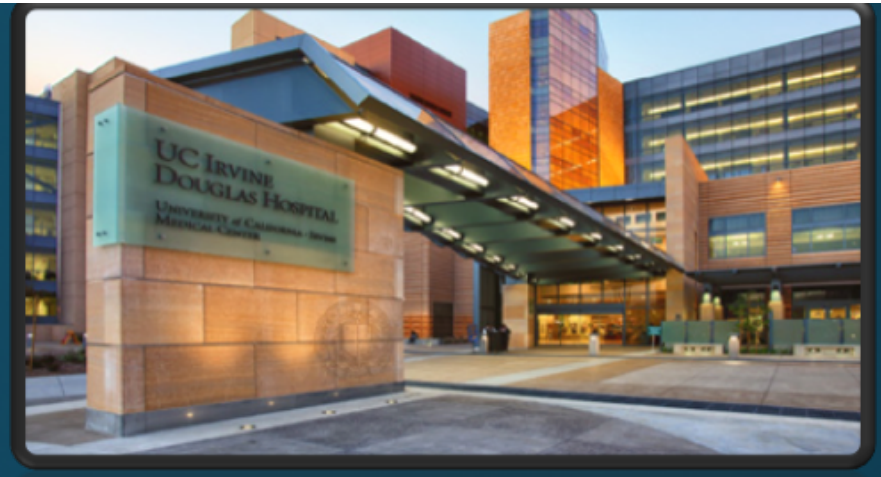
UC Irvine Health



The search for the ideal paradigm for detecting and treating Barrett's esophagus and Esophageal cancer

Jason B. Samarasena MD
Associate Clinical Professor of Medicine
Director – Advanced Endoscopic Imaging
Interventional Gastroenterology
H.H. Chao Comprehensive Digestive Disease Center
University of California, Irvine

