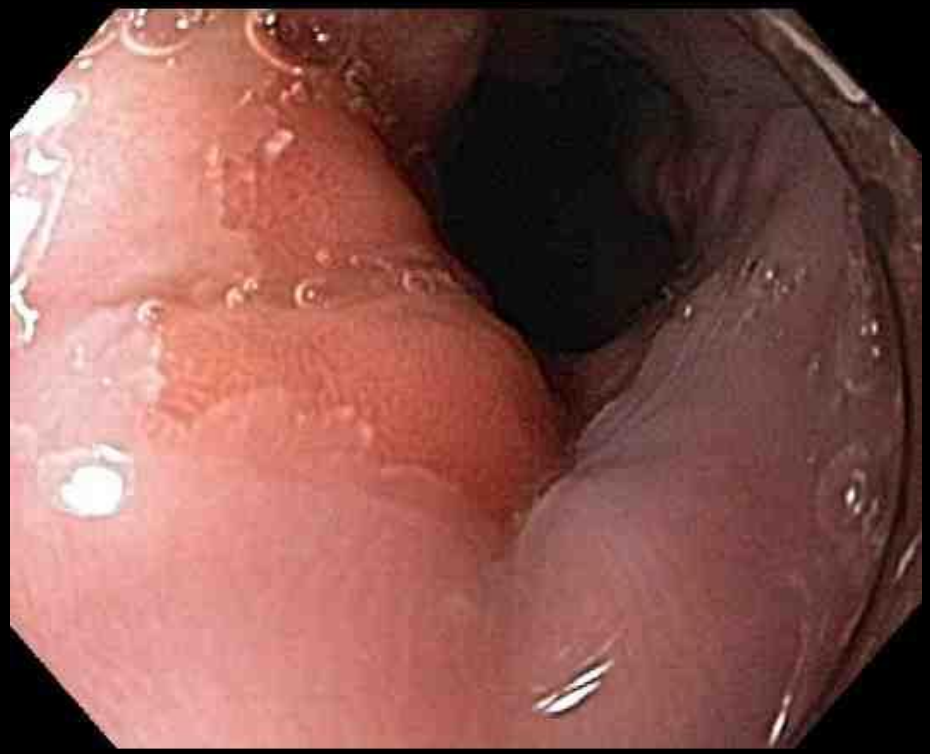
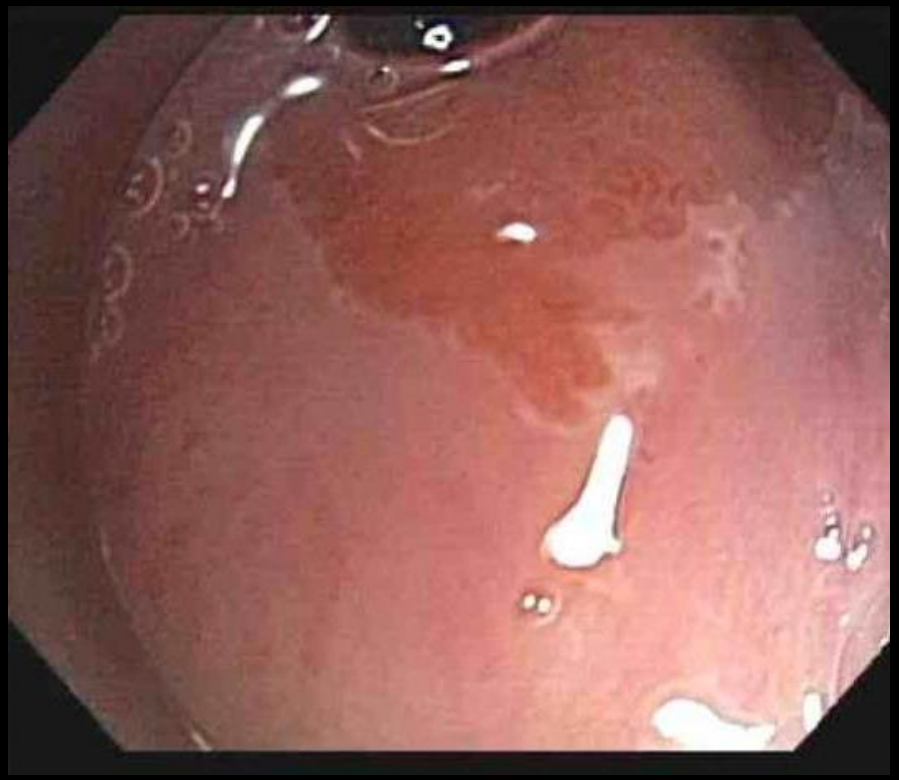
Barrett Esophagus in 2018: the pathologist's perspective

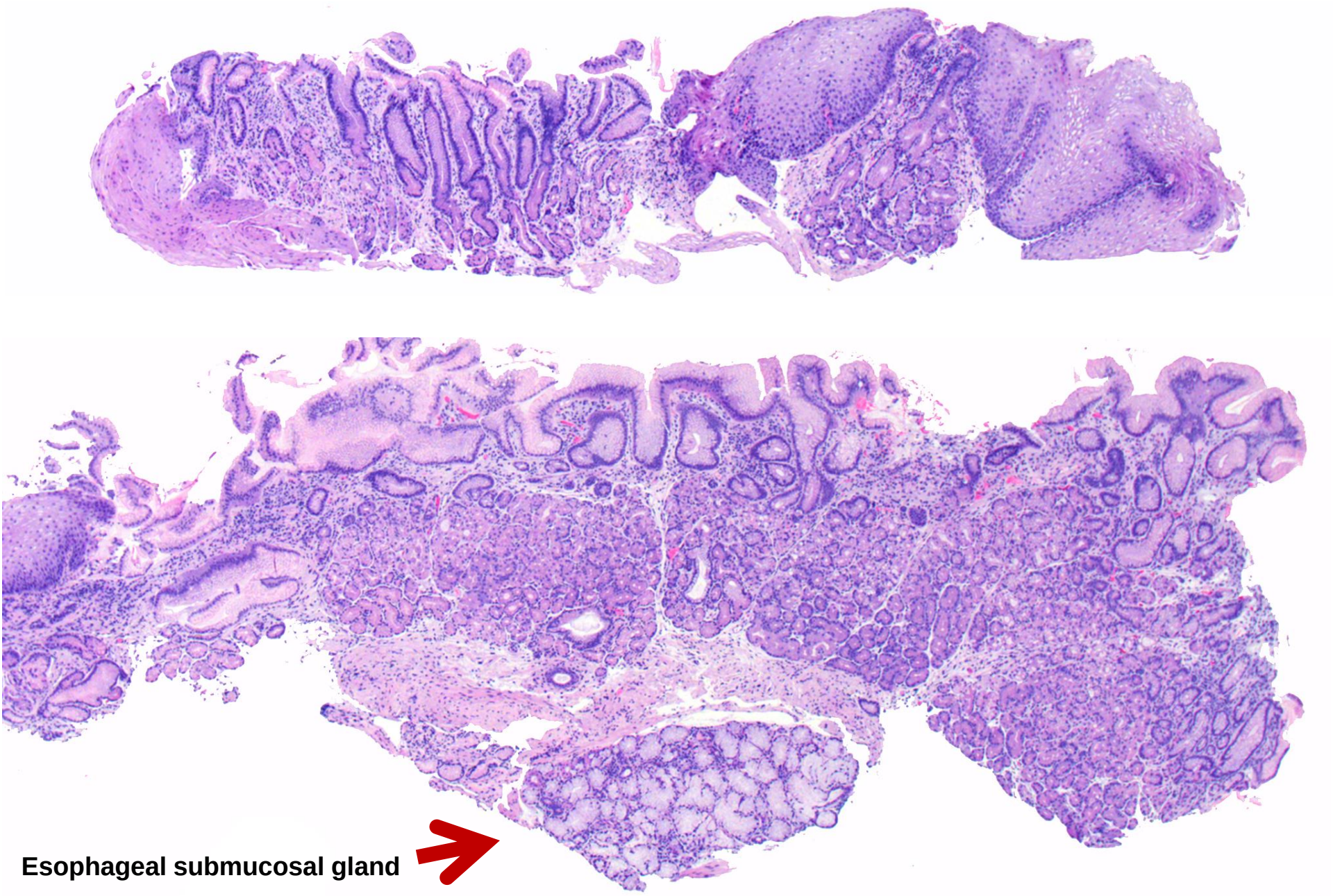
John Hart, MD
Professor of Surgical Pathology & Gastroenterology
Director of GI & Hepatic Pathology
University of Chicago Medical Center

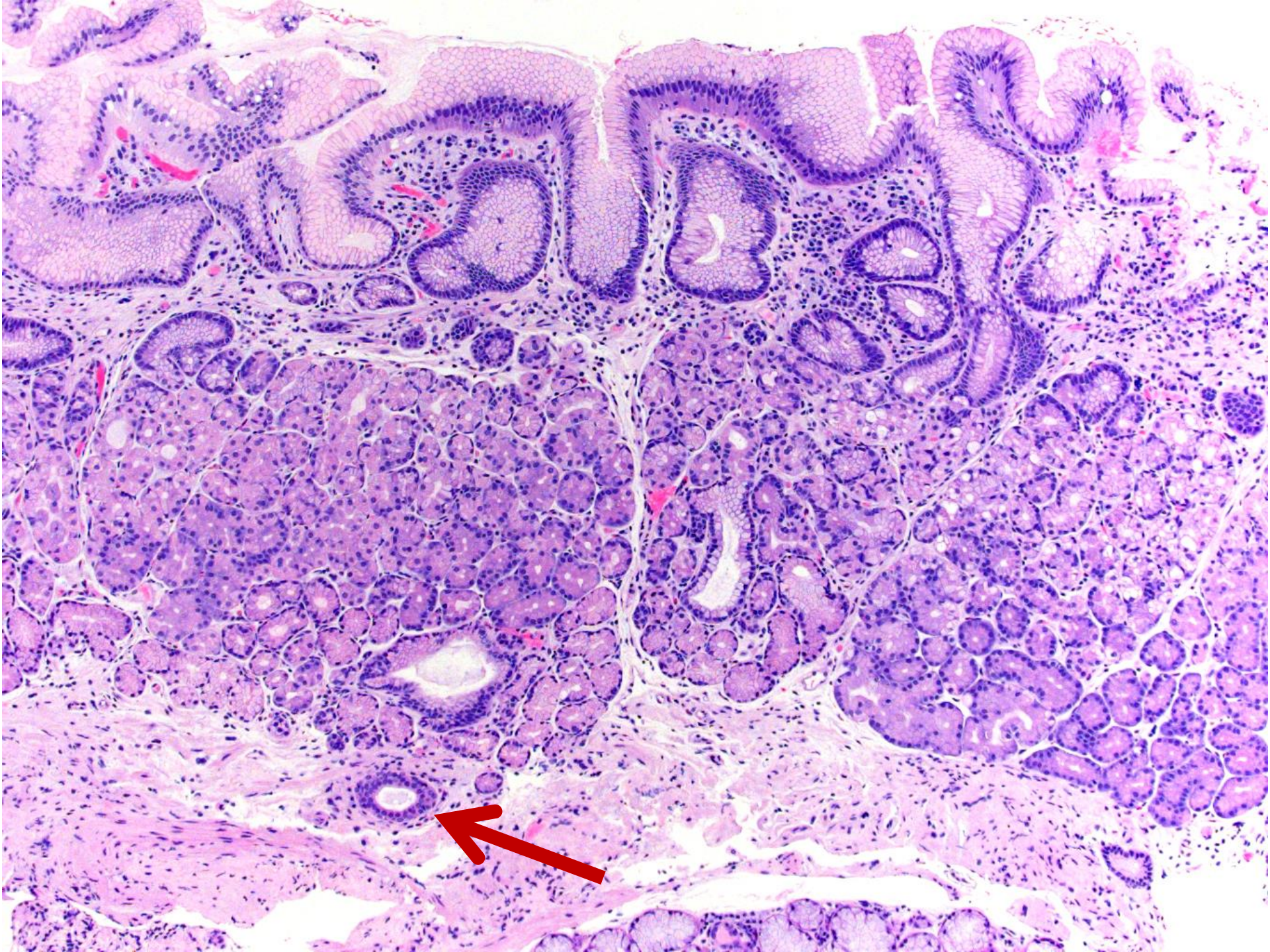
- 71 y.o. M with nocturnal heartburn
- Upper GI endoscopy reveals an irregular Z-line
- Three biopsies obtained from “possible short tongues of Barrett esophagus”





NO GOBLET CELLS





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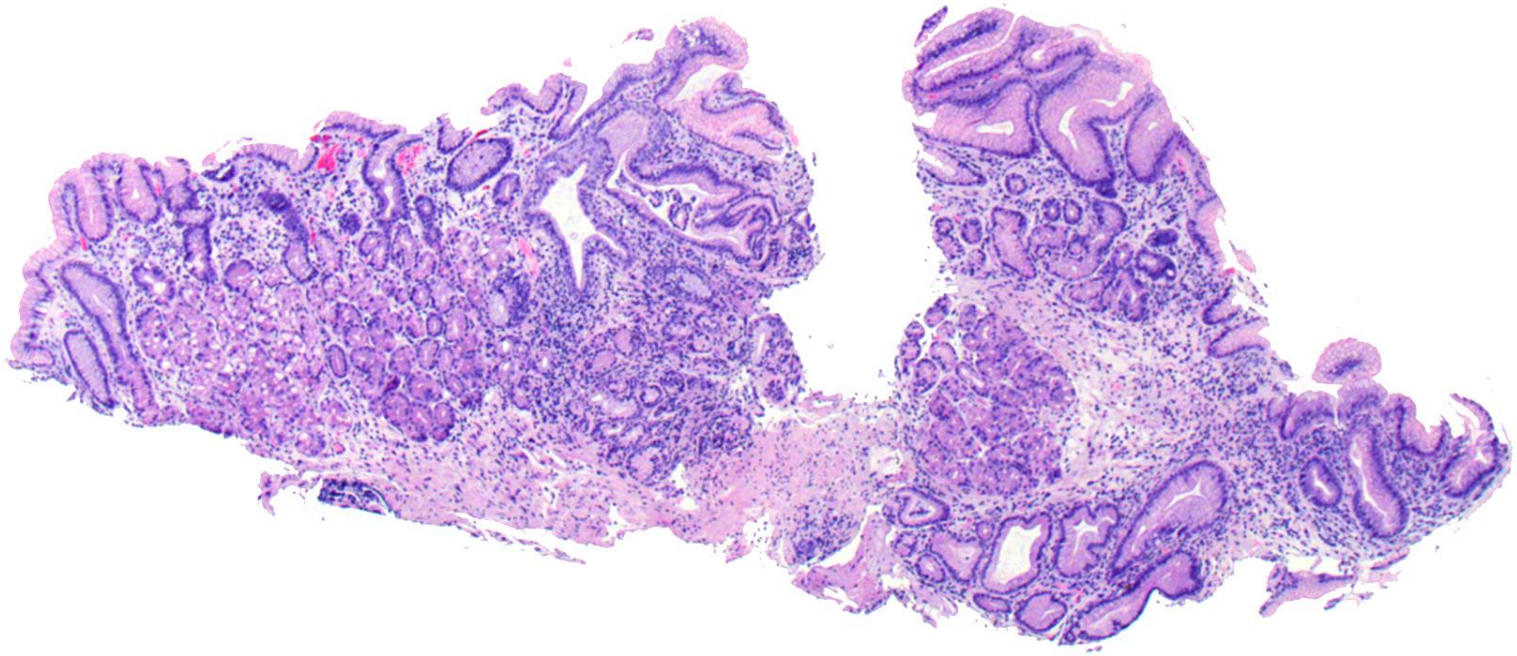
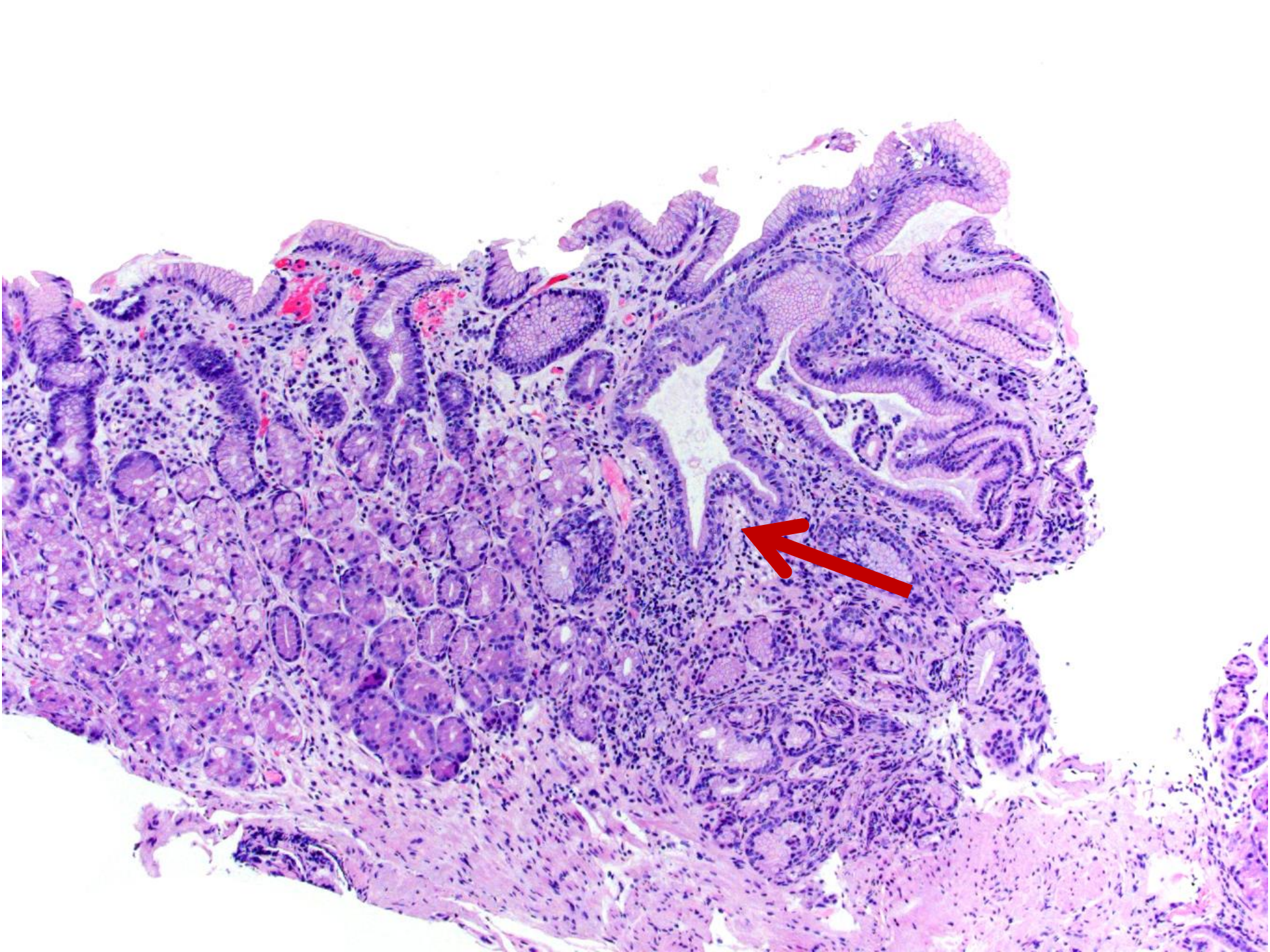
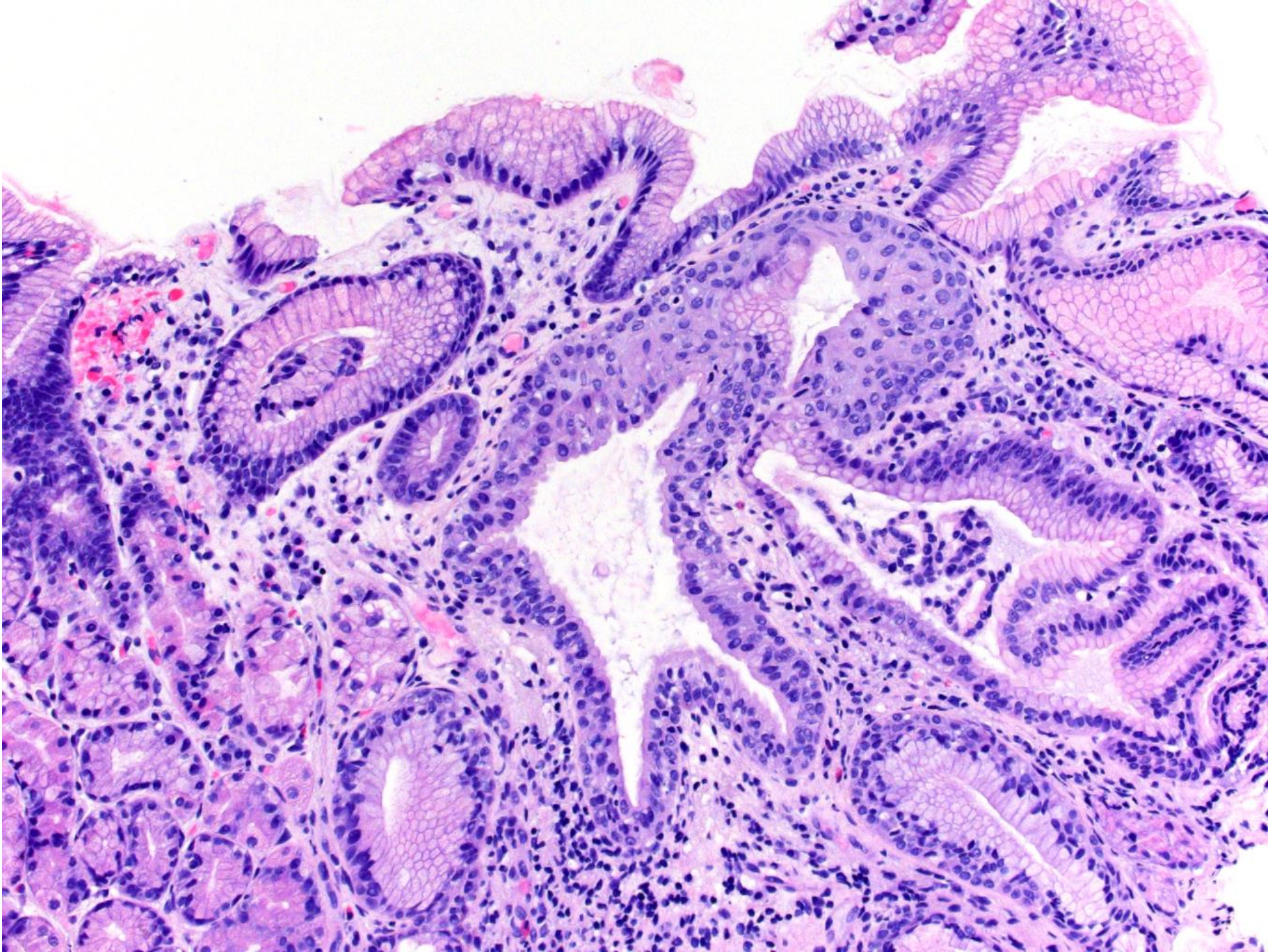
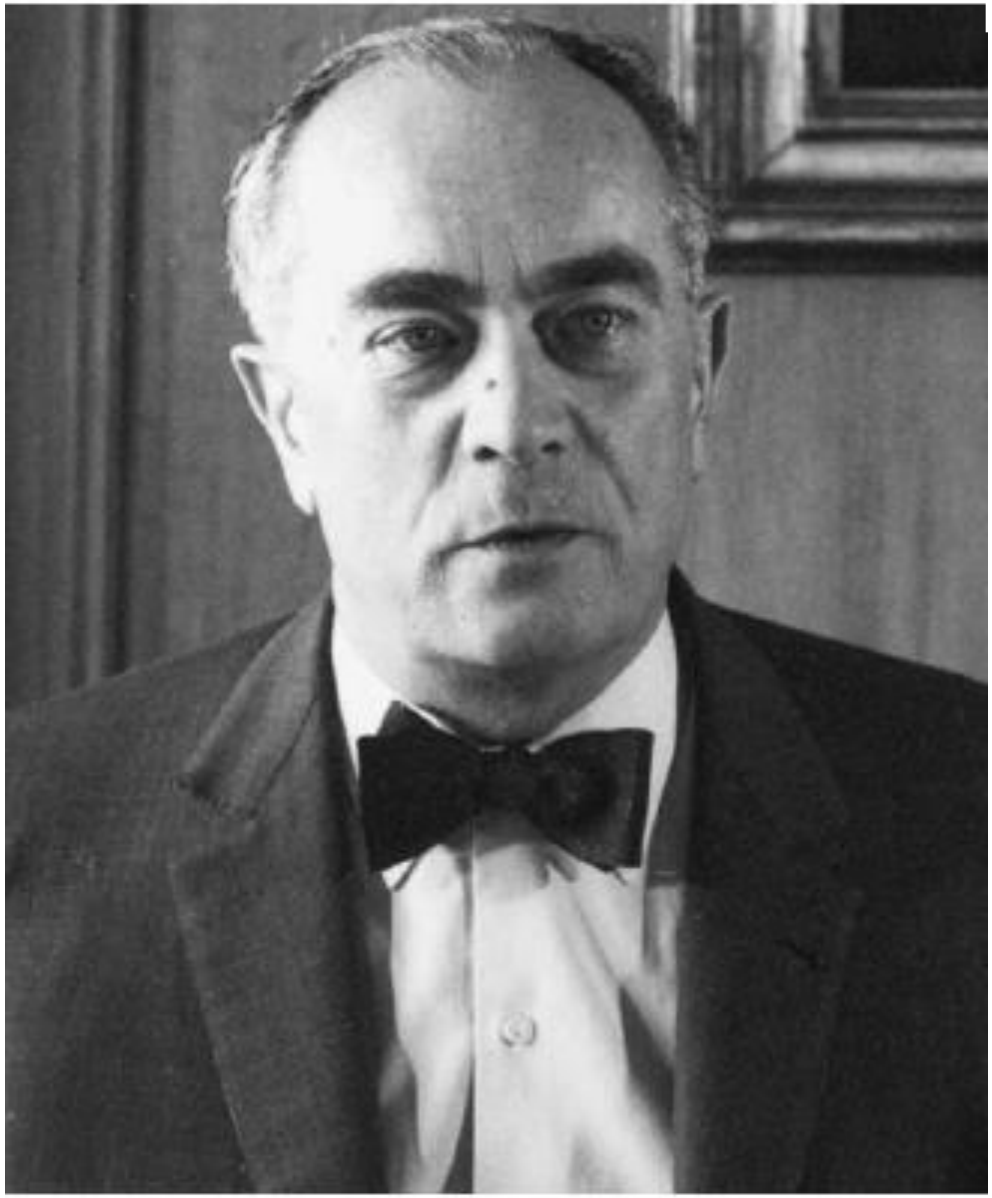




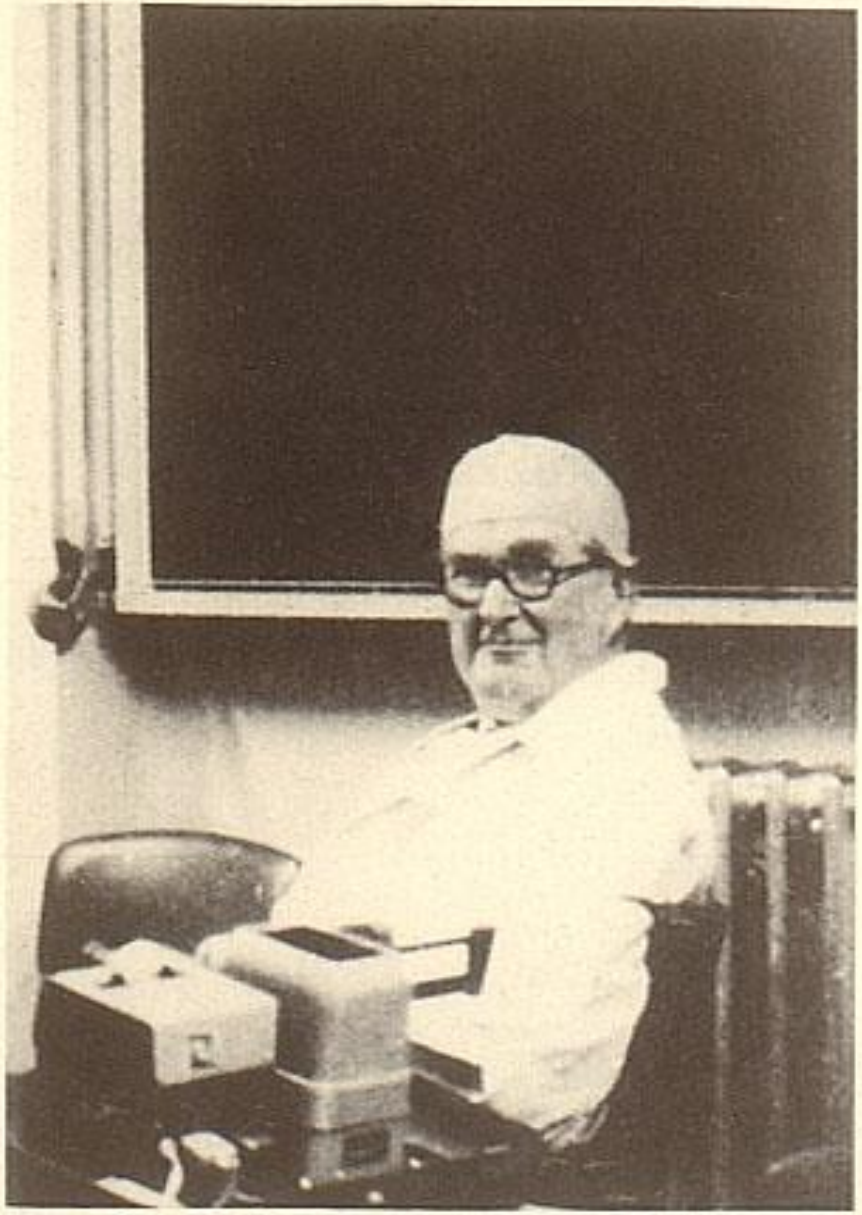



Barrett ?
Not Barrett ?

Jean-Louis Lortat-Jacob



Norman Rupert Barrett



AJG – Vol. 93, No. 7, 1998

Practice Guidelines on the Diagnosis, Surveillance, and Therapy of Barrett's Esophagus

Richard E. Sampliner, M.D., and The Practice Parameters Committee of the American College of Gastroenterology

DEFINITION OF BARRETT'S ESOPHAGUS

Barrett's esophagus is a change in the esophageal epithelium of any length that can be recognized at endoscopy and is confirmed to have intestinal metaplasia by biopsy.

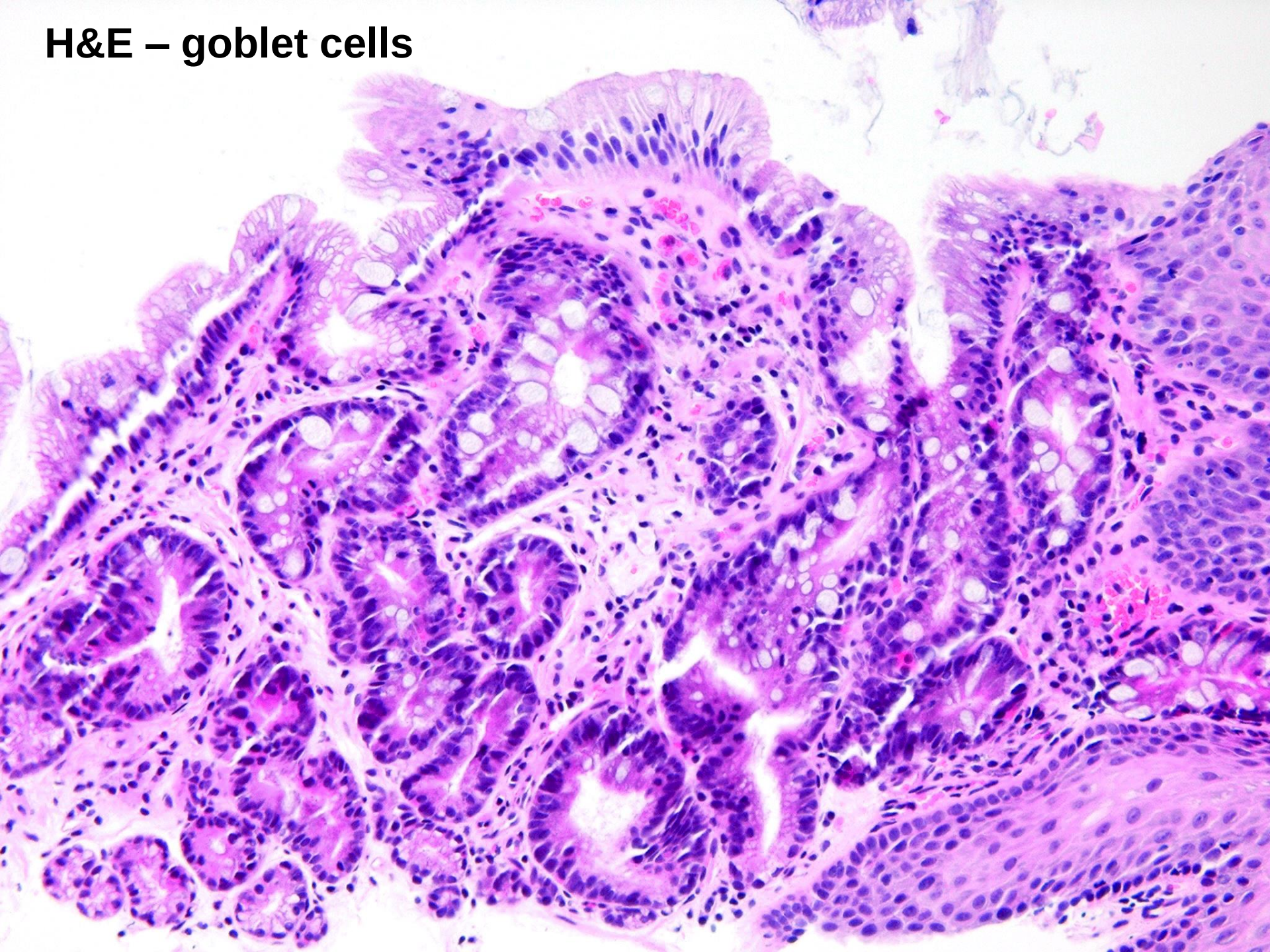
The diagnosis of Barrett's esophagus requires systematic biopsy of the abnormal appearing esophageal mucosa to document intestinal metaplasia and to detect dysplasia.

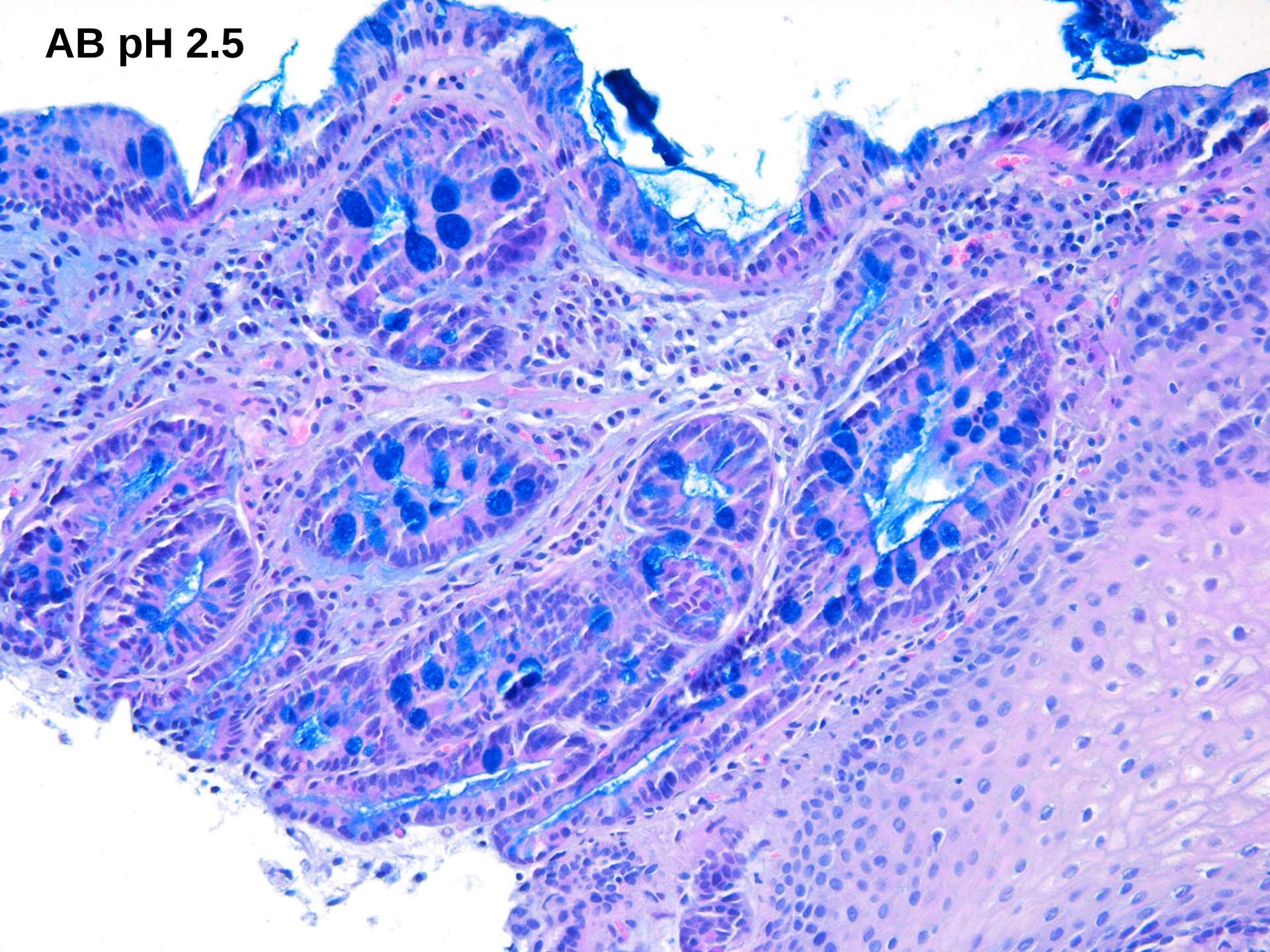
Comparison of Benign and Malignant Cases

DAVID B. SKINNER, M.D., BRUNO C. WALTHER, M.D., ROBERT H. RIDDELL, M.D., HELMUT SCHMIDT, M.D., CLEMENT IASCONE, M.D., THOMAS R. DeMEESTER, M.D.

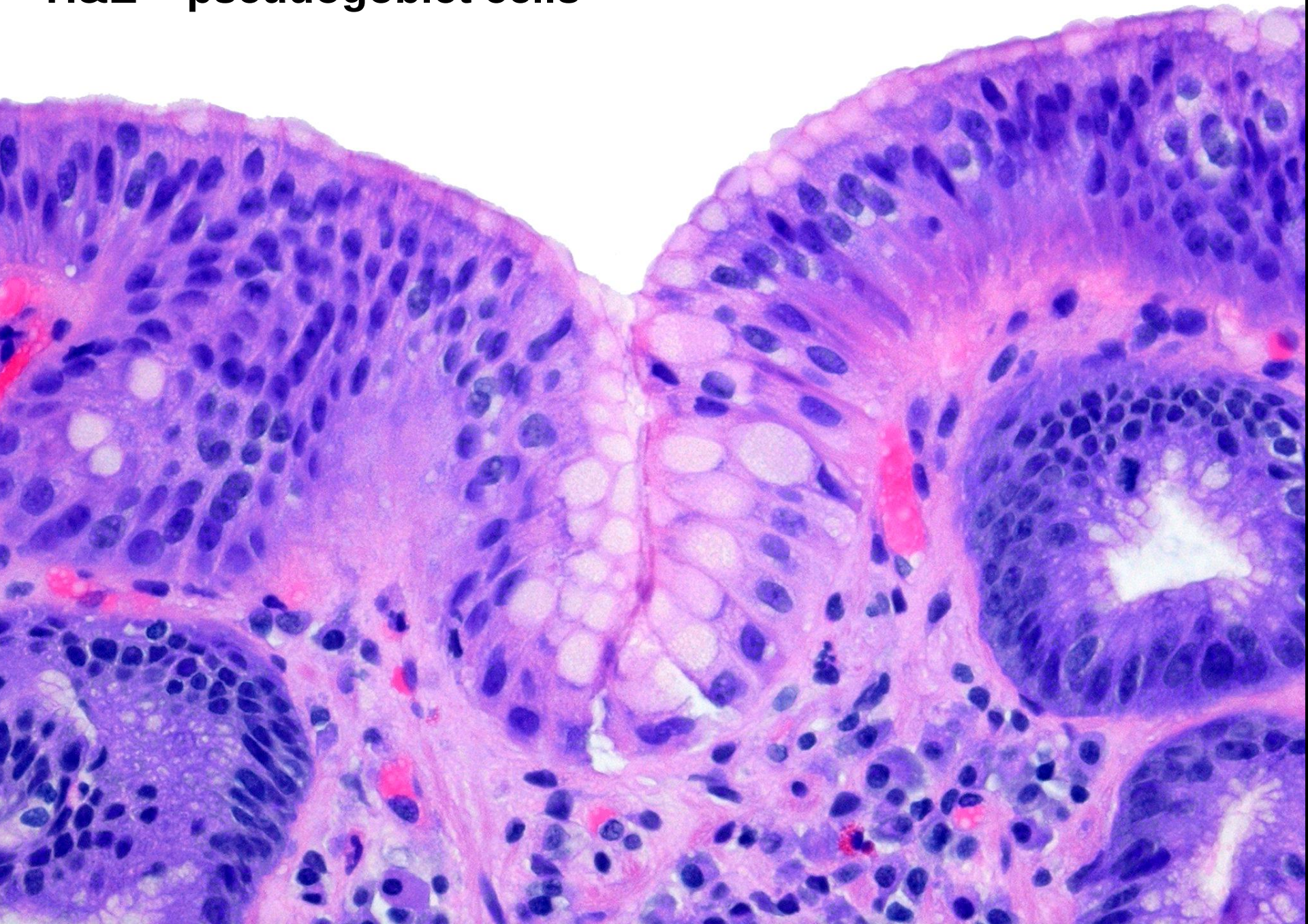
Among the malignant cases in which more thorough pathological examination could be made in the resected specimens, IT epithelium was identified in all 20 specimens, CT in the tubular esophagus 3 or more cm above the junction in eight specimens, and FT in two. In 12 of the specimens, IT was the only type epithelium identified, IT and CT were found together in six, and all three types were identified in two specimens. There were no significant differences in the patterns of epithelium identified between the benign and malignant cases. It appeared that the specialized intestinal type epithelium, featuring goblet cells, was the hallmark of Barrett's esophagus, particularly in patients at risk to develop carcinoma.

