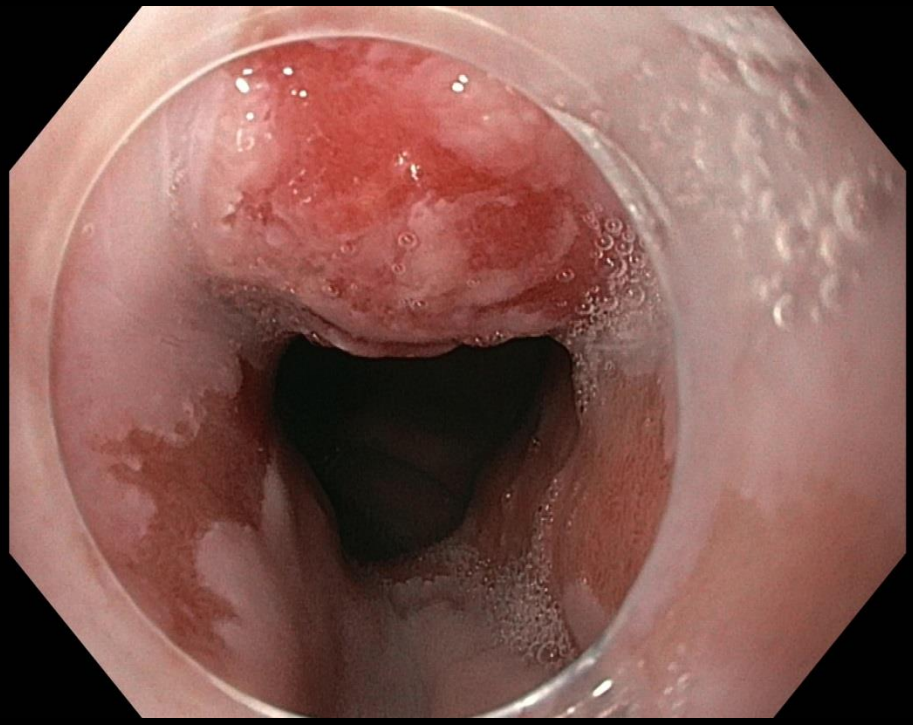
ESD for Barrett's neoplasia?

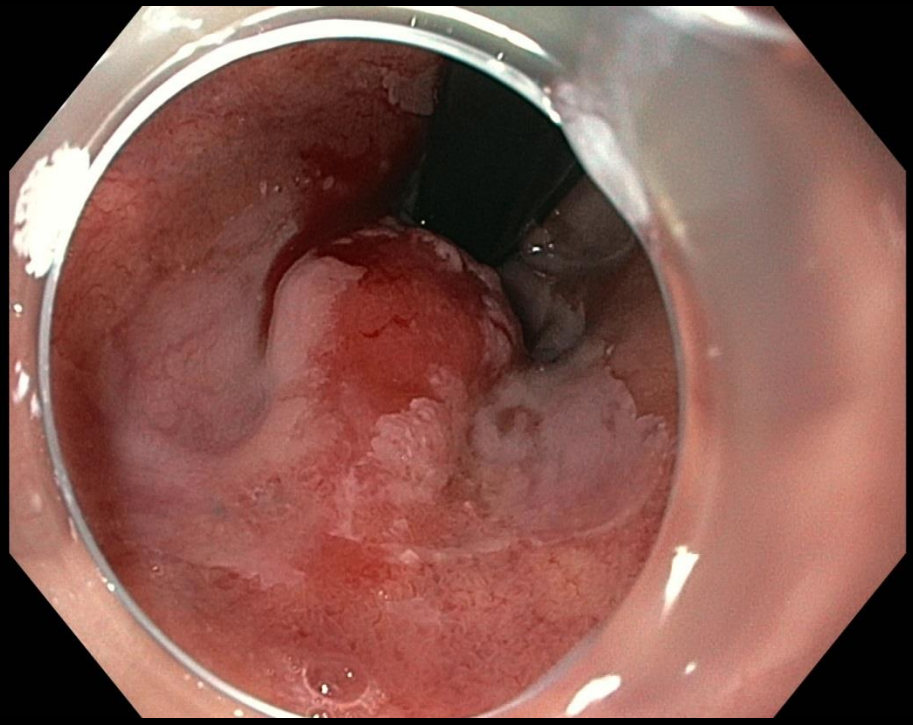


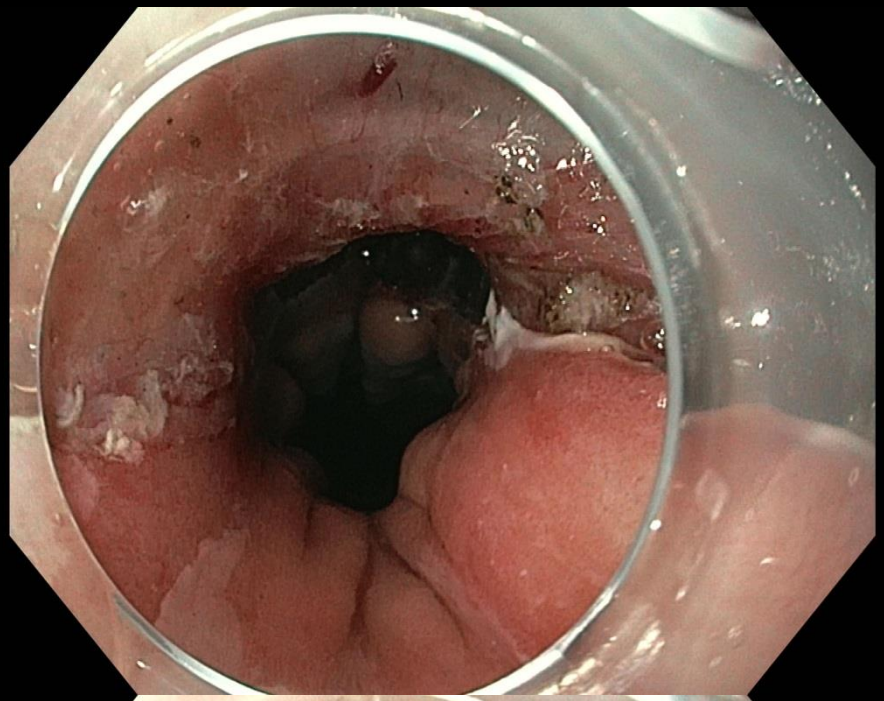
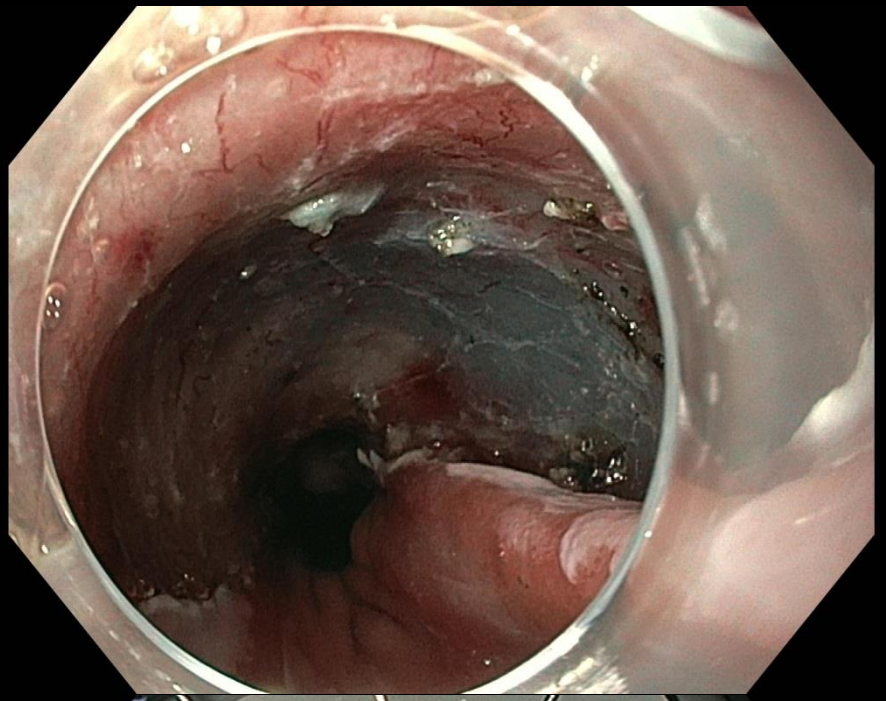
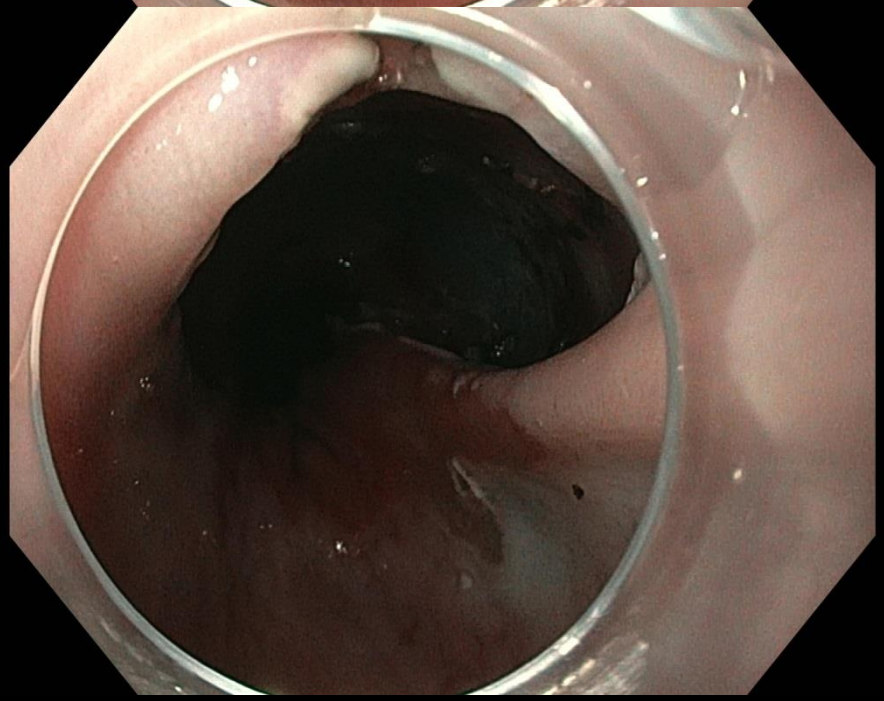
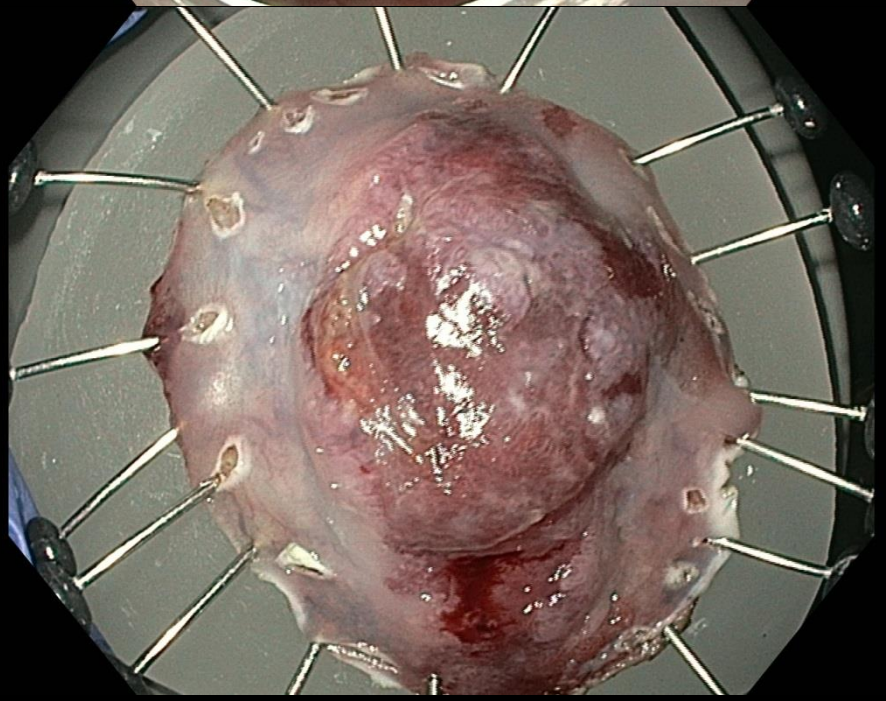
ESD for Barrett's: selected cases only!