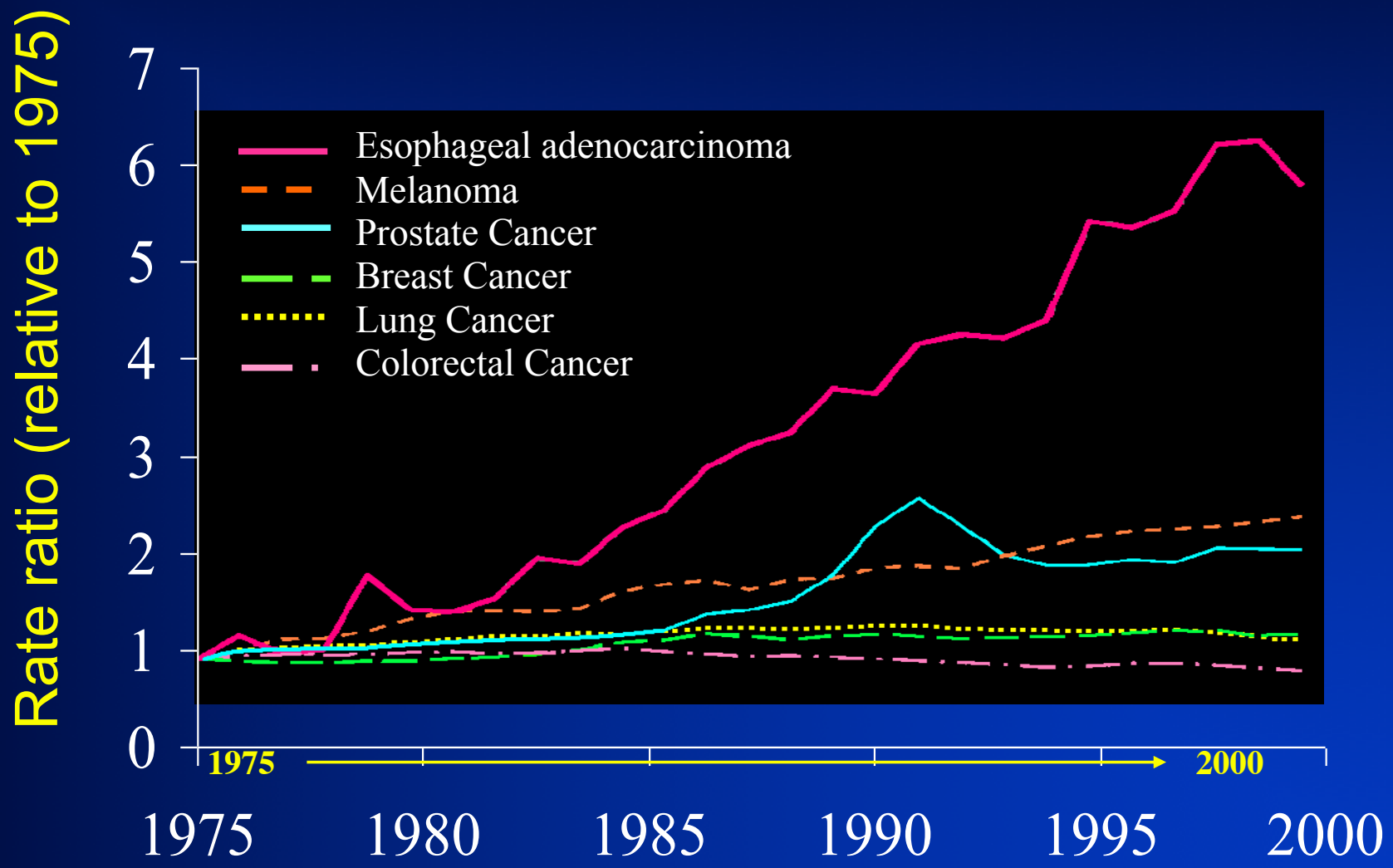
February 2nd 2018

Esophageal Cancer - Worldwide

- Statistics in 2012 (World-wide)
  - ~456,300 new cases
  - ~410,400 deaths
- 5 year-survival rate: 19%
  - ~> 50% invasive or metastatic at diagnosis
- 7th most common tumor worldwide
- In the US in 2016, 16,910 estimated new esophageal cancer cases and 15,690 deaths

Ferlay J, et al GLOBOCAN 2012 v1.1, Cancer Incidence and Mortality Worldwide, International Agency for Research on Cancer; 2014.

U.S. Esophageal Adenocarcinoma Rise



Pohl H and Welch HG. *J Natl Cancer Inst* 2005;95:142-146

Esophageal Cancer: A Dismal Prognosis

	INCIDENCE* 2008-2012	MORTALITY 2008-2012	5-YEAR SURVIVAL (%) 2005-2011
Esophageal Cancer (all types)	4.4	4.2	17.9
Breast Cancer (females only)	124.8	21.9	89.4
Melanoma	21.6	2.7	91.5
Prostate Cancer	62.7	8.5	98.9

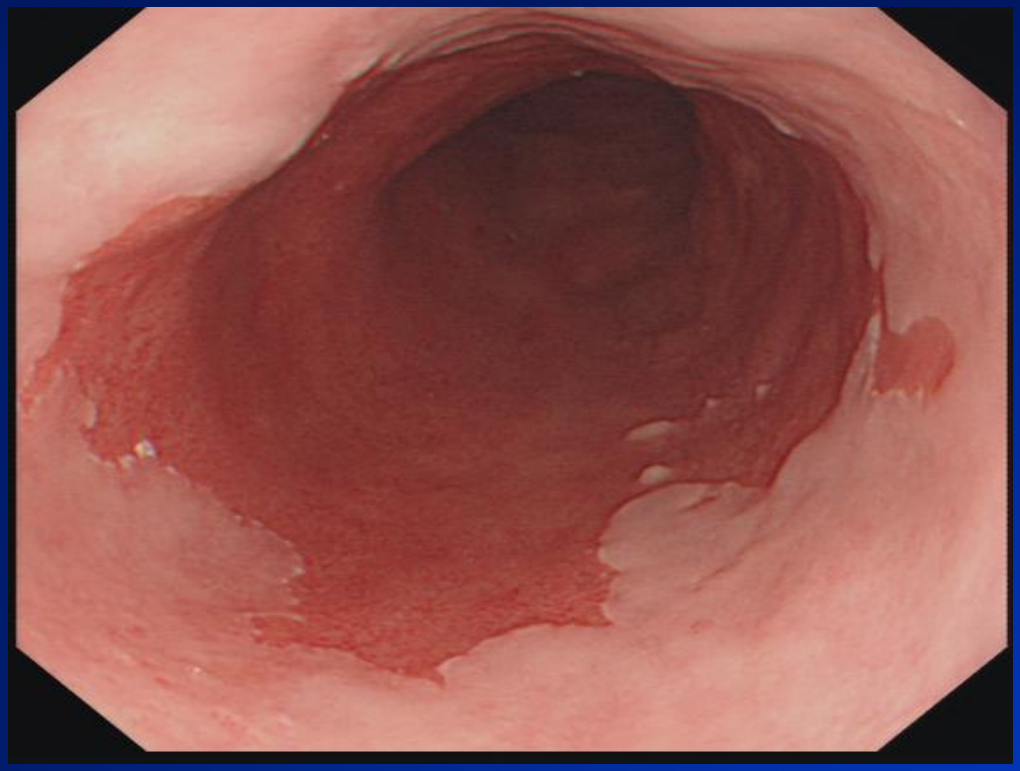
ESOPHAGEAL CANCER 2015 Estimates[2]	NEW CASES	DEATHS
	16,980	15,590