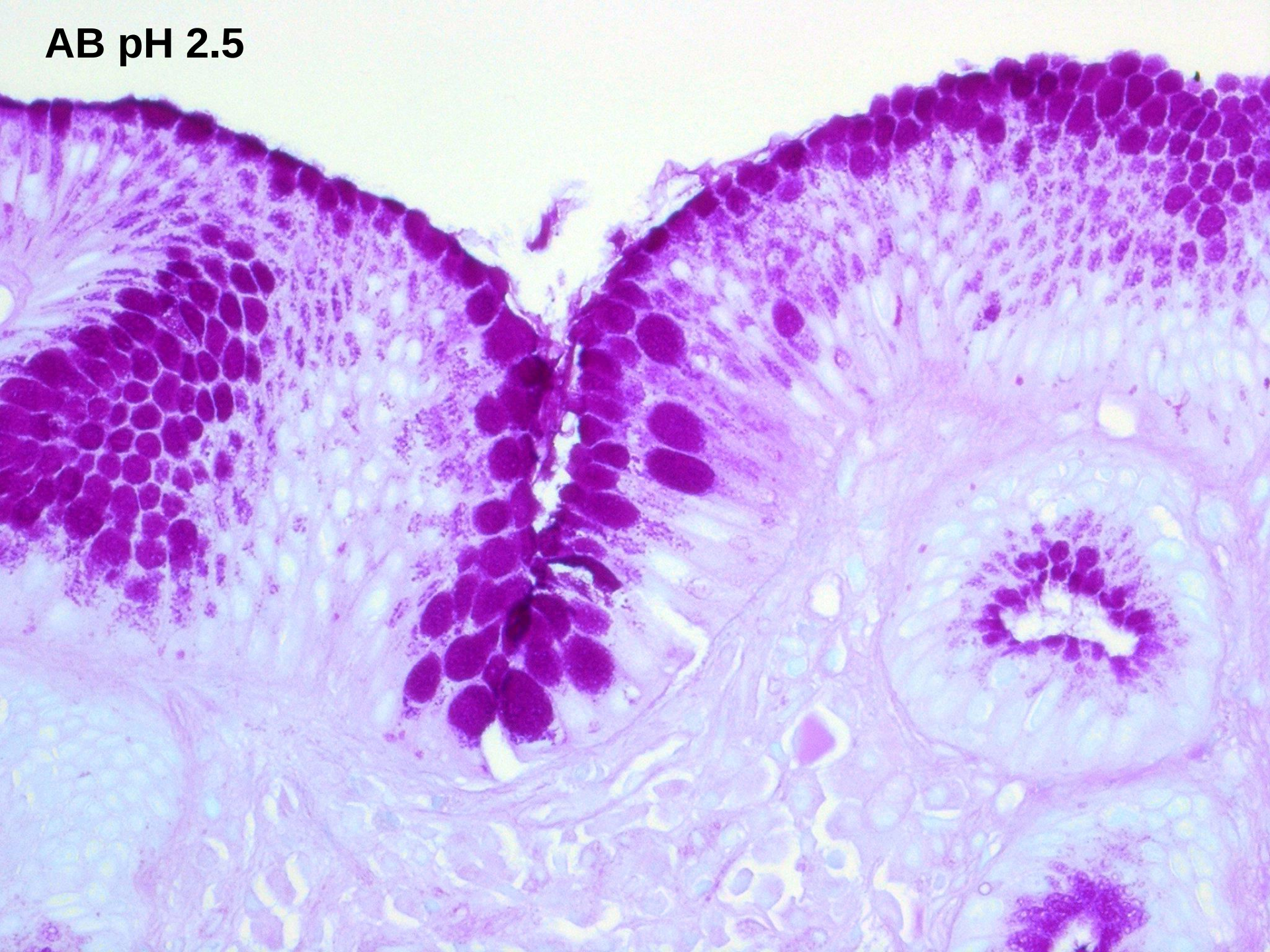
H&E – goblet cells




AB pH 2.5

H&E – pseudogoblet cells




AB pH 2.5

Guidelines for the diagnosis and management of Barrett's columnar-lined oesophagus

A Report of the Working Party of
the British Society of Gastroenterology

August 2005
http://www.bsg.org.uk

BRITISH SOCIETY
OF GASTROENTEROLOGY

diagnosis. The insistence on identification of intestinal metaplasia to establish a diagnosis of "Barrett's oesophagus" or to signify malignant potential is not supported by UK pathological opinion which believes that intestinal metaplasia can always be identified in endoscopically-visible columnar metaplasia providing a sufficient number of biopsies are taken over an adequate time-scale, and therefore a modified definition to encompass this is shown below.

An appropriate definition of "Barrett's oesophagus" (more appropriately referred to as columnar-lined oesophagus[CLO]) is an oesophagus in which any portion of the normal squamous lining has been replaced by a metaplastic columnar epithelium which is visible macroscopically. In order to make a positive diagnosis of "Barrett's oesophagus", a segment of columnar metaplasia of any length must be visible endoscopically above the oesophago-gastric junction and confirmed or corroborated histologically

Give me your tired, your poor,
Your huddled masses yearning to be free
Of Barrett oesophagus

Why the Difference?

- American position:
  - Cancer only arises when intestinal metaplasia is present
  - Endoscopists are often unsure if their biopsies are from short segment Barrett or the gastric cardia
- British position:
  - Since few biopsies are obtained initially, goblet cells may be easily missed
  - If goblet cells are missed, the patient will not be labeled as Barrett esophagus and will not be enrolled in a surveillance program
  - British endoscopists can be trusted

Detection of Intestinal Metaplasia in Barrett's Esophagus: An Observational Comparator Study Suggests the Need for a Minimum of Eight Biopsies

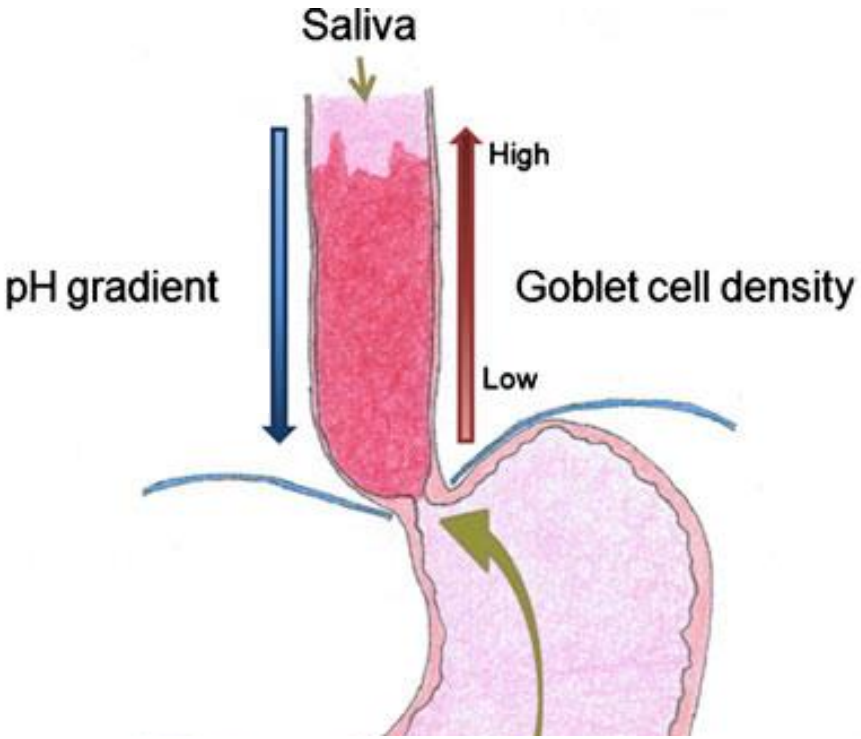
Rebecca Harrison, M.B.Ch.B., B.Sc. (Hons), F.R.C.Path.,[1] Ian Perry, M.B.Ch.B., Ph.D., M.R.C.P.,[2] William Haddadin, M.B.Ch.B., M.R.C.Path.,[3] Stuart McDonald, Ph.D.,[4] Richard Bryan, M.B.Ch.B., Ph.D., M.R.C.S.,[5] Keith Abrams, Ph.D.,[6] Richard Sampliner, M.D., Ph.D., F.A.C.G.,[7] Nicholas J. Talley, M.D., Ph.D., F.A.C.G.,[8] Paul Moayyedi, M.B.Ch.B., Ph.D., M.P.H., F.R.C.P., F.R.C.P.C.,[9] and Janusz A. Jankowski, M.D., Ph.D., F.R.C.P., F.A.C.G.[1,4]

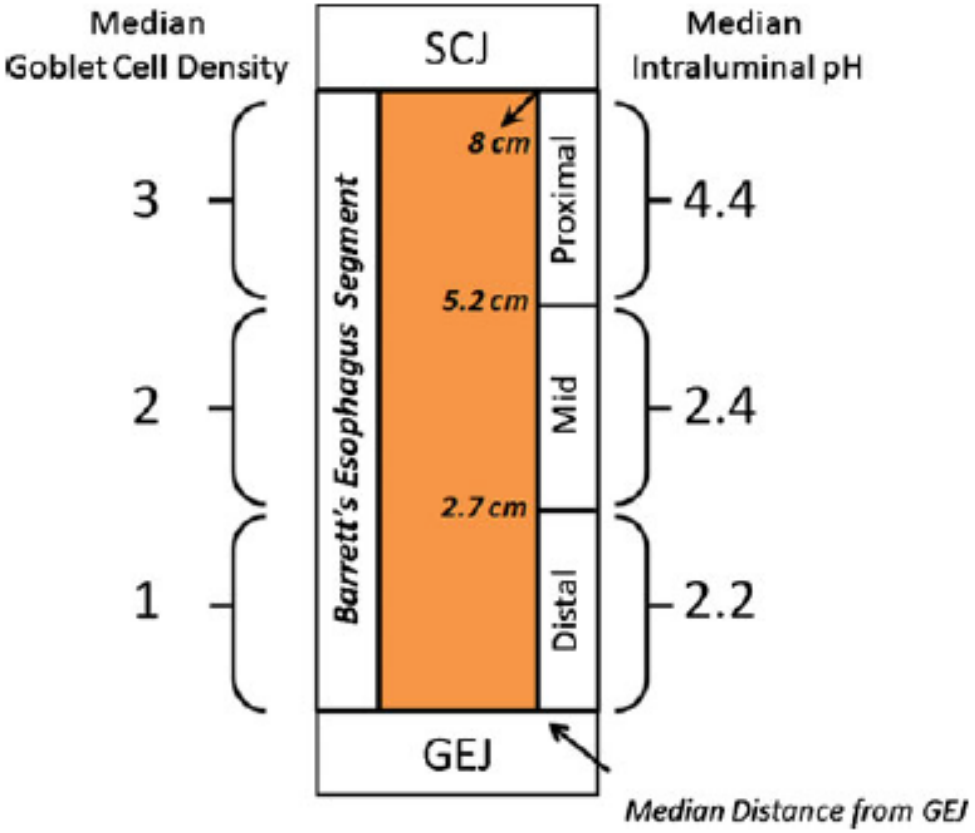
(Am J Gastroenterol 2007;102:1154–1161)

Table 2. The Relationship Between the Detection of Intestinal Metaplasia (IM) With Number of Biopsies

Number of Biopsies Per Endoscopy	Number of Endoscopies	% of Endoscopies With IM	Mean % for Each Grouping
1	15	20	
2	21	33	34.6
3	52	37	
4	62	37	
5	40	58	
6	30	63	67.9
7	19	74	
8	17	94	
9	10	80	
10	10	70	74.1
11	4	75	
12	3	67	
13	1	100	
14	–	No patient	71.4
15	4	75	
16	2	50	
>16 (19–34)	6		100

Goblet cell density in BE is related to luminal pH





The highest density of goblet cells is seen where the pH is from 3 to 5

Theodorou, D., et al. J Gastrointest Surg. 2012;16:469-74.

PRACTICE GUIDELINES

Updated Guidelines 2008 for the Diagnosis, Surveillance and Therapy of Barrett's Esophagus

Kenneth K. Wang, M.D. and Richard E. Sampliner, M.D.
The Practice Parameters Committee of the American College of Gastroenterology

(Am J Gastroenterol 2008;103:788–797)

Barrett's esophagus is a change in the distal esophageal epithelium of any length that can be recognized as columnar type mucosa at endoscopy and is confirmed to have intestinal metaplasia by biopsy of the tubular esophagus. (Grade B

Table 2. Dysplasia Grade and Surveillance Interval

Dysplasia	Documentation	Follow-Up
None	Two EGDs with biopsy within 1 year	Endoscopy every 3 years
Low Grade	• Highest grade on repeat EGD * with biopsies within 6 months • Expert pathologist confirmation	1 year interval until no dysplasia x 2
High Grade	• Mucosal irregularity • Repeat EGD with biopsies to rule out EAC * within 3 months • Expert pathologist confirmation	ER * Continued 3 month surveillance or intervention based on results and patient

*EGD – esophagogastroduodenoscopy; ER – endoscopic resection; EAC – esophageal adenocarcinoma.

American Gastroenterological Association Medical Position Statement on the Management of Barrett's Esophagus

GASTROENTEROLOGY 2011;140:1084–1091

The AGA Institute Medical Position Panel consisted of the authors of the technical review (Stuart J. Spechler, MD, AGAF, Prateek Sharma, MD, Rhonda F. Souza, MD, AGAF, John M. Inadomi, MD, AGAF, Nicholas J. Shaheen, MD, MPH,

Definition of Barrett's Esophagus

- Any extent of metaplastic columnar epithelium that ***predisposes to cancer development*** which replaces the stratified squamous epithelium that normally lines the distal esophagus.

- Intestinal metaplasia is required for the diagnosis of Barrett's esophagus because ***intestinal metaplasia is the only type of esophageal columnar epithelium that clearly predisposes to malignancy***.

***italics* added**

American Gastroenterological Association Medical Position Statement on the Management of Barrett's Esophagus

GASTROENTEROLOGY 2011;140:1084–1091

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Presently, there are insufficient data to make meaningful recommendations regarding management of patients who have solely cardia-type epithelium in the esophagus, and we do not recommend use of the term "Barrett's esophagus" for those patients. Based on this lack of data, it is justified not to perform endoscopic surveillance for patients solely with cardia-type epithelium in the esophagus.

Consensus Statements for Management of Barrett's Dysplasia and Early-Stage Esophageal Adenocarcinoma, Based on a Delphi Process

CATHY BENNETT,[1] NIMISH VAKIL,[2] JACQUES BERGMAN,[3] REBECCA HARRISON,[4] ROBERT ODZE,[5] MICHAEL VIETH,[6] SCOTT SANDERS,[7] LAURA GAY,[8] OLIVER PECH,[6] GAIUS LONGCROFT–WHEATON,[9] YVONNE ROMERO,[10] JOHN INADOMI,[11] JAN TACK,[12] DOUGLAS A. CORLEY,[13] HENDRIK MANNER,[14] SUSI GREEN,[9] DAVID AL DULAIMI,[15] HAYTHEM ALI,[16] BILL ALLUM,[17] MARK ANDERSON,[18] HOWARD CURTIS,[19] GARY FALK,[20] M. BRIAN FENNERTY,[21] GRANT FULLARTON,[22] KAUSILIA KRISHNADATH,[3] STEPHEN J. MELTZER,[23] DAVID ARMSTRONG,[24] ROBERT GANZ,[25] GIANPAOLO CENGIA,[26] JAMES J. GOING,[22] JOHN GOLDBLUM,[27] CHARLES GORDON,[28] HEIKE GRABSCH,[30] CHRIS HAIGH,[31] MICHIO HONGO,[32] DAVID JOHNSTON,[33] RICKY FORBES–YOUNG,[34] ELAINE KAY,[35] PHILIP KAYE,[36] TONI LERUT,[12] LAURENCE B. LOVAT,[37] LARS LUNDELL,[38] PHILIP MAIRS,[39] TADAKUZA SHIMODA,[40] STUART SPECHLER,[41] STEPHEN SONTAG,[42] PETER MALFERTHEINER,[43] IAIN MURRAY,[44] MANOJ NANJI,[8] DAVID POLLER,[9] KRISH RAGUNATH,[36] JAROSLAW REGULA,[45] RENZO CESTARI,[26] NEIL SHEPHERD,[46] RAJVINDER SINGH,[47] HUBERT J. STEIN,[48] NICHOLAS J. TALLEY,[49] JEAN–PAUL GALMICHE,[50] TONY C. K. THAM,[51] PETER WATSON,[1] LISA YERIAN,[27] MASSIMO RUGGE,[29] THOMAS W. RICE,[27] JOHN HART,[52] STUART GITTENS,[53] DAVID HEWIN,[46] JUERGEN HOCHBERGER,[54] PETER KAHRILAS,[55] SEAN PRESTON,[56] RICHARD SAMPLINER,[57] PRATEEK SHARMA,[58] ROBERT STUART,[59] KENNETH WANG,[10] IRVING WAXMAN,[52] CHRIS ABLEY,[4] DUNCAN LOFT,[60] IAN PENMAN,[34] NICHOLAS J. SHAHEEN,[61] AMITABH CHAK,[62] GARETH DAVIES,[63] LORNA DUNN,[64] YNGVE FALCK–YTTER,[65] JOHN DECAESTECKER,[4] PRADEEP BHANDARI,[9] CHRISTIAN ELL,[6] S. MICHAEL GRIFFIN,[64] STEPHEN ATTWOOD,[66] HUGH BARR,[46] JOHN ALLEN,[67] MARK K. FERGUSON,[52] PAUL MOAYYEDI,[24] and JANUSZ A. Z. JANKOWSKI[4,8,68]

GASTROENTEROLOGY 2012;143:336–346

Non-goblet columnar metaplasia of the esophagus can progress to cancer, but the magnitude of risk is unknown. *Agreement: A+ 59%, A 33%, U 6%, D 2%, D+ 0%. Evidence: Low.*

Barrett's esophagus: A historical perspective, an update on core practicalities and predictions on future evolutions of management

Journal of Gastroenterology and Hepatology **26** (2011) Suppl. 1; 11–30

John Dent

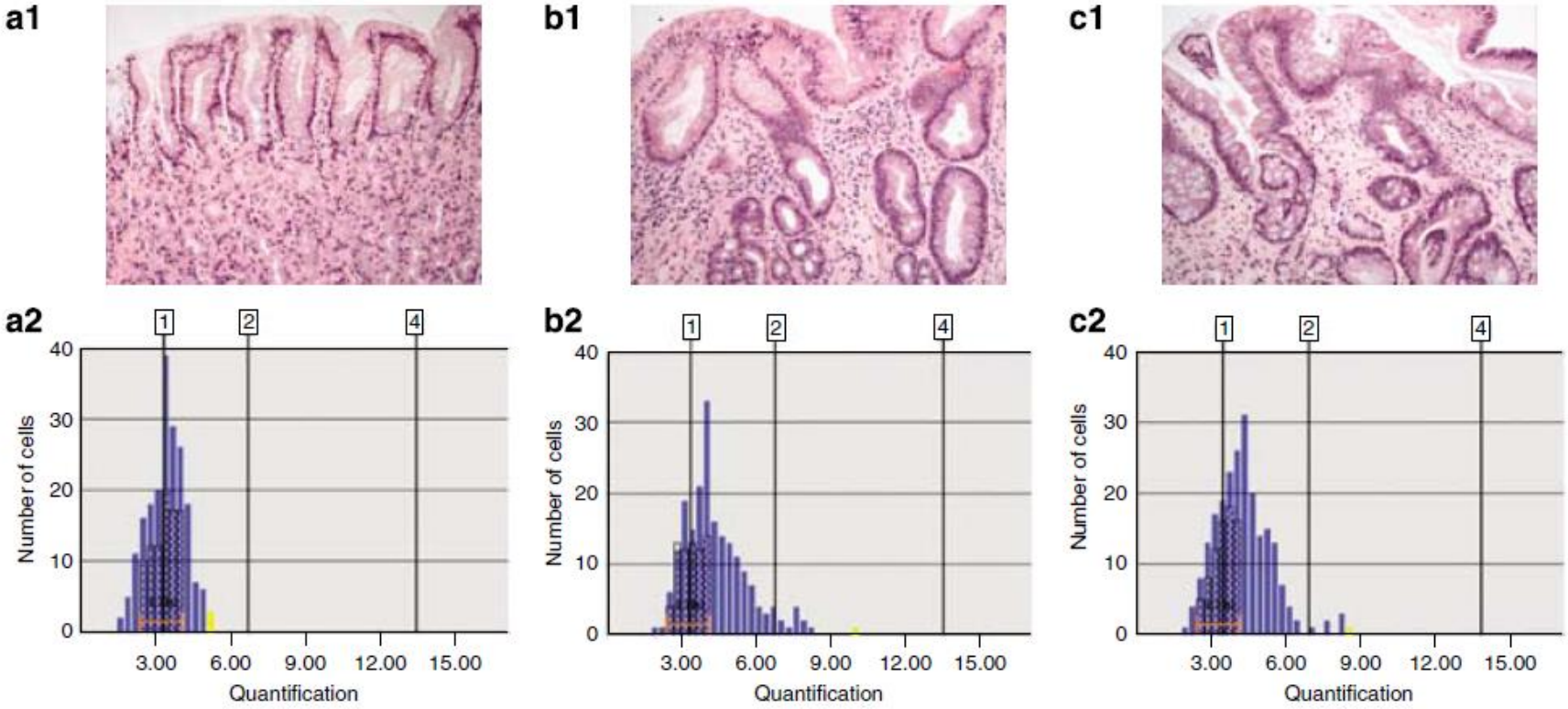
1. Risk for cancer should not be part of the definition for Barrett esophagus
2. Not enough biopsies are taken in routine practice to always find goblet cells
3. Goblet cells may develop over time
4. Abnormal DNA histograms in non-goblet cell columnar mucosa (Liu *et al*)
5. Cancer is documented to arise in columnar mucosa without goblet cells (Tabuko *et al*)
6. Cancer occurs with equal frequency in columnar mucosa without goblet cells (Gatenby *et al* and Kelty *et al*)

Metaplastic Esophageal Columnar Epithelium Without Goblet Cells Shows DNA Content Abnormalities Similar to Goblet Cell–Containing Epithelium

Am J Gastroenterol 2009; 104:816–824;

Weitian Liu, MD, PhD[1,2], Hejin Hahn, MD, PhD[1], Robert D. Odze, MD, FRCPC[1,3] and Raj K. Goyal, MD[1–3]

Gastric body **Cardia type** **Barrett (GC)**

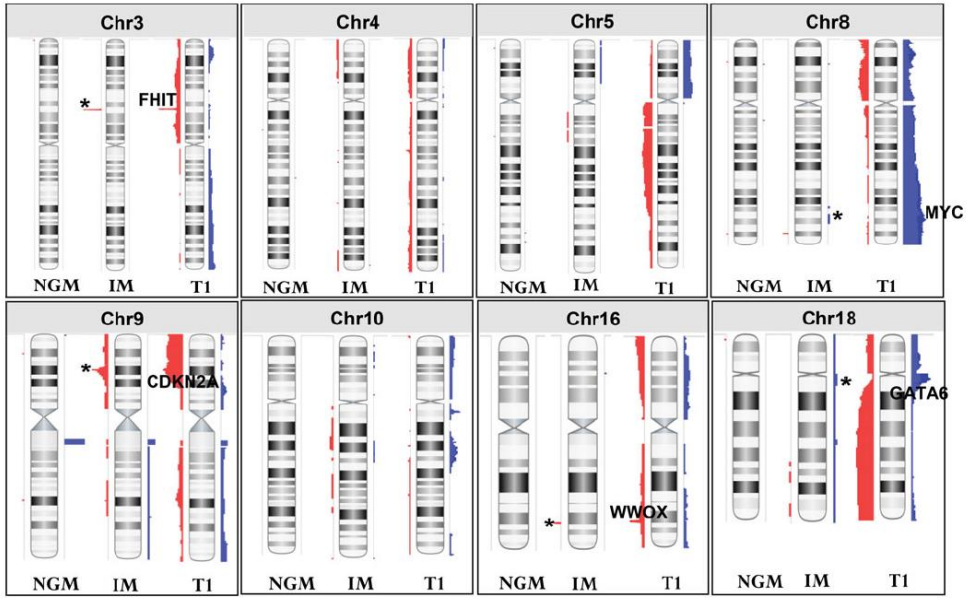


Comparison of Cancer-Associated Genetic Abnormalities in Columnar-Lined Esophagus Tissues With and Without Goblet Cells

Annals of Surgery • Volume 260, Number 1, July 2014

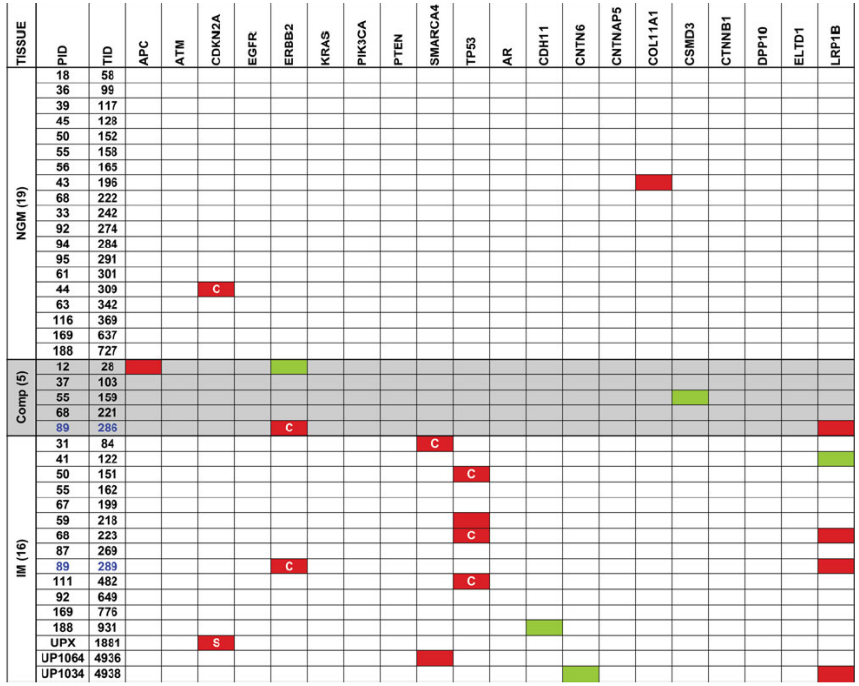
Santhoshi Bandla, PhD, Jeffrey H. Peters, MD,* David Ruff, PhD,† Shiaw-Min Chen, PhD,† Chieh-Yuan Li, BS,†*

DNA Copy Number Aberrations in NGM and IM



	n	*FHIT*	*c-MYC*	*CDKN2A*/p16	*WWOX*	*GATA6*
NGM	25	0	0	0	0	0
IM	26	54%	4%	35%	15%	8%
T1	36	61%	56%	44%	33%	31%

Targeted Resequencing of Frequently Mutated EAC Genes in NGM and IM



Conclusions: This study reports the largest and most comprehensive comparison of DNA aberrations in IM and NGM genomes. Our results show that IM has a much higher frequency of cancer-associated mutations than NGM.

Cardiac rather than intestinal-type background in endoscopic resection specimens of minute Barrett adenocarcinoma

Human Pathology (2009) **40**, 65–74

Kaiyo Takubo MD[a,*], Junko Aida DDS, PhD[a], Yoshio Naomoto MD[b], Motoji Sawabe MD[c], Tomio Arai MD[c], Hiroaki Shiraishi MD[d], Masaaki Matsuura PhD[e], Christian Ell MD[f], Andrea May MD[f], Oliver Pech MD[f], Manfred Stolte MD[g], Michael Vieth MD[g]

- **141 esophageal adenocarcinomas resected by EMR:**
  - **All tumors less than 2 cm**
  - **Only 22% of cases had GCs adjacent to the tumor**
  - **Only 56% of case had GCs anywhere in the EMR**
- **Conclusions:**
  - **Some tumors arise from columnar mucosa without GCs**
  - **The requirement for GCs should be dropped**

Does not mean there were no GCs elsewhere in the esophagus!

Intestinal or gastric? The unsolved dilemma of Barrett's metaplasia

doi:10.1016/j.humpath.2009.03.019

Massimo Rugge
Matteo Fassan
Giorgio Battaglia
Giovanni Zaninotto
Ermanno Ancona

To the Editor:

The valuable article published by Takubo et al [1] focuses on the role of intestinal metaplasia (IM) in Barrett's oncogenesis.

Table 1 Clinicopathologic characteristics of 335 consecutive Barrett's esophagus patients

	IM positive (n = 206, 61.5%)	IM negative (n = 129, 38.5%)	Total (n = 335)	*P*
Sex, no. of males (%)	161 (78.2%)	63 (48.8%)	224 (66.9%)	.003
Age, mean ± SD (median and range)	60.3 ± 3.1 (61.1, 26.1-88.0)	53.0 ± 6.4 (53.6, 17.3-96.0)	57.5 ± 14.8 (59.3, 17.3-96.0)	<.001
Biopsies per patient, mean ± SD (median and range)	8.0 ± 6.7 (6.0, 1-37)	3.4 ± 3.7 (2.0, 1-18)	6.2 ± 6.1 (4.0, 1-37)	<.001
IM-positive biopsy samples (%)	1145/1643 (69.7%)	0/445 (0%)	1145/2088 (54.8%)	–
Velvel mucosa segment length, mean ± SD (median and range) (cm)	3.5 ± 2.9 (3.0, 0.5-16.0)	2.0 ± 1.7 (2.0, 0.5-16.0)	2.9 ± 2.6 (2.0, 0.5-16.0)	.018
Velvet mucosa ≥3 cm (%)	107 (51.9%)	32 (24.8%)	139 (41.5%)	<.001
Prevalence of preneoplastic/neoplastic lesions[a] (%)	30 (14.6%)	0 (0%)	30 (9.0%)	<.001

NOTE. Only patients at initial endoscopy (years 2005-2008) were considered, all with detailed information about biopsy sampling protocol and location of squamous-columnar junction, gastroesophageal junction, and diaphragmatic pinchcocks.

[a] Indefinite for NiN, low-grade NiN, high-grade NiN, and adenocarcinoma are merged together.

prevalence study

Columnar-Lined Esophagus Without Intestinal Metaplasia Has No Proven Risk of Adenocarcinoma

Parakrama Chandrasoma, MD, Sulochana Wijetunge, MBBS, MD (Path),*† Steven DeMeester, MD,‡ Yanling Ma, MD,* Jeffrey Hagen, MD,‡ Lindsay Zamis, MD,* and Tom DeMeester, MD‡*

Am J Surg Pathol • Volume 36, Number 1, January 2012

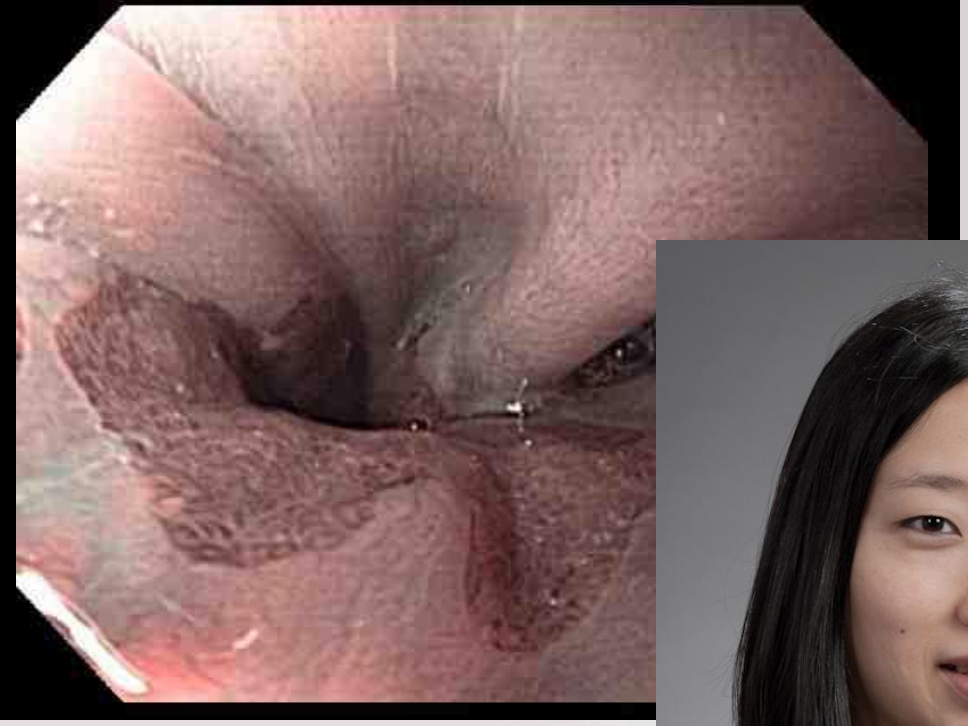
TABLE 1. Prevalence of Intestinal Metaplasia and Dysplasia/Adenocarcinoma in 214 Patients With Systematic Protocol Biopsies of a Visible CLE

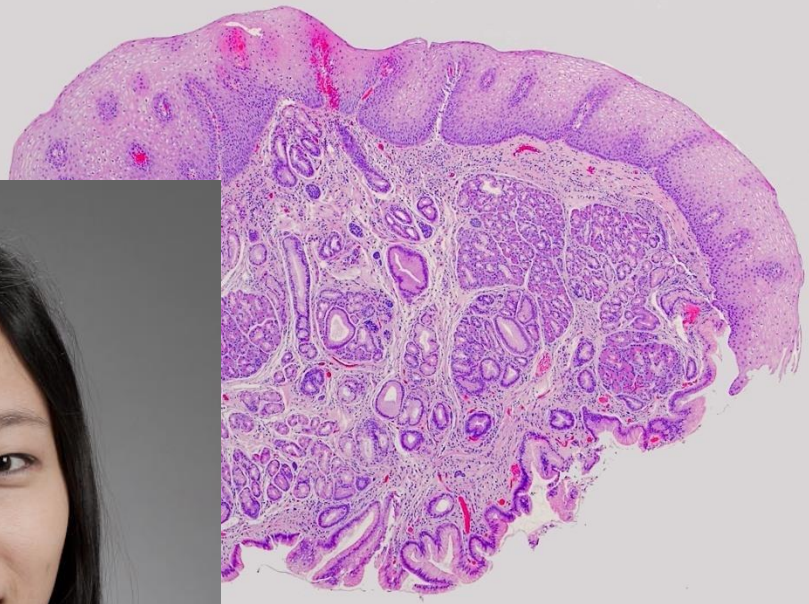
Length of Visible CLE	Number	IM^+	$Dysplasia/CA^+$	$Dysplasia/CA^+$ in IM^+ Patients	IM^-	$Dysplasia/CA^+$ in IM^- Patients
1 cm	34	19 (55.9%)	3/34 (8.8%)	3/19 (15.8%)	15 (44.1%)	0
2 cm	38	31 (81.6%)	10/38 (26.3%)	10/31 (26.3%)	7 (18.4%)	0
3 cm	15	13 (86.7%)	4/15 (26.7%)	4/13 (30.8%)	2 (14.3%)	0
4 cm	39	37 (94.9%)	8/39 (20.5%)	8/37 (21.6%)	2 (5.1%)	0
5 cm	8	7 (87.5%)	2/8 (25.0%)	2/7 (28.6%)	1 (12.5%)	0
> 5 cm	80	80 (100%)	28/80 (35.0%)	28/80 (35.0%)	0	0
Total	214	187 (87.4%)	55/214 (25.7%)	55/187 (29.4%)	27 (12.6%)	0

TABLE 2. Selected Esophagectomy Studies With the Most Complete Sampling to Demonstrate the Prevalence of Residual Intestinal Metaplasia in Patients With Esophageal Adenocarcinoma

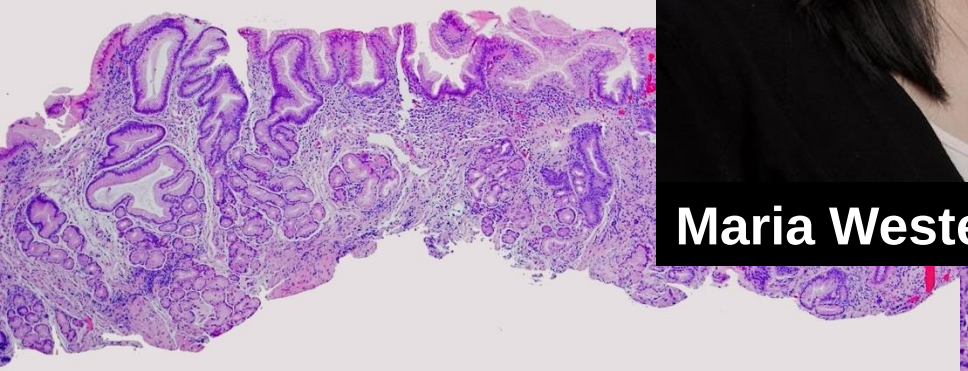
Reference	Place of Origin	No. Patients With adenoCA of Esophagus	Number (%) With Intestinal Metaplasia
Ruol et al[28]	Padova, Italy	26	25 (96.2%)
Skinner et al[29]	Chicago, IL	20	20 (100%)
Cameron et al[4]	Rochester, MN	9	9 (100%)
Rosenberg et al[27]	Detroit, MI	9	9 (100%)
Paraf et al[19]	Paris, France	67	66 (98.5%)
Van Sandick et al[34]	The Netherlands	32	32 (100%)

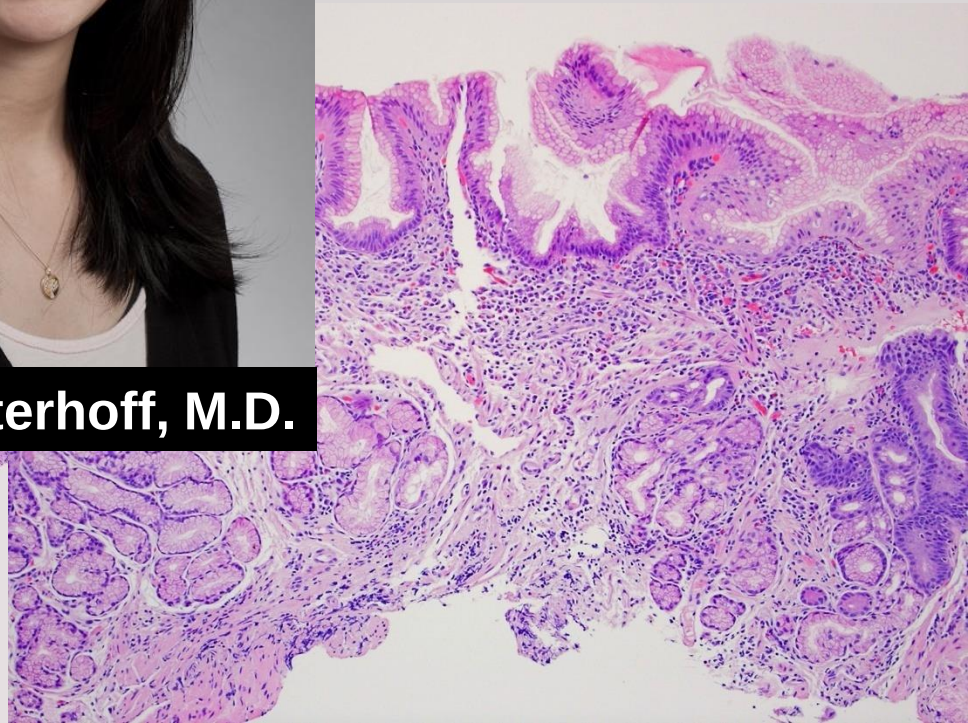
prevalence study





Maria Westerhoff, M.D.