Larger lesions (>2cm) with:

- High likelihood for submucosal invasion
- a bulky intraluminal component (this will fill your cap upon suctioning and this will result in a positive vertical resection margin)
- Generally <15% of cases.
- 2 cases per week in our unit



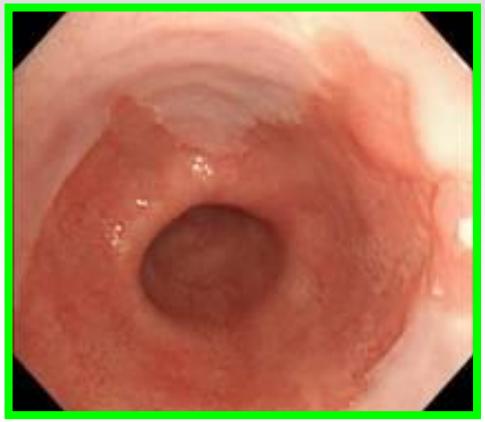


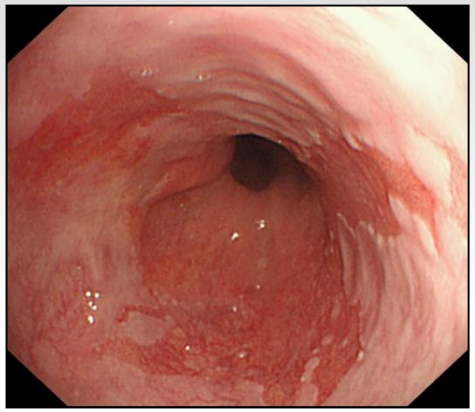
Who to treat endoscopically?

Low grade dysplasia

High grade dysplasia



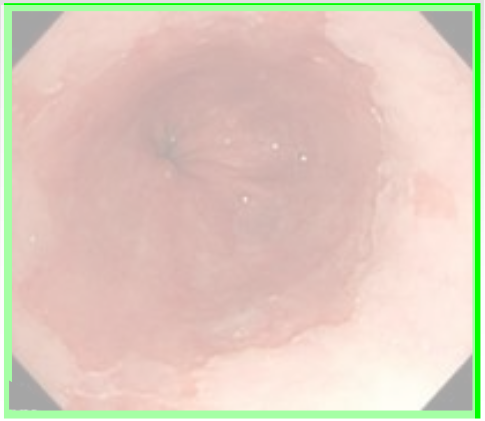
Mucosal cancer



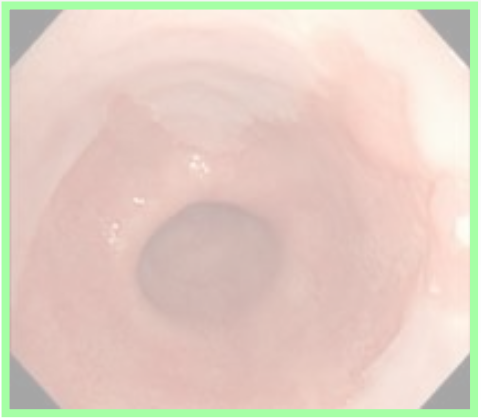
Submucosal cancer

What about low-grade dysplasia?