*Incidence rates are per 100,000 and are age-adjusted to the 2000 US Std Population

1.SEER Cancer Statistics Review (CSR) 1975-2012. National Cancer Institute. Bethesda, MD http://seer.cancer.gov/csr/1975_2012/results_single/sect_01_table.05_2pgs.pdf

2.SEER Cancer Statistics Factsheets: Esophageal Cancer. National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/statfacts/html/esoph.html

Barrett's Esophagus



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

Prevalence & Incidence of Barrett's

- 1.6% of Swedish adult population
- 3.5 million Americans (extrapolated)
- 5.6% of US population (based on a SEER data simulation model)
- 13% of a VA population with GERD had Barrett's upon screening endoscopy

Ronkainen, Gastroenterology, 2005

Sampliner, Gastroenterology, 2005

Spechler, Dis Esoph, 2010

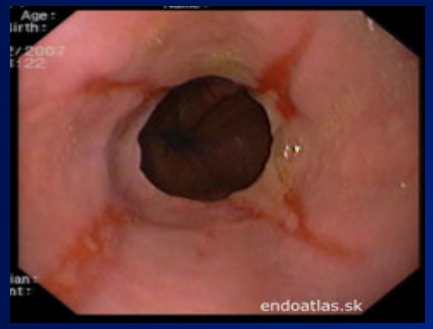
Westhoff, GI Endoscopy, 2005

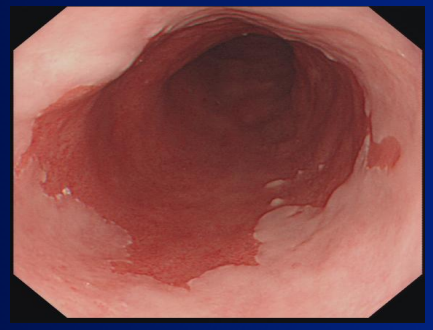
Epidemiology: Barrett's Esophagus

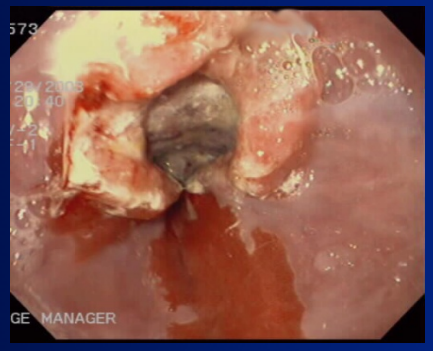
- Mean age is 55
- Caucasian
- Uncommon in Blacks and Asians
- Male: Female 2:1 Barrett's