Endoscopic Columnar Mucosa Identified and Biopsied

New diagnosis only
No dysplasia in initial bx

N = 690

53
squamous mucosa sampled only

379
columnar mucosa without goblet cells (- GC)

258
columnar mucosa with goblet cells (+ GC)

CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2012

Effects of Dropping the Requirement for Goblet Cells From the Diagnosis of Barrett's Esophagus

MARIA WESTERHOFF,* LINDSEY HOVAN,‡ CHRISTINE LEE,‡ and JOHN HART‡

Endoscopic Columnar Mucosa Identified and Biopsied

New diagnosis only
No dysplasia in initial bx

N = 690

53
squamous mucosa sampled only

379
columnar mucosa without goblet cells (- GC)

258
columnar mucosa with goblet cells (+ GC)

- **Native gastric cardia**
- **GC were missed (not enough biopsies taken)**
- **Barrett's mucosa without GC**

Original Diagnostic Guidelines

	Endoscopic Finding of Columnar Lined Esophagus	n = 690
BARRETT ESOPHAGUS	Goblet Cells Present	258
Not consistent with Barrett esophagus	No Goblet Cells Present	379
Not consistent with Barrett esophagus	Squamous Mucosa Only	53

37% of patients (258/690) diagnosed with BE based on 2011 AGA guidelines

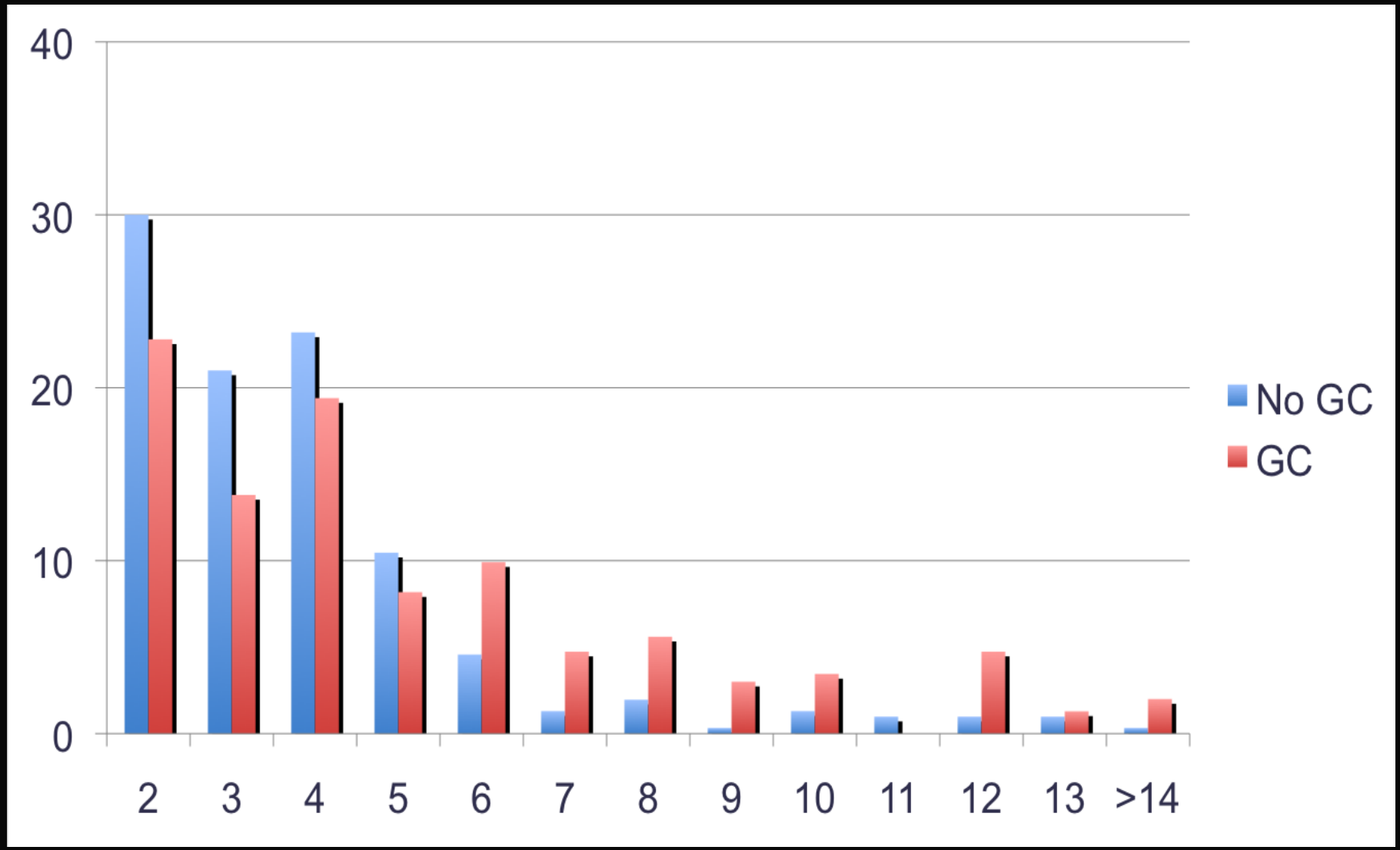
Reclassification using British Diagnostic Guidelines

	Endoscopic Finding of Columnar Lined Esophagus	n = 690
BARRETT ESOPHAGUS	Columnar Mucosa With GCs	258
	Columnar Mucosa Without GCs	379
Not consistent with Barrett esophagus	Squamous Mucosa Only	53

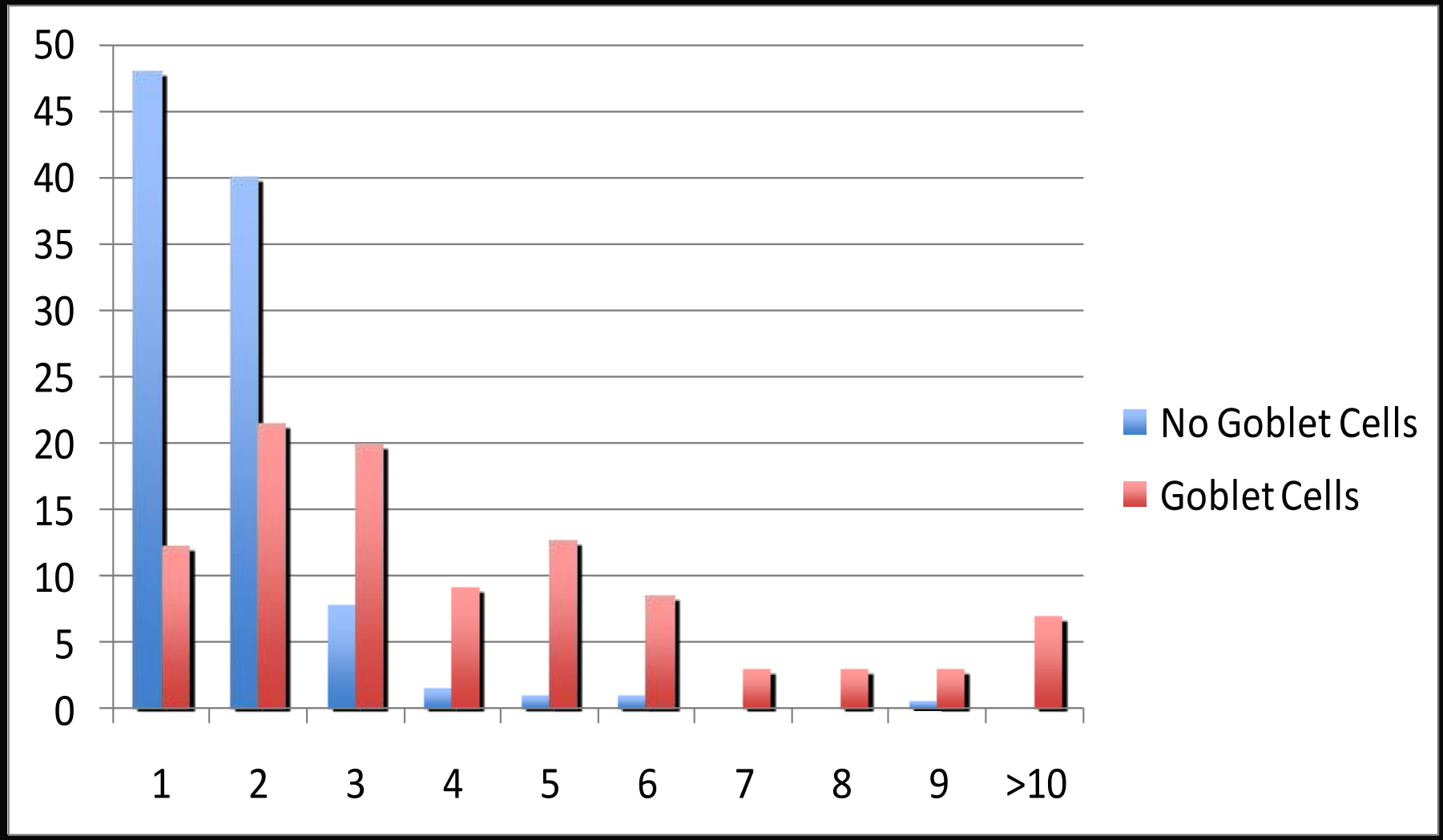
92.3% of patients (637/690) diagnosed with BE

Diagnosis of BE increased by 147%

Number of Biopsies Obtained at Initial Endoscopy

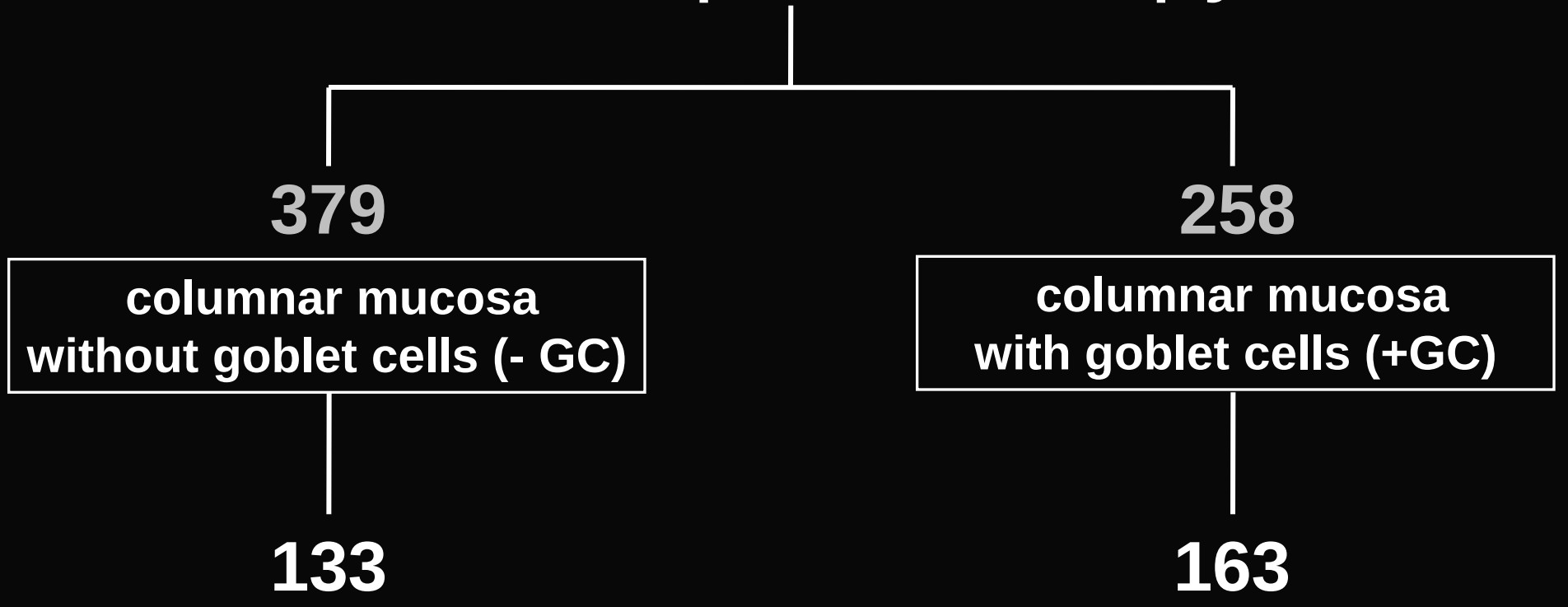


Length of Endoscopic Columnar Mucosa

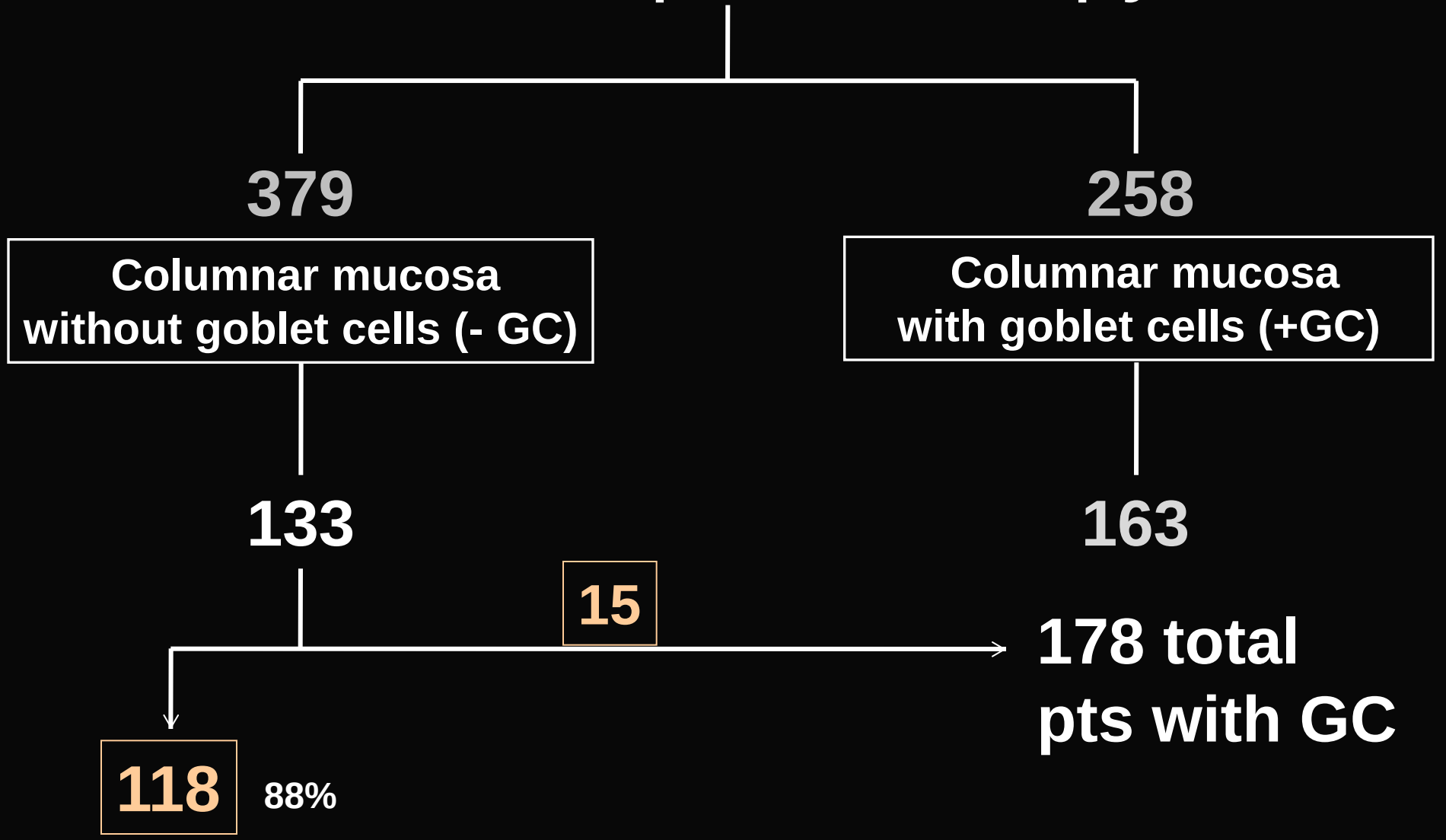


	Pts with GC	Pts without GC	p value
Average endoscopic length (cm)	4.6	1.6	<0.05
Average # biopsies taken on initial endoscopy	5	4	0.3

Patients who Underwent Follow-up Endoscopy



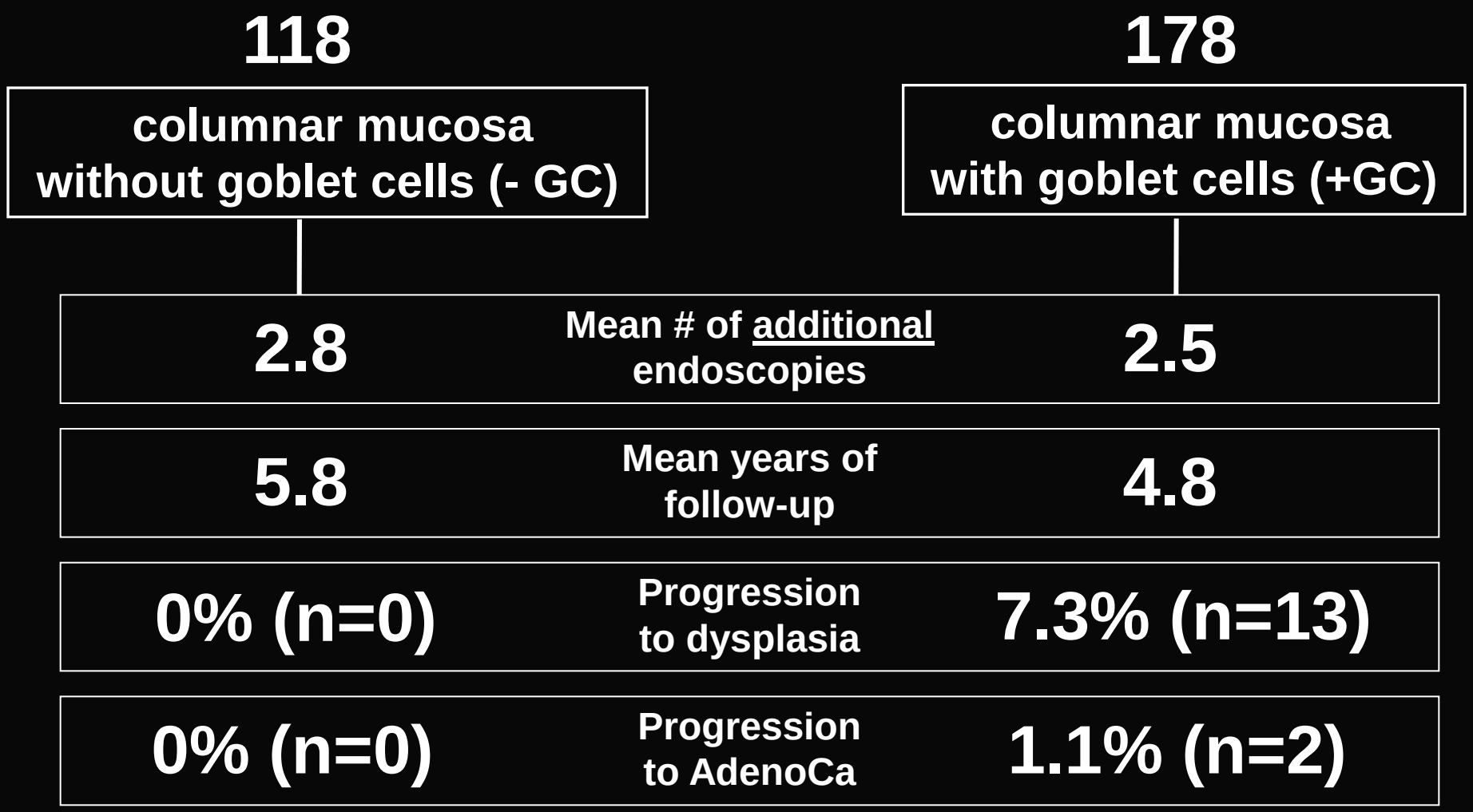
Patients who Underwent Follow-up Endoscopy



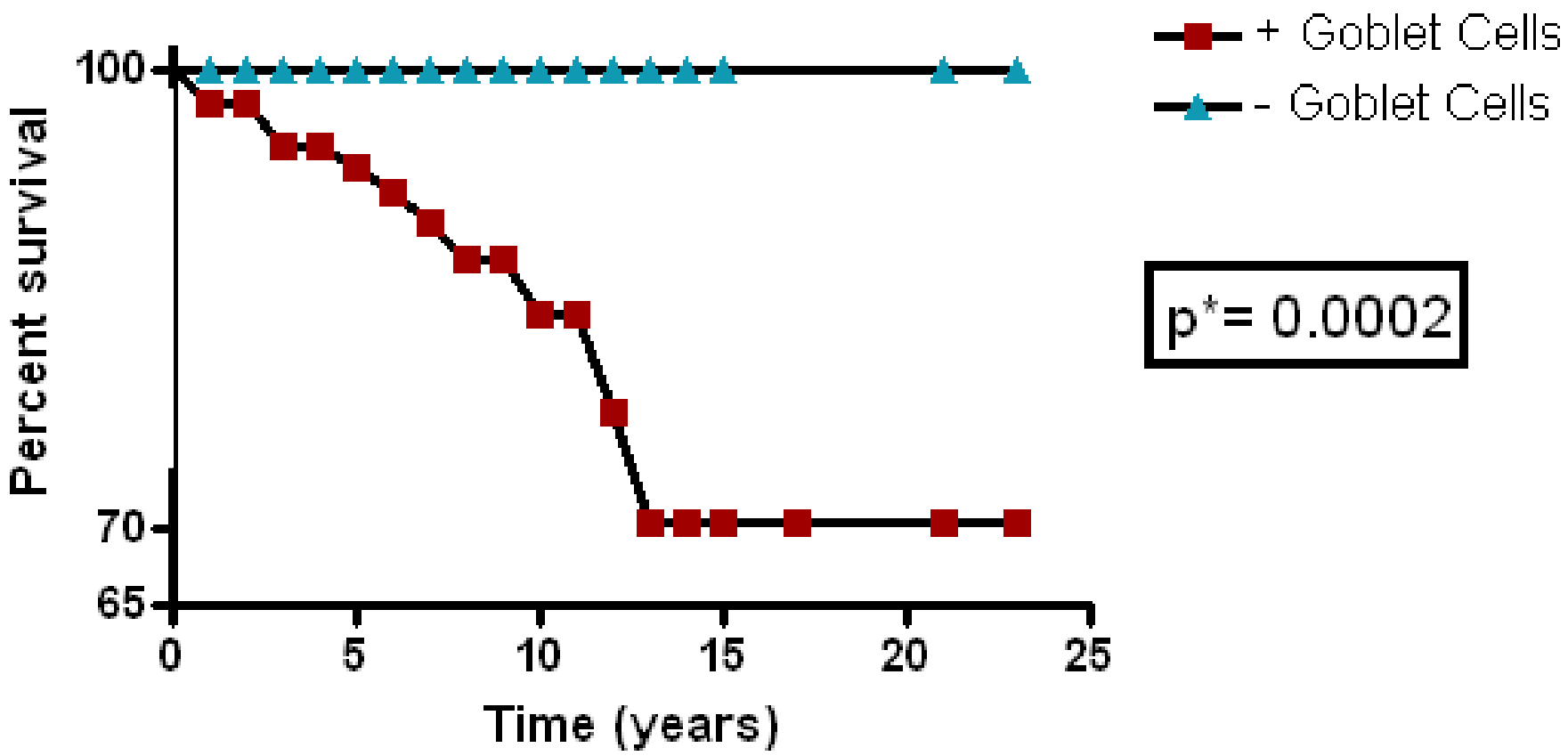
Patients without GC at Initial Endoscopy Who Underwent Follow-up Endoscopy (n = 133)

	No GC on subsequent biopsies (n = 118)	GC identified on subsequent biopsies (n = 15)
Average number of additional endoscopic procedures	2.8	2.1
Average number of additional biopsies	7.0	6.2
Average years of follow-up	5.8	4.9
Average endoscopic length of columnar mucosa (cm)	1.6	4.1

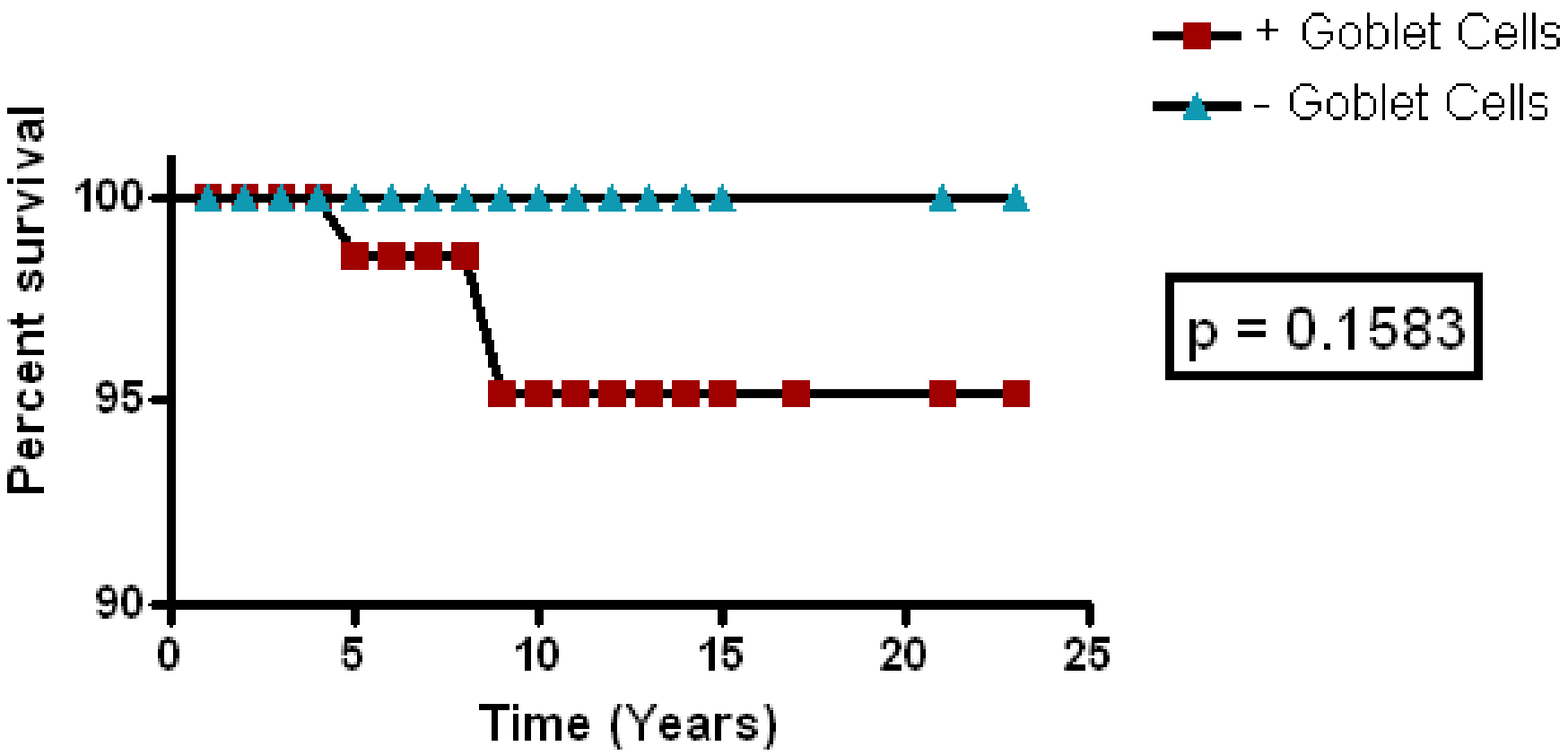
All Pts without GC vs. All Pts with GC



Development of Dysplasia



Development of Adenocarcinoma



- 1 EAC per 442 patient years (GC) vs. 0 EAC per 664 patient years (no GC)

Conclusions

Endoscopy-Identified Esophageal Columnar Mucosa

columnar mucosa without goblet cells (- GC)

- **0% developed dysplasia**
- **0% developed adenoCa**

columnar mucosa with goblet cells (+GC)

- **7% developed dysplasia**
- **1% developed adenoCa**

Dropping the requirement for GCs increased initial diagnosis of BE by 147%

Endoscopy-Identified Esophageal Columnar Mucosa

Columnar mucosa with goblet cells (+GC) = Barrett Esophagus

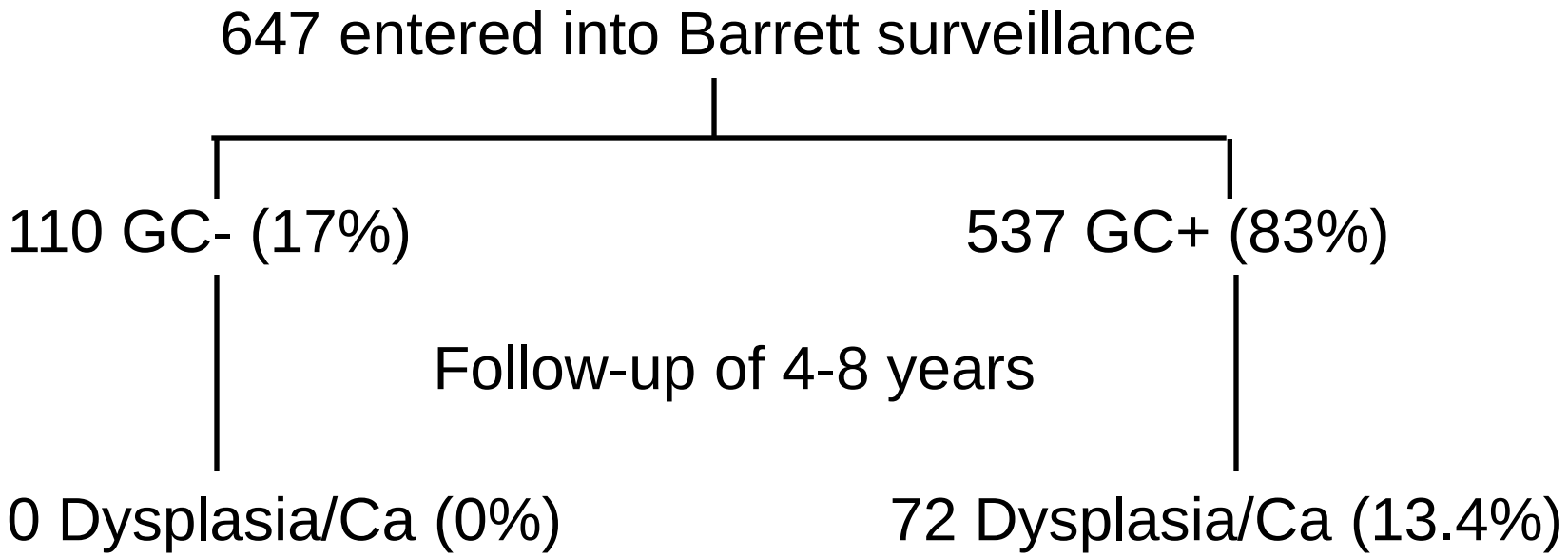
Columnar mucosa without goblet cells (- GC)

- **Native gastric cardia**
- **Barrett esophagus and GC were missed (12% missed)**
- **Barrett esophagus without GC (and no cancer risk?)**

Intestinal metaplasia in Barrett's oesophagus: An essential factor to predict the risk of dysplasia and cancer development

Marianna Salemme[a], Vincenzo Villanacci[a], Gianpaolo Cengia[b], Renzo Cestari[b], Guido Missale[b], Gabrio Bassotti[c,*]

Digestive and Liver Disease 48 (2016) 144–147



Conclusion: The histological identification of intestinal metaplasia seems to be an essential factor for the progression towards dysplasia and cancer in BE patients.

ACG Clinical Guideline: Diagnosis and Management of Barrett's Esophagus

Am J Gastroenterol 2016; 111:30–50;

Nicholas J. Shaheen, MD, MPH, FACG[1], Gary W. Falk, MD, MS, FACG[2], Prasad G. Iyer, MD, MSc, FACG[3] and Lauren B. Gerson, MD, MSc, FACG[4]

Recommendations

1. BE should be diagnosed when there is extension of salmon-colored mucosa into the tubular esophagus extending ≥1 cm proximal to the gastroesophageal junction (GEJ) with biopsy confirmation of IM (strong recommendation, low level of evidence).
2. Endoscopic biopsy should not be performed in the presence of a normal Z line or a Z line with <1 cm of variability (strong recommendation, low level of evidence).

Why at least 1 cm?

Epidemiology and Natural History of Intestinal Metaplasia of the Gastroesophageal Junction and Barrett's Esophagus: A Population-Based Study *Am J Gastroenterol.* 2011 August ; 106(8): 1447–1455.

Kee Wook Jung, MD[1], Nicholas J. Talley, MD, PhD[1,2], Yvonne Romero, MD[1,3,4,5], David A.

Comparison of :
Patients with > 1 cm segment of biopsy proven BE (GC+)
versus
Patients with < 1 cm segment – designated as "intestinal metaplasia of the GE junction" (IMGEJ)

Subjects with IMGEJ in the population do not progress to high-grade dysplasia (HGD) or adenocarcinoma over a substantial length of follow-up.

Survival in subjects with IMGEJ and BE is comparable to that of age- and gender-matched subjects.

Surveillance in subjects with IMGEJ may not be required.

BE patients cumulative risk of progression to AdenoCa was 7% at 10 years, compared to 0% for IMGEJ

ACG Clinical Guideline: Diagnosis and Management of Barrett's Esophagus

Am J Gastroenterol advance online publication, 3 November 2015; doi:10.1038/ajg.2015.322

Nicholas J. Shaheen, MD, MPH, FACG[1], Gary W. Falk, MD, MS, FACG[2], Prasad G. Iyer, MD, MSc, FACG[3] and Lauren Gerson, MD, MSc, FACG[4]

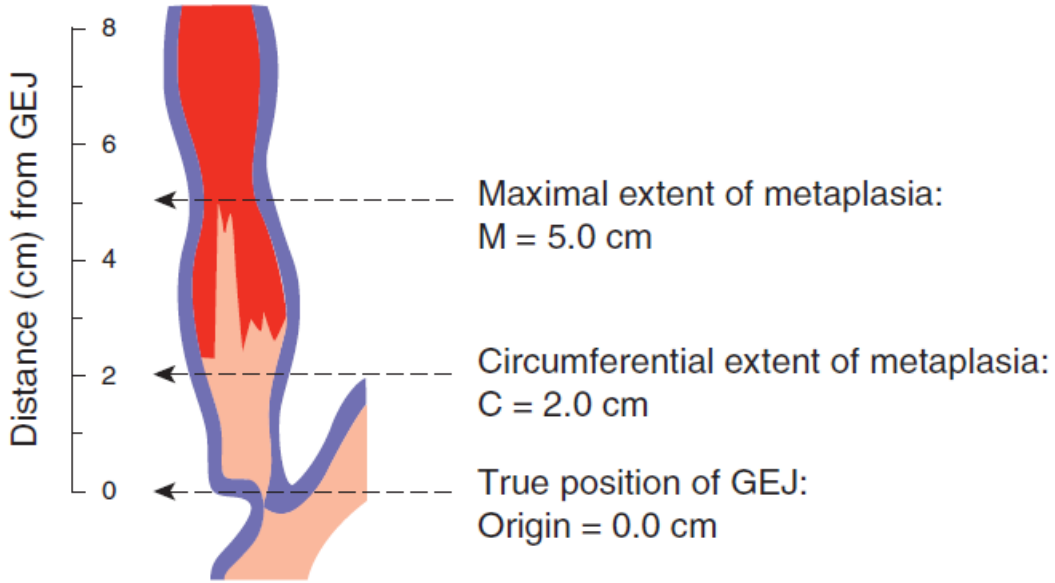


Figure 1. Illustration of Prague Classification for Barrett's esophagus (BE)

there were high reliability coefficients (RCs) for recognition of BE segments >1 cm (RC 0.72), locations of the EGJ (RC 0.88), and diaphragmatic hiatus (RC 0.85), but not for BE segments <1 cm (RC 0.22).

ACG Clinical Guideline: Diagnosis and Management of Barrett's Esophagus

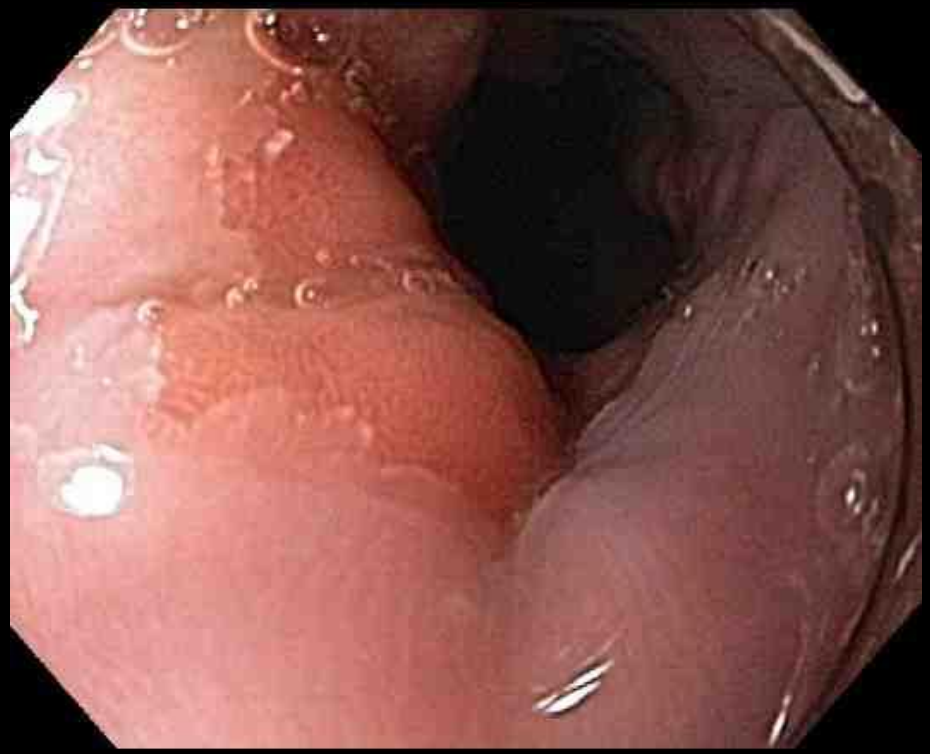
Am J Gastroenterol 2016; 111:30–50;

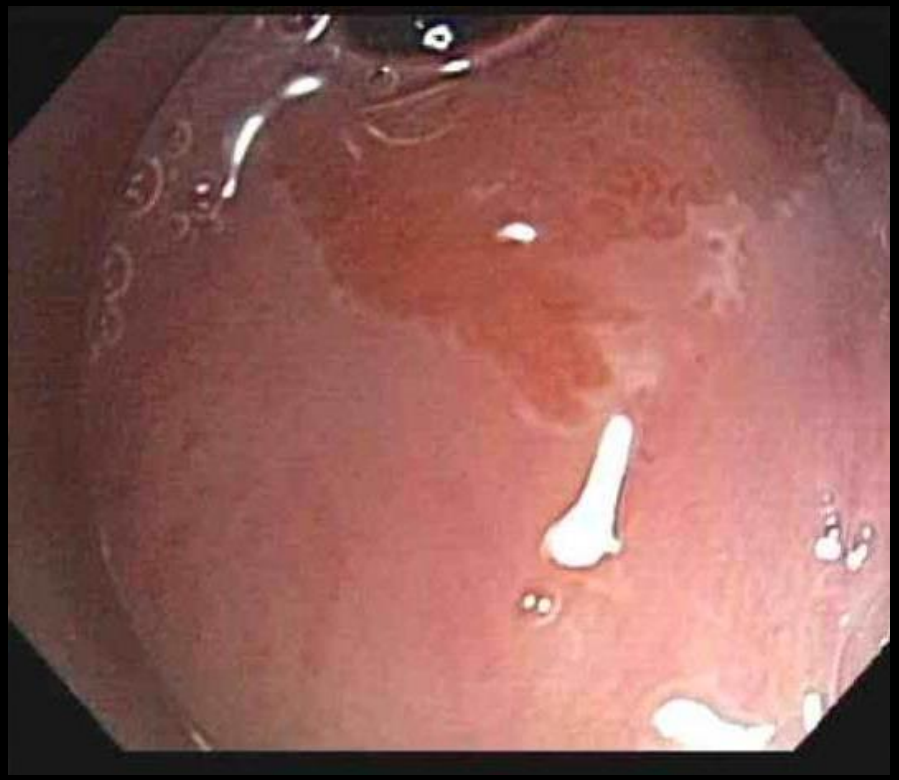
Nicholas J. Shaheen, MD, MPH, FACG[1], Gary W. Falk, MD, MS, FACG[2], Prasad G. Iyer, MD, MSc, FACG[3] and Lauren B. Gerson, MD, MSc, FACG[4]

5. In patients with suspected BE, at least 8 random biopsies should be obtained to maximize the yield of IM on histology. In patients with short (1–2 cm) segments of suspected BE in whom 8 biopsies may be unobtainable, at least 4 biopsies per cm of circumferential BE, and one biopsy per cm in tongues of BE, should be obtained (conditional recommendation, low level of evidence).
6. In patients with suspected BE and lack of IM on histology, a repeat endoscopy should be considered in 1–2 years of time to rule out BE (conditional recommendation, very low level of evidence).

were performed (15). Despite the incompletely elucidated risk of EAC in non-IM CLE, and acknowledging the potential for sampling error, we continue to suggest that only CLE containing IM be defined as BE, given the apparent differential cancer risk between CLE containing IM and CLE without IM. Until and unless further work substantiates a markedly elevated risk of EAC in non-IM CLE patients, it is unwise to give these patients a disease diagnosis that has a documented negative impact on insurance status and quality of life (16,17).

- 71 y.o. M with nocturnal heartburn
- Upper GI endoscopy reveals an irregular Z-line
- Three biopsies obtained from “possible short tongues of Barrett esophagus”





DIAGNOSIS

1. ~~X~~ Barrett esophagus, no evidence of dysplasia
2. Squamous and gastric cardia and fundic type mucosa, no evidence of Barrett esophagus

Rule out Barrett's

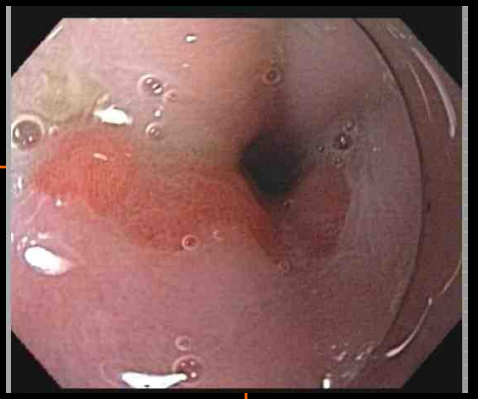
Upper GI endoscopic biopsies, "distal esophagus":

- Gastric cardiac-type mucosa with focal intestinal metaplasia (goblet cells).

See comment

Comment: The histologic findings are c/w intestinal metaplasia of gastric cardia mucosa or Barrett's esophagus, depending on the exact site of the biopsies and the endoscopic findings. There is no evidence of dysplasia.

Single 1 cm tongue of salmon colored mucosa – r/o Barrett's esophagus



Upper GI endoscopic biopsies:

"tongue of possible Barrett's"

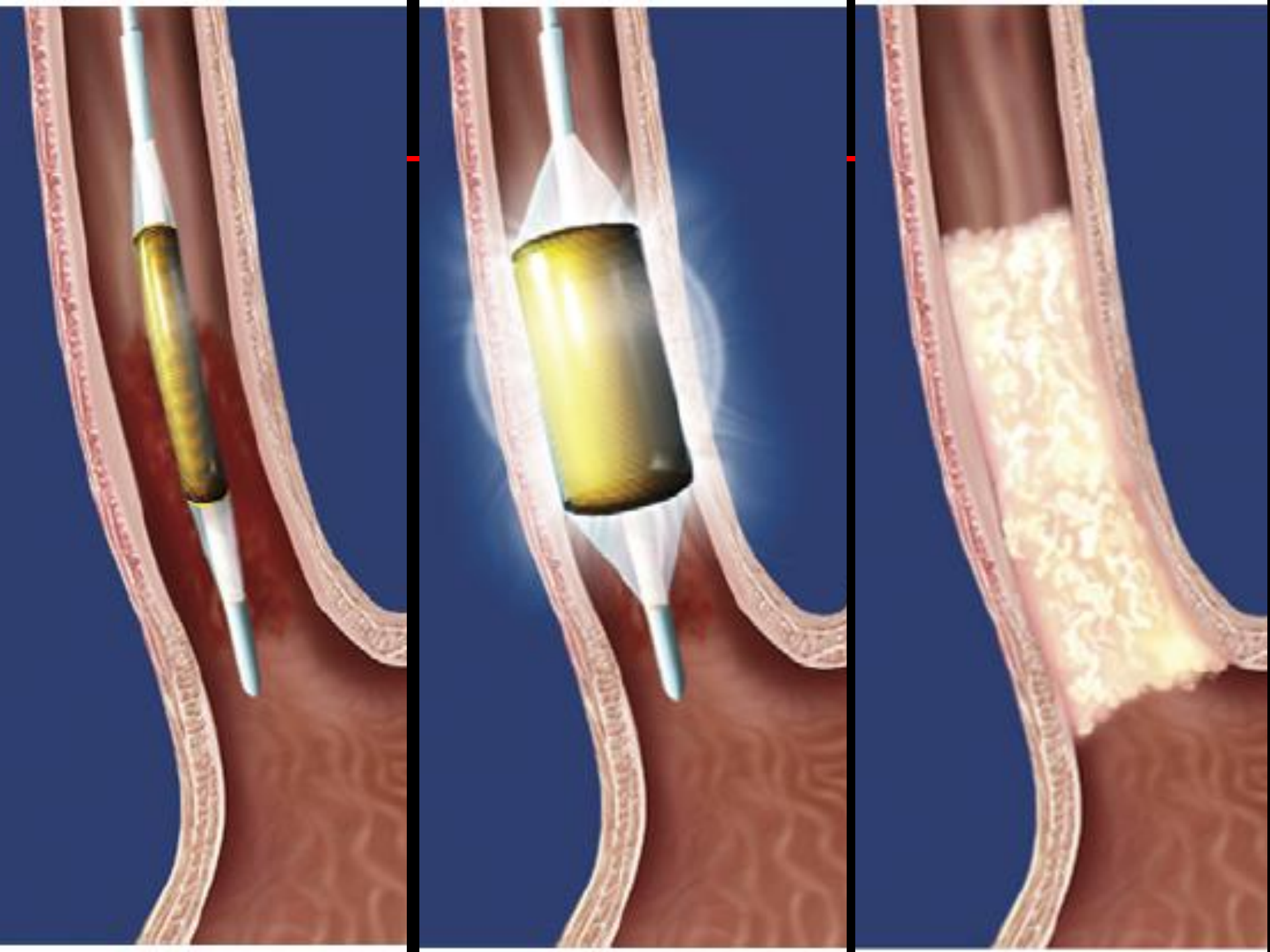
- specialized columnar mucosa, c/w Barrett's esophagus, negative for dysplasia.

"gastric cardia"

- mildly inflamed gastric cardia mucosa.