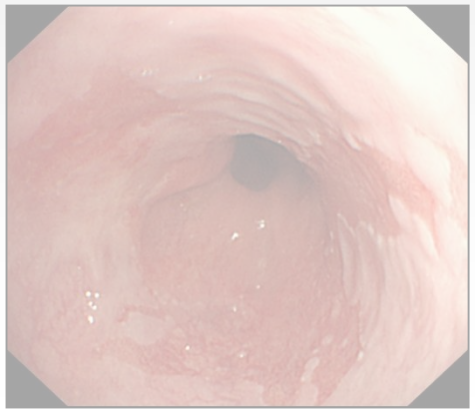
Low grade dysplasia



High grade dysplasia



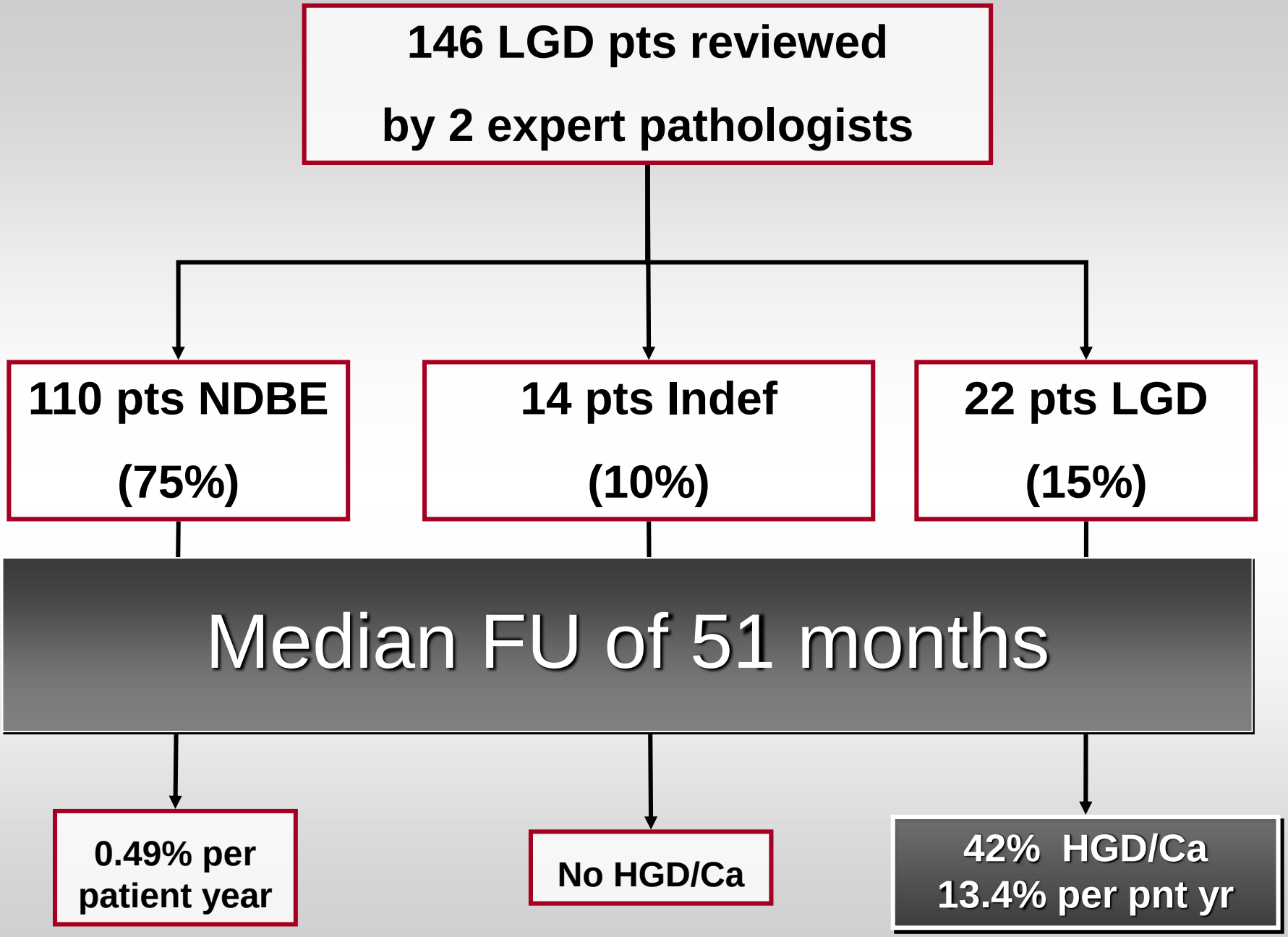
Mucosal cancer



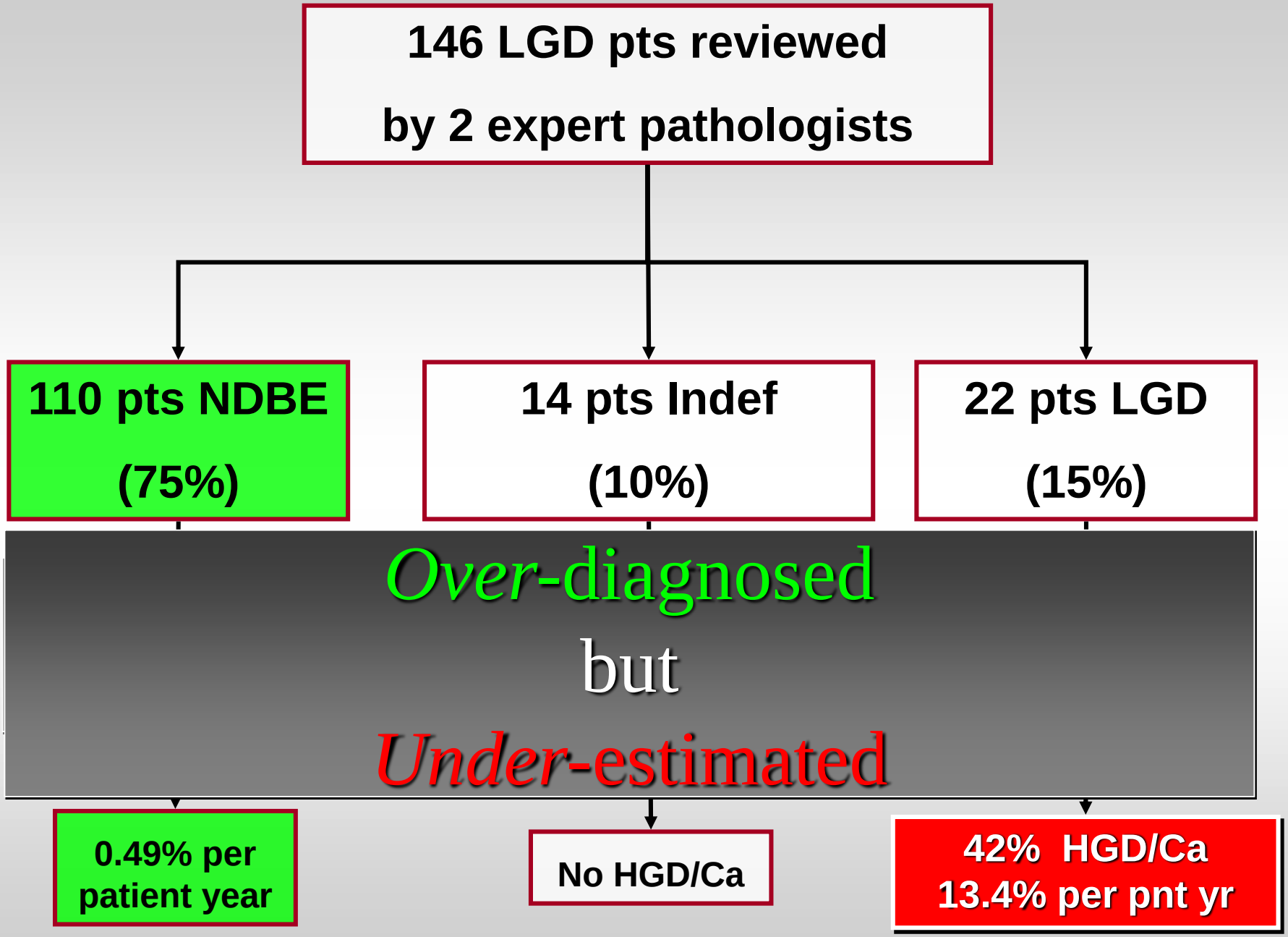
Submucosal cancer

Is LGD an innocent disease?

Depends on which pathologist makes the diagnosis.



Curvers et al. Am. J. Gastro. 2010

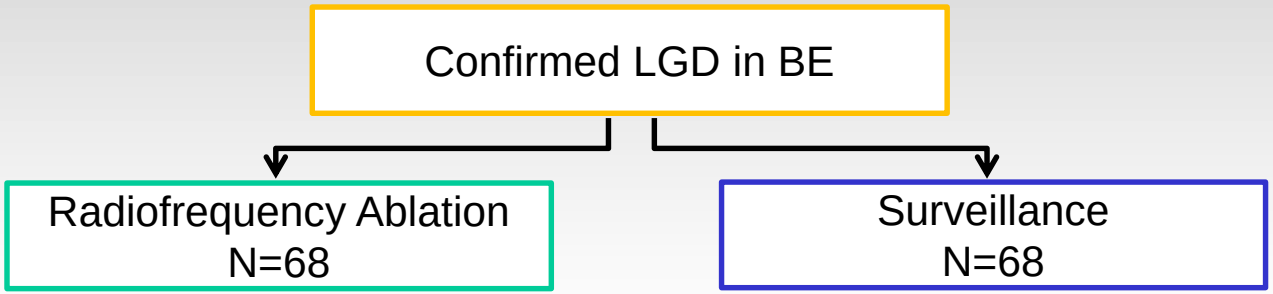


Curvers et al. Am. J. Gastro. 2010

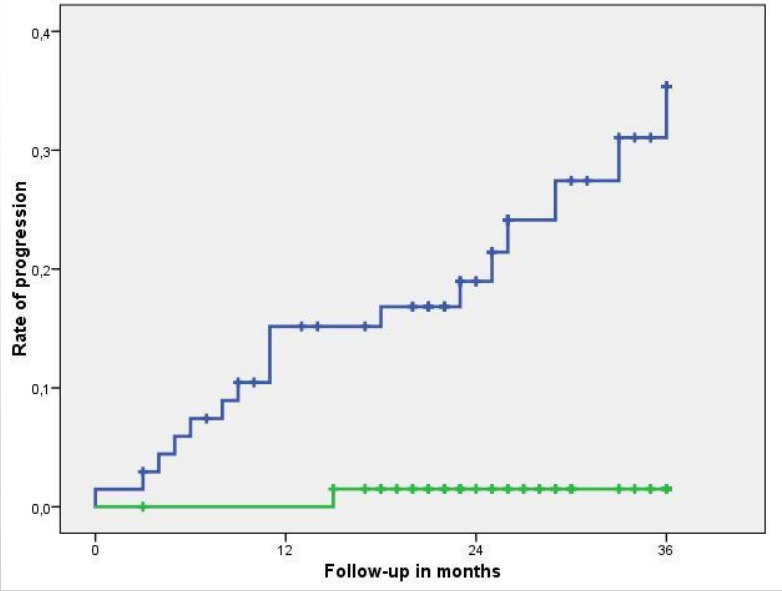
SURF-Trial

European multicenter RCT

Phoa *et al.* JAMA 2014

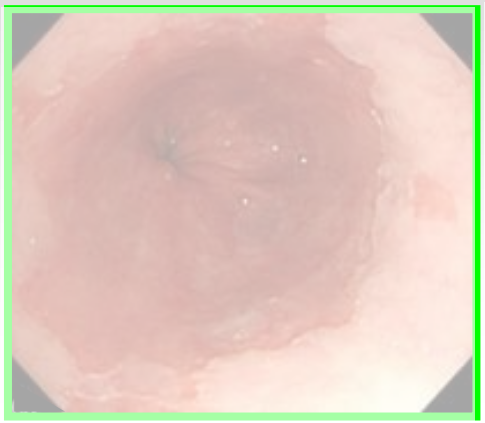


HGD/cancer	1 (1%)	18 (27%)	<0.001

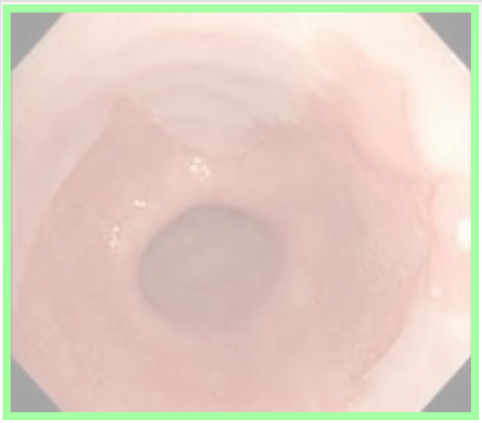


What about low-grade dysplasia?

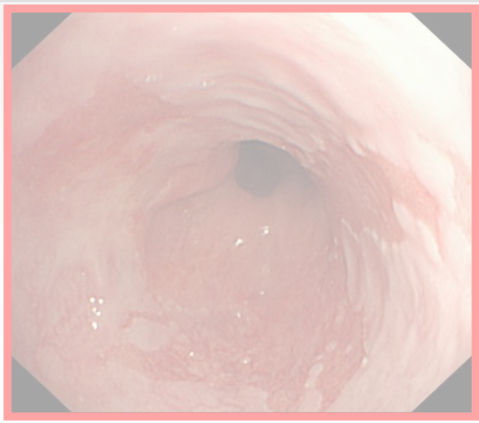
Low grade dysplasia



High grade dysplasia



Mucosal cancer



Submucosal cancer

- Confirmed LGD is a strong indication for treatment (Need for good quality expert pathology panels).