Pathophysiology

Evolution of Barrett's







Squamous esophagus

Chronic inflammation

Barrett's metaplasia

Low-grade dysplasia

High-grade dysplasia

Adenocarcinoma

Injury: Acid & bile reflux

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

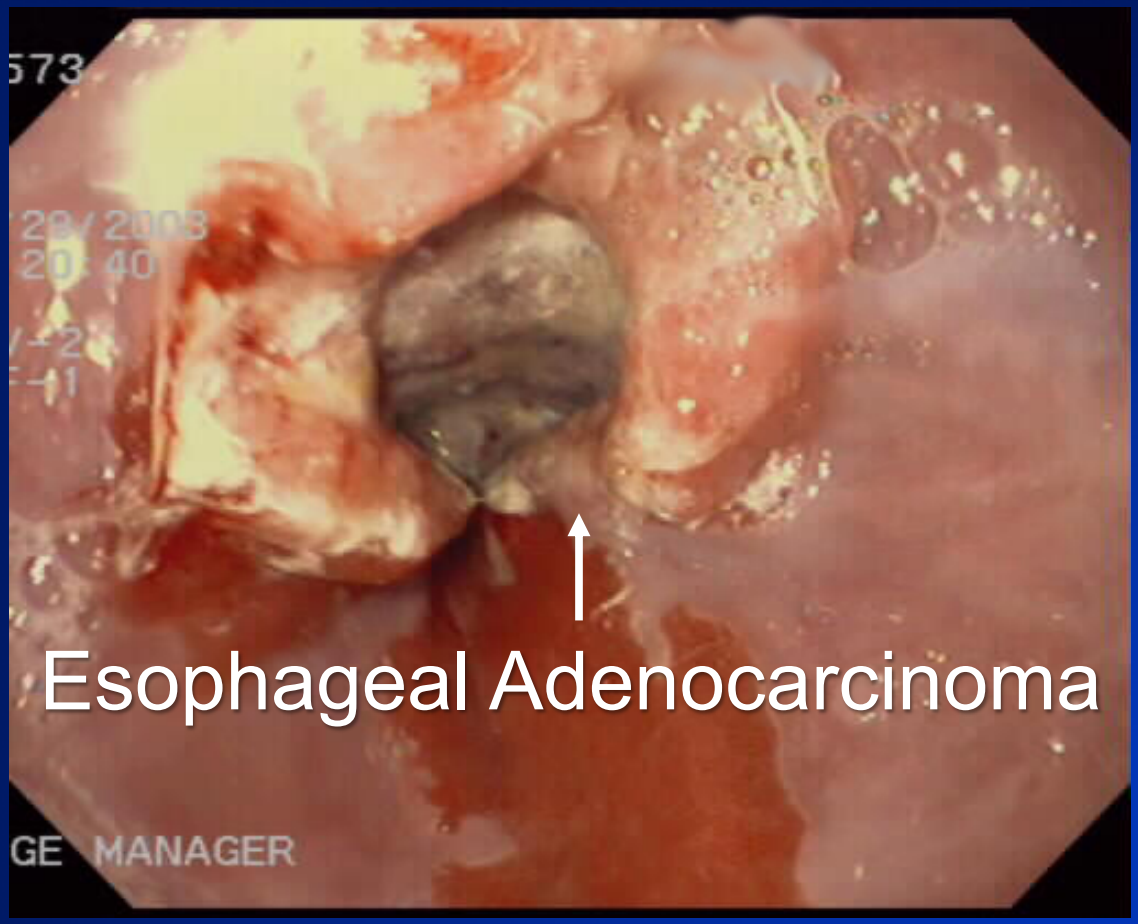
Accumulate Genetic Changes

Progression Risk

Risk of Progression

Barrett's Esophagus

Risk of Progression



Clinical Factors that Contribute to Increased Progression Risk

- Male
- Caucasian
- Smoker
- Obese

Chak, Gut, 2002
Gopal, Dig Dis Sci, 2003
Weston, Am J Gastroenterol, 2004
Hage, Scand J Gastroenterol, 2004
Iftikhar, Gut, 1992
Bani-Hani, World J Gastroenterol, 2005
Ramus, Eur J Cancer Prev, 2012
de Jonge, Gut, 2010
Prasad, Am J Gastroenterol, 2010

- Family history
- Length of Barrett's
- Size of hiatal hernia
- Duration of Barrett's
- Young Age

Reid, Am J Gastroenterol, 2000
Weston, Am J Gastroenterol, 2001
Suspiro, Am J Gastroenterol, 2003
Sikkema, Am J Gastroenterol, 2011
Sappati Biyyani , Dis Esophagus, 2007
Munitiz, J Clin Gastroenterol, 2008
Abnet, Eur J Cancer, 2008
de Jonge, Am J Gastroenterol, 2006
Lagergren, Ann Intern Med, 1999
Jung, Am J Gastroenterol, 2011

Non-Dysplastic BE Progression to Cancer in Several Large 2010/11 Studies Averaged .29% per Year

Oesophagus

Risk of malignant progression in patients with Barrett's oesophagus: a Dutch nationwide cohort study