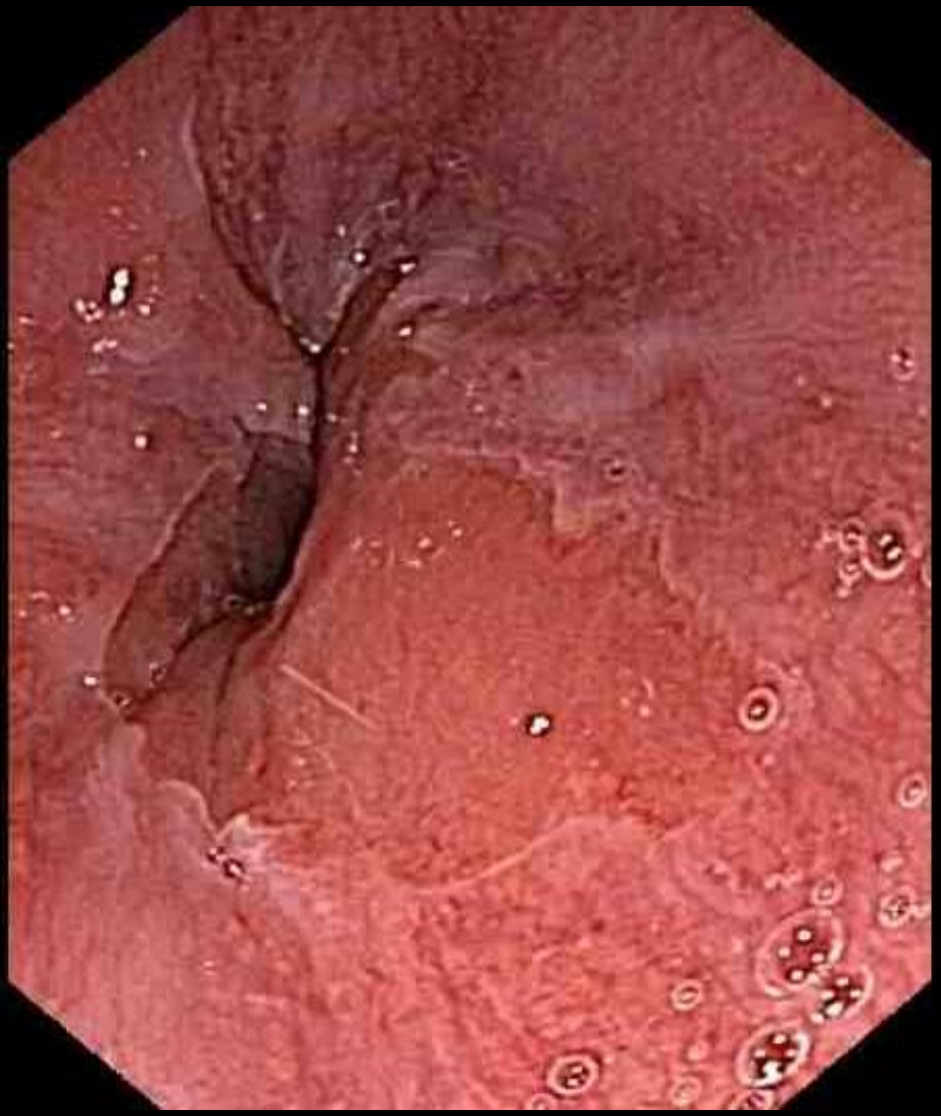
Ablation of Barrett's Mucosa

- **Methods:**
  - Argon plasma coagulation
  - Photodynamic therapy
  - Cryoablation
  - Radiofrequency ablation
- **Advantages:**
  - Avoid surgery
  - Removes all Barrett's mucosa (?)
- **Disadvantages:**
  - Limited depth of ablation
  - No tissue samples for diagnosis
  - Development of "buried Barrett's" upon re-epithelialization
  - Post-therapy stricture formation

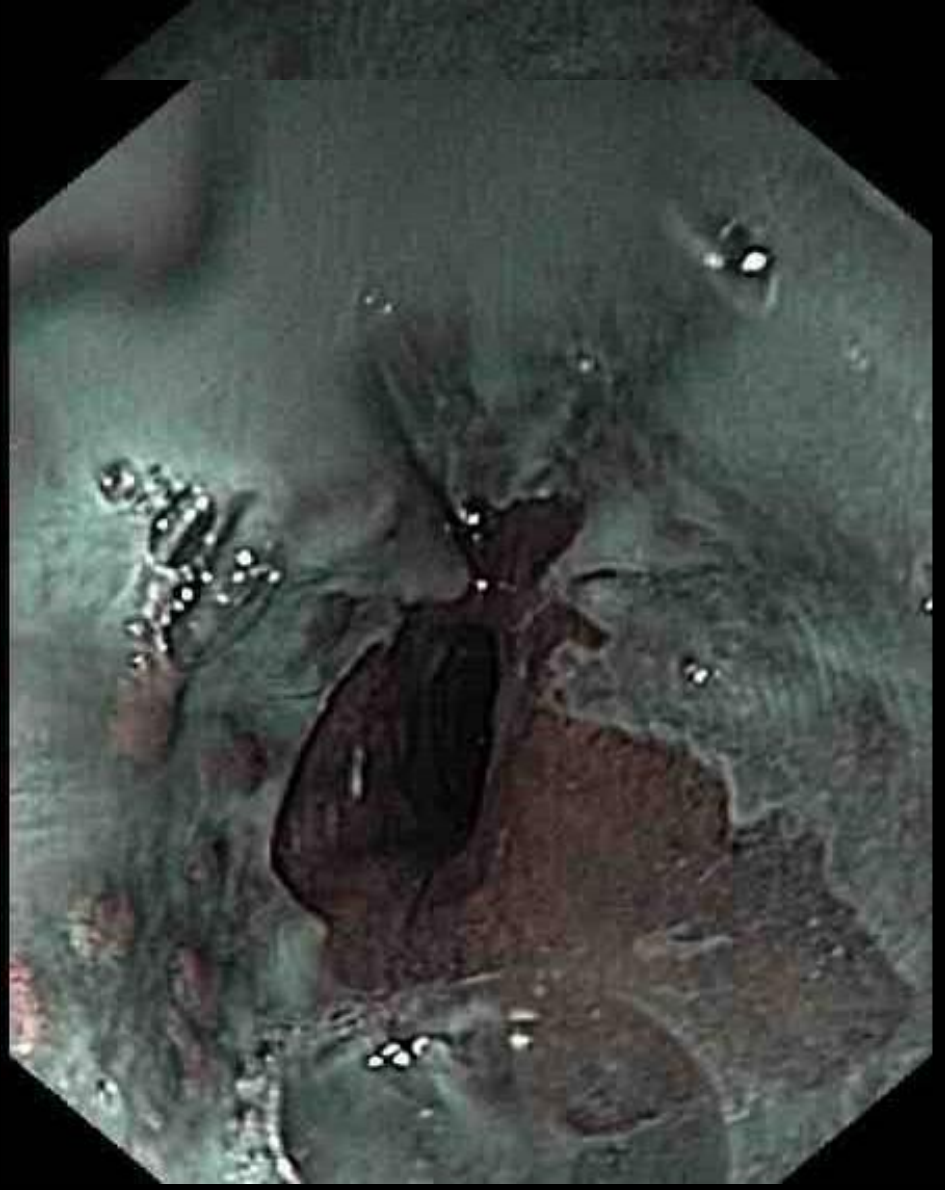


“Next-Generation” Endoscopy

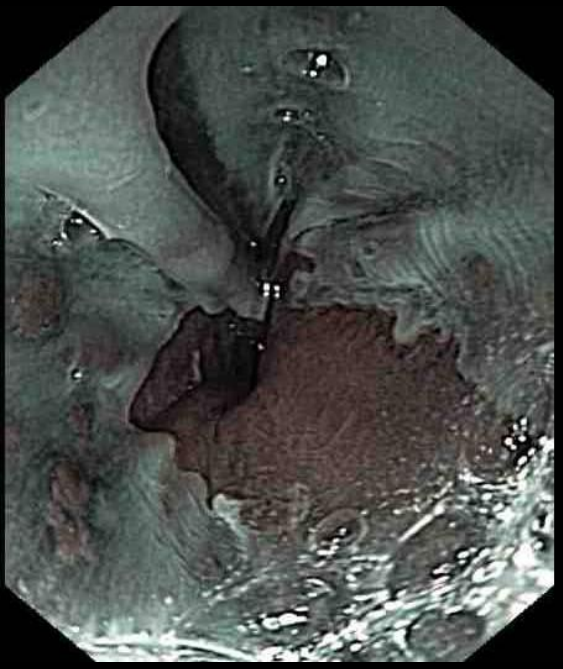
- **Narrow-Band Imaging**
  - White light→Filters→R/G/B bands →Image processing
  - Better contrast between squamous and columnar epithelium
  - Pit pattern and microvascular abnormalities
  - Widely available and relatively inexpensive
- **Confocal Endomicroscopy:**
  - In vivo microscopic imaging (IV contrast required)
  - Glandular and microvascular architecture are visible
  - Can identify dysplastic foci directly
- **Volumetric Laser Endomicroscopy:**
  - Superior depth of penetration (3 mm)
  - Faster acquisition of 360º images
  - Cost is higher; limited experience

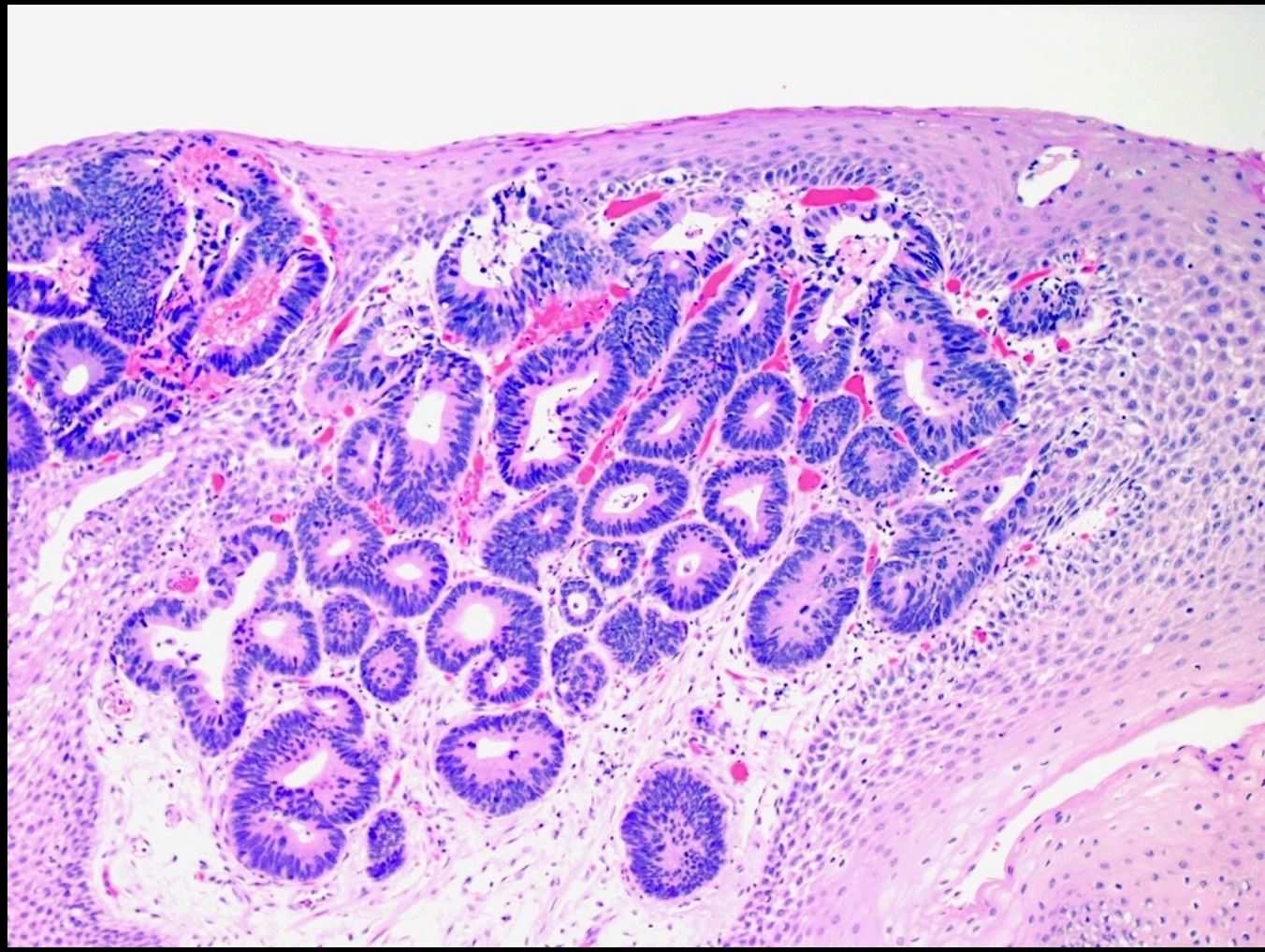


Regular white light exam

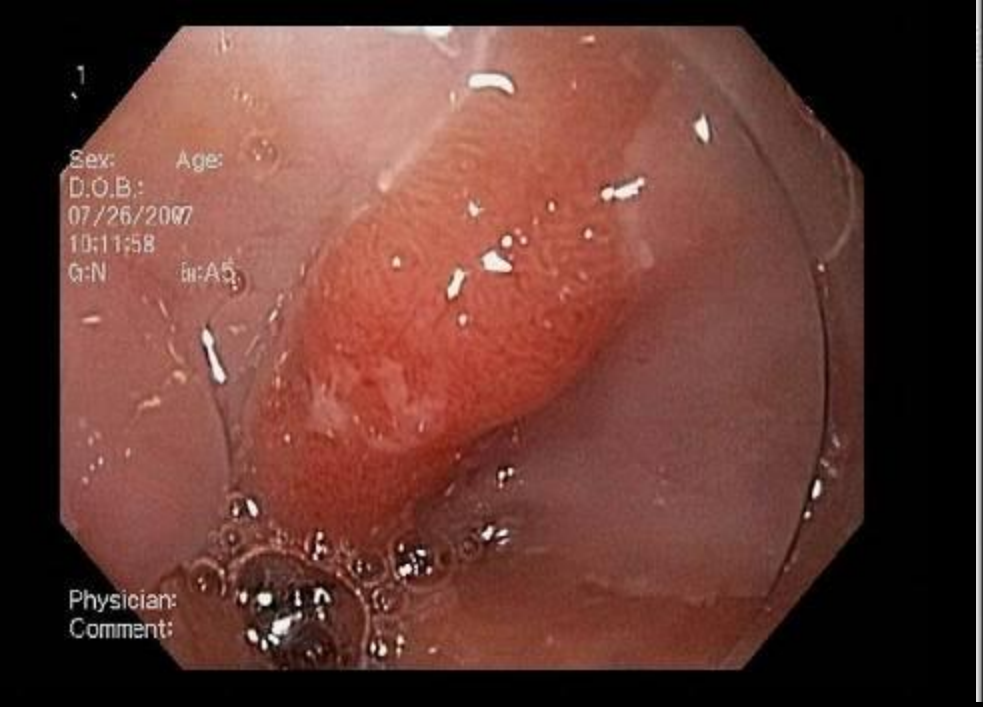


Narrow band imaging





Buried dysplastic Barrett’s mucosa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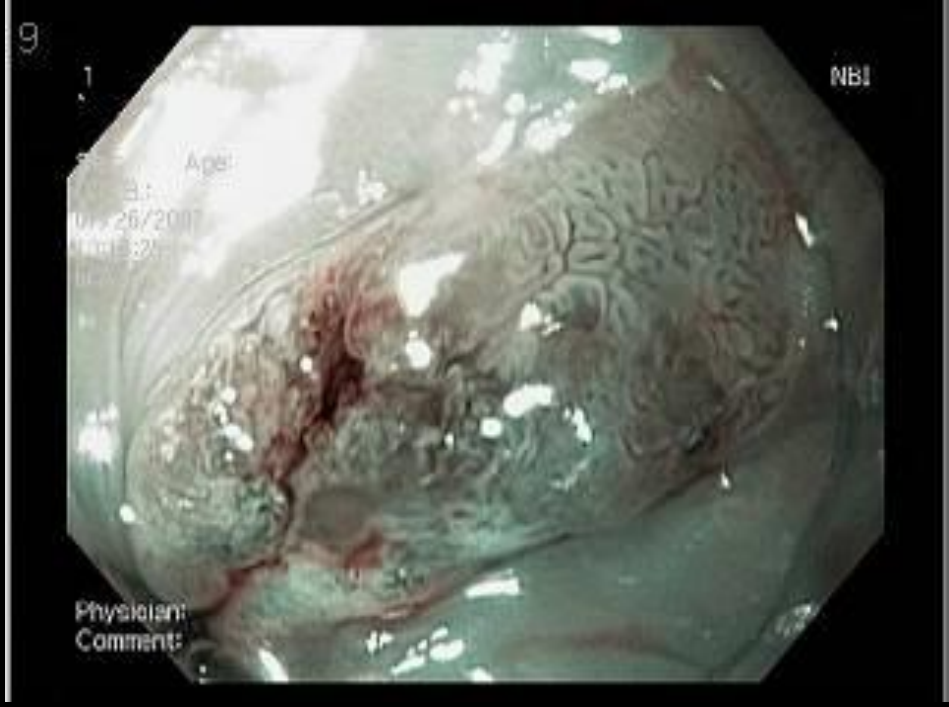
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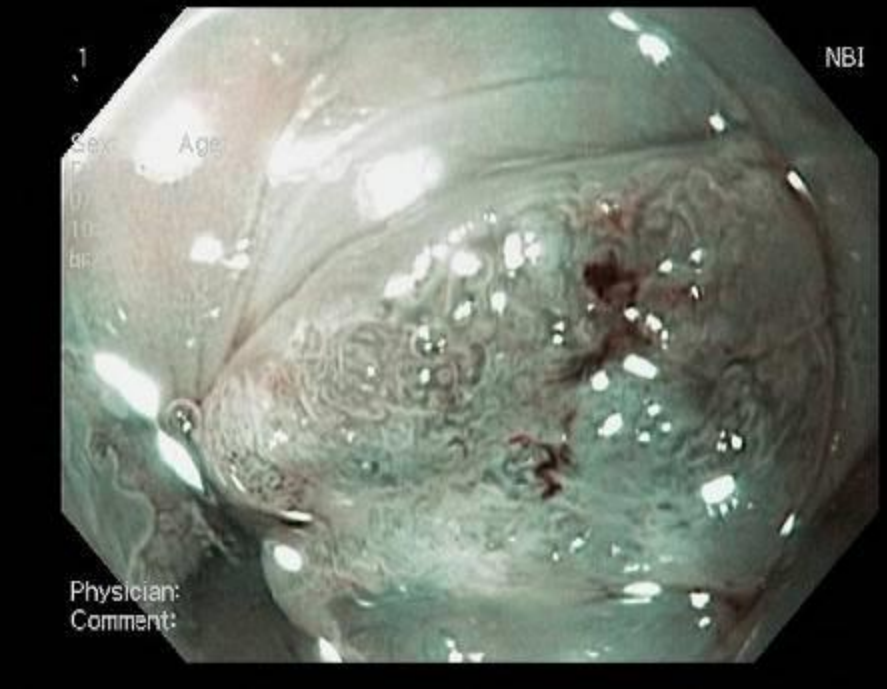
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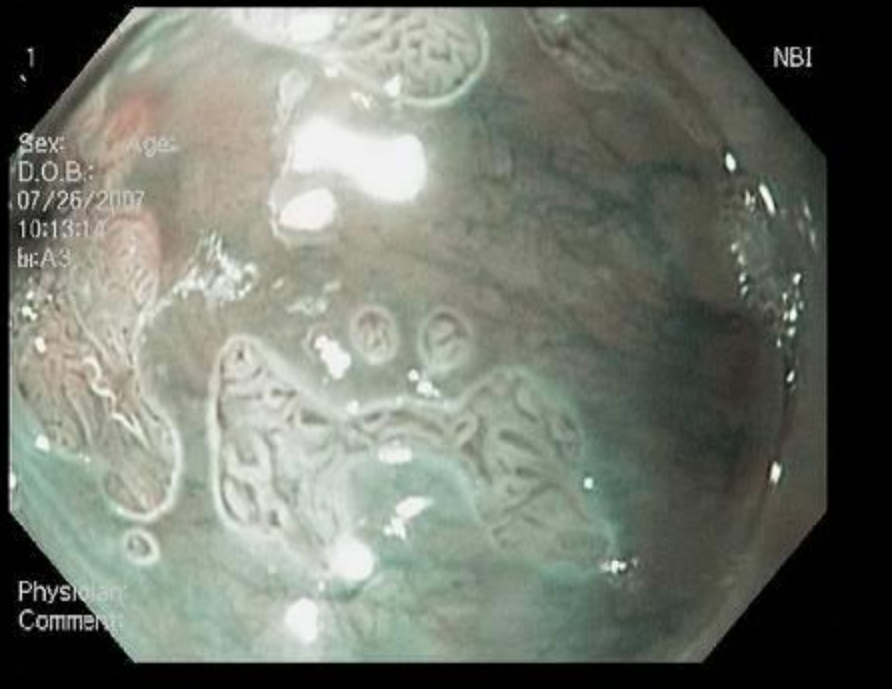
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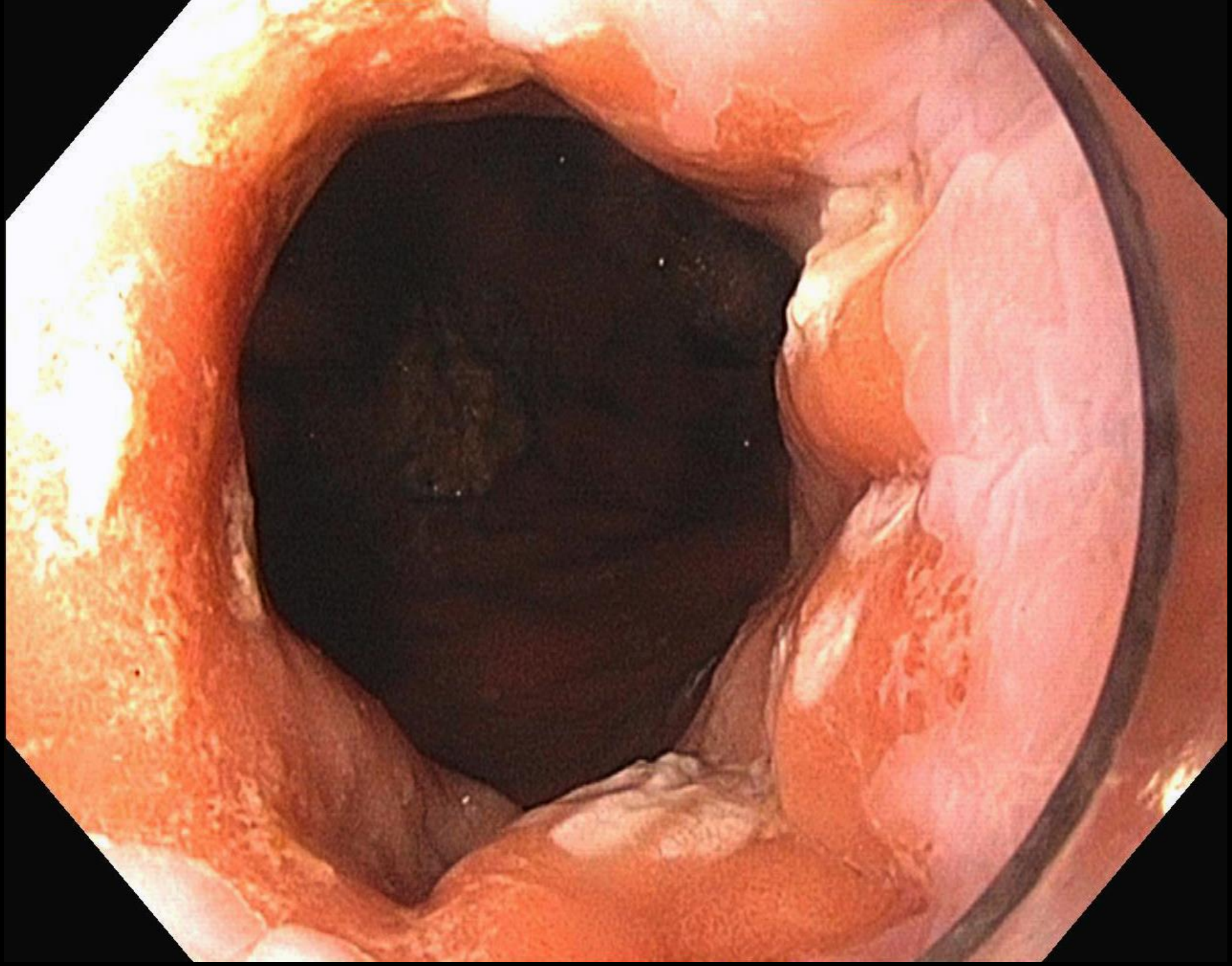
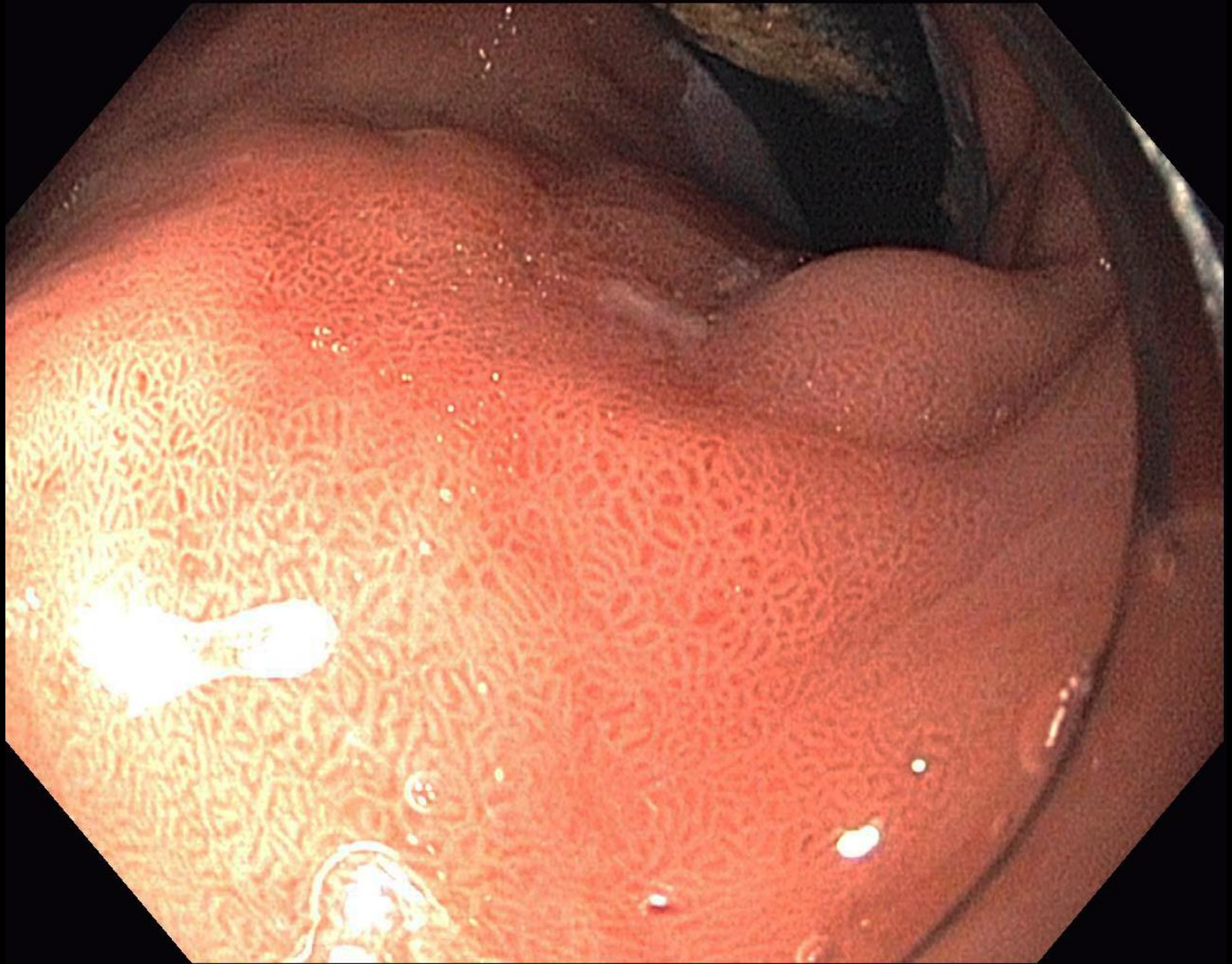
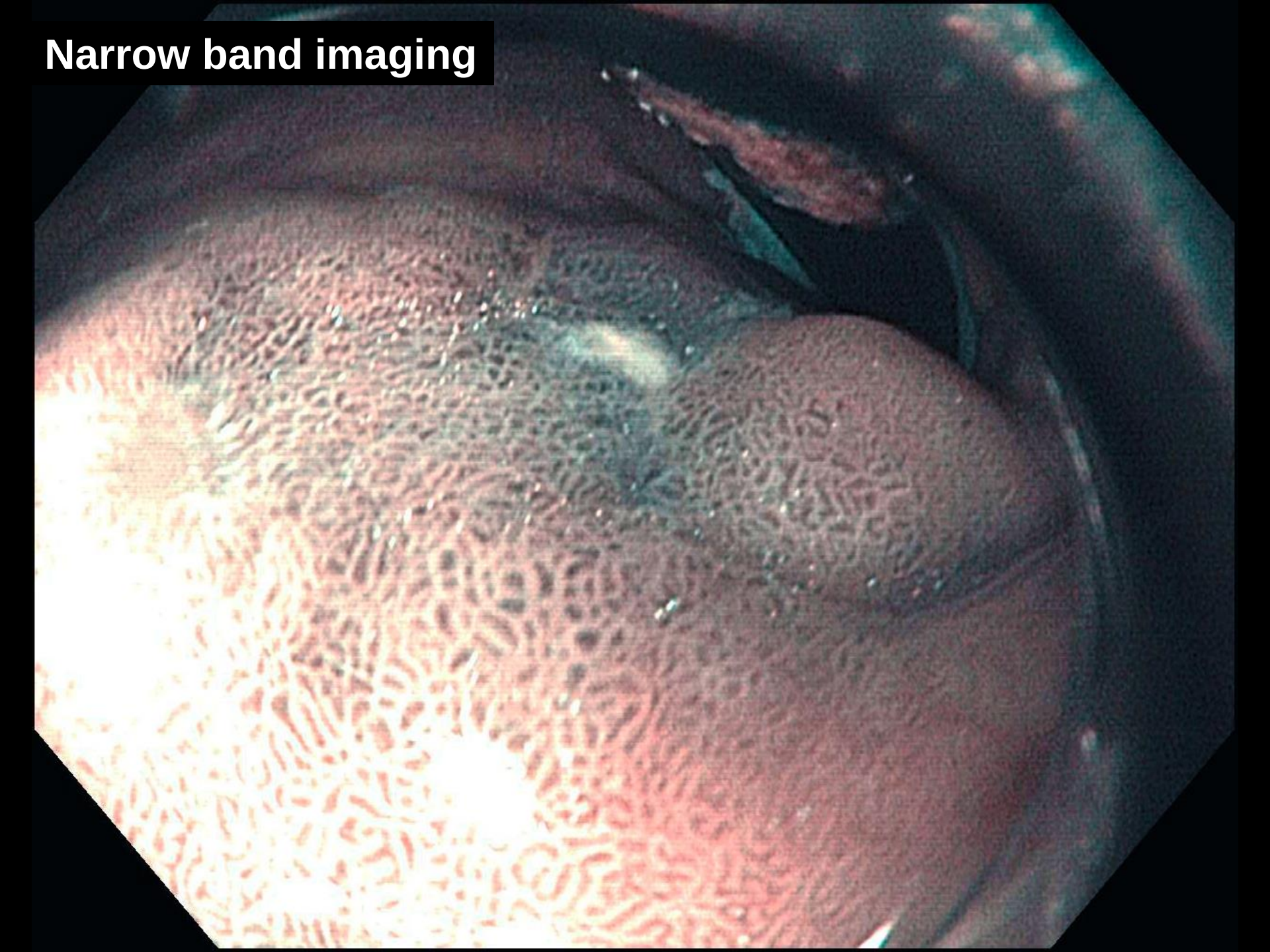
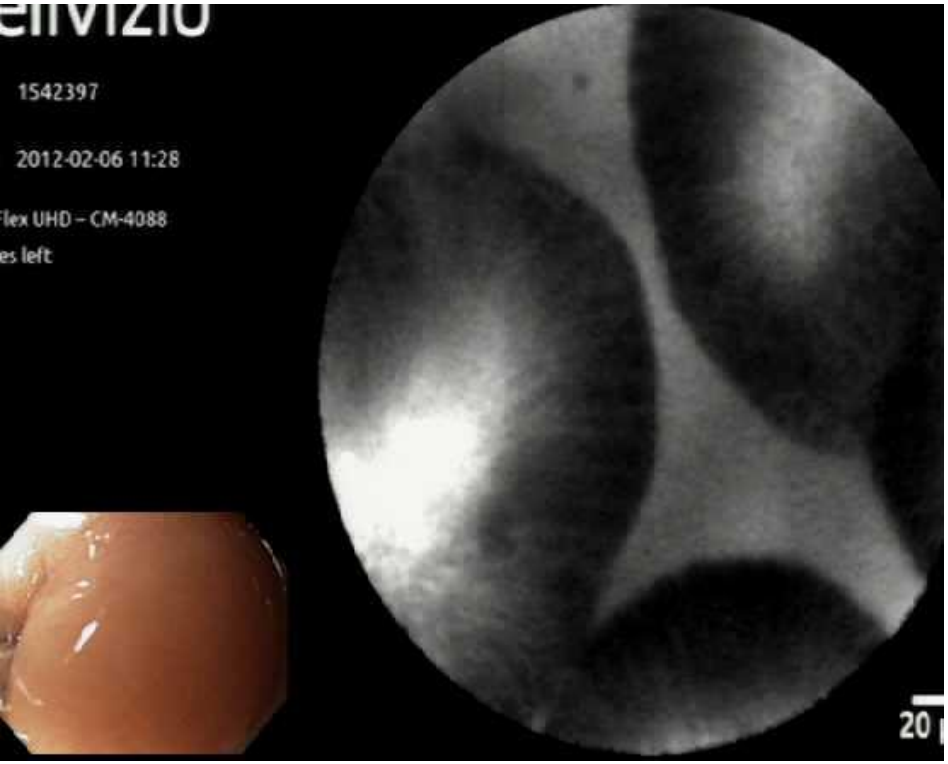
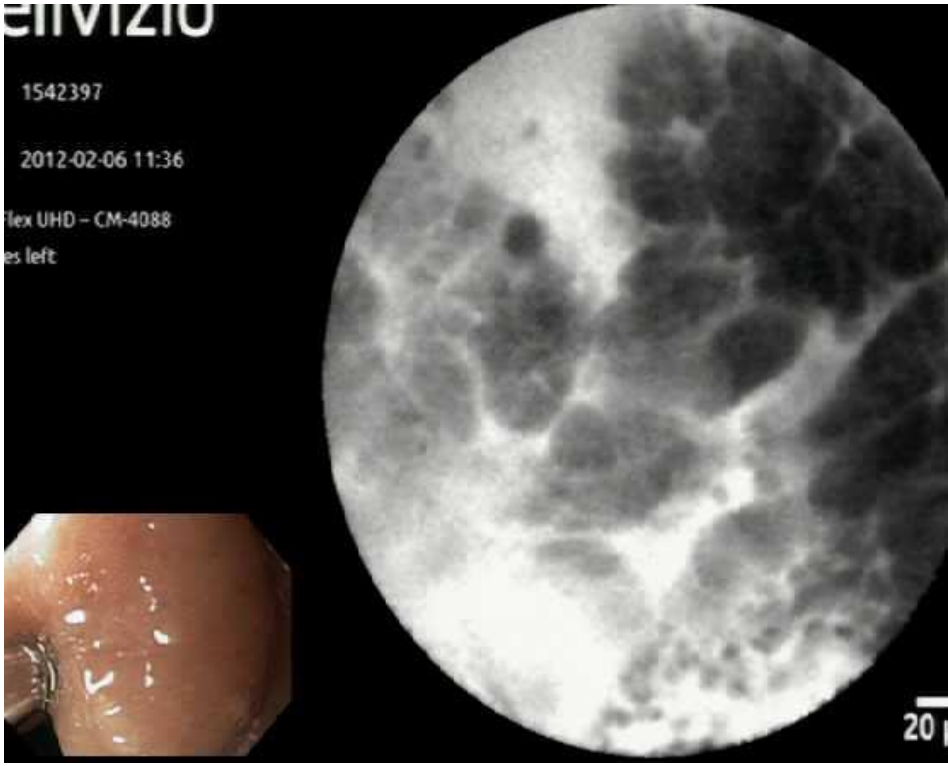