Web-based BE advisory platform

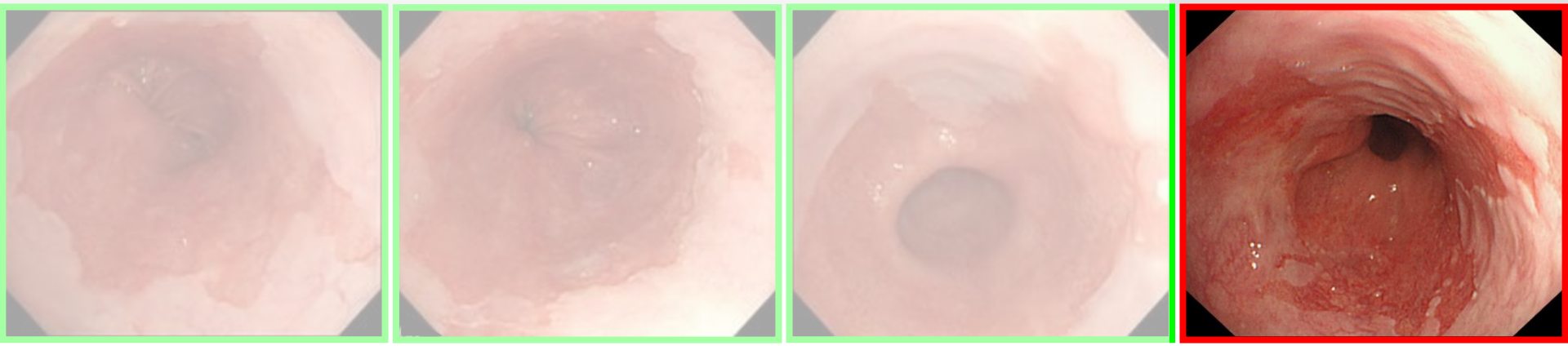
Implemented in the Netherlands in 2017

- Central registration on www.Barrett.nl
- Histology slides shipped to central lab and scanned
- Digital slides reviewed online by expert pathologists
- Annotate and store relevant images
- Feedback plus annotated images to referring centers

Endoscopic Tx of upper GI neoplasia is centralized in the Netherlands

- Since 2007 8 centers: AMC, EMC,UMZG, N'gein, UMCU, Zwolle, Haga ZH, CZH Eindhoven.
- 10-12 endoscopists; 14 pathologists
- Joint training program; 3-4 teaching days/year; joint treatment protocol and registration; consensus meetings; hand-on trainings.
- Expand beyond these 8? Volume is rate limiting factor.

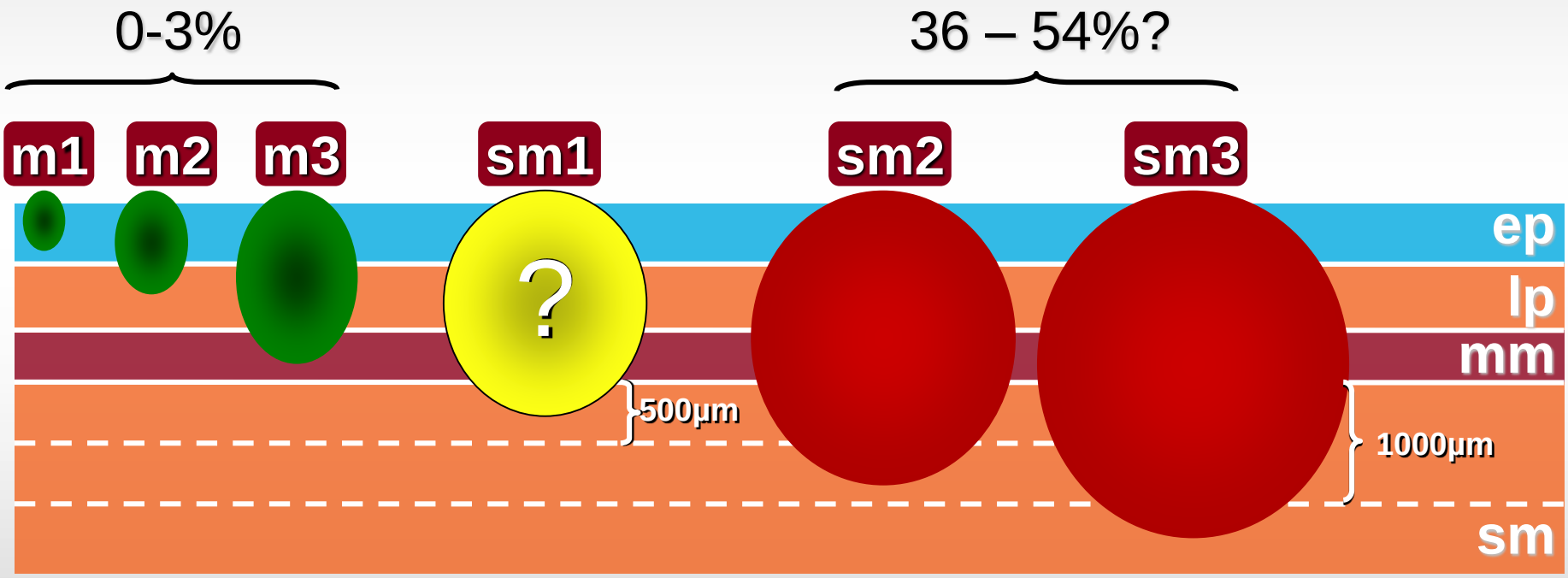
What about submucosal cancers?



Low grade dysplasia | High grade dysplasia | Mucosal cancer | Submucosal cancer

- Really an indication for surgery?
- Endoscopic management justified for some?

Invasion depth and risk of LNM



Further risk stratification

- Lower risk of LNM in case:

  Well-moderately differentiated cancers

  No invasion in lymphatic vessels

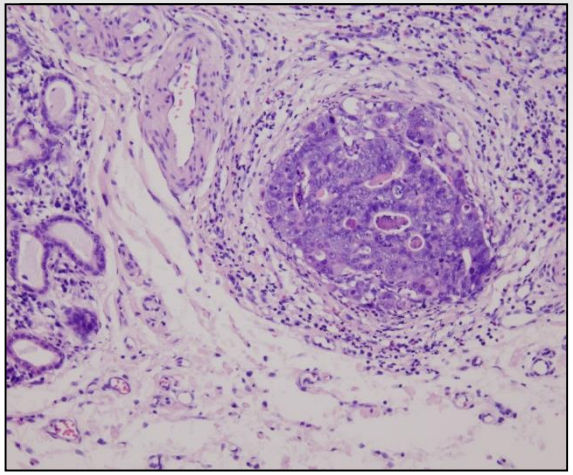


Table 3. Early gastric cancer with no risk of lymph node metastasis

Criteria	Incidence	95% C.I.
Minute submucosal penetration (SM1) Differentiated adenocarcinoma No lymphovascular invasion Tumor less than 3 cm in size	0/145; 0%	0–2.5%

Gotoda et al. J. Gastroenterol. 2006

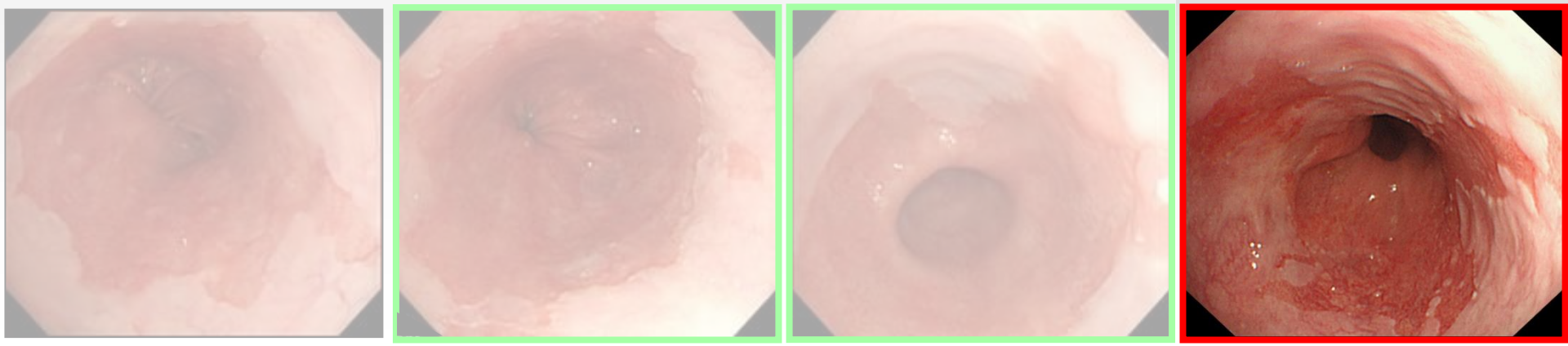
Esophageal preservation for Sm1?

- >90% of Sm1-patients will have no LNM.
- This holds especially for “low-risk” submucosal cancers.
- Esophagectomy: 3% mortality; 40% morbidity.

Esophageal preservation for Sm1?

- >90% of Sm1-patients will have no LNM.
- This holds especially for “low-risk” submucosal cancers.
- Esophagectomy: 3% mortality; 40% morbidity.
- Manner et al. (Clin. Gastro Hep 2013):
  - 61 patients with T1sm1G1-2Ly-
  - 47 mo follow-up: no tumor related deaths.
  - 1/61 (1.9%) developed a single Lnn metastasis (curative surgery).