Pieter J F de Jonge,[1] Mark van Blankenstein,[1] Caspar W N Looman,[2] Mariël K Casparie,[3] Gerrit A Meijer,[4] Ernst J Kuipers[1,5]

GI cancer

ce of oesophageal adenocarcinoma in stic Barrett's oesophagus: a meta-analysis

mar Krishnan,[2] Niharika Samala,[1] Jashanpreet Singh,[1] iah Perla,[3] Colin W Howden[2]

W ENGLAND AL of MEDICINE

OCTOBER 13, 2011 VOL. 365 NO. 15

denocarcinoma among Patients Barrett's Esophagus

ABSTRACT

CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2011;9:220–227

Barrett's Esophagus Have Low Risks for phageal Adenocarcinoma

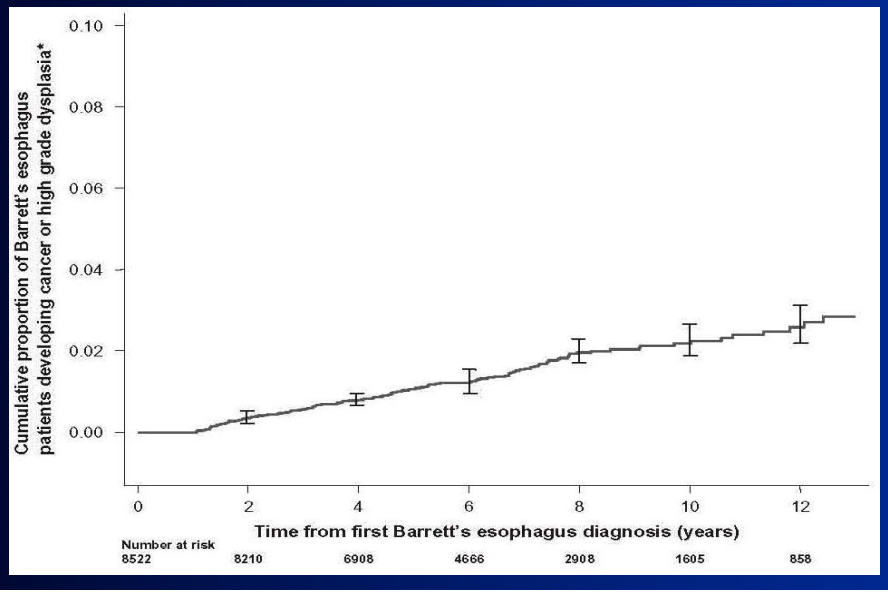
n in Barrett's Esophagus Patients: ion-Based Study

de Jonge, Gut, 2010
Desai, Gut, 2011
Hvid-Jensen, N Engl J Med, 2011
Wani, Clin Gastroenterol Hepatol, 2011
Bhat, J Natl Cancer Inst, 2011

CLE/IM Progression to HGD/EAC

(Bhat, JNCI, 2011)

- Population-based study (Northern Ireland Barrett's Register or NIBR) from 1993 to 2005
- 8522 IM pts were followed for a mean of 7 yrs
- "Results from the NIBR demonstrate a constant risk of progression to cancer over time."



ARTICLE

Risk of Malignant Progression in Barrett's Esophagus Patients: Results from a Large Population-Based Study

Shivaram Bhat, Helen G. Coleman, Fouad Yousef, Brian T. Johnston, Damian T. McManus, Anna T. Gavin, Liam J. Murray

Manuscript received October 7, 2010; revised May 9, 2011; accepted May 9, 2011.

Correspondence to: Shivaram Bhat, MB, BCh, MRCP, Centre for Public Health, Queens University Belfast, Institute of Clinical Sciences Building, Belfast BT12 6BA, Northern Ireland (e-mail: shiv_bhat@doctors.org.uk).

Background Barrett's esophagus (BE) is a premalignant lesion that predisposes to esophageal adenocarcinoma. However, the reported incidence of esophageal adenocarcinoma in patients with BE varies widely. We examined the risk of malignant progression in patients with BE using data from the Northern Ireland Barrett's esophagus Register (NIBR), one of the largest population-based registries of BE worldwide, which includes every adult diagnosed with BE in Northern Ireland between 1993 and 2005.