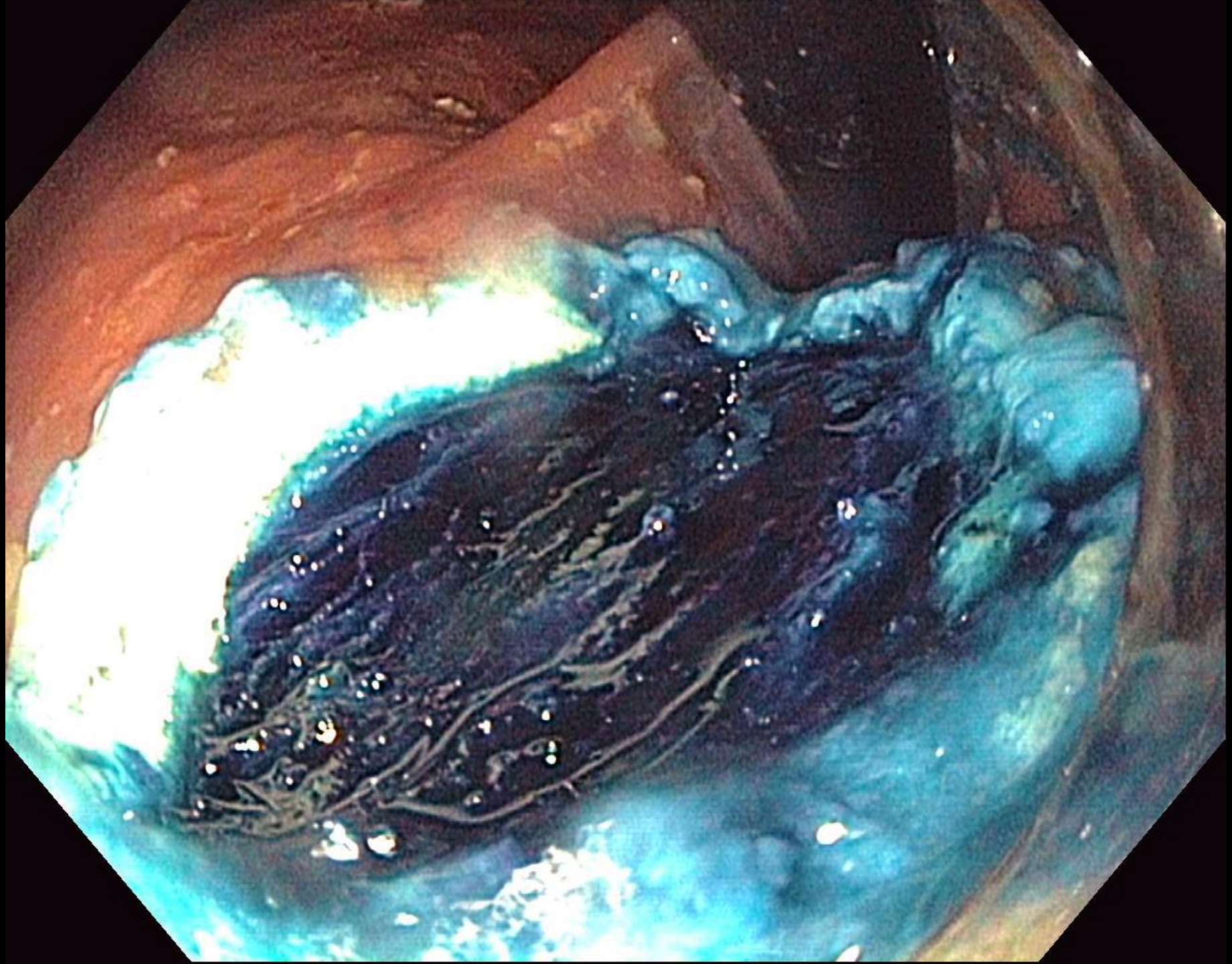



Narrow band imaging

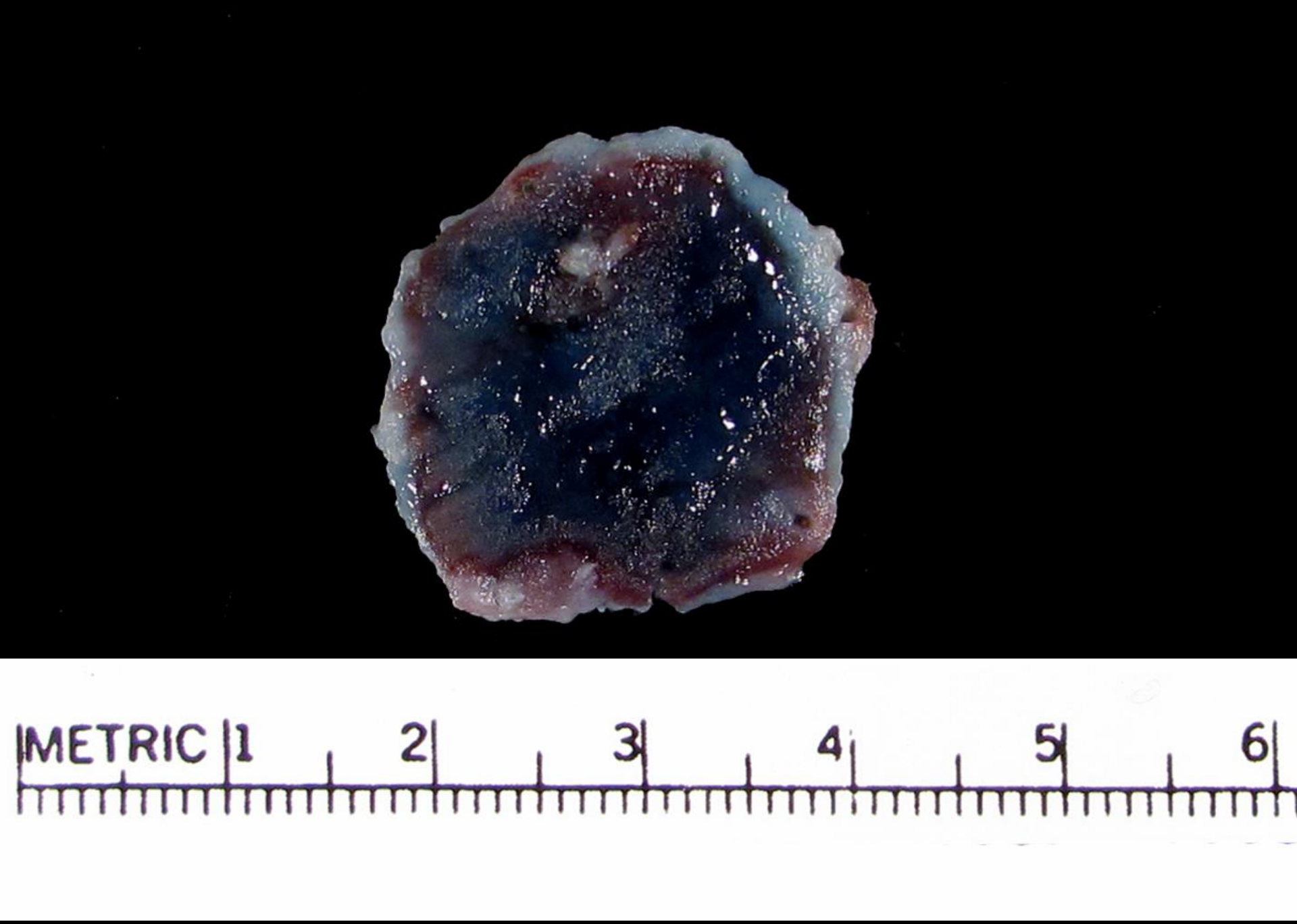
Confocal Endomicroscopy







Specimen pinned out in endoscopy suite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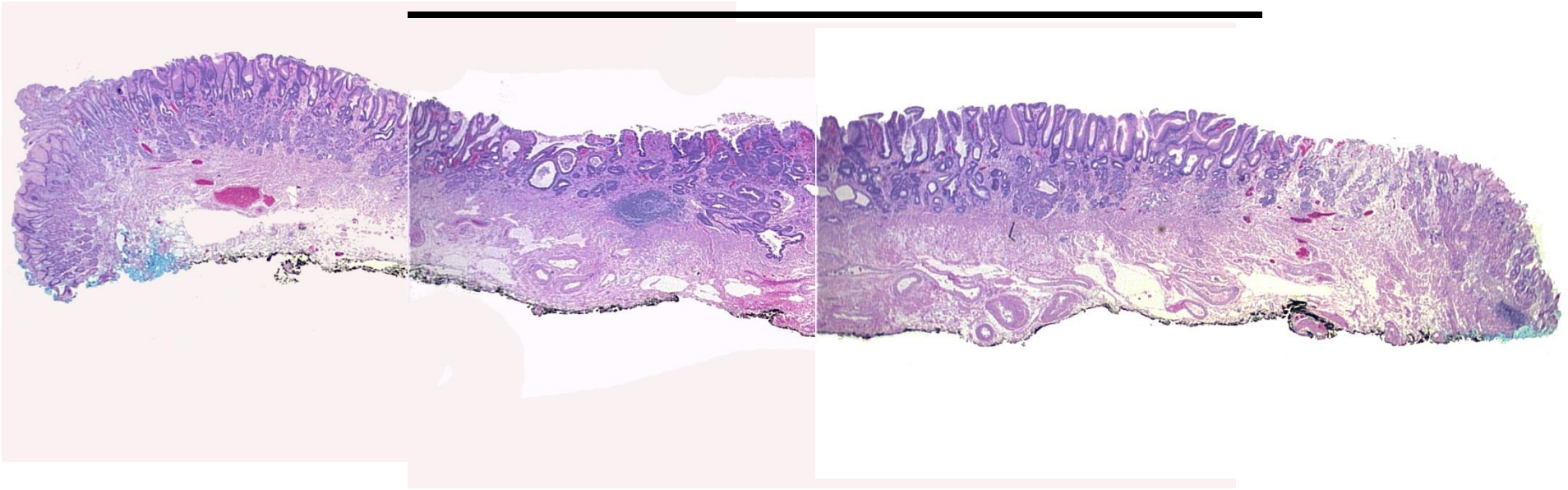
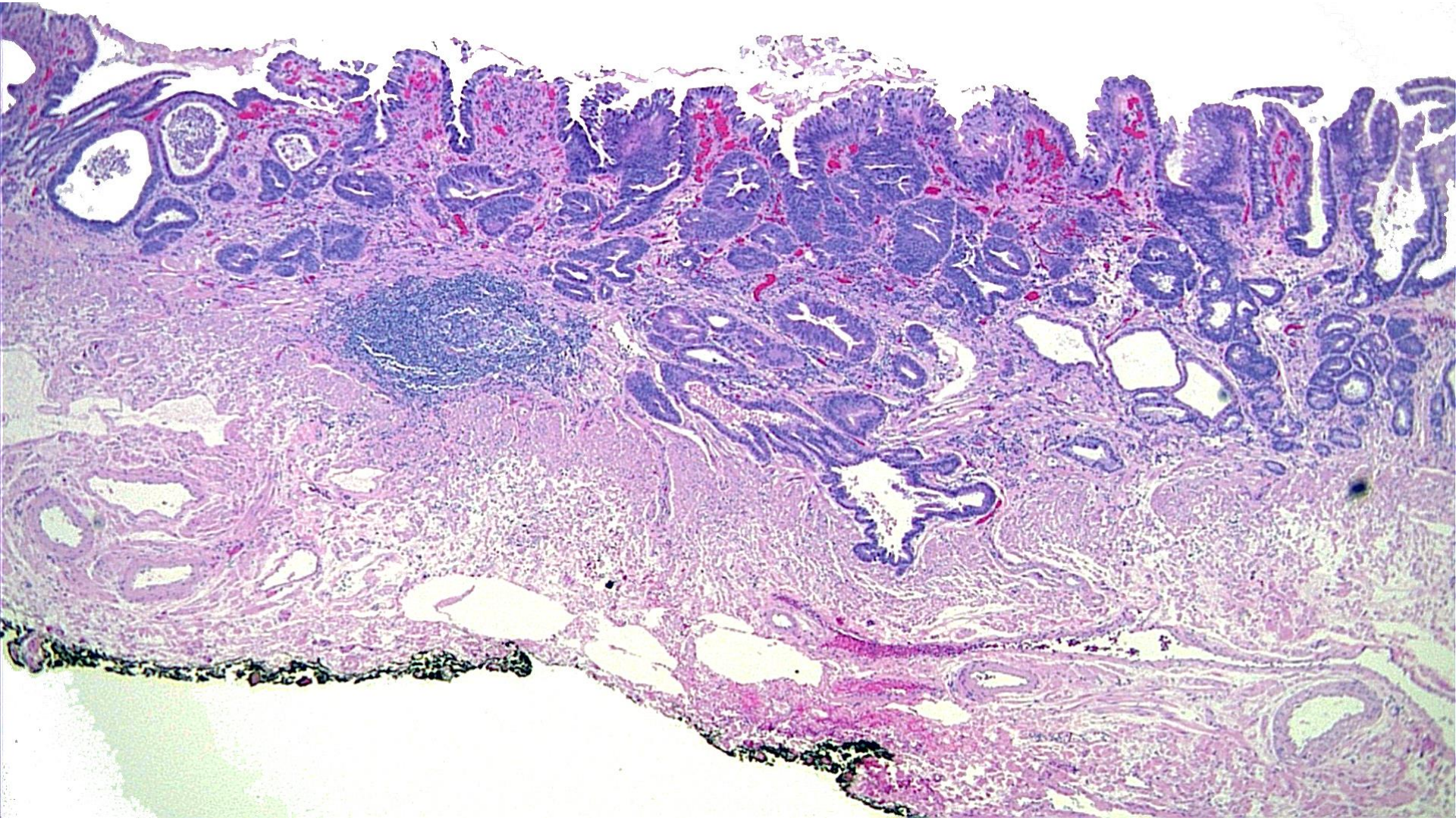
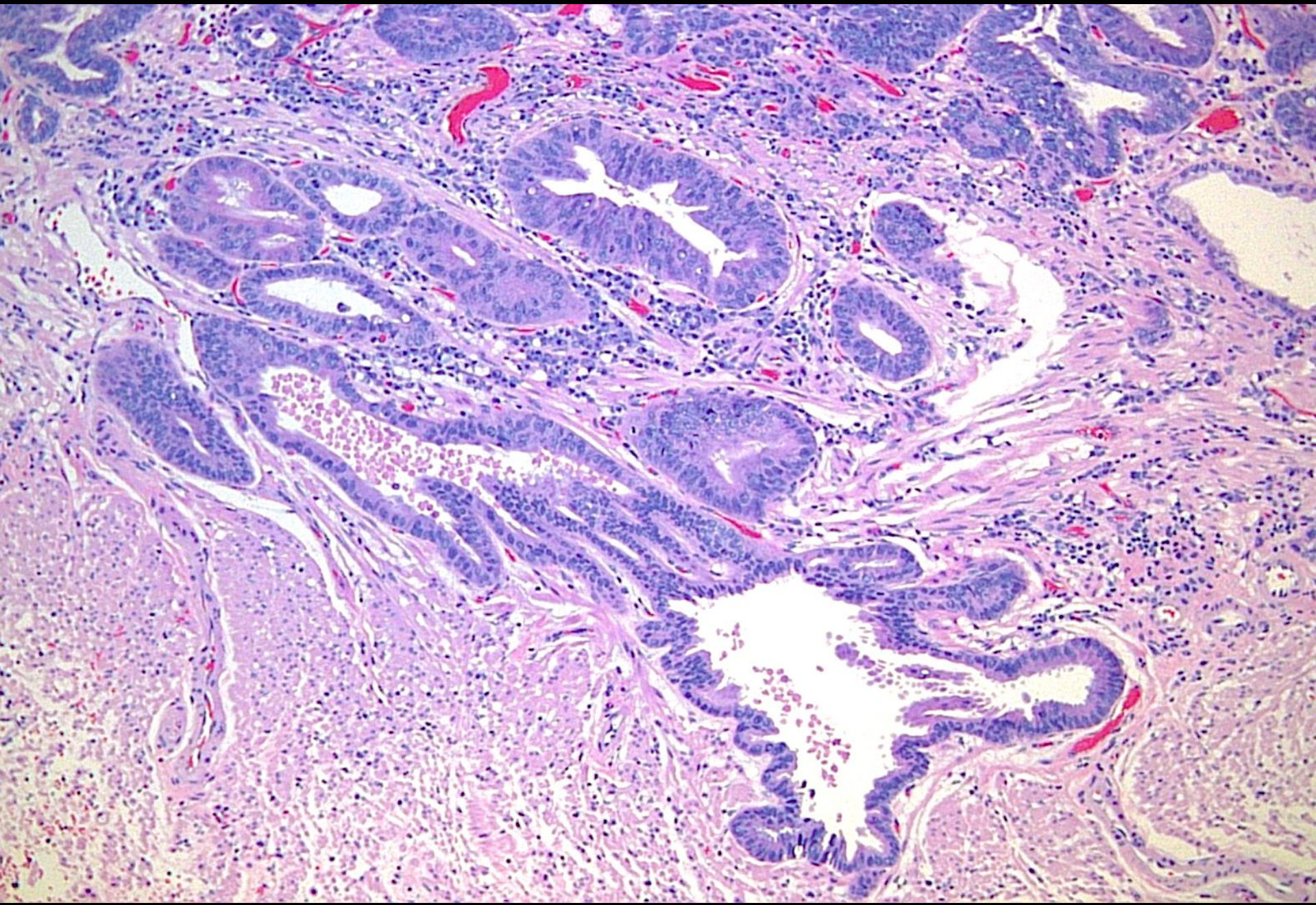
DYSPLASTIC FOCUS

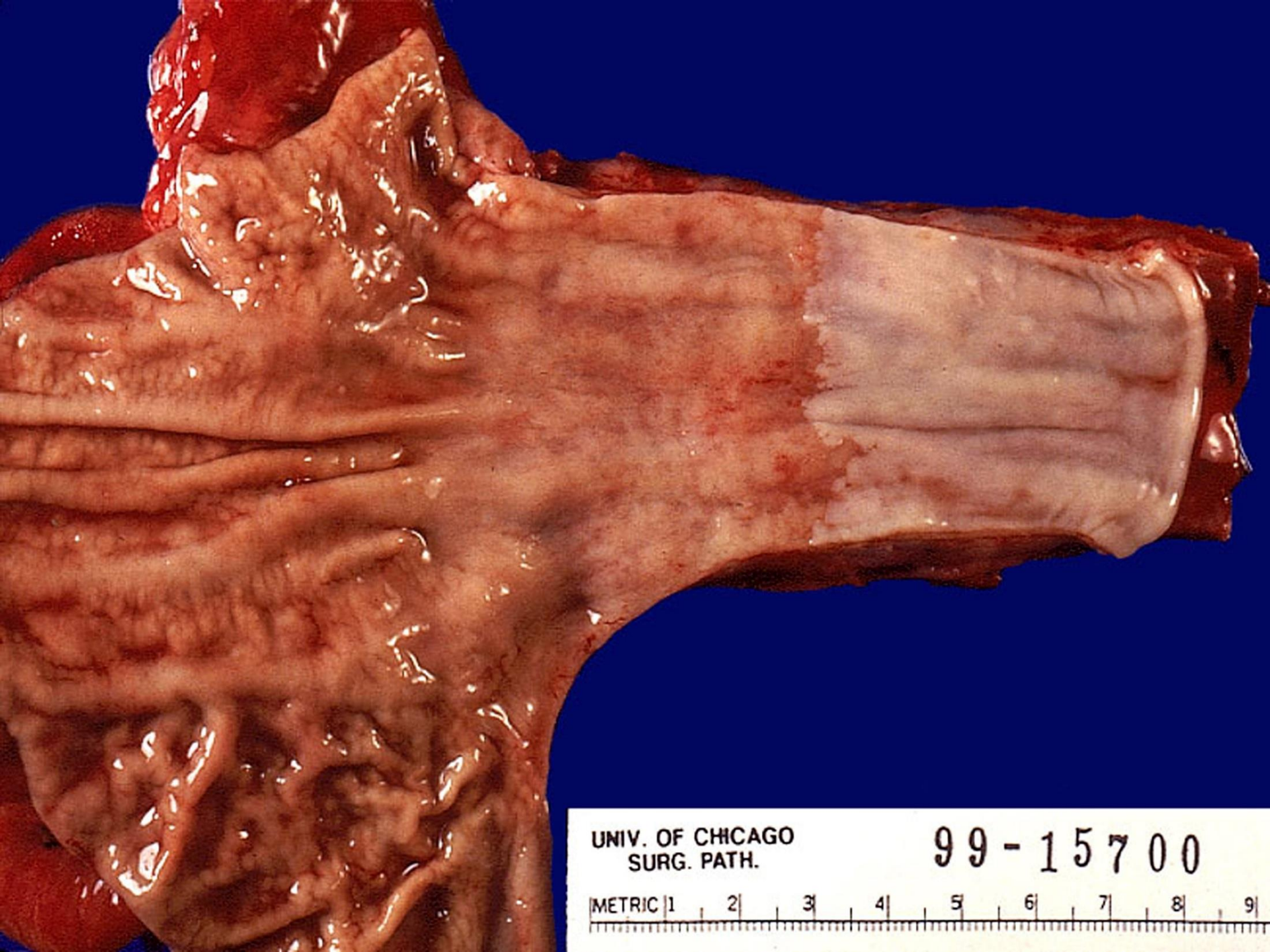


Blue ink = lateral margins
Black ink = deep margins



intramucosal adenocarcinoma




UNIV. OF CHICAGO
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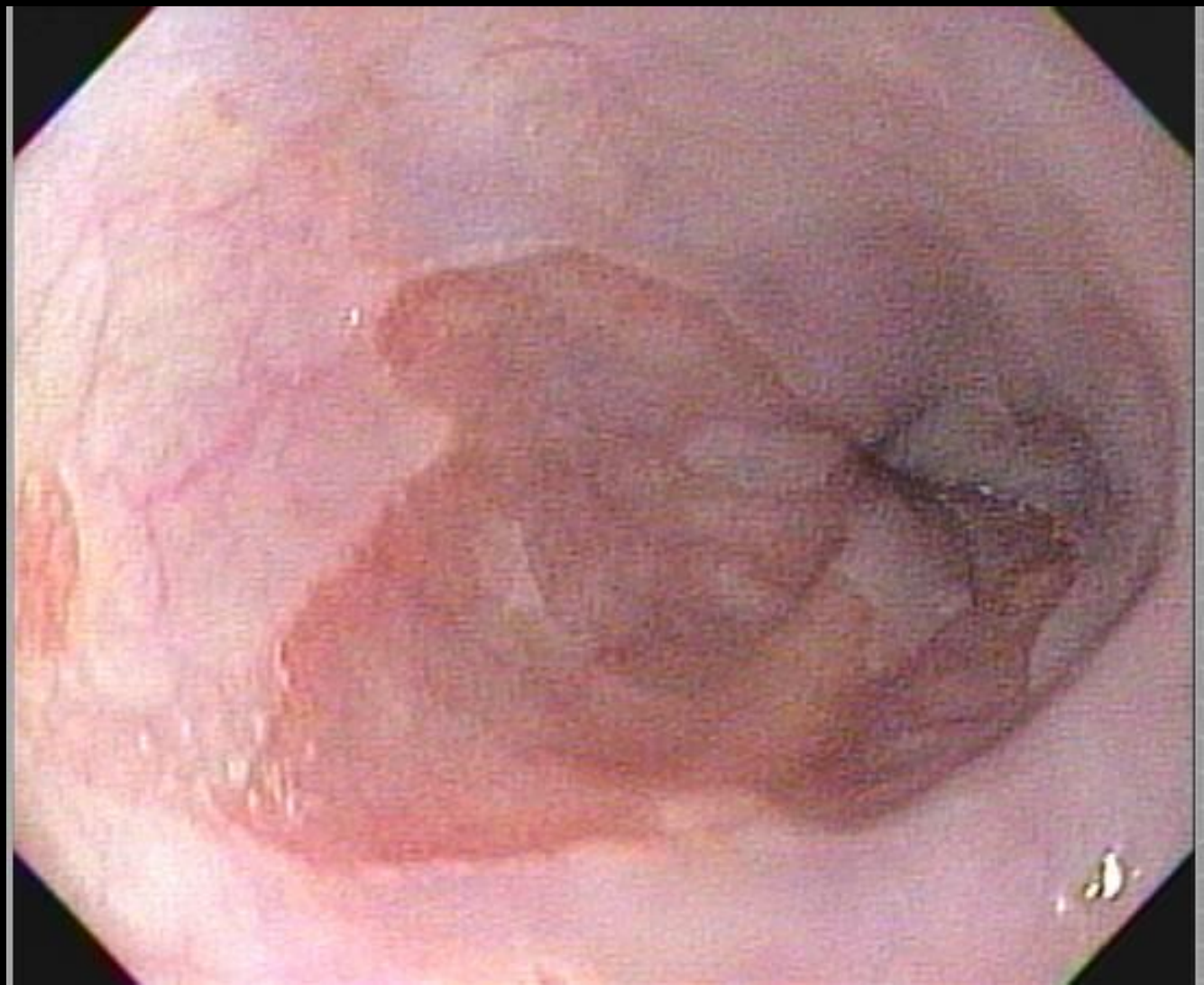
Long-term follow-up of complete Barrett's eradication endoscopic mucosal resection (CBE-EMR) for the treatment of high grade dysplasia and intramucosal carcinoma

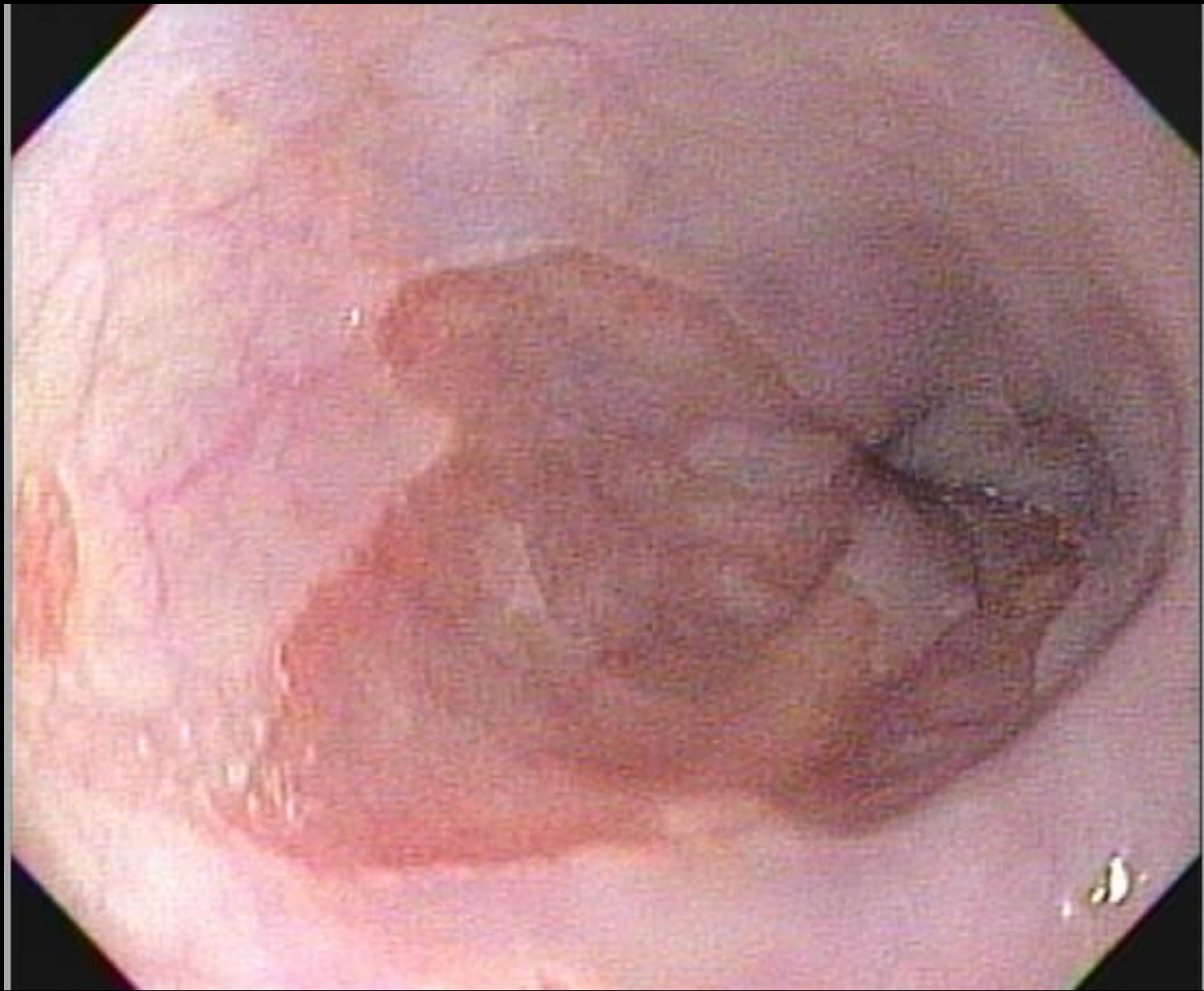
Am J Gastroenterol 2009; 104:2684-92.

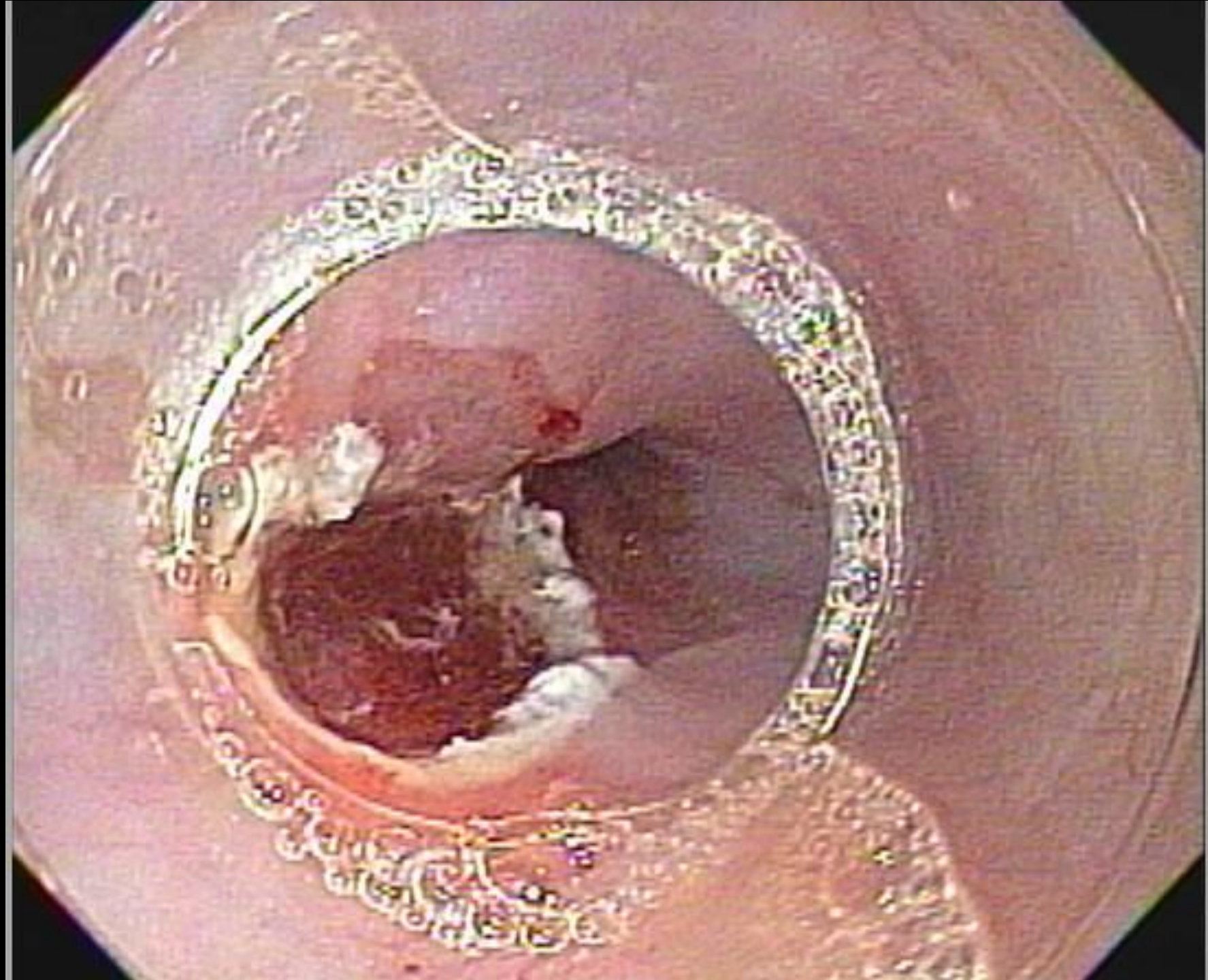
A. Larghi[1], C. J. Lightdale[2], A. S. Ross[1], P. Fedi[2], J. Hart[3], H. Rotterdam[4], A. Noffsinger[3], L. Memeo[4], G. Bhagat[4], I. Waxman[1]

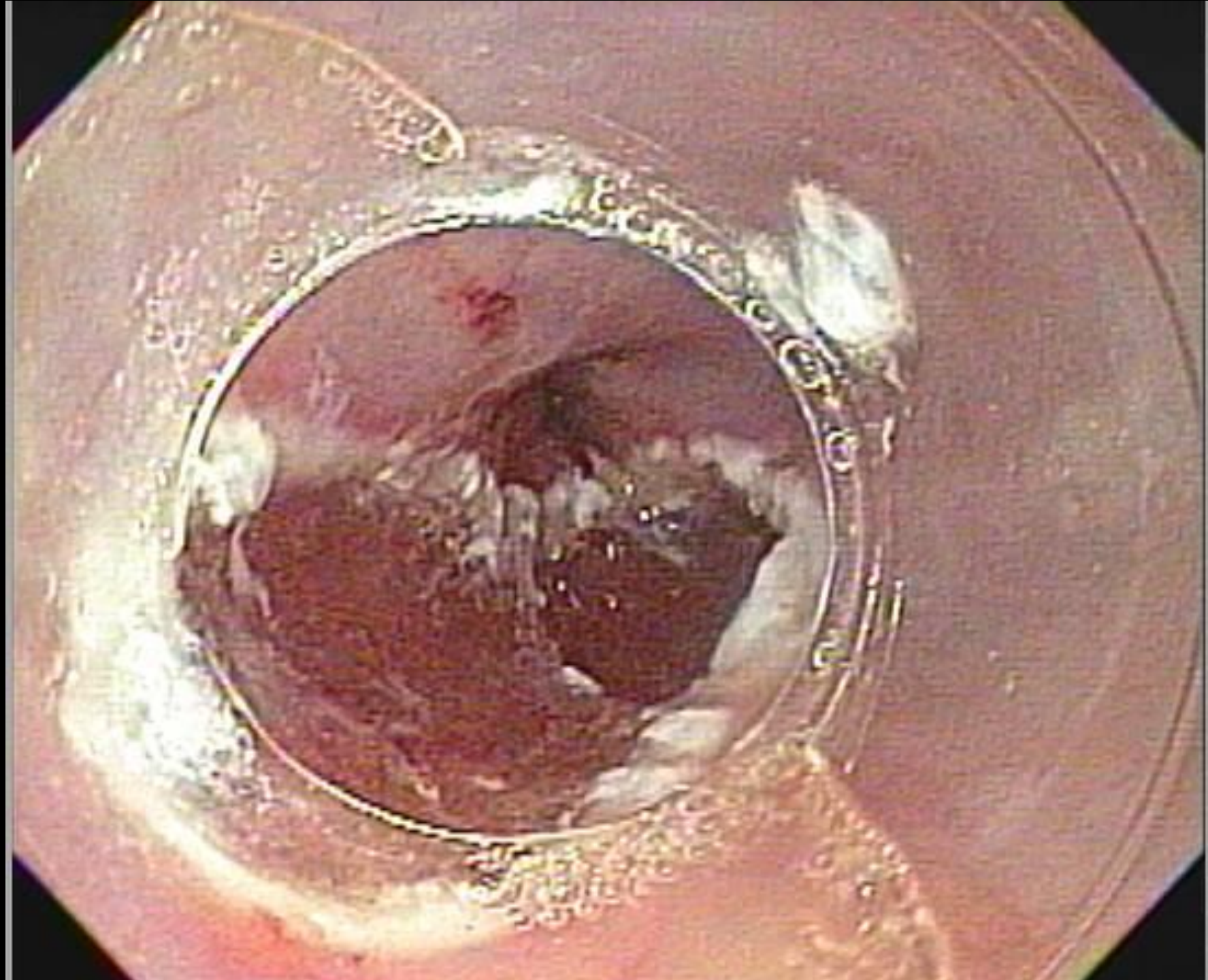
CBE-EMR is the endoscopic removal of all Barrett's epithelium with curative intent.

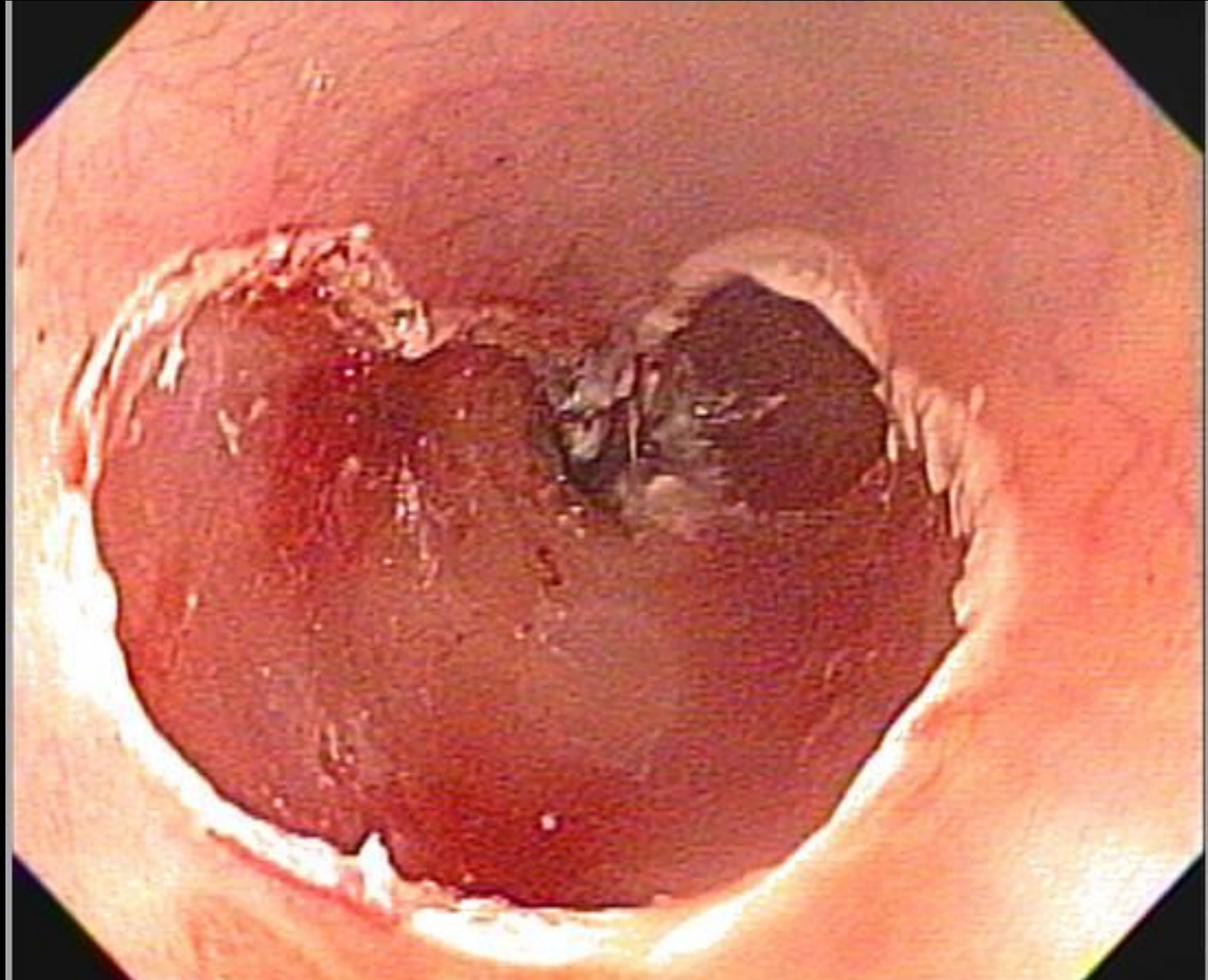
It is intended to eliminate HGD/IMC and reduce the risk of metachronous lesion development.