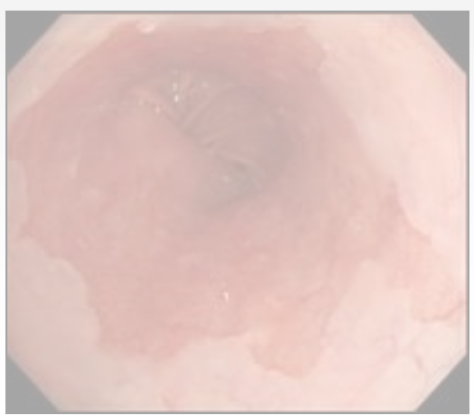
Submucosal cancers in 2017



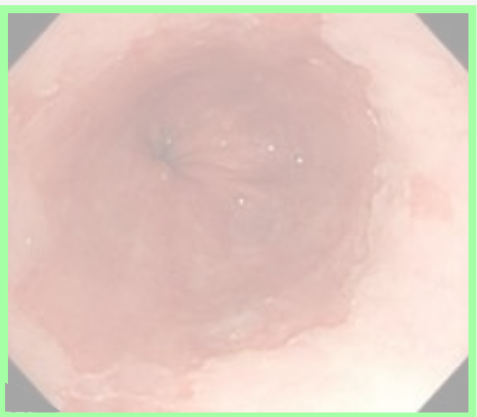
Low grade dysplasia | High grade dysplasia | Mucosal cancer | Submucosal cancer

- Not automatically an indication for surgery

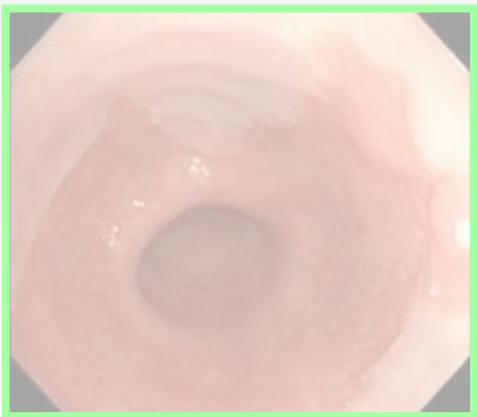
Submucosal cancers in 2017



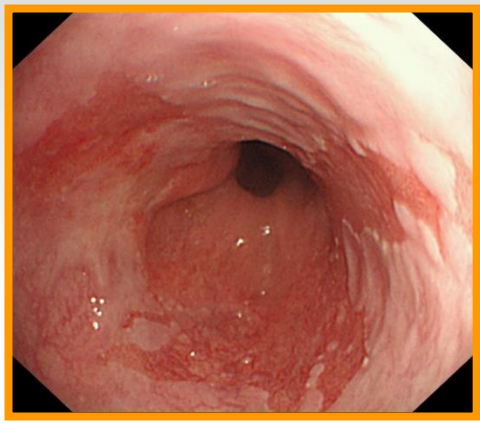
Low grade dysplasia



High grade dysplasia



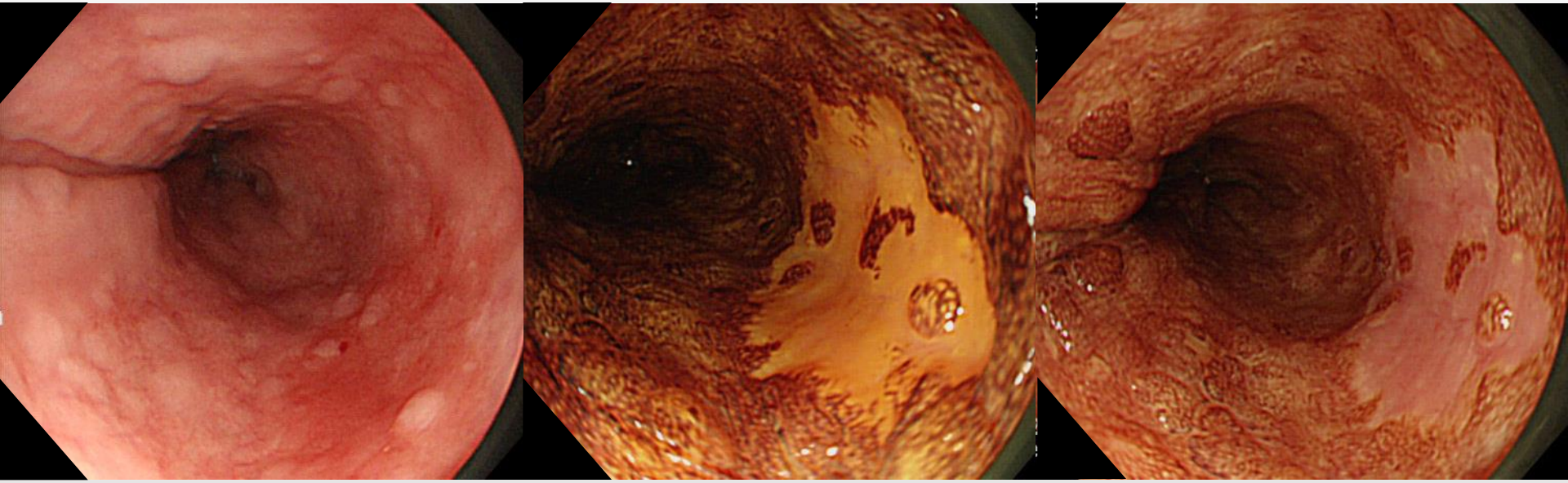
Mucosal cancer

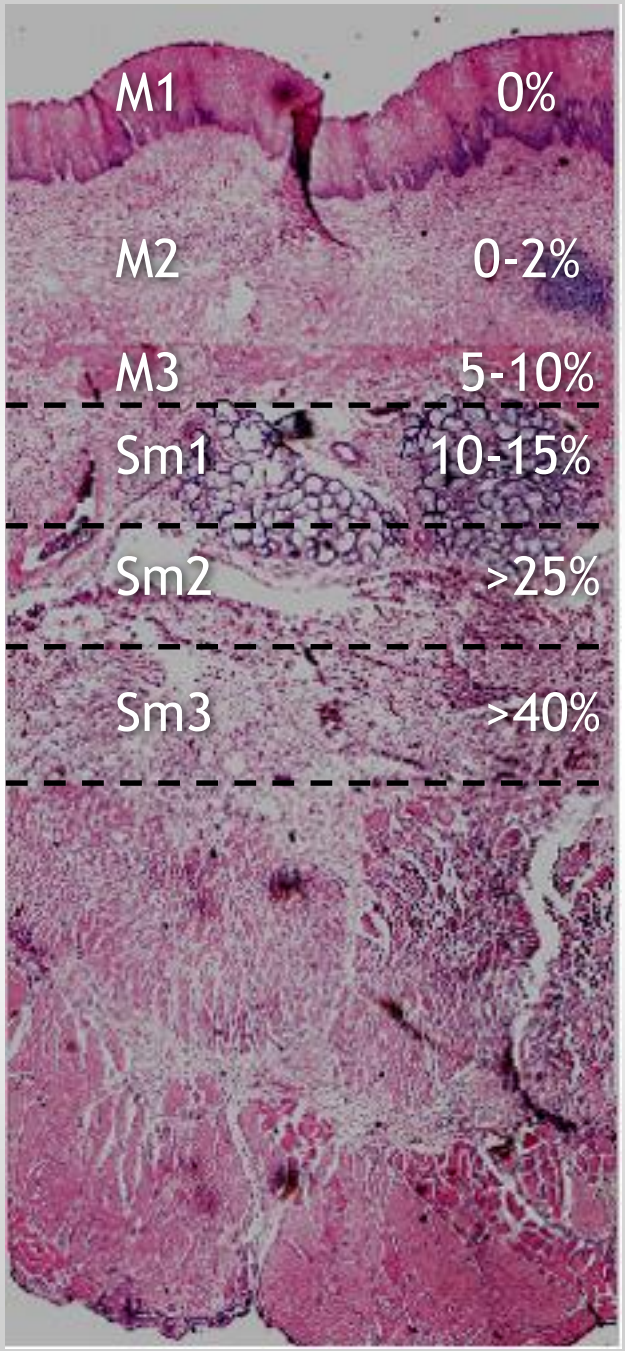


Submucosal cancer

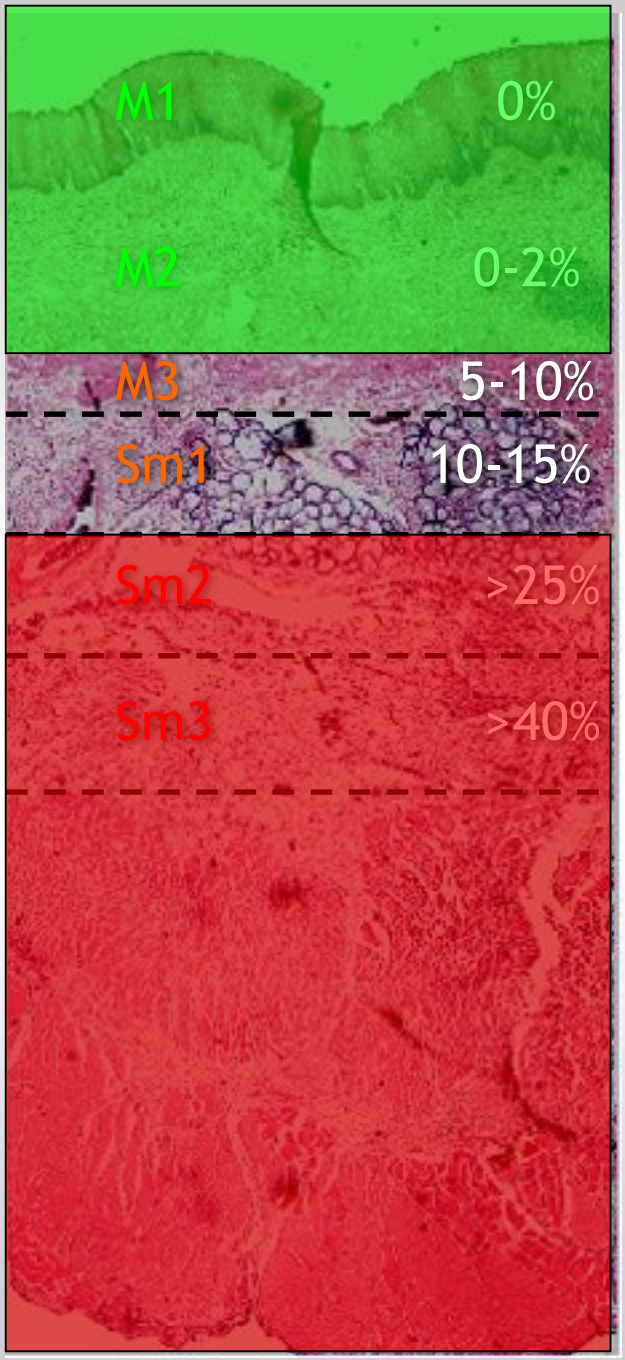
- Not automatically an indication for surgery
- Sm1-ca with low-risk histology: esophageal preservation
- Future: more esophageal preservation strategies for other submucosal cancers.

Treatment of squamous neoplasia





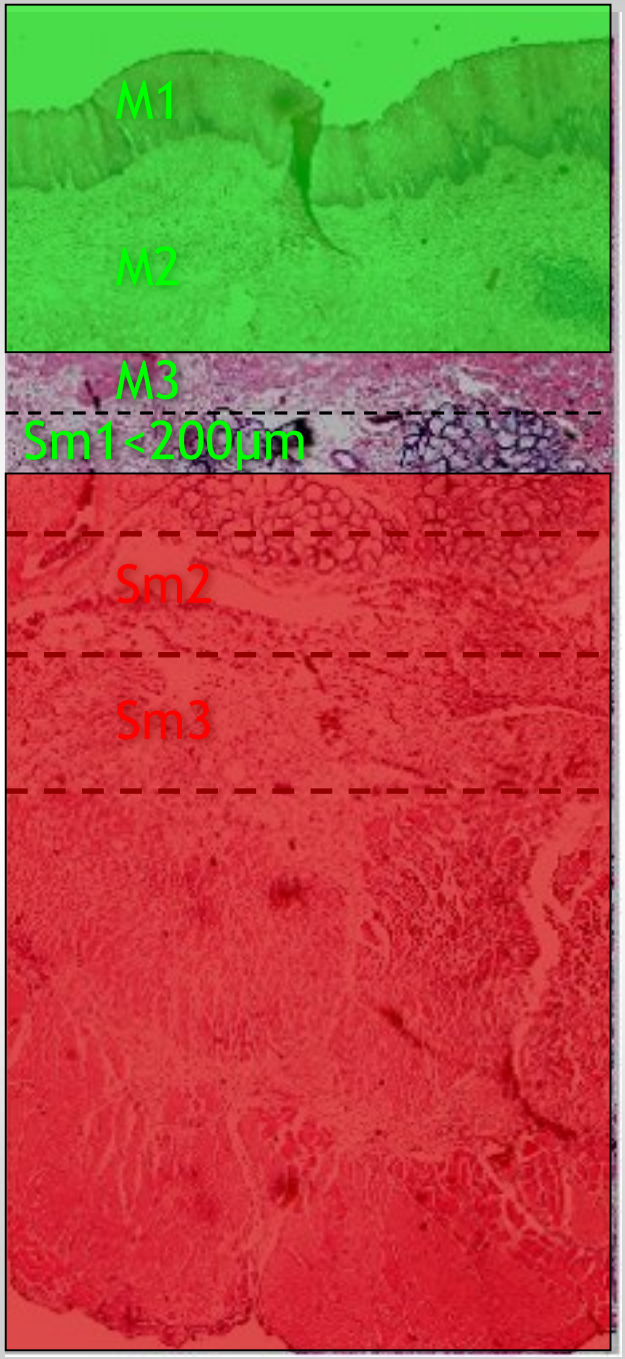
Risk of lymph node metastasis



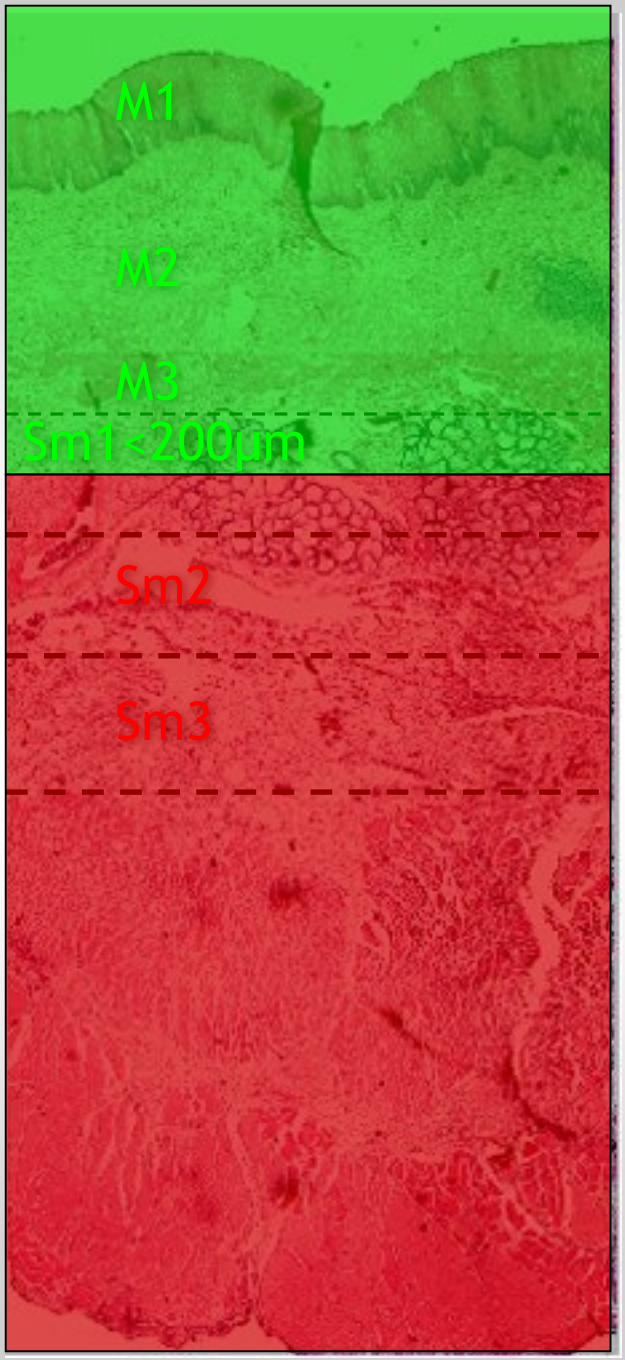
Endoscopic treatment

?????