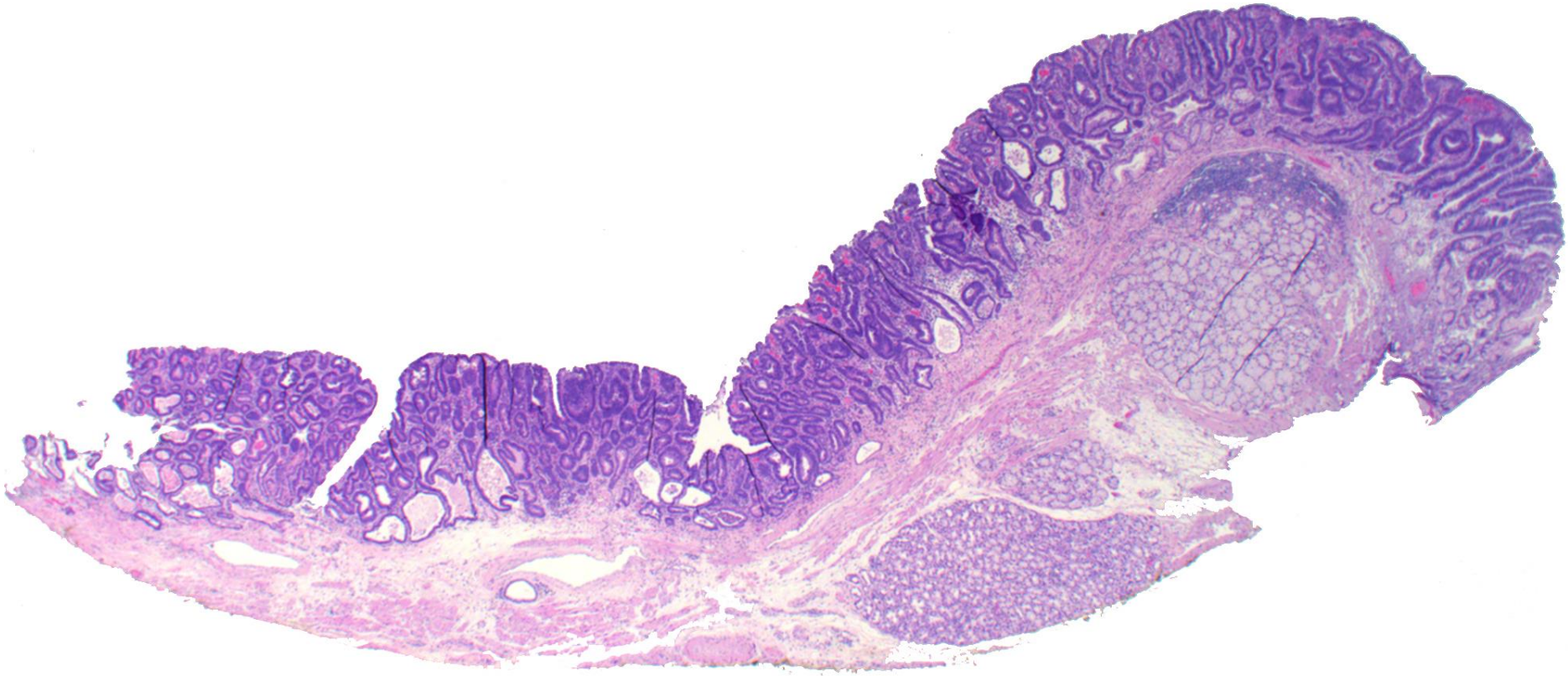


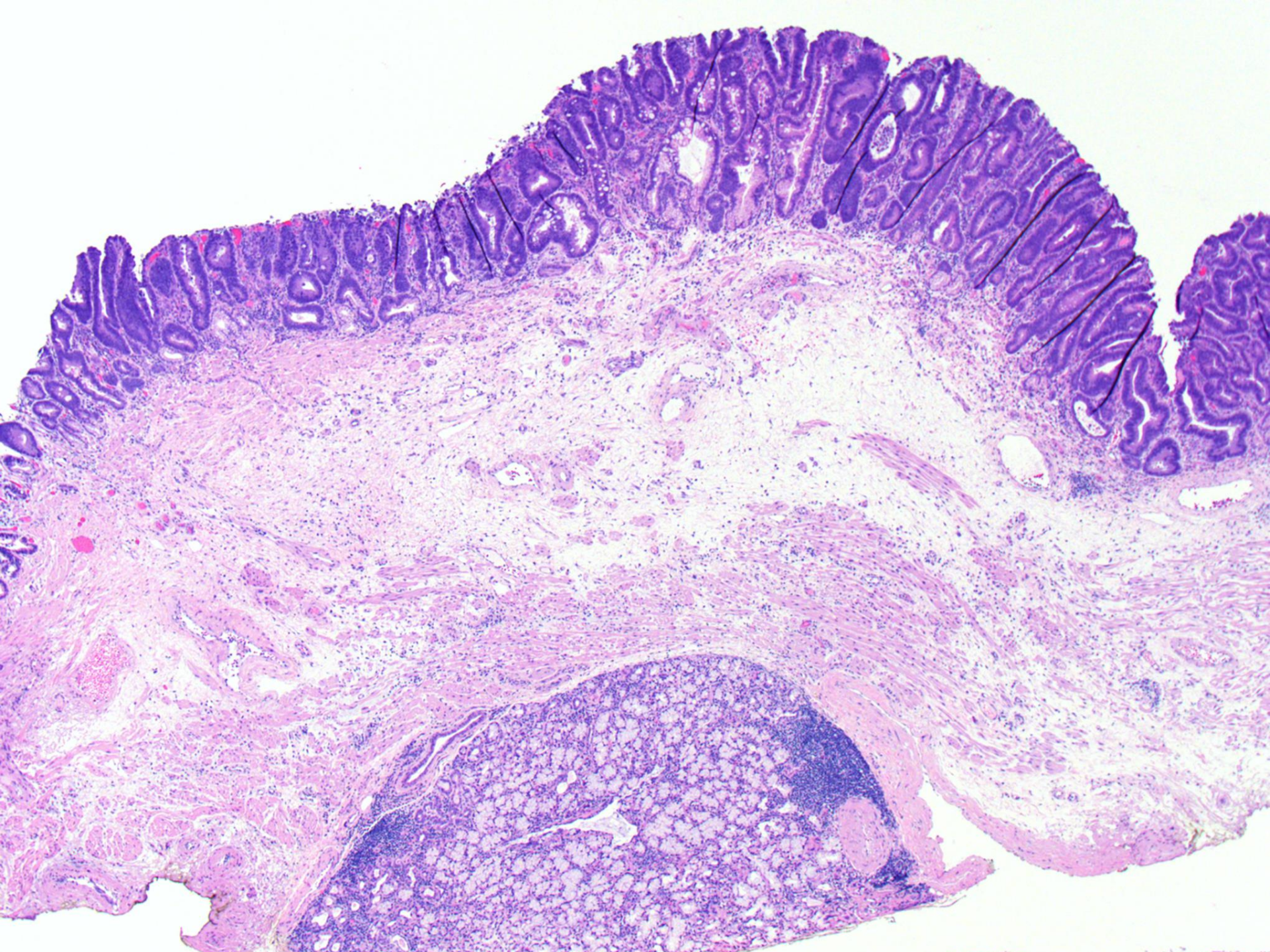




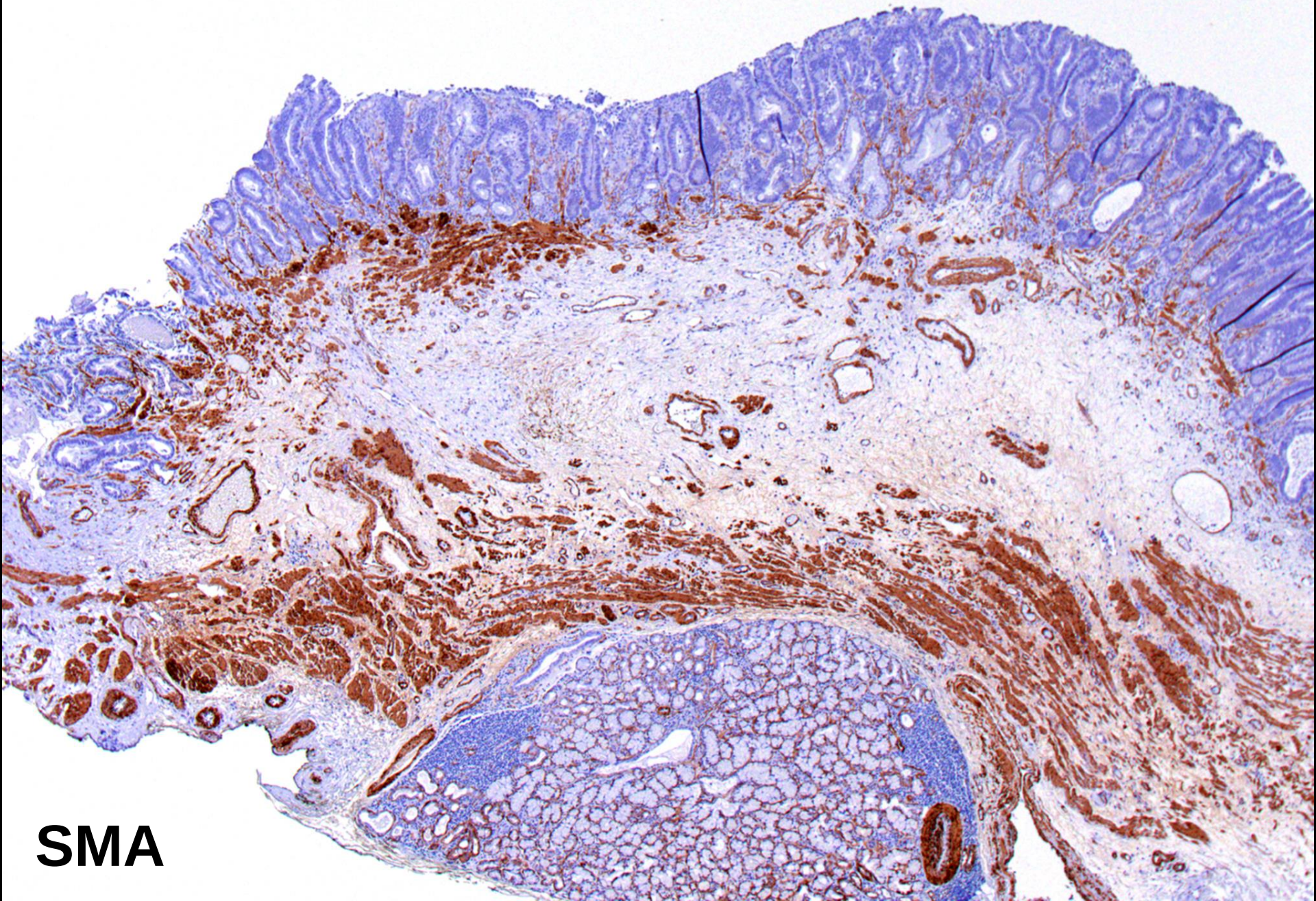






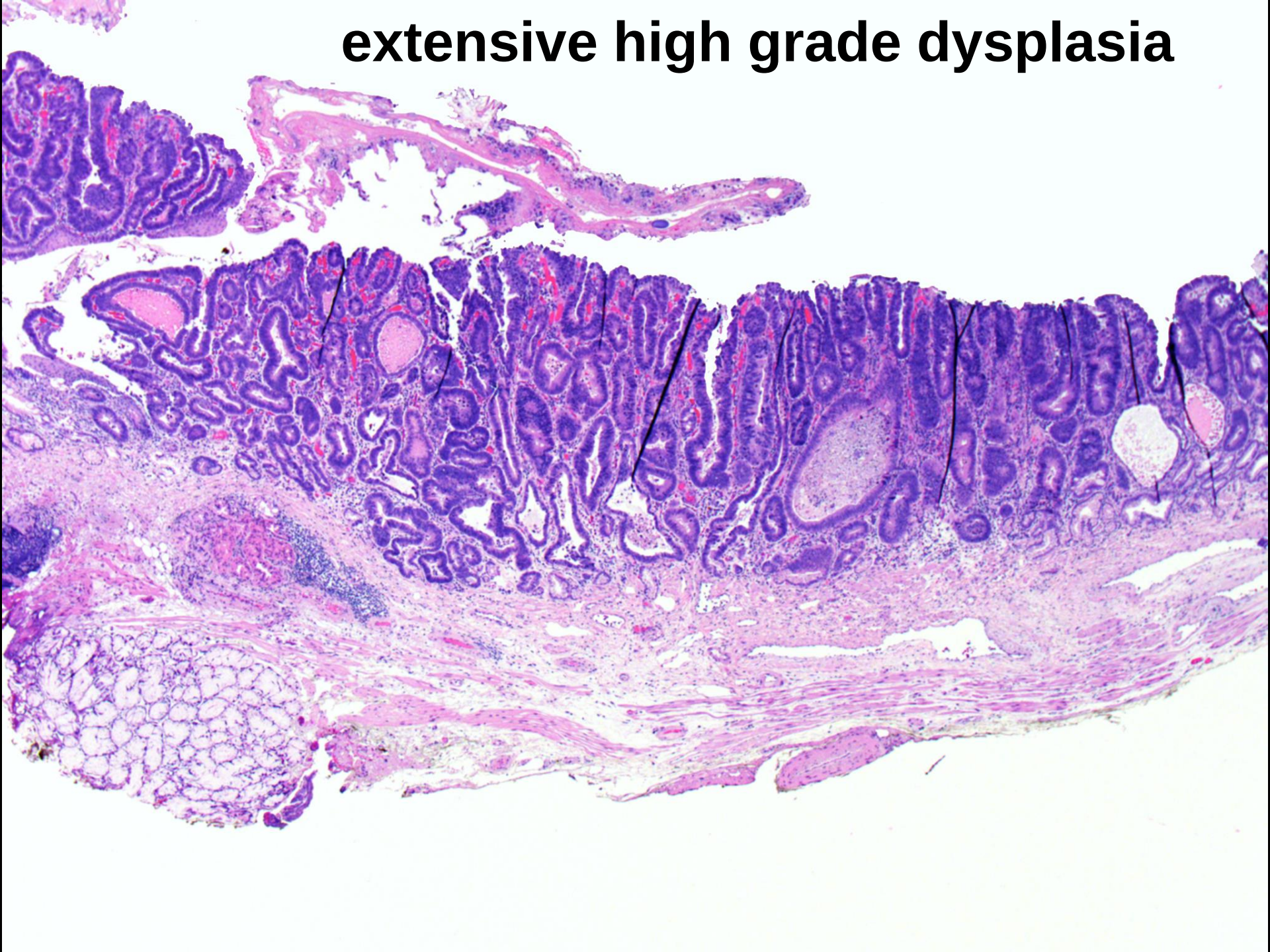


Duplicated muscularis mucosae

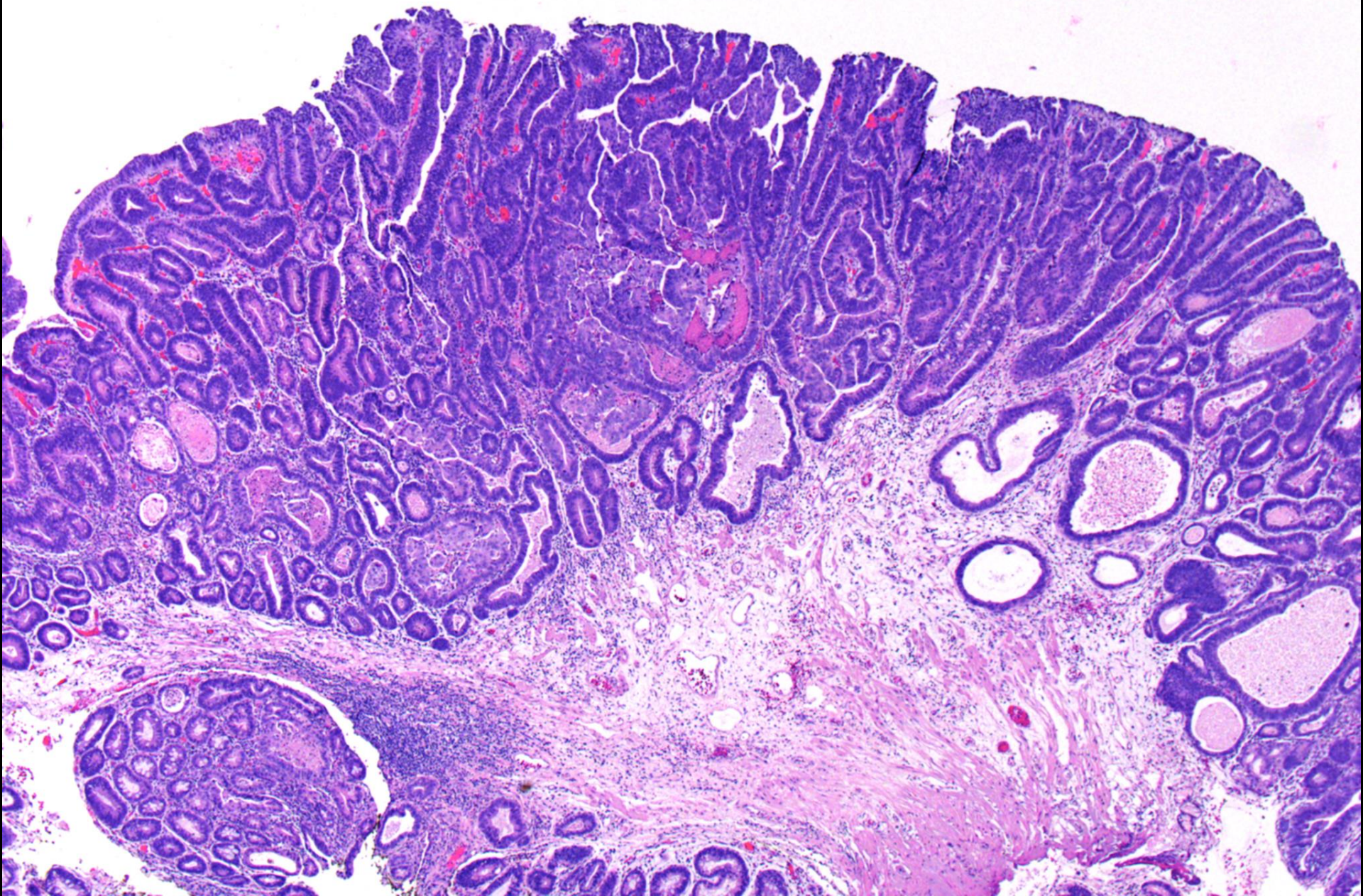


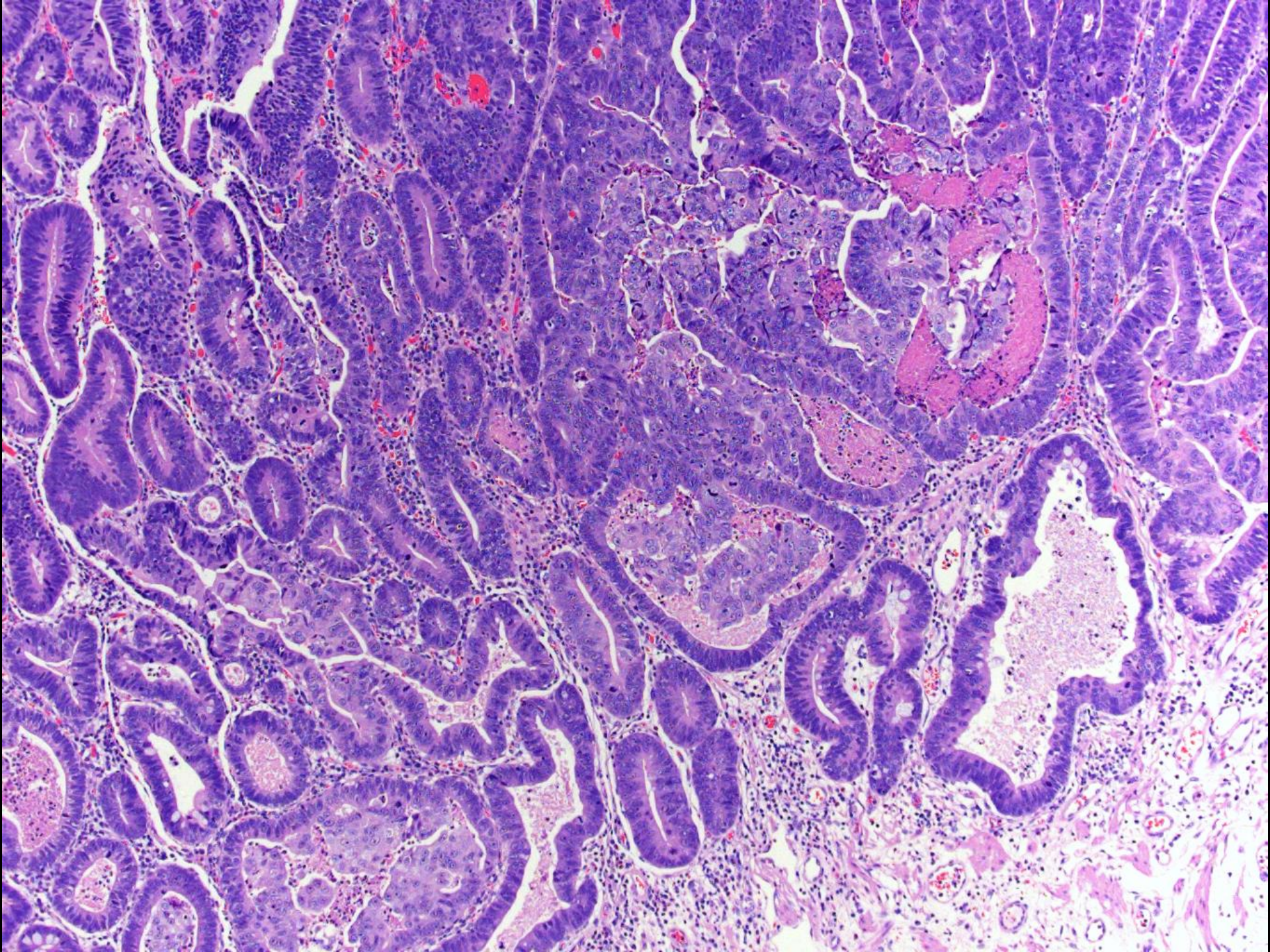
SMA

extensive high grade dysplasia



Intramucosal adenocarcinoma





Complete Endoscopic Mucosal Resection Is Effective and Durable Treatment for Barrett's-Associated Neoplasia

Vani J. A. Konda,[*] Mariano Gonzalez Haba Ruiz,[*] Ann Koons,[*] John Hart,[‡] Shu–Yuan Xiao,[‡] Uzma D. Siddiqui,[*] Mark K. Ferguson,[§] Mitchell Posner,[§] Marco G. Patti,[§] and Irving Waxman[*]

Clinical Gastroenterology and Hepatology 2014;12:2002–2010

Table 1. Characteristics of Patients Undergoing Complete EMR

Characteristic	N = 107
Age, average, *y*	67.5
Sex, M:F ratio	2.7:1
BE segment length	
Median	2.5
SD	2.83
Range	1–17
Interquartile range	2–5
Pre-EMR diagnosis	
LGD/indeterminate (with visible lesions)	4/1
HGD	63
IMC	39
Visible lesions	
Present	71/107 (66%)
I-s	5
I-p	7
II-a	43
II-b	10
II-c	3
III	1
Mixed IIa–IIc	2

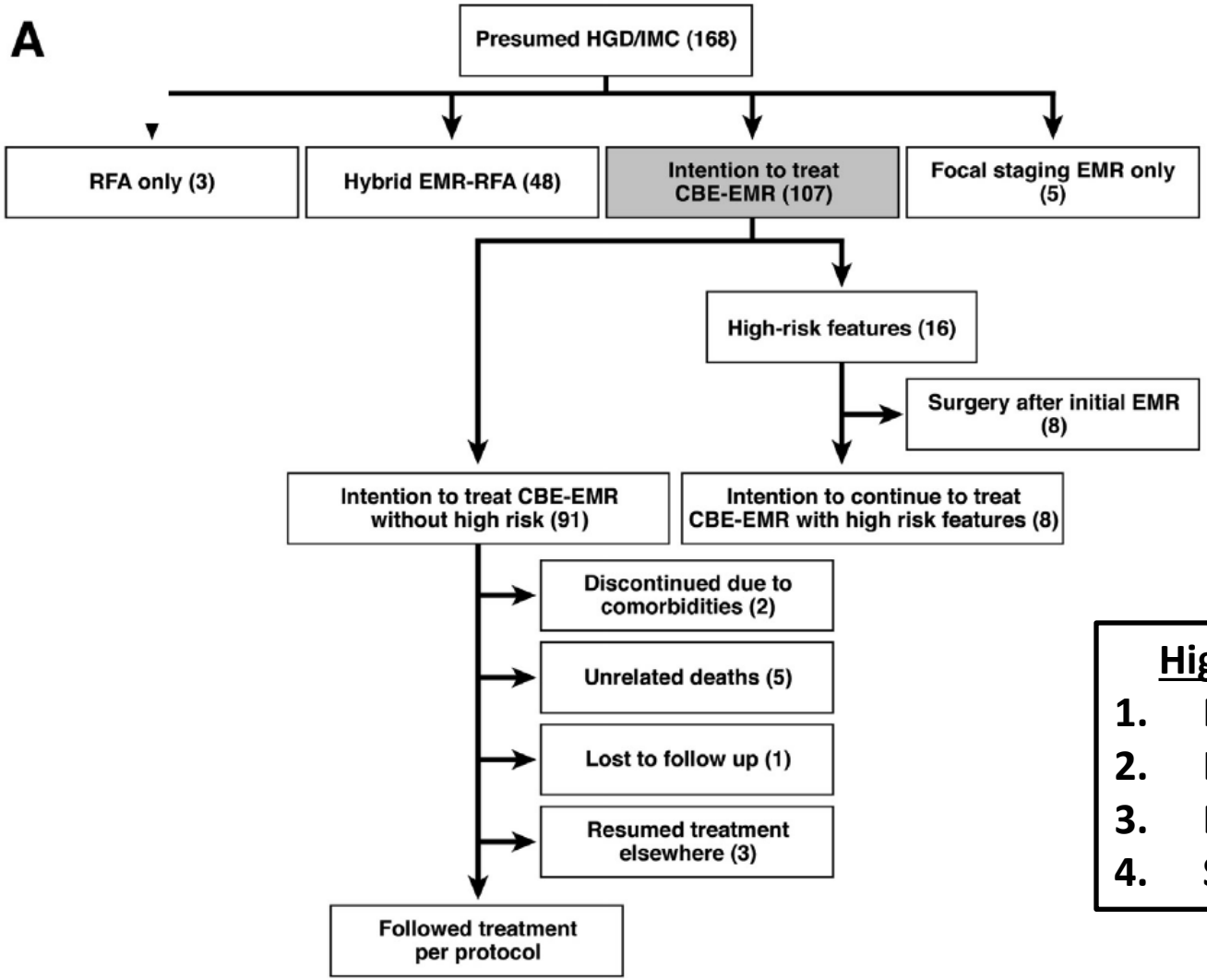
Table 2. Complications Associated With Complete EMR Protocol

Complication		Comments
Associated with EMR	N = 107	
Perforation	1.9% (2/107)	1 requiring esophagectomy 1 managed with endoscopic clips
Tear	2.8% (3/107)	Managed with endoscopic clips
Bleeding	3.7% (4/107)	Requiring repeat endoscopy 1 requiring transfusion
Stricture	41.5% (44/106)	
Symptomatic stricture	37.8% (40/106)	
Associated with stricture management		
Perforation after dilation	1	1 requiring esophagectomy
Stent placement for stricture	2	1 patient had stent migration
Required steroid injection	9	

Complete Endoscopic Mucosal Resection Is Effective and Durable Treatment for Barrett's-Associated Neoplasia

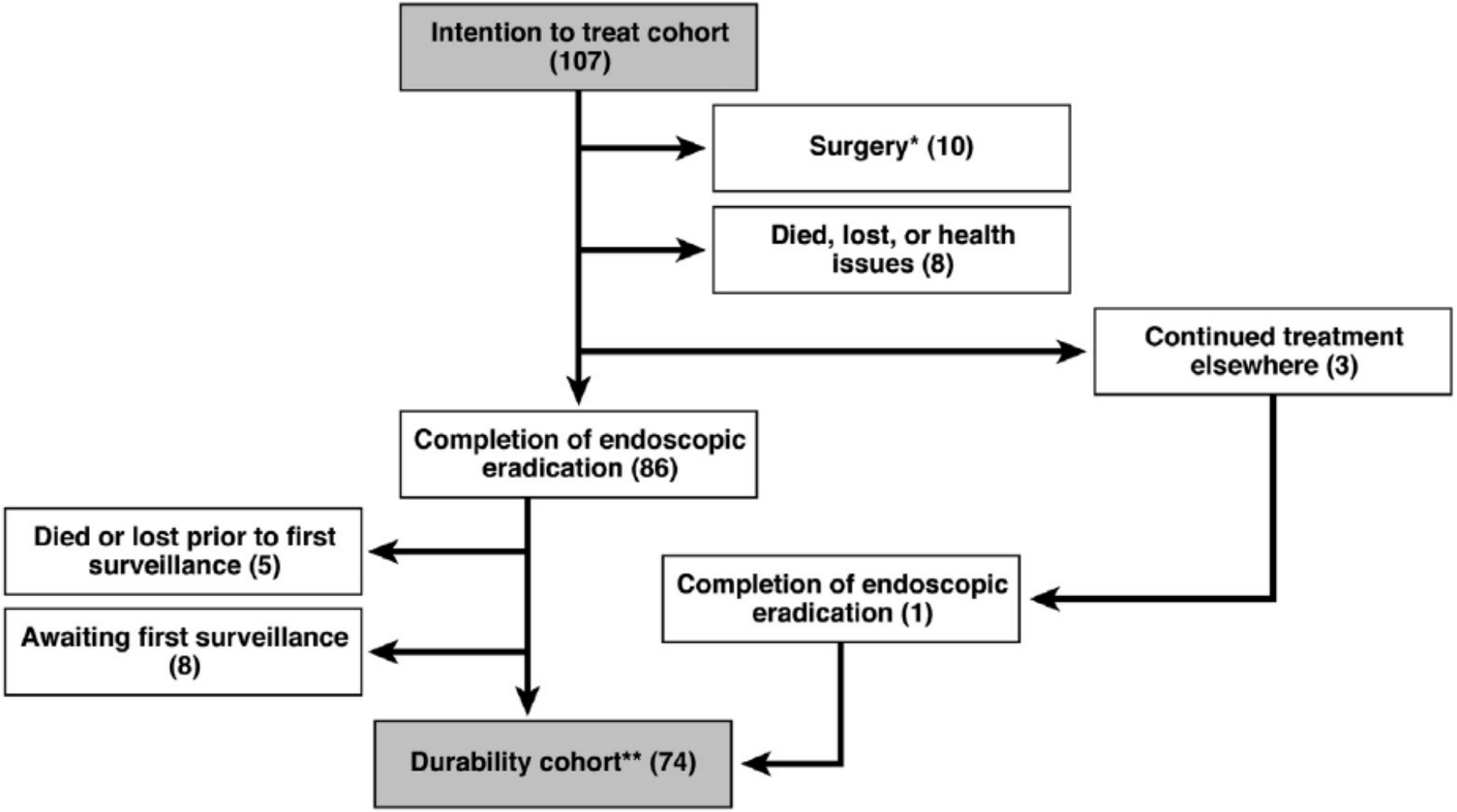
Vani J. A. Konda,* Mariano Gonzalez Haba Ruiz,* Ann Koons,* John Hart,‡ Shu–Yuan Xiao,‡ Uzma D. Siddiqui,* Mark K. Ferguson,§ Mitchell Posner,§ Marco G. Patti,§ and Irving Waxman*

Clinical Gastroenterology and Hepatology 2014;12:2002–2010



High Risk Features:

1. Poorly diff IMC
2. LVI
3. Deep margin +
4. Submucosal tumor

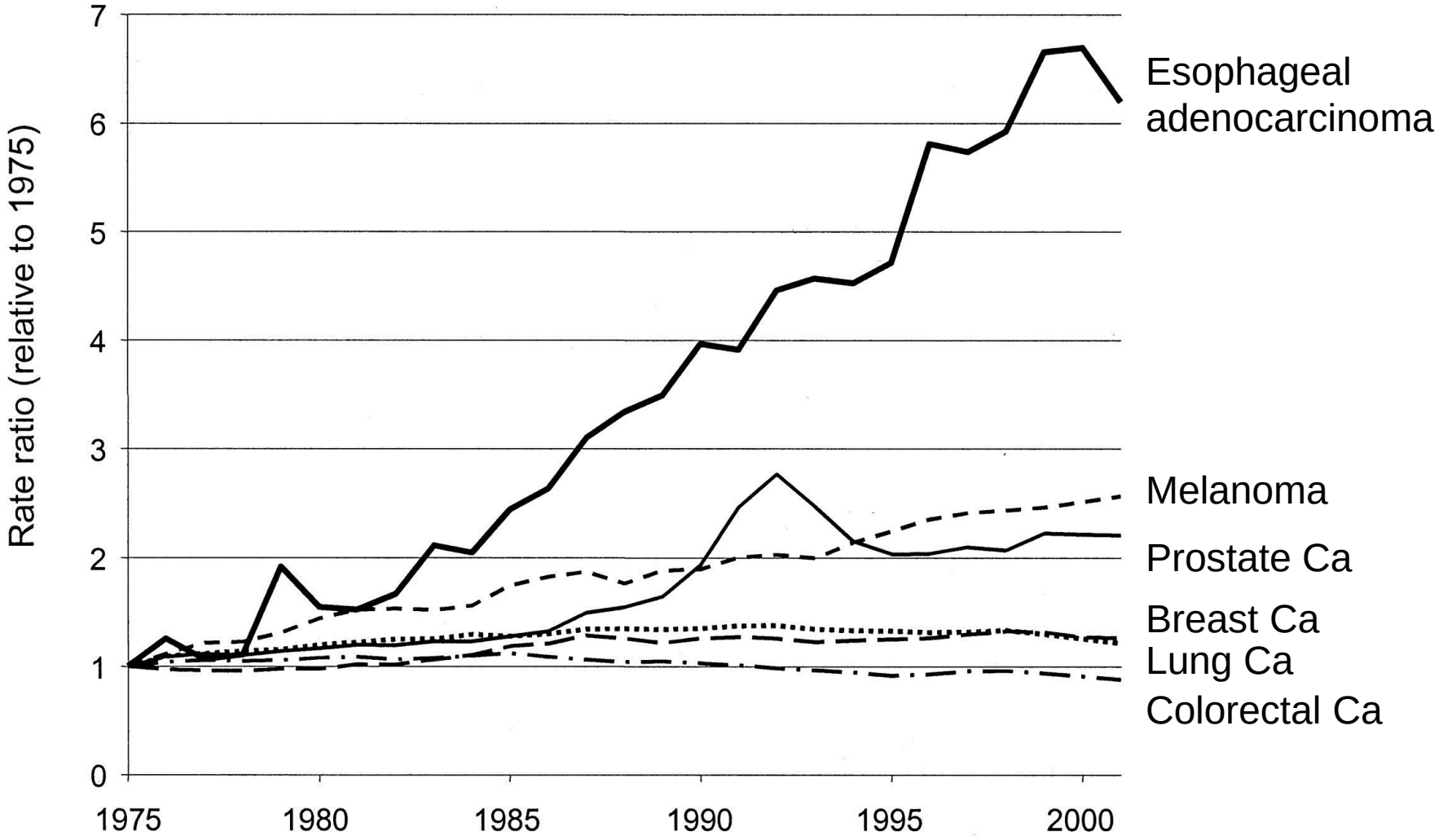

Intention to treat cohort (107)
Surgery* (10)
Died, lost, or health issues (8)
Continued treatment elsewhere (3)
Completion of endoscopic eradication (86)
Died or lost prior to first surveillance (5)
Awaiting first surveillance (8)
Completion of endoscopic eradication (1)
Durability cohort** (74)

	Intention to treat					
	Including advanced disease		Excluding advanced disease		Per protocol	
Durability, n	74		68		67	
Median follow-up period, *mo*	33.0		33.5		40.0	
Recurrence of disease						
Cancer	1.4%	(1/74)	0		0	
HGD	1.4%	(1/74)	1.5%	(1/68)	1.5%	(1/67)
LGD	8.1%	(6/74)	7.4%	(5/68)	7.5%	(5/67)
Complete remission						
Cancer	100%	(74/74)	100%	(68/68)	100%	(67/67)
HGD	100%	(74/74)	100%	(68/68)	100%	(67/67)
Dysplasia	95.9%	(71/74)	97.1%	(66/68)	97.0%	(65/67)
Intestinal metaplasia	71.6%	(53/74)	75%	(51/68)	74.6%	(50/67)

	Intention to treat					
	Including advanced disease		Excluding advanced disease		Per protocol	
Efficacy (n)	107		91		80	
Required surgery	10		1		1	
For advanced disease	9[a]		0		0	
For complications	2[a]		1		1	
Related death	1[a]		0		0	
Disease progression	1		1		0	
Complete endoscopic eradication	86	(80.4%)	80	(87.9%)	79	(98.8%)

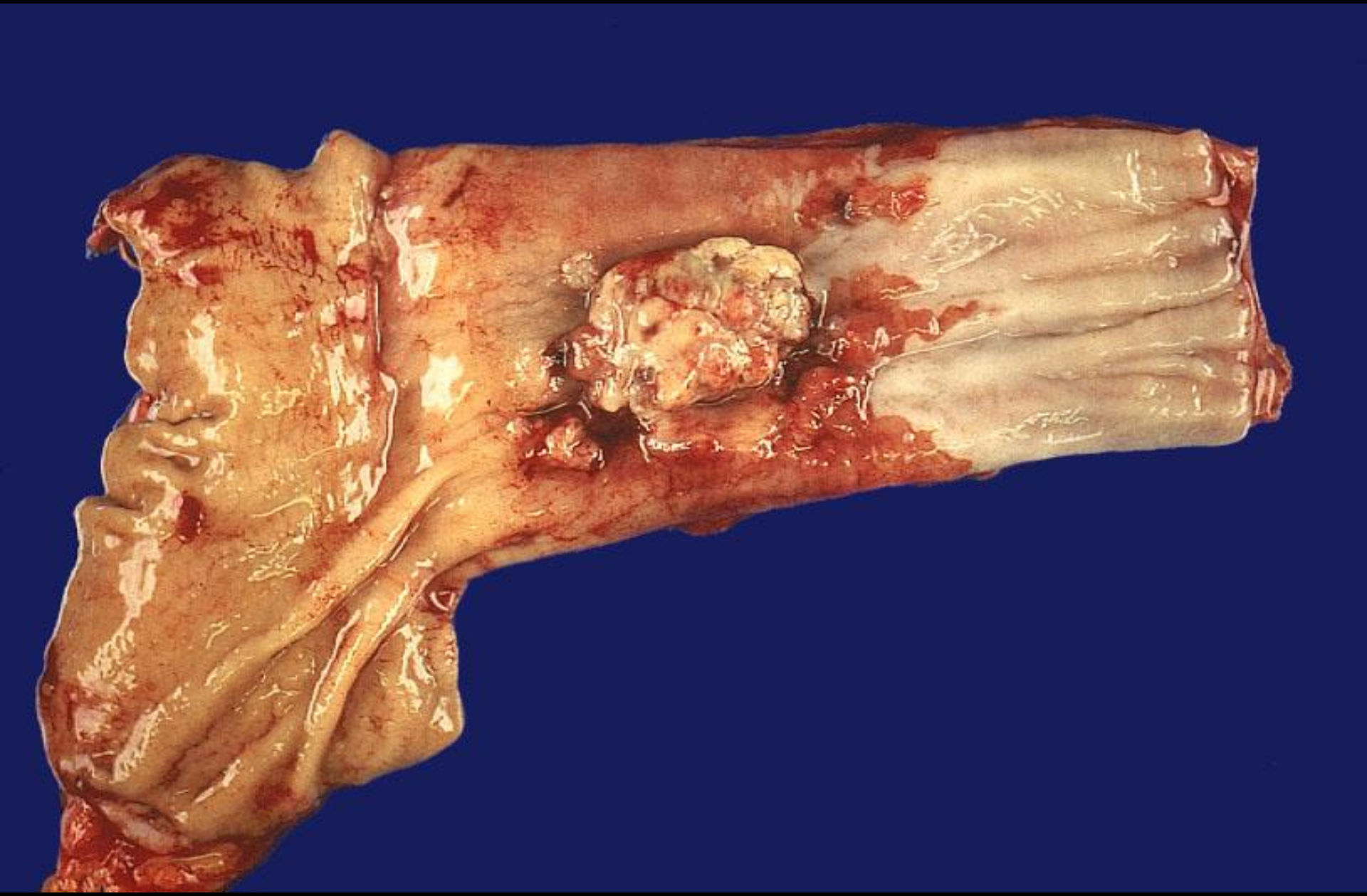
[a]One patient who had a perforation after EMR underwent esophagectomy. The surgical specimen showed submucosal invasion. The same patient died after a complicated postoperative course.

Esophageal adenocarcinoma is the fastest rising malignancy in the United States (1975–2001)



Pohl H, Welch HG. J Natl Cancer Inst. 2005;97:142-146

JNCI



Observer Variation in the Diagnosis of Dysplasia in Barrett's Esophagus

B. J. REID, MD, PHD,* R. C. HAGGITT, MD,* C. E. RUBIN, MD,* G. ROTH, MD,*
C. M. SURAWICZ, MD,* G. VAN BELLE, PHD,* K. LEWIN, MD,†
W. M. WEINSTEIN, MD,† D. A. ANTONIOLI, MD,‡ H. GOLDMAN, MD,‡
W. MACDONALD, MD,§ AND D. OWEN, MD§

Hum Pathol 1988;19(2):166-78.

- **No dysplasia – minimal cytologic atypia**
- **Indefinite – cytologic atypia suspicious for dysplasia**
- **Low grade – mild cytologic & architectural atypia**
- **High grade – prominent cytologic & architectural atypia**
- **Intramucosal Ca – invasion beyond basement membrane**

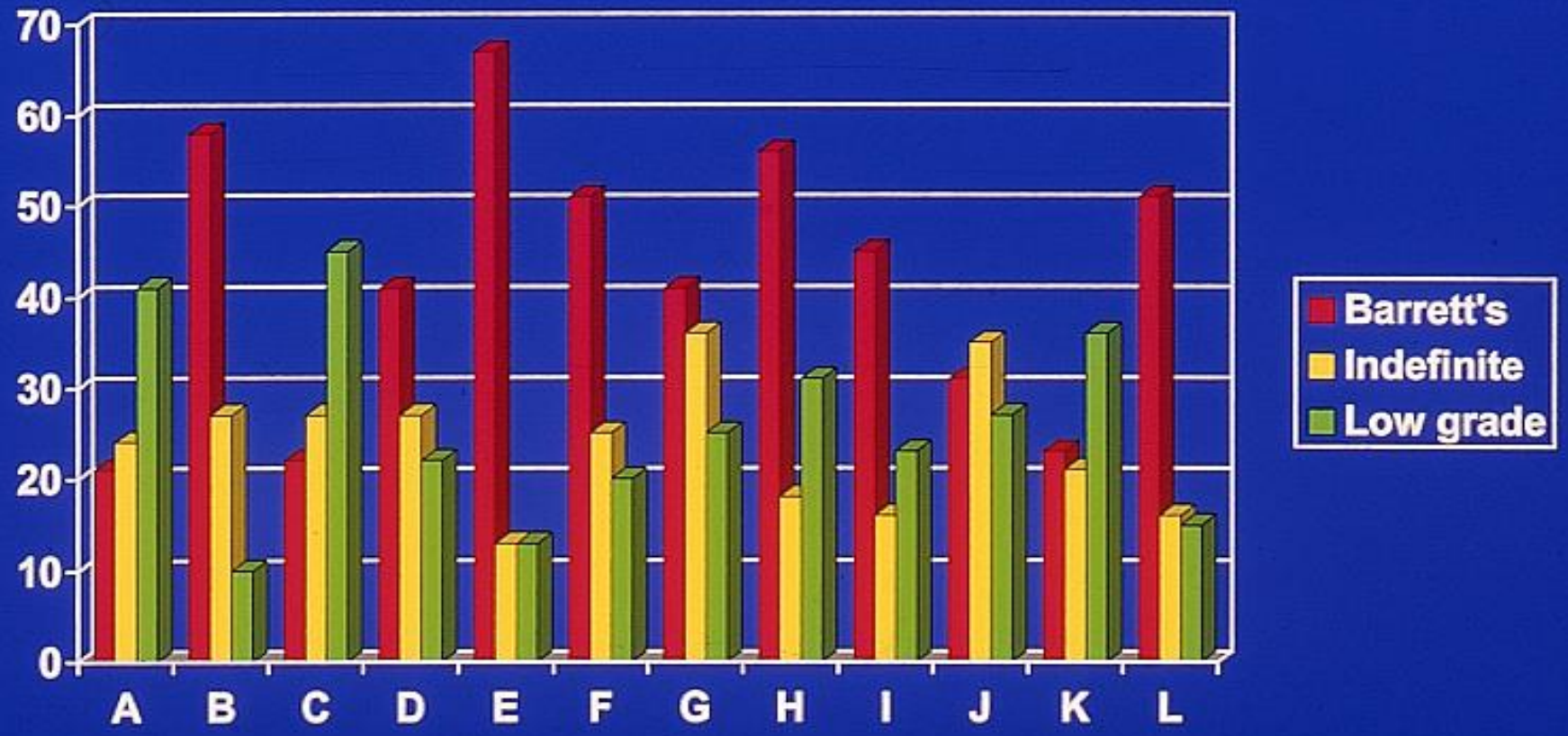
Reproducibility of the Diagnosis of Dysplasia in Barrett Esophagus: A Reaffirmation

ELIZABETH MONTGOMERY, MD, MARY P. BRONNER, MD,
JOHN R. GOLDBLUM, MD, JOEL K. GREENSON, MD,
MARIAN M. HABER, MD, JOHN HART, MD, LAURA W. LAMPS, MD,
GREGORY Y. LAUWERS, MD, AUDREY J. LAZENBY, MD,
DAVID N. LEWIN, MD, MARIE E. ROBERT, MD,
ALICIA Y. TOLEDANO, ScD, YU SHYR, PhD,
AND KAY WASHINGTON, MD, PhD

Human Pathol 2001; 32(4):368-78.

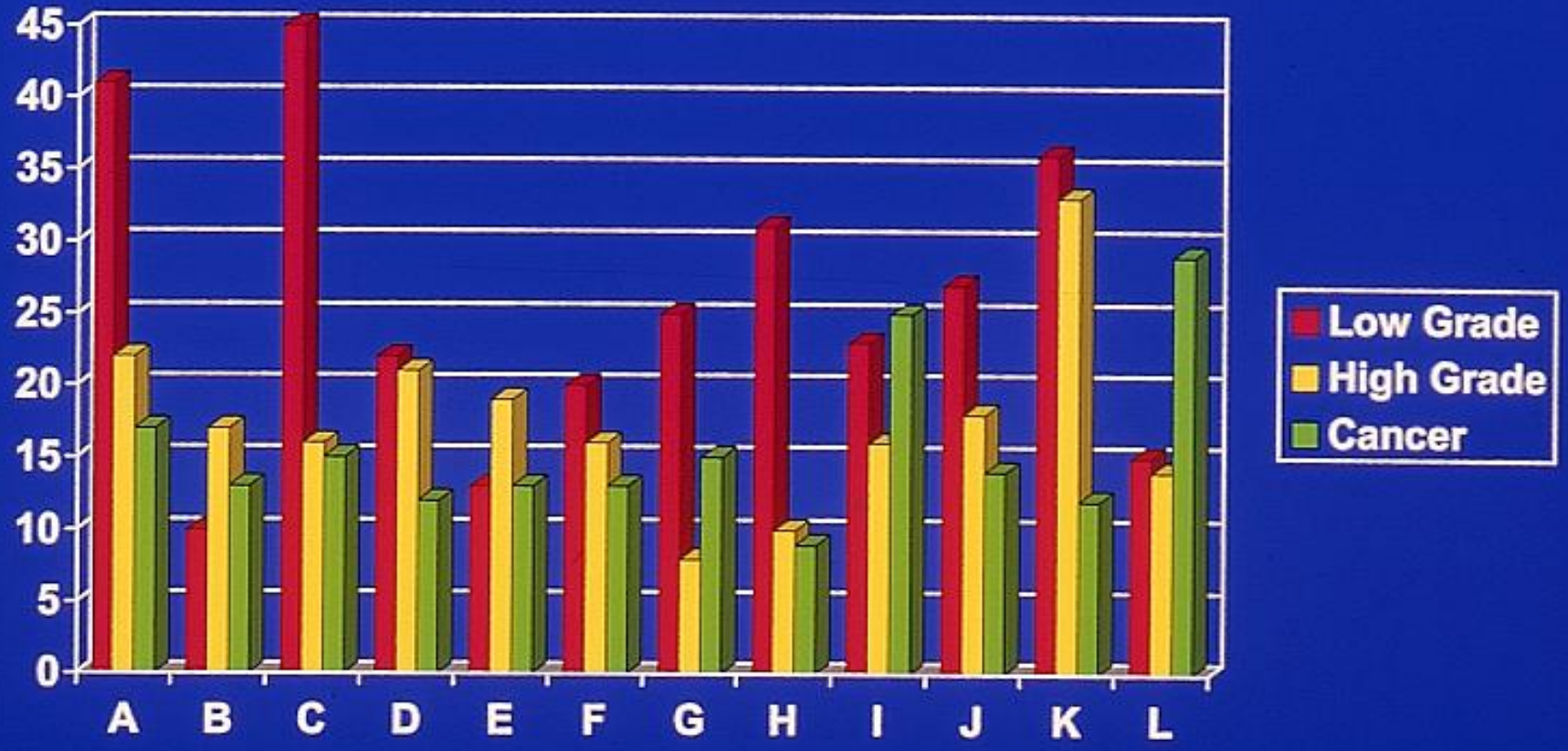
- **Pathologists submitted 25 slides each**
- **No dysplasia, indefinite, LGD, HGD, Carcinoma**
- **125 cases read blindly twice 6 months apart**
- **No prior discussion of criteria**
- **Meeting to develop consensus criteria**
- **New batch of 125 cases read twice**

Low End

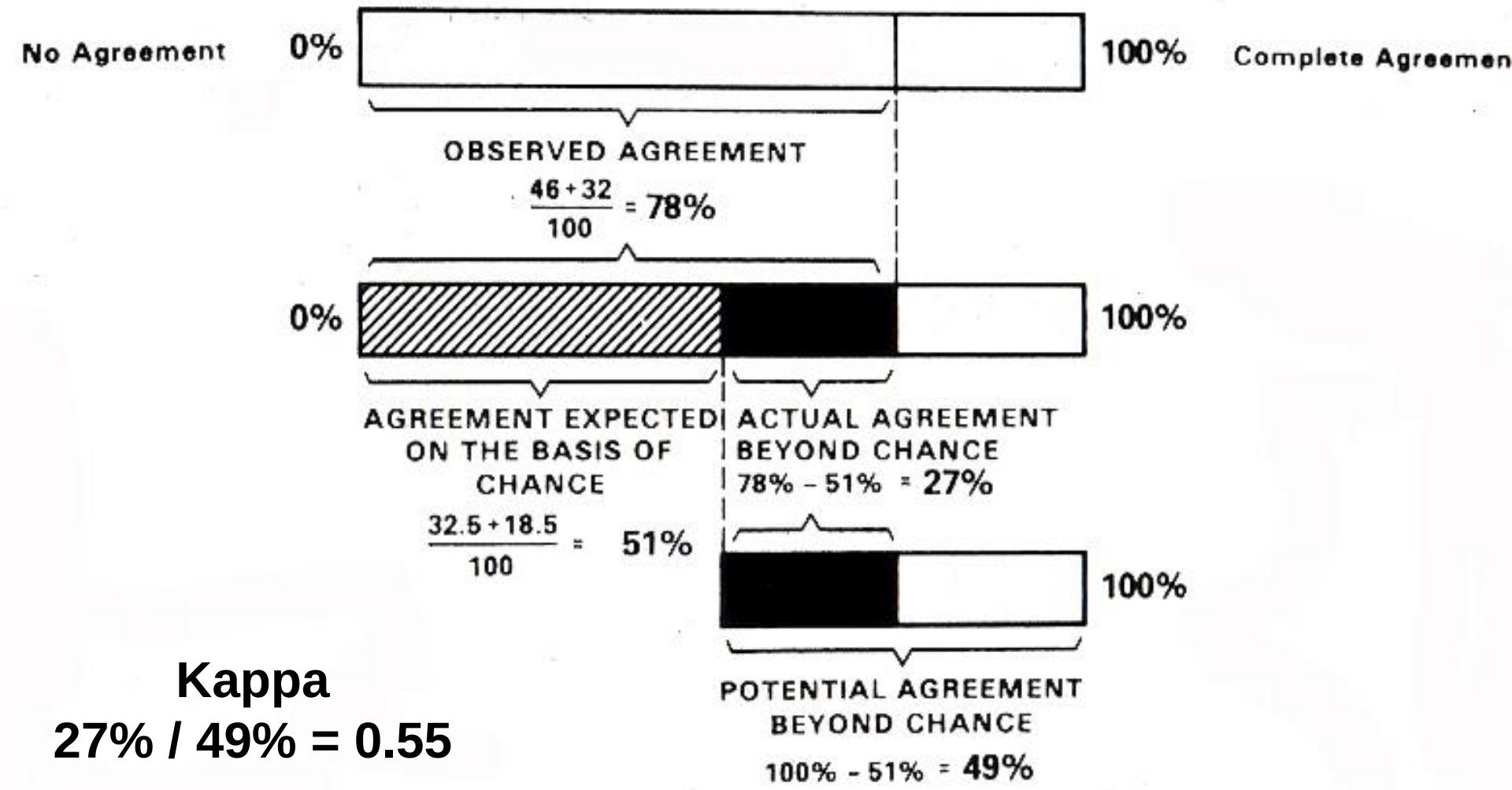


Human Pathol 2001; 32(4):368-78.

High End



Human Pathol 2001; 32(4):368-78.