Surgery +/- ChemoradioTx



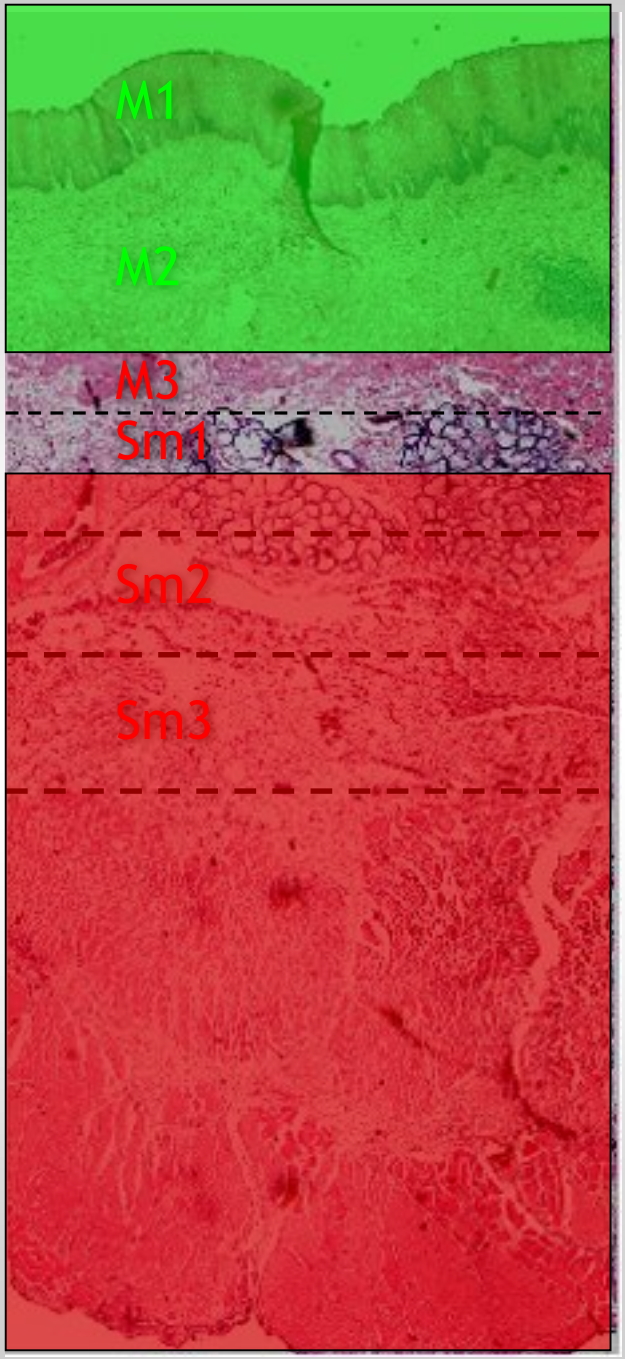
G1/G2, LVI- and Sm1<200µm



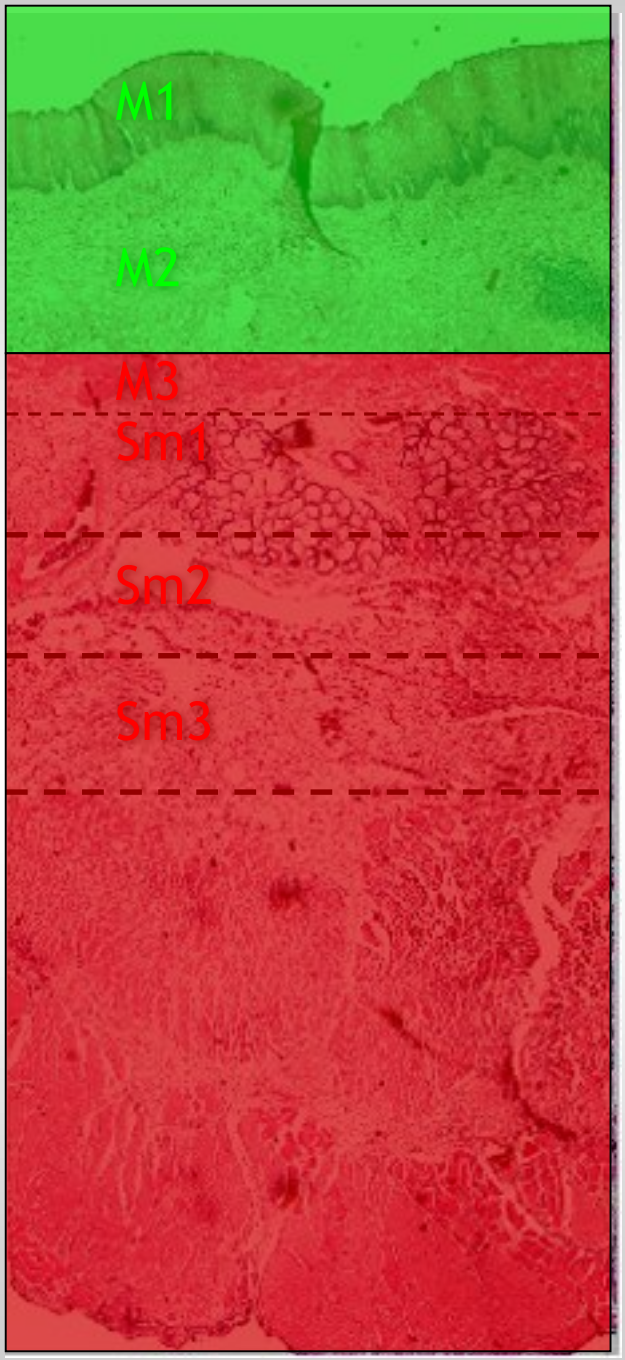
Endoscopic treatment

G1/G2, LVI- and Sm1<200µm

Surgery +/- ChemoradioTx



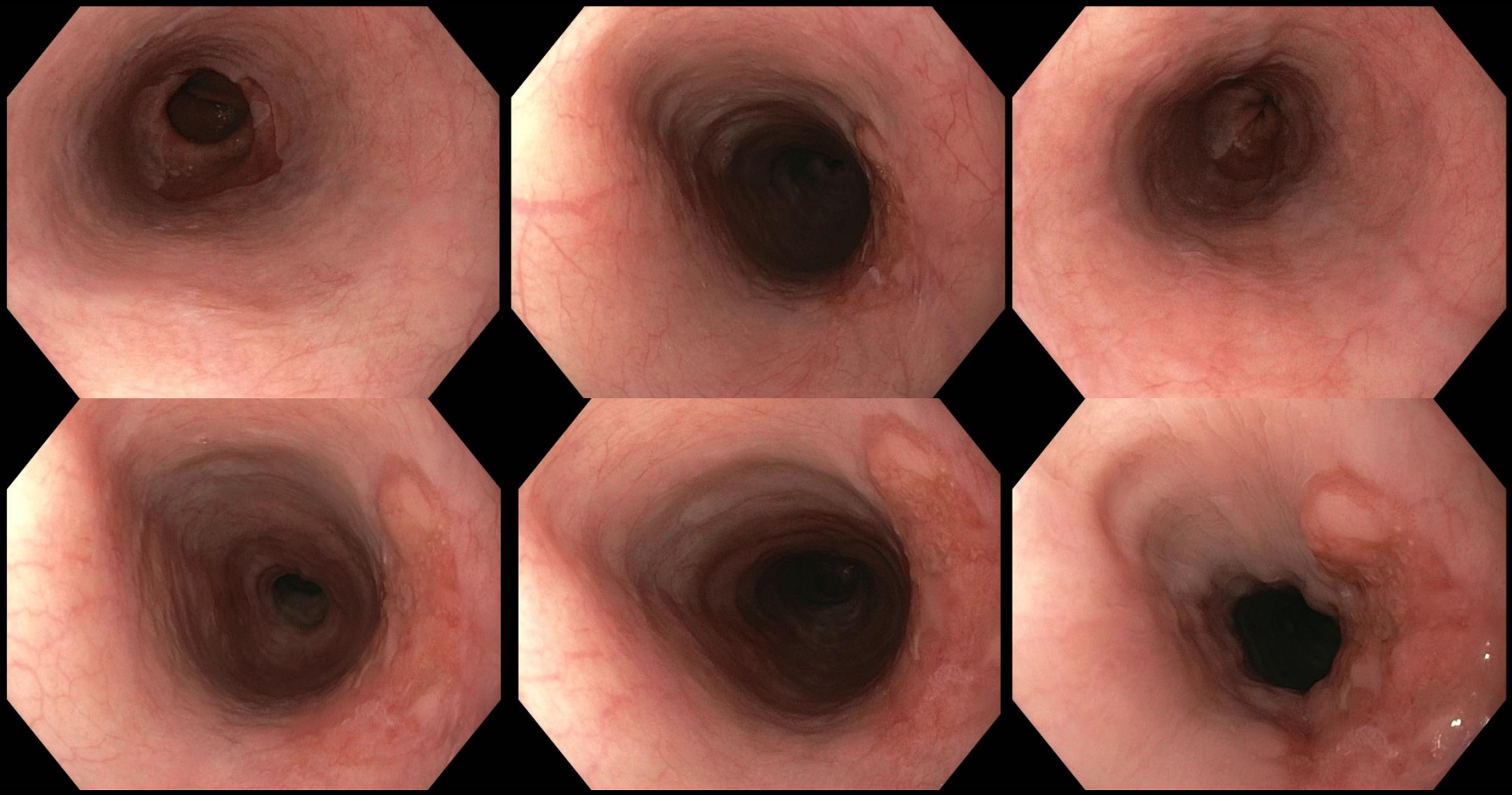
G3/G4 OR LVI+ OR Sm>200µm

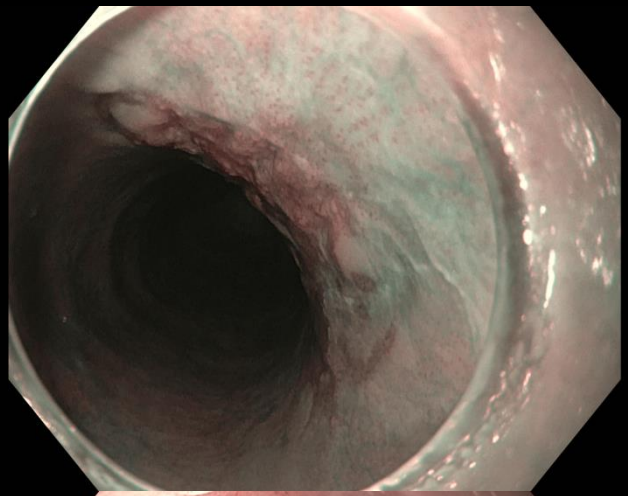


Endoscopic treatment

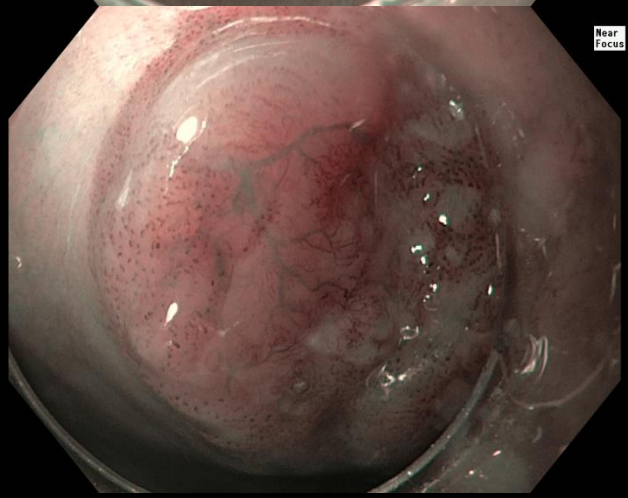
G3/G4 OR LVI+ OR Sm>200µm

Surgery +/- ChemoradioTx





Near
Focus

Near
Focus

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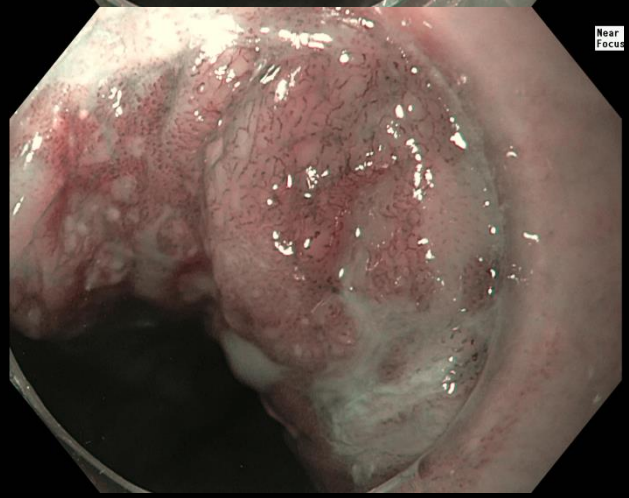
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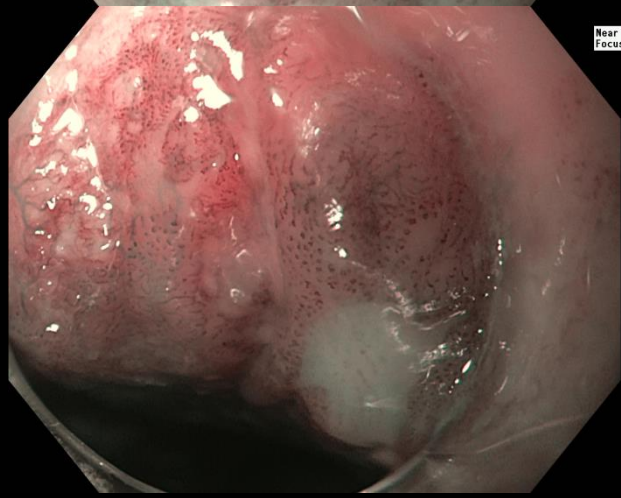
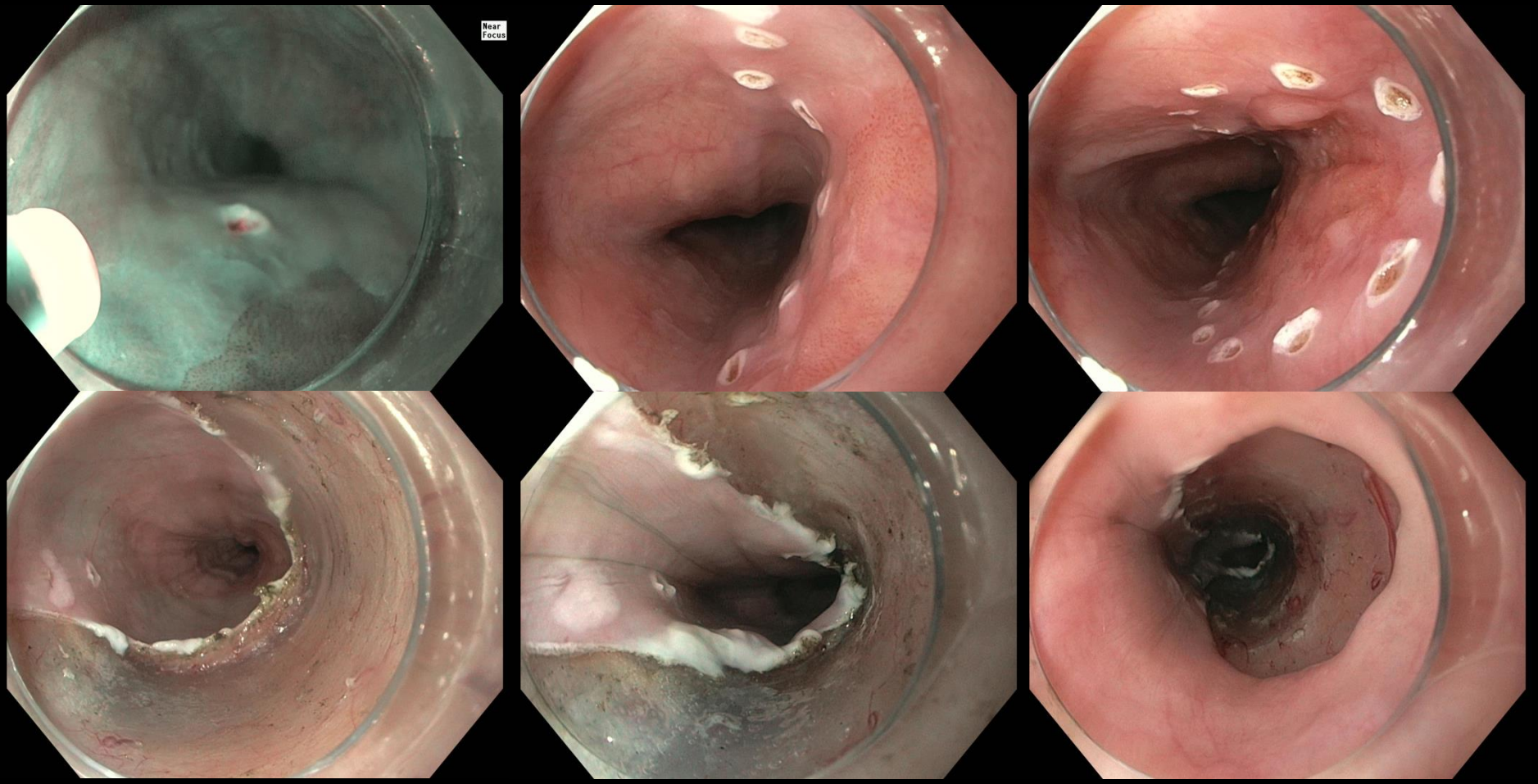
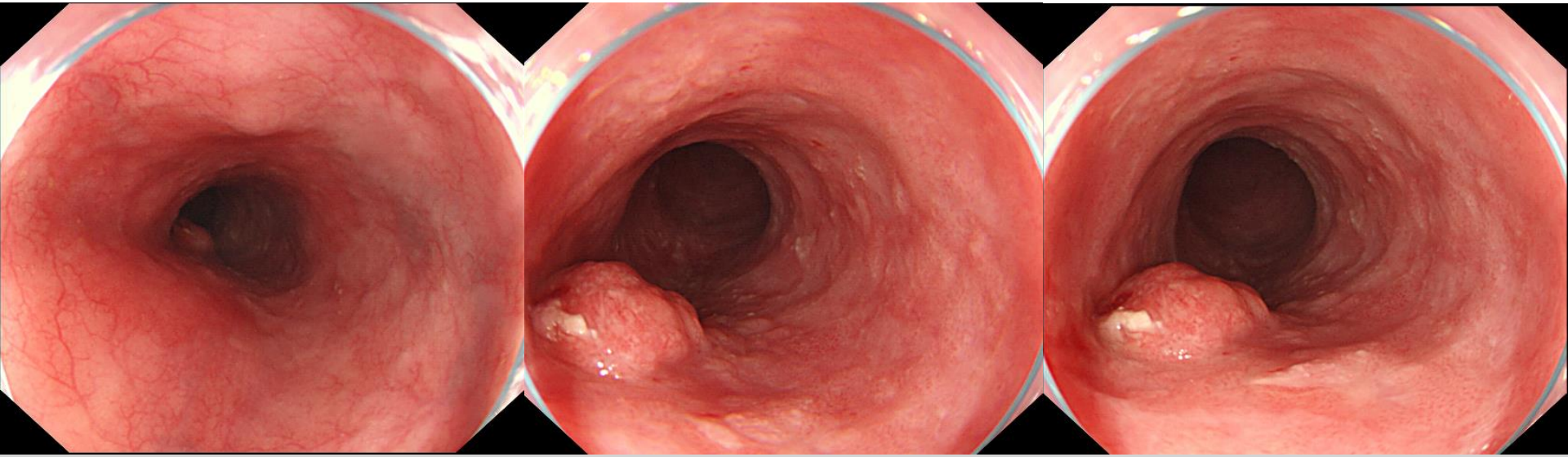

Near
Focus


Near
Focus

Squamous lesions:

Most lesions we detect are NOT amendable for curative endoscopic Tx.



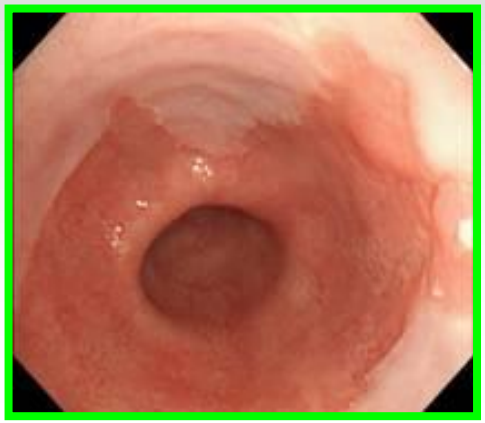
Treatment of squamous neoplasia

- Much more ugly disease than Barrett's!
- We generally miss early squamous lesions
- >75% cases referred are NOT amendable for endoscopic Tx.
- Treatment consists of resection by means of ESD.
- Centralized in 4 centers in the Netherlands

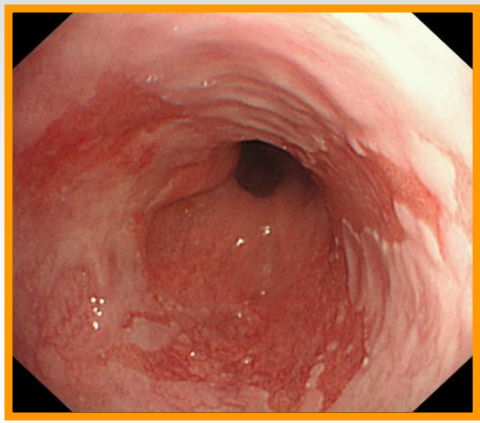
“The organ preserving revolution”

Low grade dysplasia

High grade dysplasia



Mucosal cancer



Submucosal cancer

- HGD and mucosal cancer: endoscopy first choice.
- LGD (confirmed and reproduced): ablation therapy.
- Sm1-ca: esophageal preservation.