Kappa

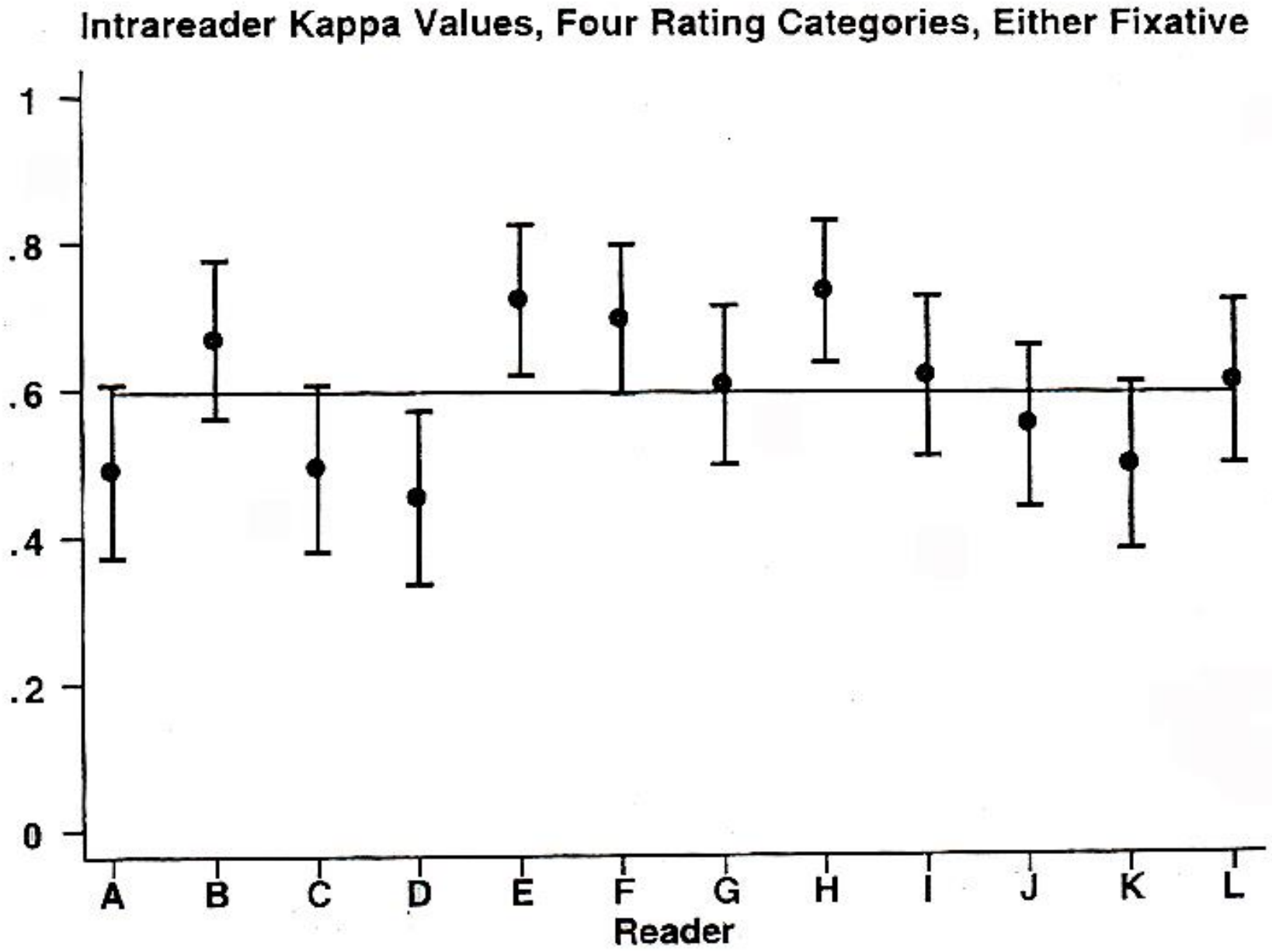
27% / 49% = 0.55

0 to 0.2 poor agreement

0.2 to 0.4 fair agreement

0.4 to 0.6 moderate agreement

0.6 to 0.8 substantial agreement



Human Pathol 2001; 32(4):368-78.

Interobserver Kappa Scores

	1st Read	2nd read
No dysplasia	0.44	0.45
Indefinite	0.13	0.15
LGD	0.23	0.23
HGD	0.36	0.44
Cancer	0.67	0.74

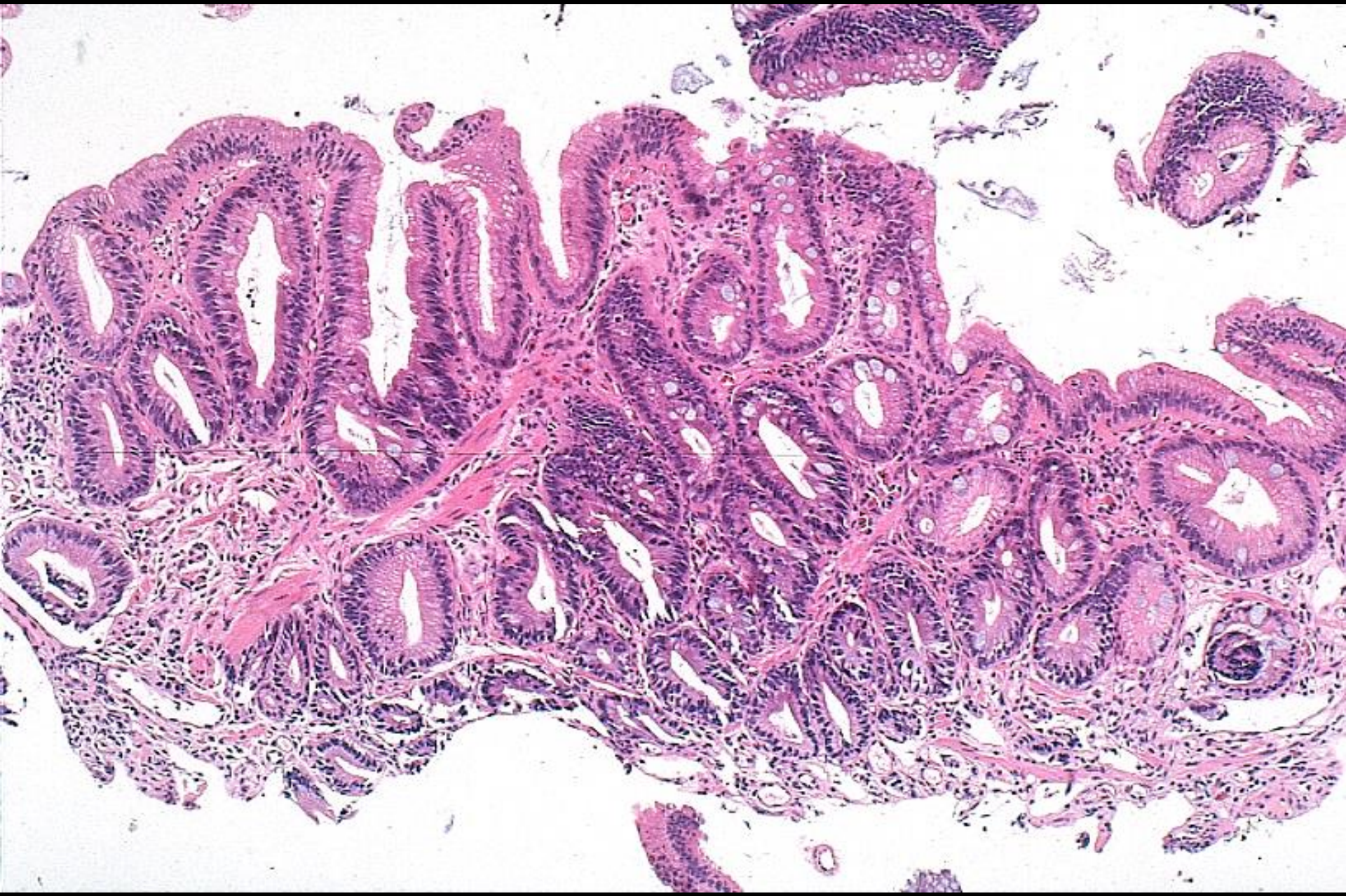
Human Pathol 2001; 32(4):368-78.

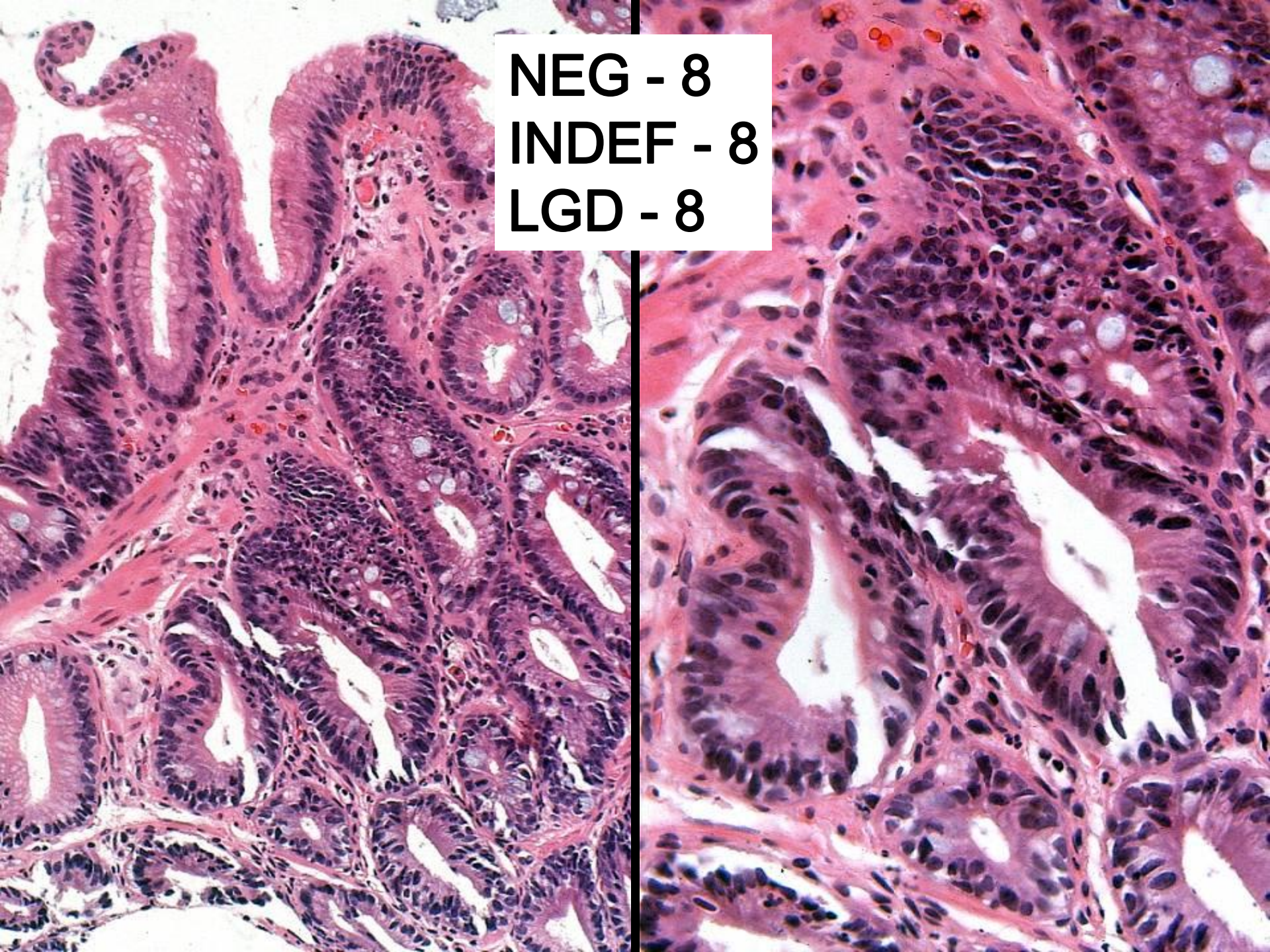
Intraobserver Kappas for Three Categories

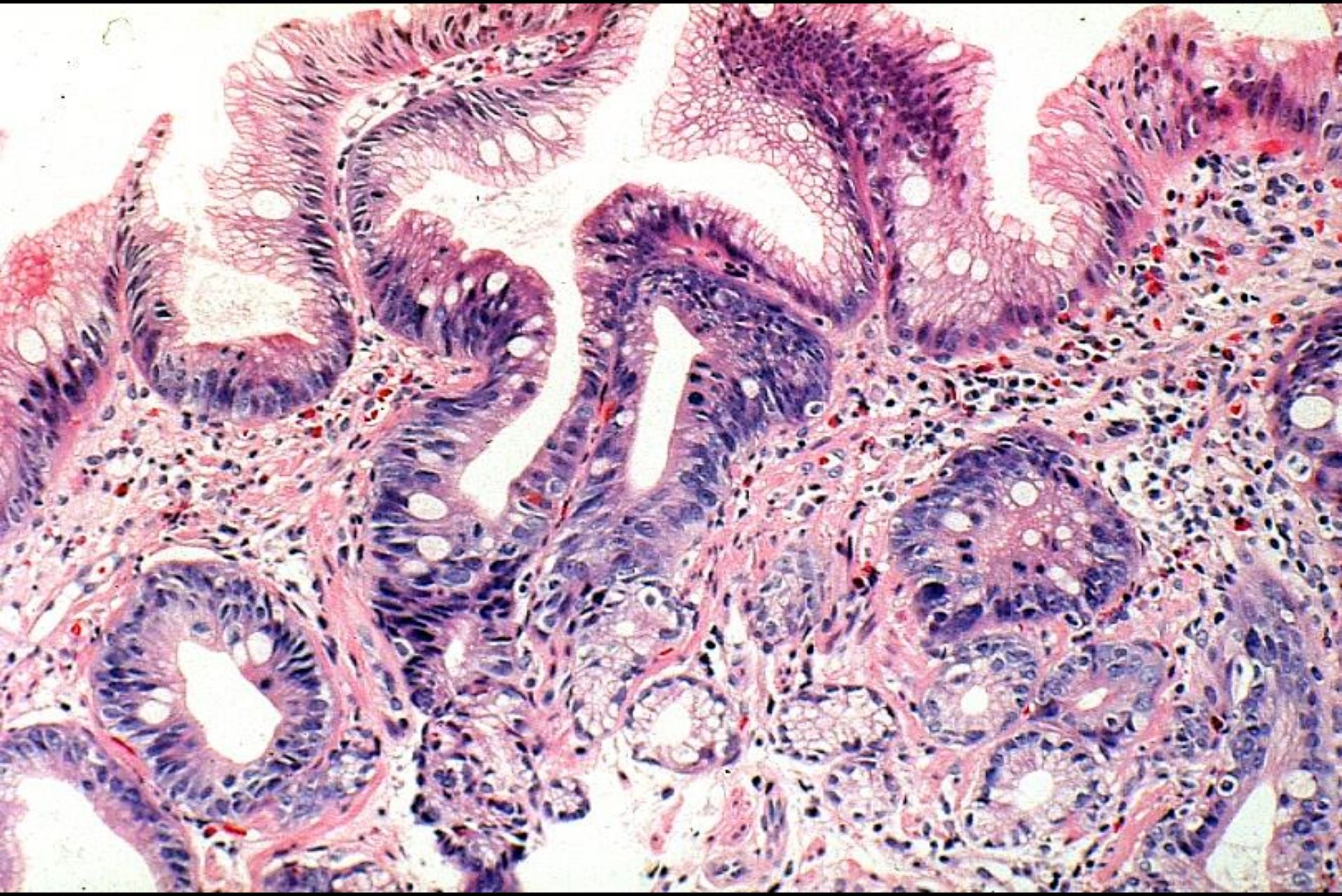
Intraobserver Premeeting	Intraobserver Postmeeting	Interobserver Premeeting	Interobserver Postmeeting
0.57	0.54	0.44	0.44
0.76	0.60	0.52	0.52
0.57	0.69	0.47	0.55
0.54	0.65	0.45	0.42
0.75	0.80	0.48	0.52
0.77	0.83	0.48	0.55
0.66	0.76	0.52	0.54
0.76	0.80	0.48	0.50
0.77	0.83	0.50	0.50
0.64	0.65	0.46	0.43
0.61	0.70	0.47	0.51
0.71	0.88	0.50	0.51
0.67	0.72	0.48	0.50

Causes of Poor Reproducibility

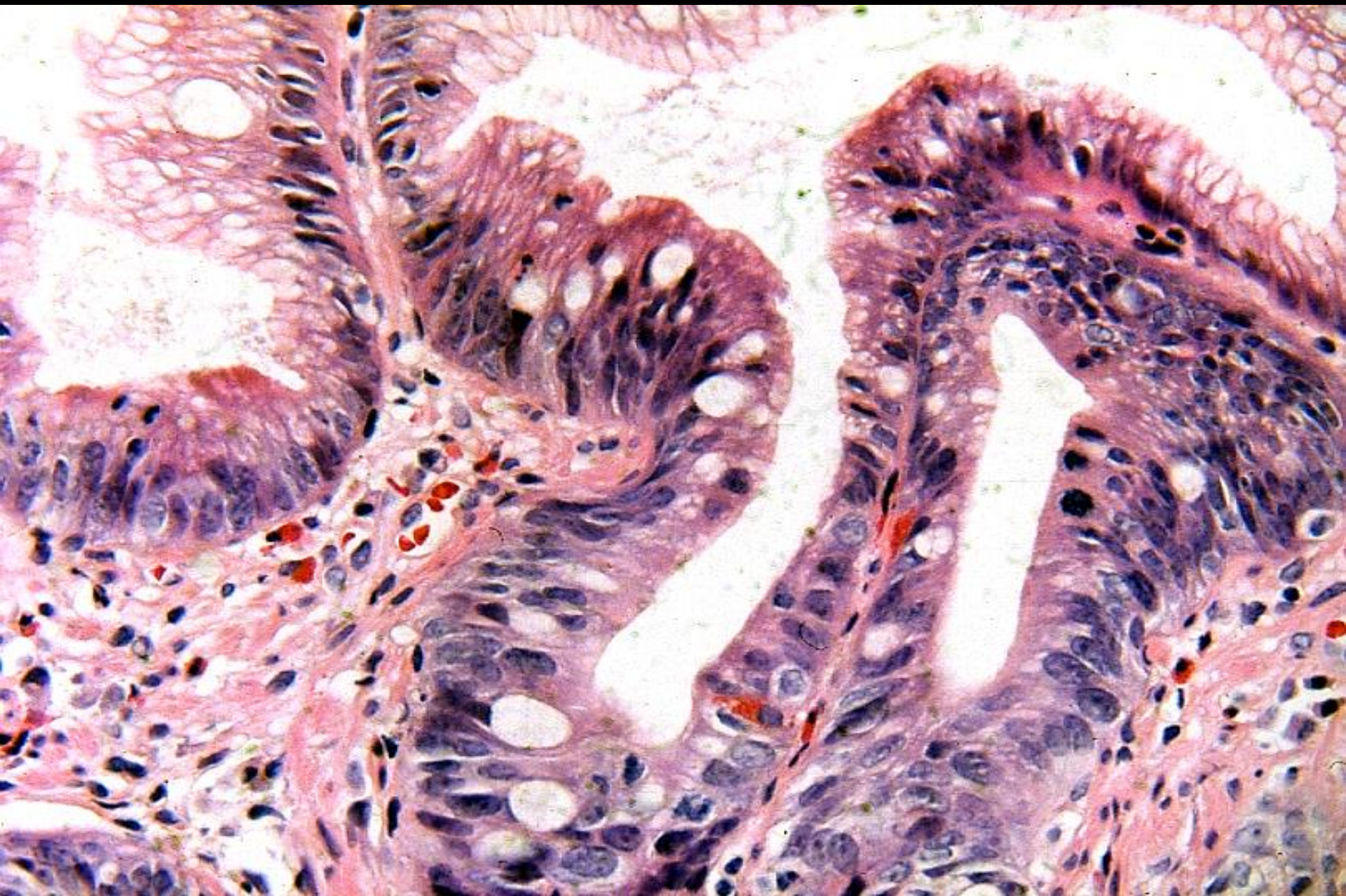
- Small, crushed, poorly fixed biopsies
- Thick and/or badly stained sections
- Very limited dysplastic change
- Confusion with inflammatory atypia
- Discordance between cytologic and architectural features
- Disagreement on criteria

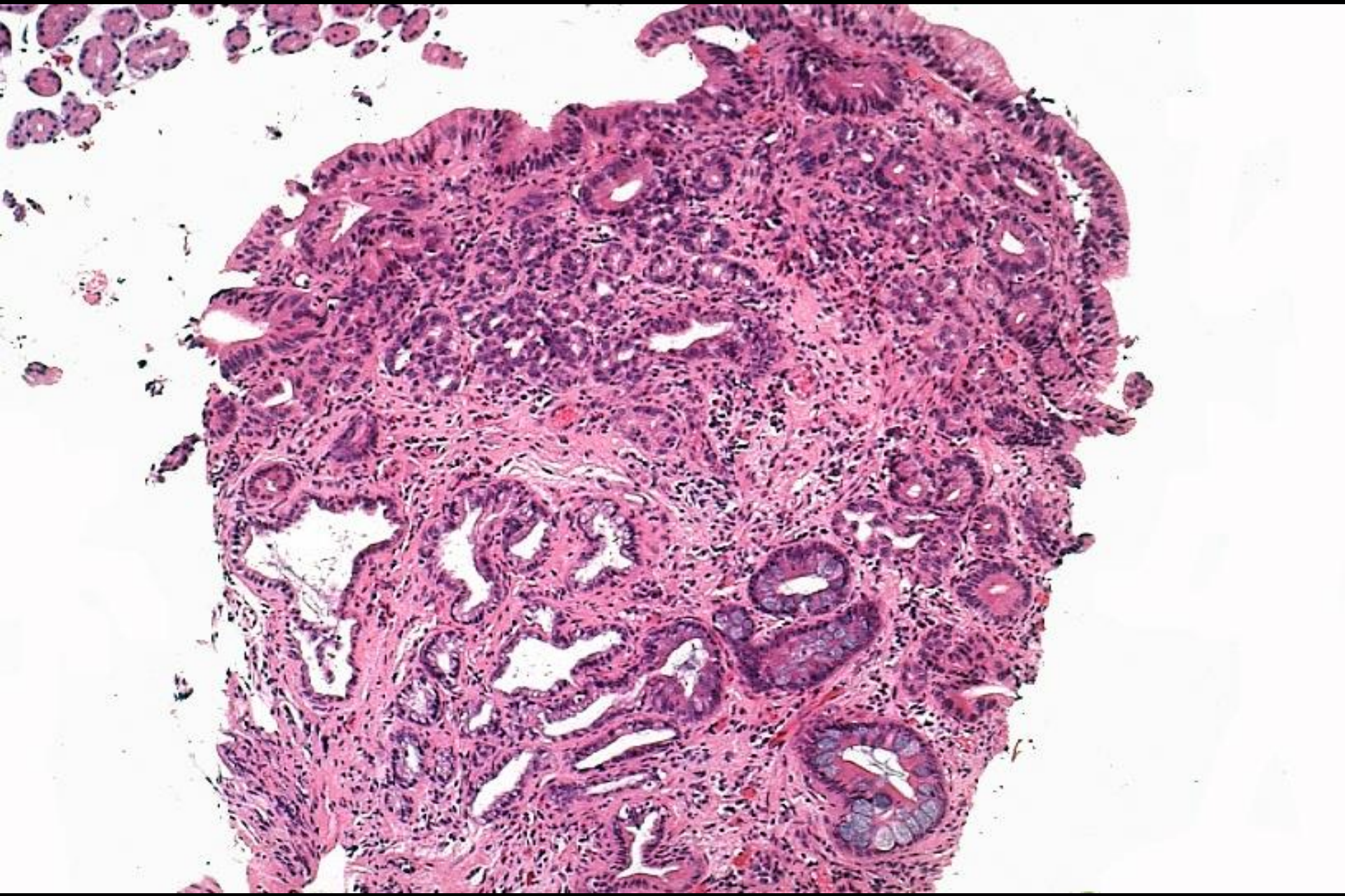


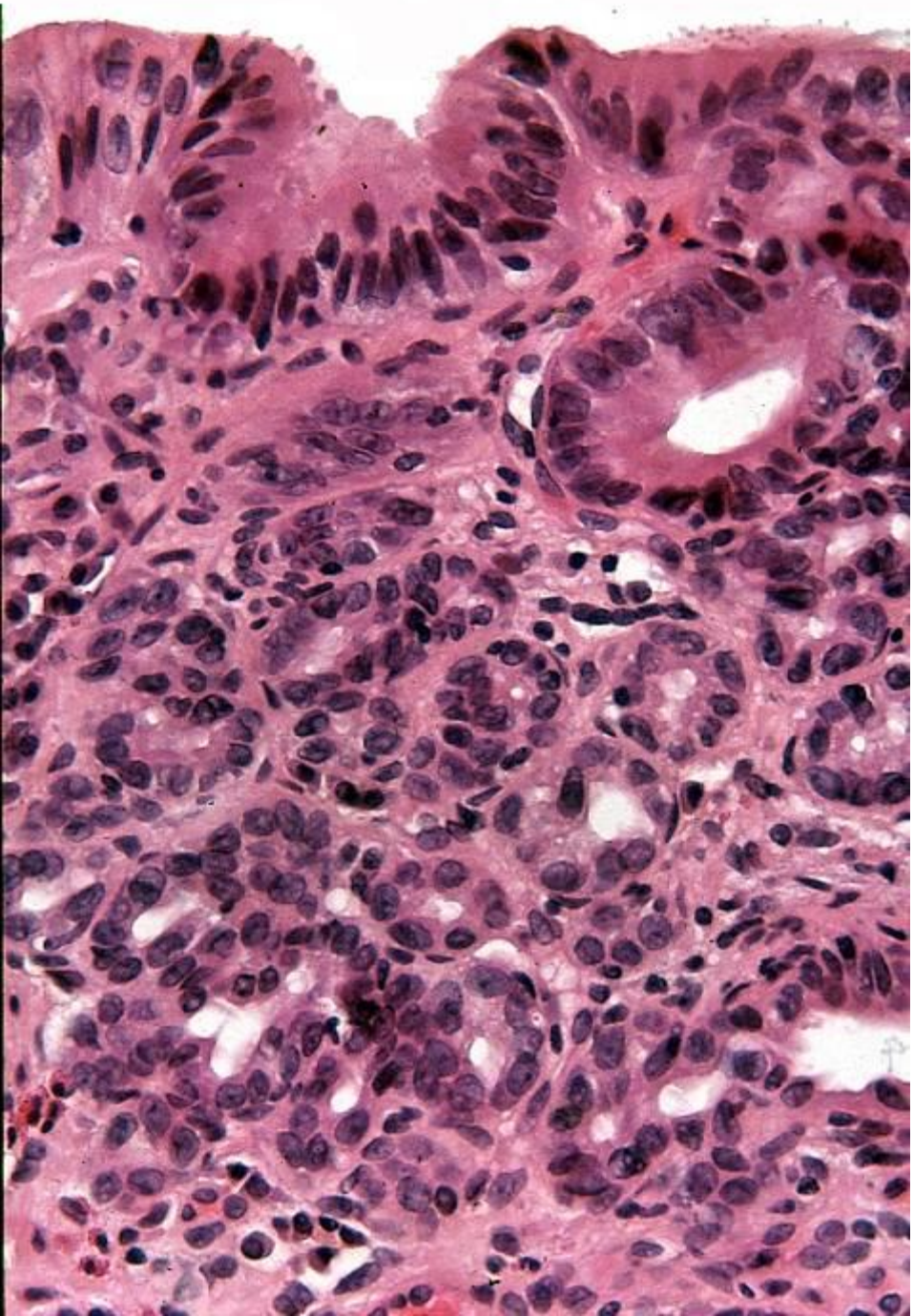

NEG - 8
INDEF - 8
LGD - 8



NEG – 3, INDEF – 8, LGD - 13





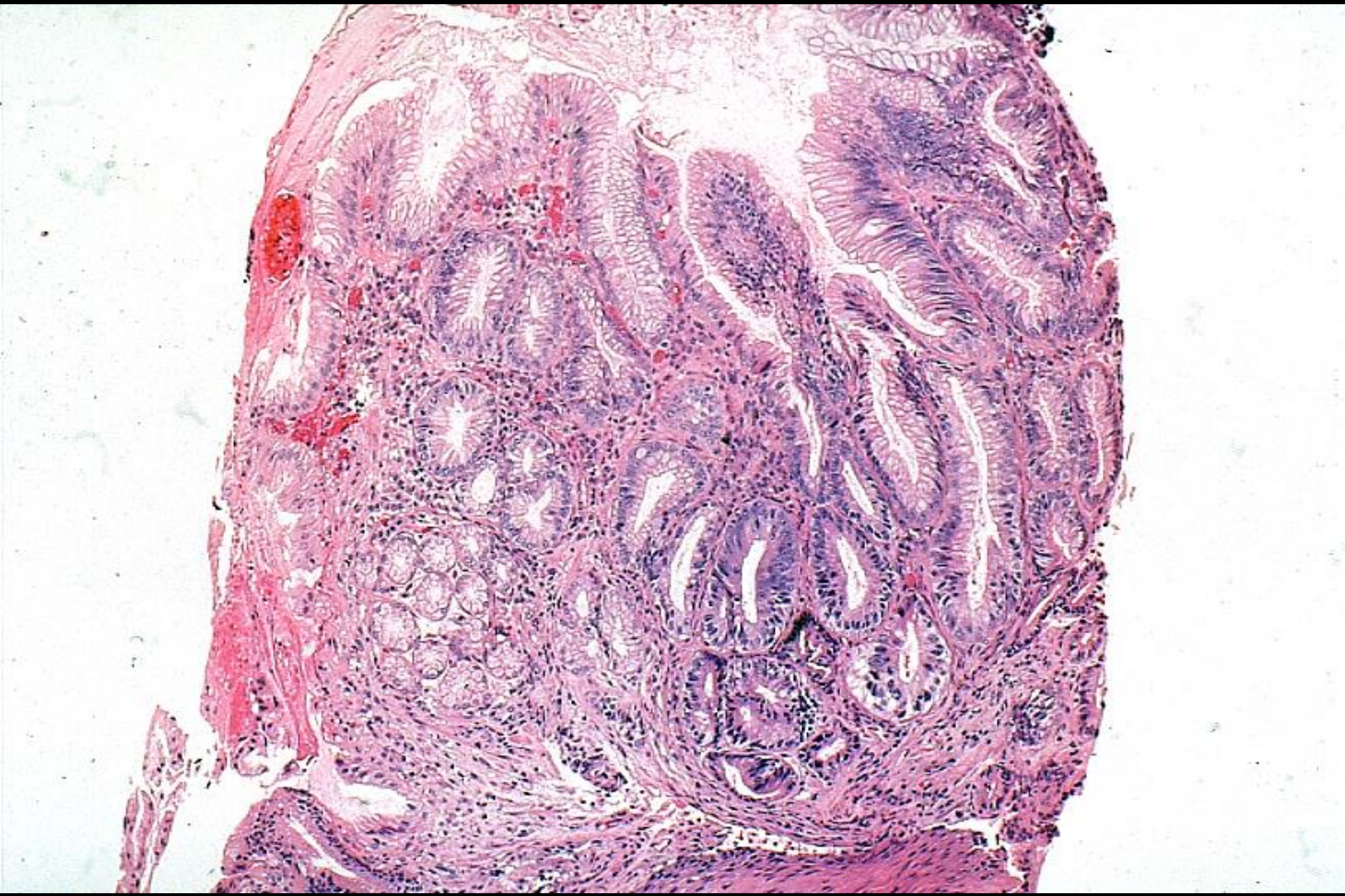


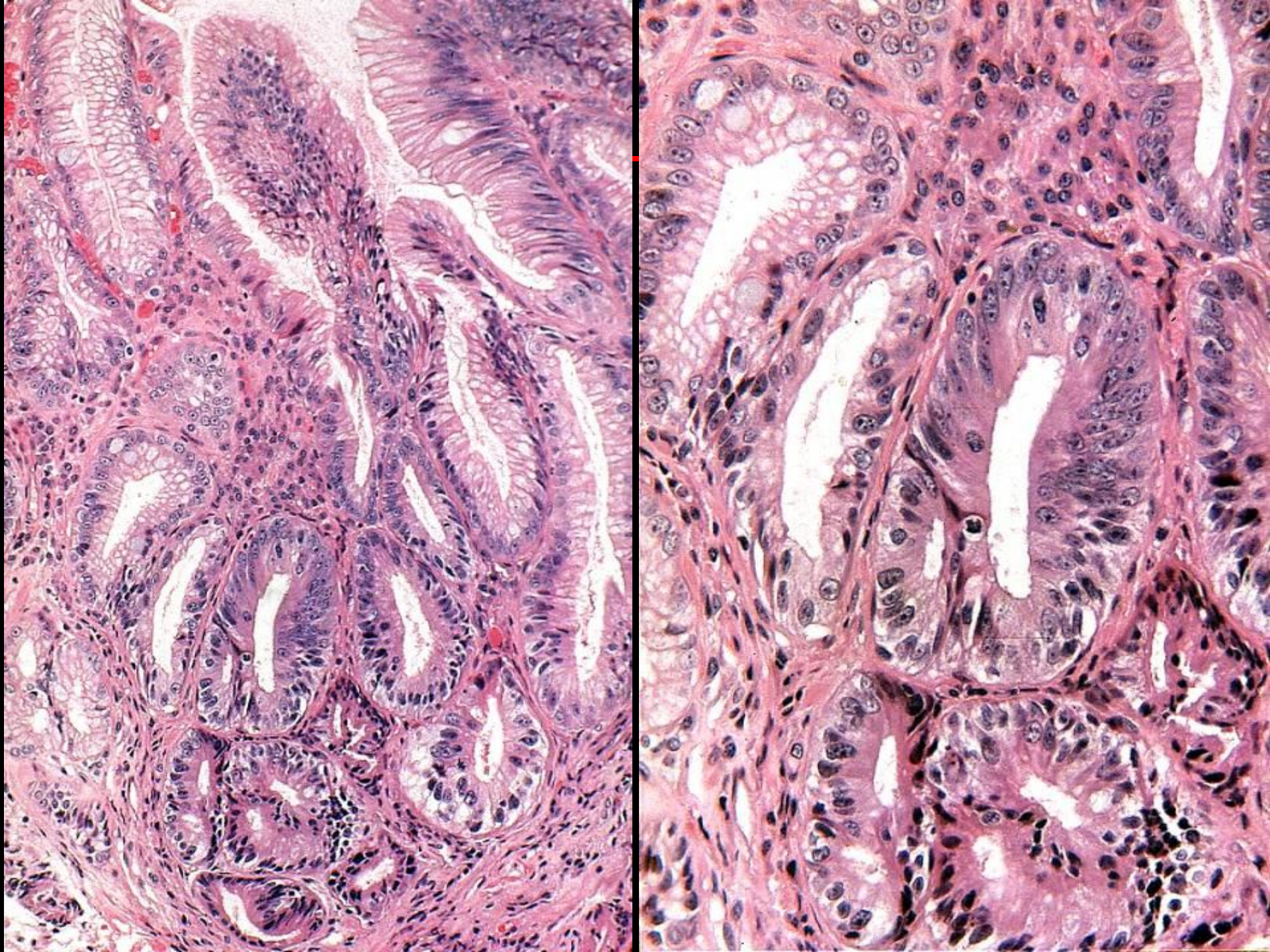
INDEF – 3

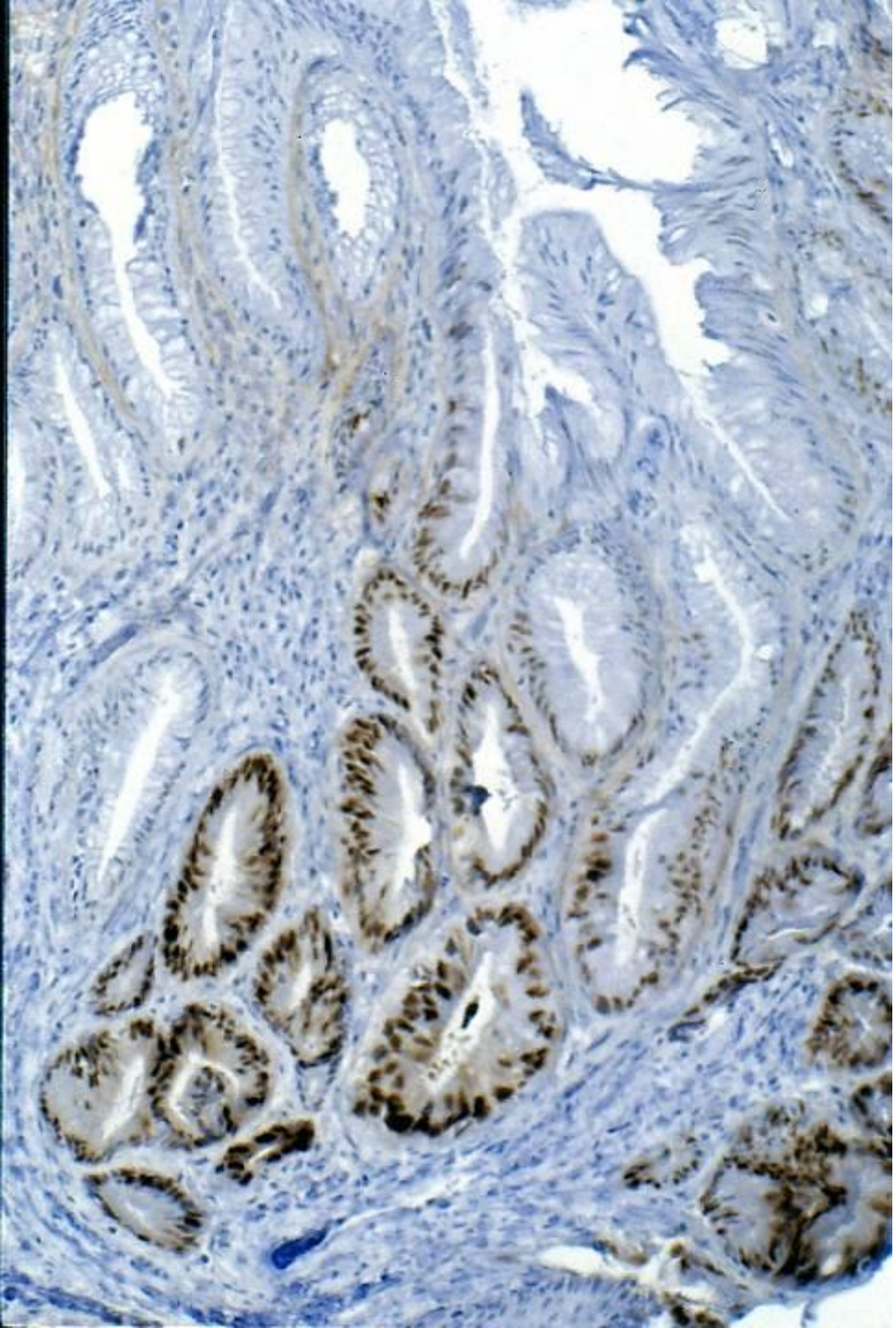
LGD – 6

HGD – 7

INTRA - 8







NEG – 2

INDEF – 8

LGD –13

HGD - 1

p53 immunostain

The Use of Ancillary Stains in the Diagnosis of Barrett Esophagus and Barrett Esophagus–associated Dysplasia

Recommendations From the Rodger C. Haggitt Gastrointestinal Pathology Society

Amitabh Srivastava, MD, Henry Appelman, MD,† Jeffrey D. Goldsmith, MD,‡ Jon M. Davison, MD,§ John Hart, MD,‖ and Alyssa M. Krasinskas, MD¶*

Am J Surg Pathol • Volume 41, Number 5, May 2017

- Recommendation for the use of special stains to diagnose dysplasia and for risk stratification in BE:
  - A diagnosis of dysplasia remains a morphologic diagnosis; ancillary stains are not recommended for diagnosing dysplasia in BE at this time.
  - Although p53 is a promising marker for identifying high-risk BE patients, existing data are insufficient to recommend p53 staining for routine use as a prognostic marker at present. Additional studies are required to address unresolved questions with regard to case selection, interpretation, integration with morphologic diagnosis, and impact on clinical outcome among other significant issues.

Discordance Among Pathologists in the United States and Europe in Diagnosis of Low-Grade Dysplasia for Patients With Barrett's Esophagus

Prashanth Vennalaganti,[1,2] Vijay Kanakadandi,[1,2] John R. Goldblum,[3] Sharad C. Mathur,[4] Deepa T. Patil,[3] G. Johan Offerhaus,[5] Sybren L. Meijer,[6] Michael Vieth,[7] Robert D. Odze,[8] Saligram Shreyas,[1,2] Sravanthi Parasa,[1,2] Neil Gupta,[9] Alessandro Repici,[10] Ajay Bansal,[1] Titi Mohammad,[1,2] and Prateek Sharma[1,2]

Gastroenterology 2017;152:564–570

Table 1. κ Values for Inter-observer Agreement Among All 7 Pathologists From the United States and Europe

Histologic diagnosis (no. of slides)	Overall κ (95% CI)
Overall (79)	0.43 (0.42–0.48)
NDBE (23)	0.22 (0.11–0.29)
LGD (22)	0.11 (0.004–0.15)
HGD (34)	0.43 (0.36–0.46)

Table 3. Inter-observer Agreement for the US-Based and European Pathologists

Diagnosis	US pathologists, κ (95% CI)	European pathologists, κ (95% CI)
Overall	0.44 (0.39–0.48)	0.65 (0.64–0.71)
NDBE	0.21 (0.05–0.35)	0.37 (0.26–0.51)
LGD	0.14 (0.09–0.22)	0.32 (0.08–0.73)
HGD	0.45 (0.42–0.49)	0.63 (0.51–0.69)

Four pathologists - 10,12, 12 & 13 HGD
Three pathologists – 19,19 & 22 HGD

Table 2. κ Values and the Level of Confidence

Variable	κ (95% CI)
All pathologists	
7	0.57 (0.45–0.62)
≥6	0.62 (0.58–0.64)
≥5	0.59 (0.53–0.64)
≥4	0.52 (0.47–0.55)
≥3	0.47 (0.42–0.50)
≥2	0.44 (0.38–0.49)
≥1	0.43 (0.42–0.48)
US-based pathologists	
4	0.63 (0.61–0.66)
≥3	0.53 (0.4–0.54)
≥2	0.46 (0.43–0.52)
≥1	0.44 (0.39–0.49)
Europe-based pathologists	
3	0.80 (0.74–0.97)
≥2	0.74 (0.71–0.80)
≥1	0.66 (0.60–0.71)

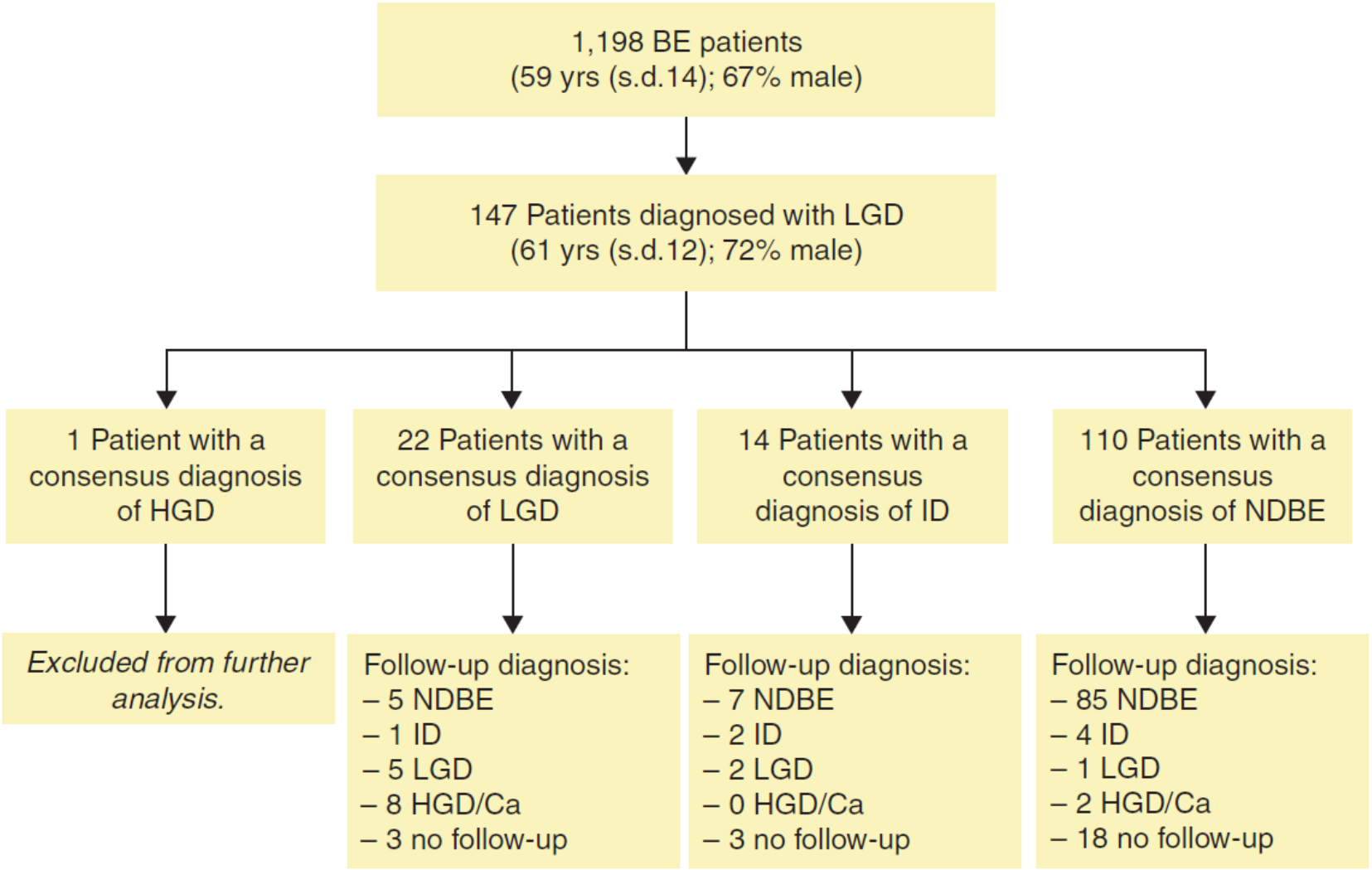
Table 2. κ Values and the Level of Confidence

Variable	κ (95% CI)
All pathologists	
7	0.57 (0.45–0.62)
≥6	0.62 (0.58–0.64)
≥5	0.59 (0.53–0.64)
≥4	0.52 (0.47–0.55)
≥3	0.47 (0.42–0.50)
≥2	0.44 (0.38–0.49)
≥1	0.43 (0.42–0.48)
US-based pathologists	
4	0.63 (0.61–0.66)
≥3	0.53 (0.4–0.54)
≥2	0.46 (0.43–0.52)
≥1	0.44 (0.39–0.49)
Europe-based pathologists	
3	0.80 (0.74–0.97)
≥2	0.74 (0.71–0.80)
≥1	0.66 (0.60–0.71)

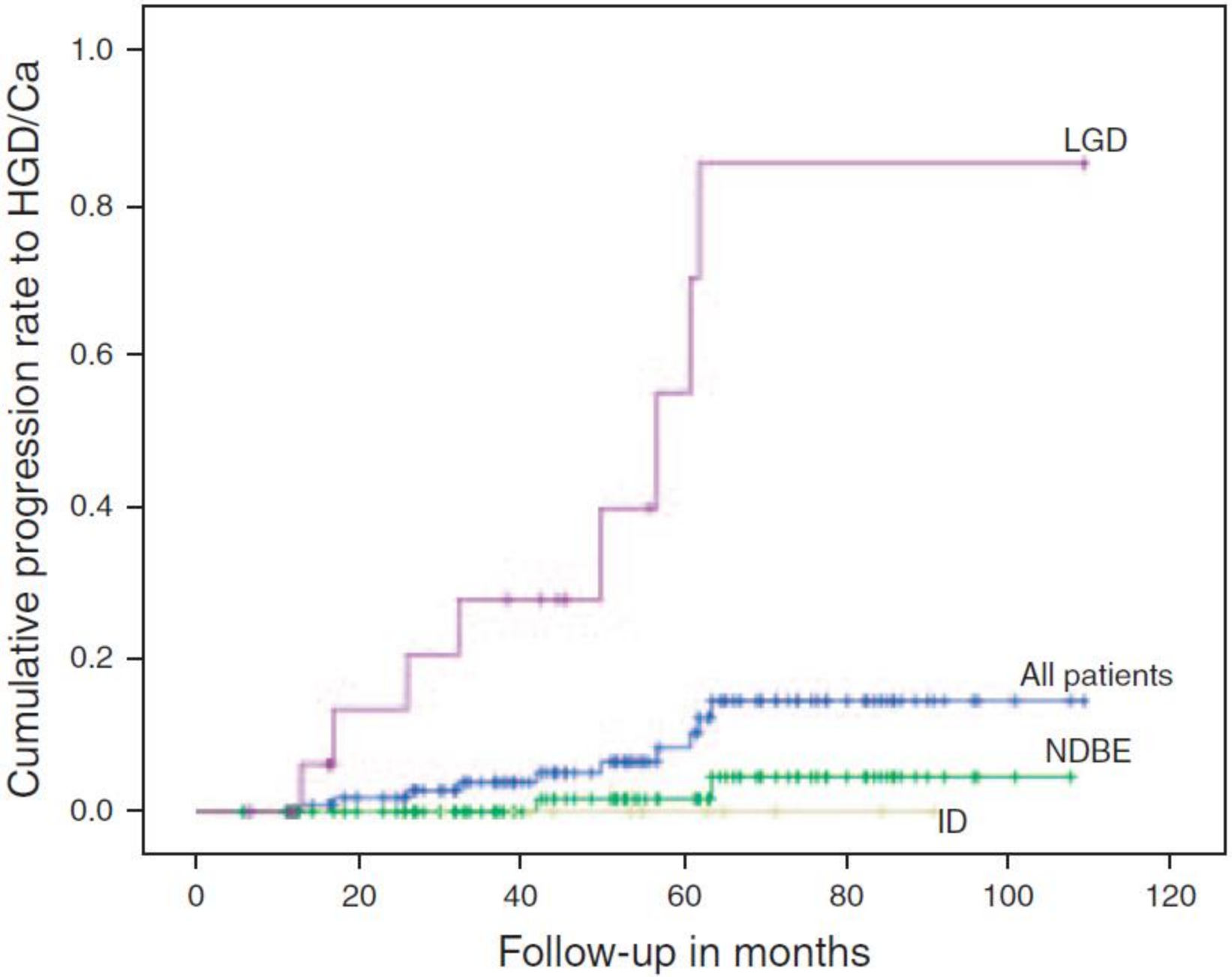
Low-Grade Dysplasia in Barrett's Esophagus: Overdiagnosed and Underestimated

Wouter L. Curvers, MD[1,12], Fiebo J. ten Kate, MD, PhD[2,12,13], Kausilia K. Krishnadath, MD, PhD[1,12], Mike Visser, MD, PhD[2,13],

Am J Gastroenterol 2010; 105:1523–1530;



Am J Gastroenterol 2010; 105:1523–1530;



Patients With Barrett's Esophagus and Confirmed Persistent Low-Grade Dysplasia Are at Increased Risk for Progression to Neoplasia

Gastroenterology 2017;152:993–1001

Lucas C. Duits,[1] Myrtle J. van der Wel,[1,2] Cary C. Cotton,[3] K. Nadine Phoa,[1]

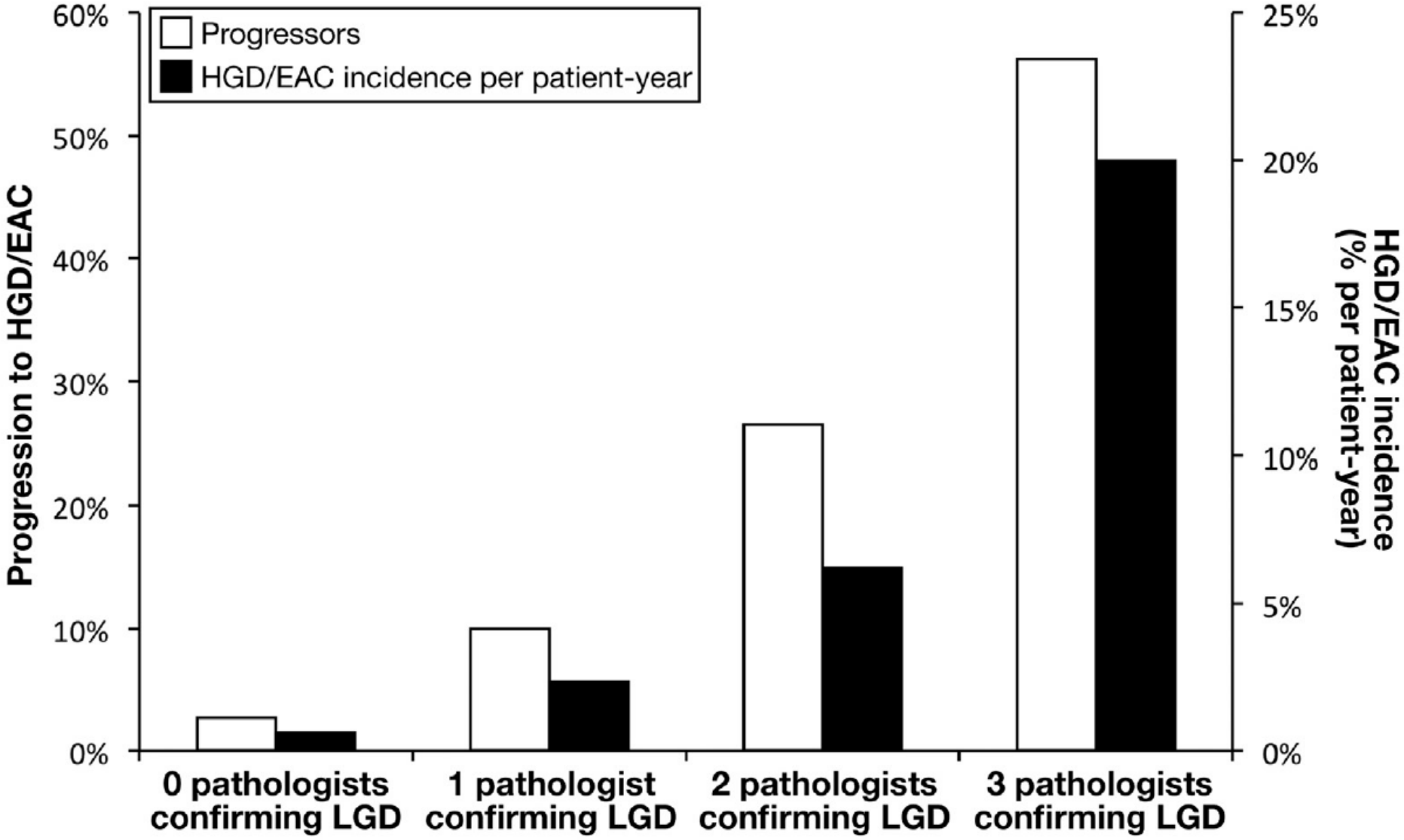
Table 1. Demographic and Clinical Characteristics

Characteristic	All patients (N = 255)
Age, *y*, mean ± SD	63.0 ± 10.2
Male, n (%)	199 (78)
Time since Barrett's diagnosis, *y*, median (IQR)	3.4 (0–8)
Length of Barrett's segment, *cm*, median (IQR)	4 (3–7)
Circumferential Barrett's extent, *cm*, median (IQR)	2 (1–5)
No. of pathologists confirming LGD, n (%)	
0	113 (44)
1	60 (24)
2	34 (13)
3	48 (19)

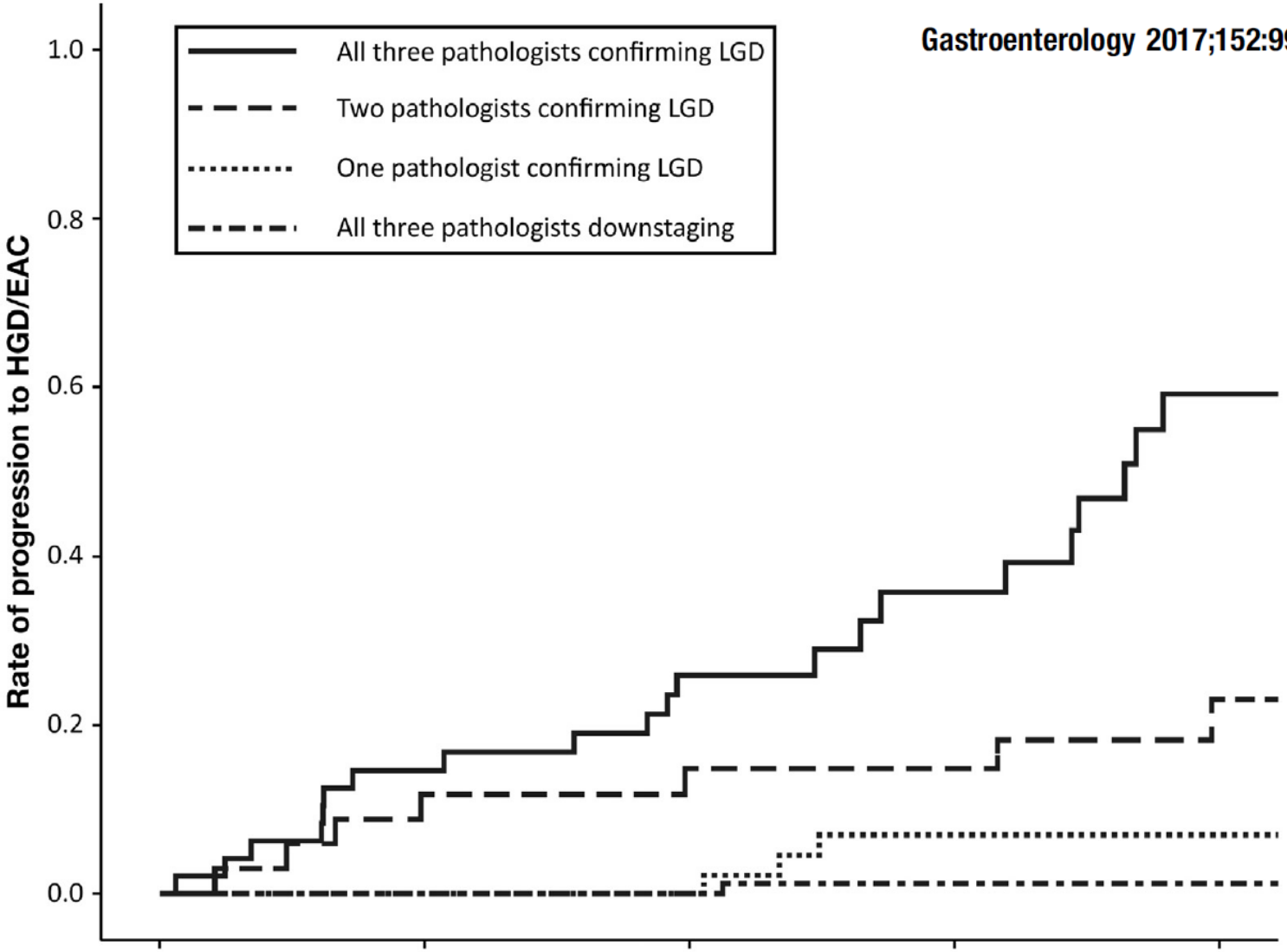
Patients With Barrett's Esophagus and Confirmed Persistent Low-Grade Dysplasia Are at Increased Risk for Progression to Neoplasia

Gastroenterology 2017;152:993–1001

Lucas C. Duits,[1] Myrtle J. van der Wel,[1,2] Cary C. Cotton,[3] K. Nadine Phoa,[1]



Gastroenterology 2017;152:993–1001



Patients at risk

3 pathologists LGD	39	31	18	10
2 pathologists LGD	30	28	27	16
1 pathologist LGD	52	46	35	27
0 pathologists LGD	105	90	77	52

Diagnosis and Management of Low-Grade Dysplasia in Barrett's Esophagus: Expert Review From the Clinical Practice Updates Committee of the American Gastroenterological Association

Gastroenterology 2016;151:822–835

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Practice Advice 2: Given the significant interobserver variability among pathologists, the diagnosis of Barrett's esophagus with LGD should be confirmed by an expert gastrointestinal pathologist (defined as a pathologist with a special interest in Barrett's esophagus–related neoplasia who is recognized as an expert in this field by his/her peers).

Practice Advice 3: Expert pathologists should report audits of their diagnosed cases of LGD, such as the frequency of LGD diagnosed among surveillance patients and/or the difference in incidence of neoplastic progression among patients diagnosed with LGD vs nondysplastic Barrett's esophagus.

ACG Clinical Guideline: Diagnosis and Management of Barrett's Esophagus

Am J Gastroenterol advance online publication, 3 November 2015; doi:10.1038/ajg.2015.322

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Importance of confirmation of dysplasia. Dysplasia remains the best clinically available marker of cancer risk in patients with BE. However, there is considerable interobserver variability in the interpretation of dysplasia in both the community and academic settings. That being said, there is reasonable interobserver agreement among GI pathologists for the extremes of dysplasia, namely IM without dysplasia and HGD/EAC (109). There is considerably more difficulty in the interpretation of indefinite for dysplasia and LGD (121). The importance of the confirmation of the diagnosis of LGD comes from two recent studies from the Netherlands.

Therefore, current evidence supports the importance of having all readings of dysplasia confirmed by a second pathologist with extensive experience in the interpretation of Barrett's associated neoplasia.

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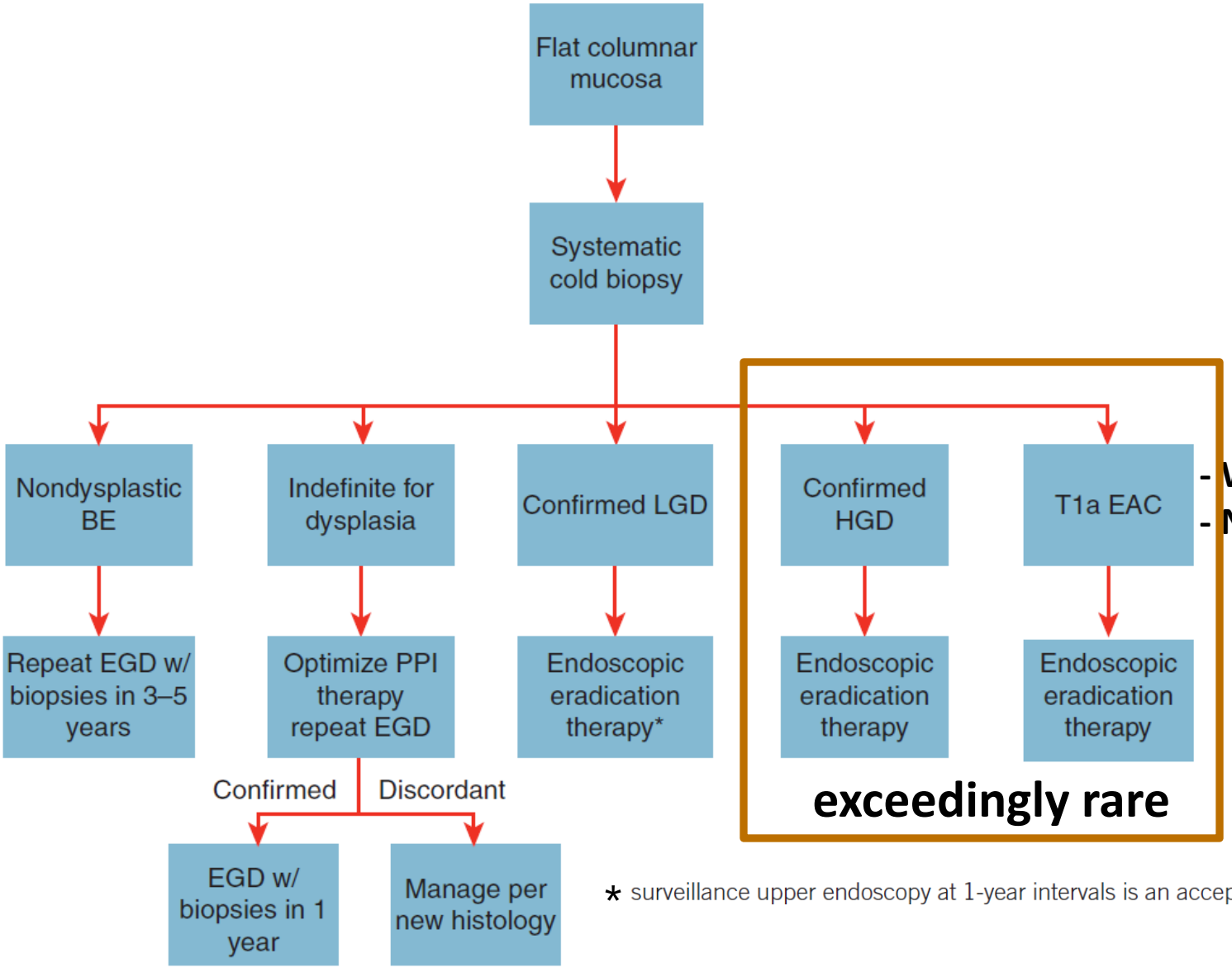

* surveillance upper endoscopy at 1-year intervals is an acceptable alternative

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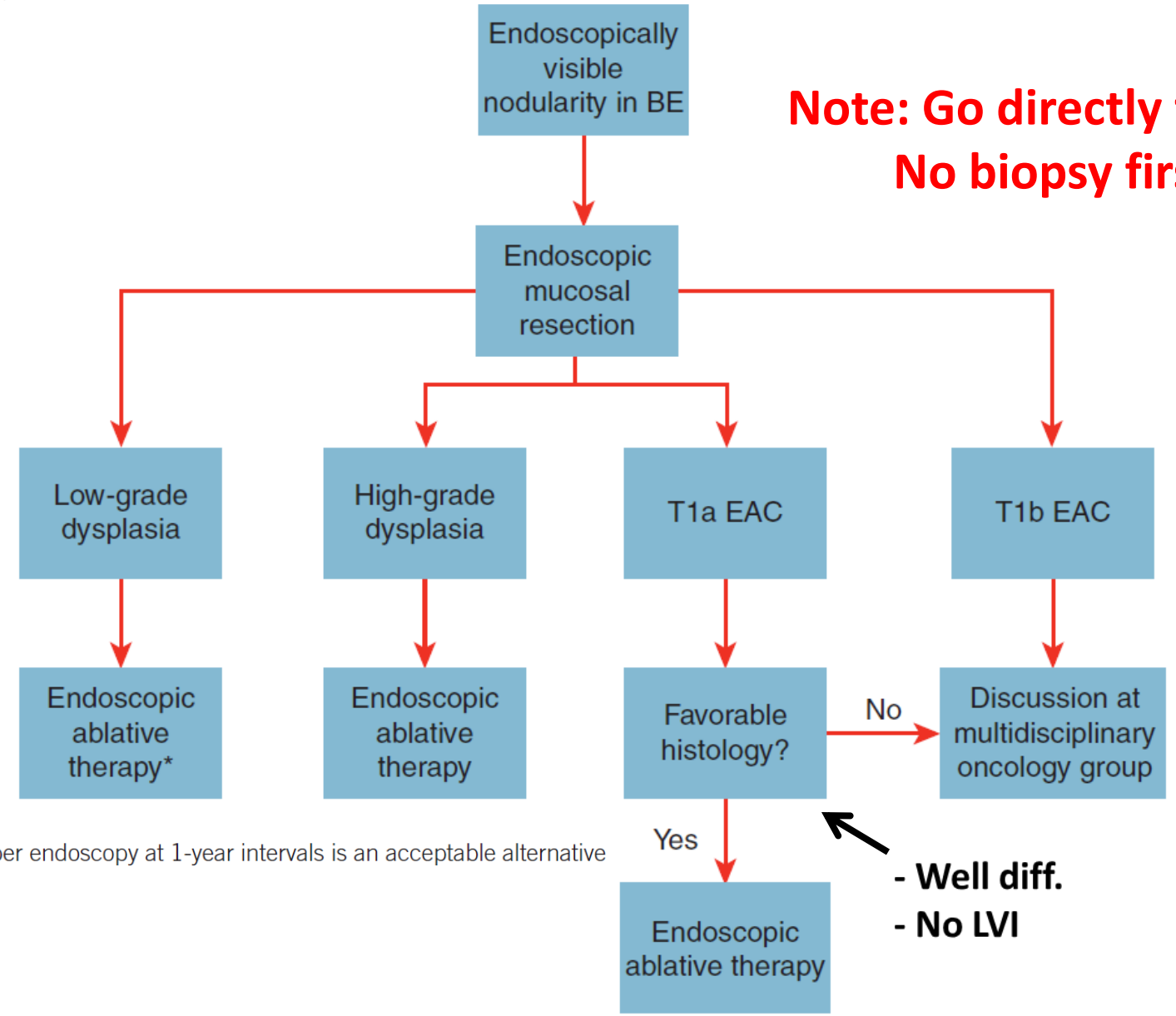


Note: Go directly to EMR
No biopsy first !

*surveillance upper endoscopy at 1-year intervals is an acceptable alternative

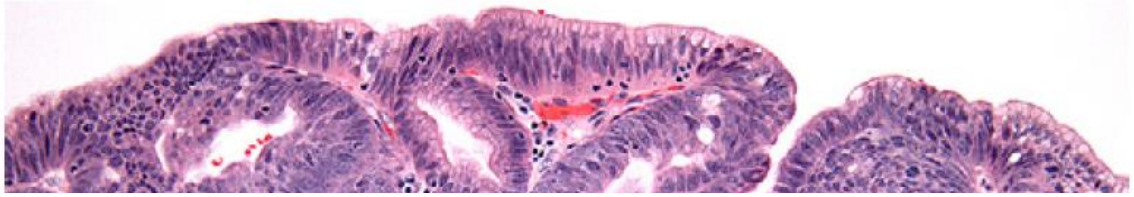
Intramucosal Carcinoma

- Tiny (but real) risk of lymph node metastasis – 1 to 10% quoted
- Invasion through the basement membrane into lamina propria or muscularis mucosae but not into submucosa
- Individual tumor cells lying free in the lamina propria
- Difficult to recognize
- Poorly reproducible

Neoplastic Precursor Lesions in Barrett's Esophagus

Gastroenterol Clin N Am 36 (2007) 775–796

Jason L. Hornick, MD, PhD, Robert D. Odze, MD, FRCPc*



Intramucosal adenocarcinoma is defined as neoplastic epithelium that has invaded beyond the basement membrane into the surrounding lamina propria or muscularis mucosae (Fig. 6). Because the esophageal lamina propria contains lymphatic vessels, adenocarcinomas limited to the mucosa may result in lymph node metastases (approximately 5% risk). Morphologically, individual cells or small clusters of cells in the lamina propria are diagnostic of intramucosal

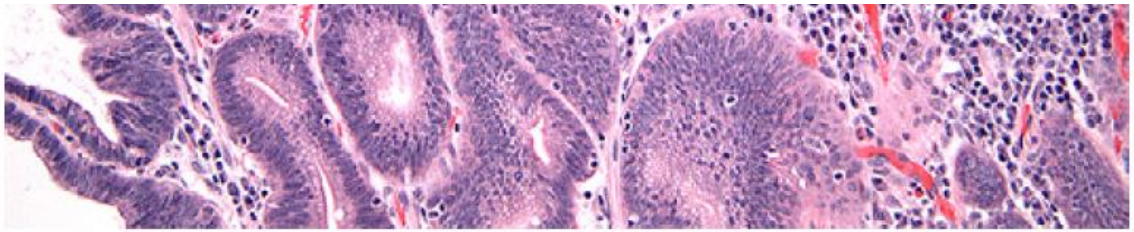
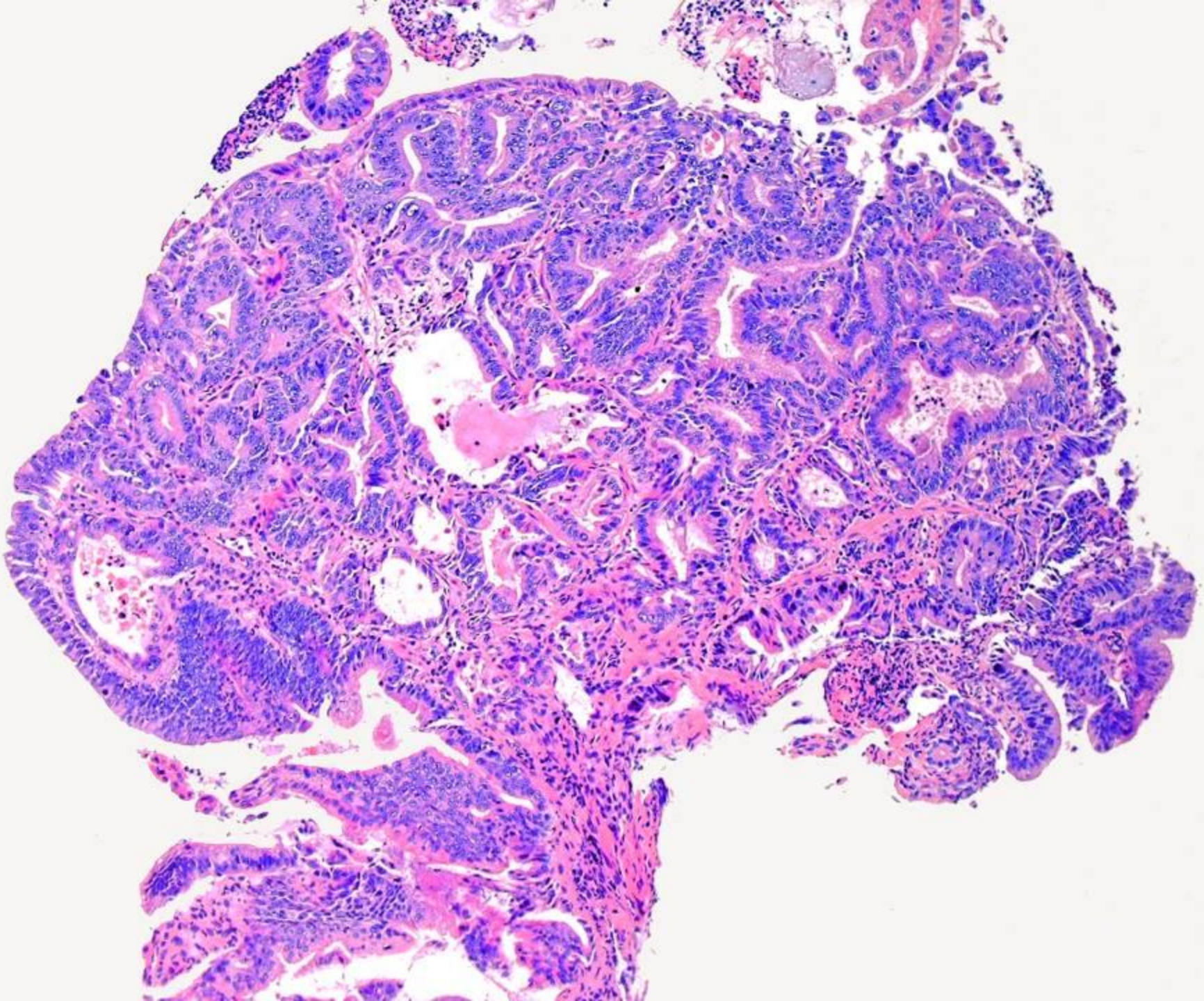
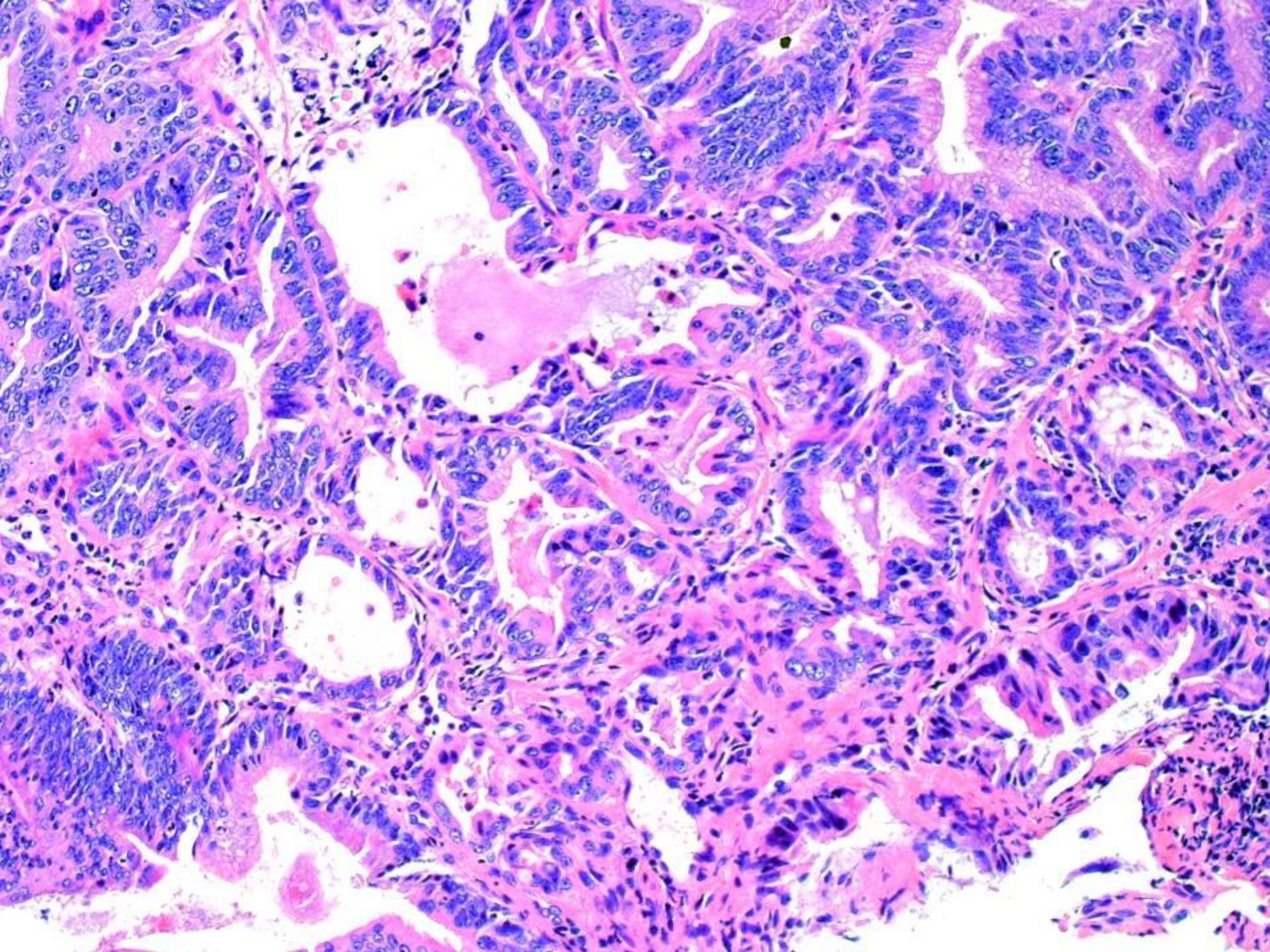
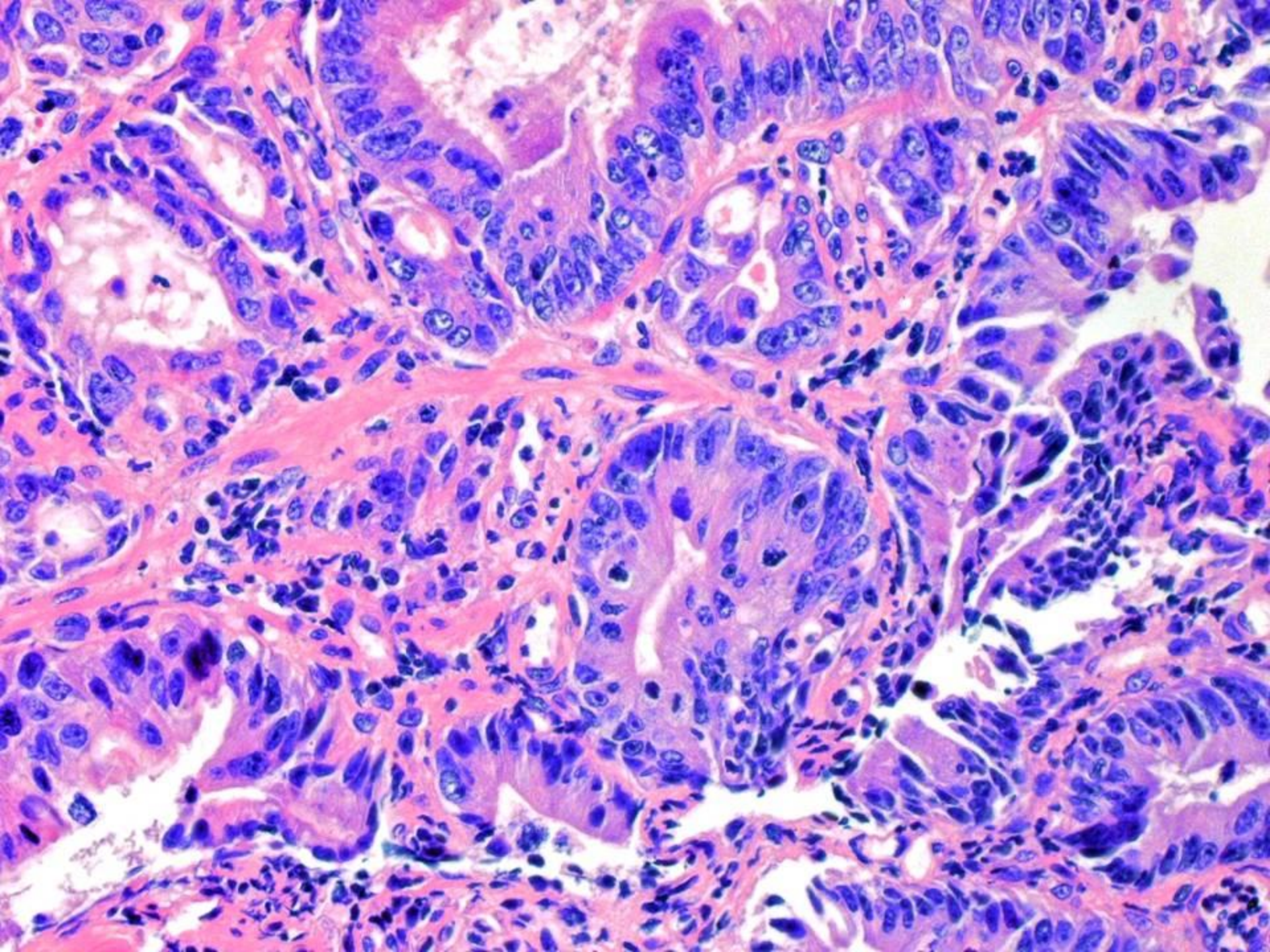


Fig. 6. Intramucosal adenocarcinoma. Similar to high-grade dysplasia, the nuclei show severe nuclear stratification, hyperchromasia, and loss of polarity. However, the architecture is markedly abnormal with cribriforming (*arrow*), which cannot be explained by preexisting Barrett's architecture.







Clinical Significance of the Duplicated Muscularis Mucosae in Barrett Esophagus-related Superficial Adenocarcinoma

Am J Surg Pathol • Volume 35, Number 5, May 2011

David K. Kaneshiro, MD, Jane C. Post, MD,* Lisa Rybicki, MS,† Thomas W. Rice, MD,‡ and John R. Goldblum, MD**

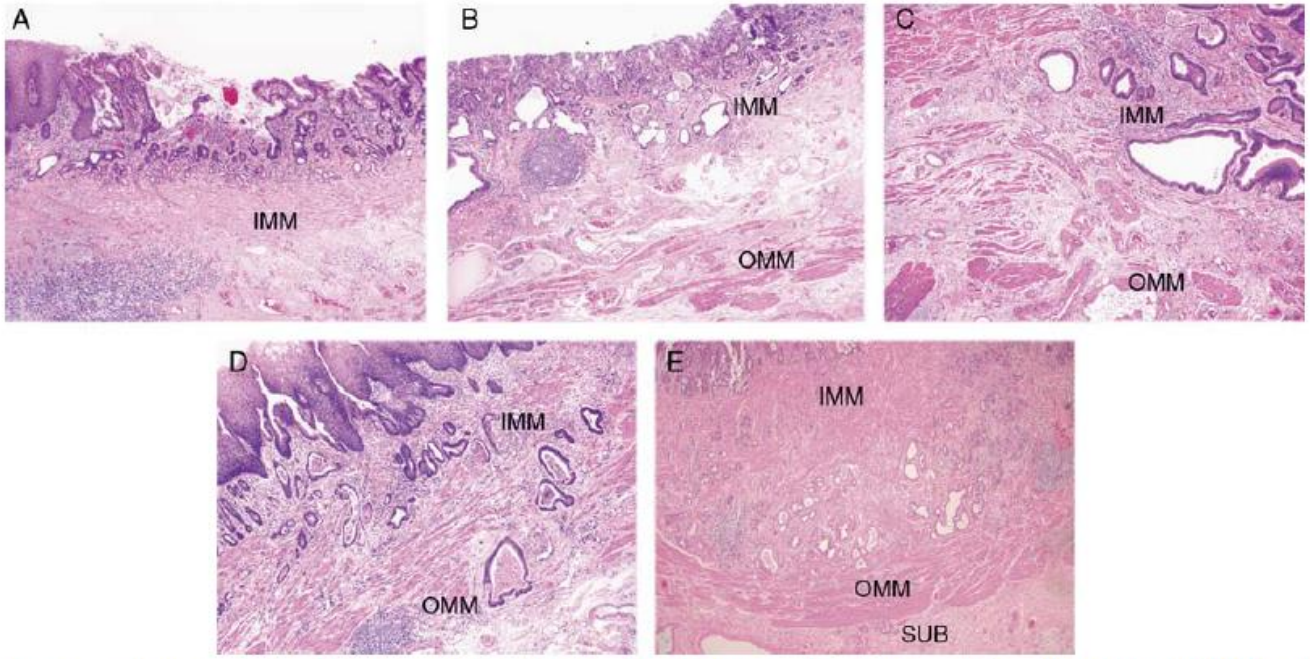


FIGURE 1. Esophageal adenocarcinoma invading the superficial lamina propria, LP (A); invading IMM (B); invading between layers of duplicated MM, BMM (C); invading the OMM (D); and invading superficial SUB (E); SUB indicates submucosa.

Group (N)	Male	Mean Age ± SD (R)	pN1	pN2
Total patients (185)	158 (85.4%)	63 ± 10 (35-81)	3 (1.6%)	1 (0.5%)
All IMC (150)	128 (85.3%)	63 ± 10 (35-80)	0	1 (0.7%)
LP (68)	55 (80.9%)	63 ± 10 (42-79)	0	1 (1.5%)
IMM (38)	33 (86.8%)	64 ± 11 (35-80)	0	0
BMM (11)	9 (81.8%)	61 ± 10 (48-74)	0	0
OMM (33)	31 (93.9%)	63 ± 11 (36-80)	0	0
SM-I (35)	30 (85.7%)	66 ± 9 (48-81)	3 (8.6%)	0
P	0.52	0.42	0.07*	

Take Home Points

- In the U.S. the Dx of Barrett esophagus requires:
  - Endoscopic evidence of columnar lined esophagus
  - Biopsies from the columnar mucosa that contain goblet cells
  - Only segments 1 cm or greater should be biopsied
- Only patients with intestinal type Barrett mucosa (GC+) have a significant risk of progression to dysplasia and adenocarcinoma
- Improved imaging modalities have allowed endoscopists to identify & target dysplastic lesions
- Complete endoscopic (or EMR + ablation) removal of all Barrett mucosa is now feasible for patients with HGD or intramucosal adenocarcinoma