Subjects and Methods We followed 8522 patients with BE, defined as columnar lined epithelium of the esophagus with or without specialized intestinal metaplasia (SIM), until the end of 2008. Patients with incident adenocarcinomas of the esophagus or gastric cardia or with high-grade dysplasia of the esophagus were identified by matching the NIBR with the Northern Ireland Cancer Registry, and deaths were identified by matching with records from the Registrar General's Office. Incidence of cancer outcomes or high-grade dysplasia was calculated as events per 100 person-years (% per year) of follow-up, and Cox proportional hazard models were used to determine incidence by age, sex, length of BE segment, presence of SIM, macroscopic BE, or low-grade dysplasia. All *P* values were from two-sided tests.

Results After a mean of 7.0 years of follow-up, 79 patients were diagnosed with esophageal cancer, 16 with cancer of the gastric cardia, and 36 with high-grade dysplasia. In the entire cohort, incidence of esophageal or gastric cardia cancer or high-grade dysplasia combined was 0.22% per year (95% confidence interval [CI] = 0.19% to 0.26%). SIM was found in 46.0% of patients. In patients with SIM, the combined incidence was 0.38% per year (95% CI = 0.31 to 0.46%). The risk of cancer was statistically significantly elevated in patients with vs without SIM at index biopsy (0.38% per year vs 0.07% per year; hazard ratio [HR] = 3.54, 95% CI = 2.09 to 6.00, $P < .001$), in men compared with women (0.28% per year vs 0.13% per year; HR = 2.11, 95% CI = 1.41 to 3.16, $P < .001$), and in patients with low-grade dysplasia compared with no dysplasia (1.40% per year vs 0.17% per year; HR = 5.67, 95% CI = 3.77 to 8.53, $P < .001$).

Conclusion We found the risk of malignant progression among patients with BE to be lower than previously reported, suggesting that currently recommended surveillance strategies may not be cost-effective.

J Natl Cancer Inst 2011;103:1–9

The incidence of esophageal adenocarcinoma is rising in the United States and Europe (1,2). Despite general improvements in cancer survival in most countries, patients with esophageal adenocarcinoma have a poor prognosis, with fewer than 20% surviving for 5 years (3,4). Barrett's esophagus (BE) is the metaplastic transformation of the native esophageal squamous epithelium into columnar epithelium in response to gastroesophageal reflux. Patients with BE, a known precursor to esophageal adenocarcinoma, are estimated to carry a 30- to 60-fold increased risk of developing esophageal adenocarcinoma (5).

Endoscopic surveillance of BE is the currently accepted standard of care and aims to reduce morbidity and mortality through early detection of dysplasia or cancer (6,7). The cost-effectiveness of surveillance is dependent on the risk of progression of BE to cancer (8–10). However, a wide variation in the incidence of esophageal adenocarcinoma in BE has been observed, ranging from 0% to 3.5% per annum (11,12). Also, it is not currently known whether the rate of progression of BE to esophageal adenocarcinoma varies with time from diagnosis of BE. Change in risk over time has implications regarding both the need for, and the frequency of, endoscopic surveillance.

The aim of this study was to examine the risk of adenocarcinoma or high-grade dysplasia in a large cohort of unselected BE patients. The risk of cancer or high-grade dysplasia was examined using both the British definition of BE, that is, columnar lined epithelium of the esophagus (CLE) and the American definition of

IM Progression to HGD/EAC

(Falk, Sampliner, Sharma et al, CGH, 2011)

- Multi-center outcomes project
- 1204 pts were followed for a mean of 5.5 yrs
- 2.9% of IM pts developed cancer in 10 yrs
- 7.3% of IM pts developed HGD or cancer in 10 yrs

CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2011;9:220–227

Patients With Nondysplastic Barrett's Esophagus Have Low Risks for Developing Dysplasia or Esophageal Adenocarcinoma

SACHIN WANI,* GARY FALK,‡ MATTHEW HALL,* SRINIVAS GADDAM,* AMY WANG,§ NEIL GUPTA,* MANDEEP SINGH,* VIKAS SINGH,* KENG-YU CHUANG,‖ VIKRAM BOOLCHAND,‖ HEMANTH GAVINI,‖ JOHN KUCZYNSKI,‖ PRITI SUD,‖ SAVIO REDDYMASU,* AJAY BANSAL,* AMIT RASTOGI,* SHARAD C. MATHUR,* PATRICK YOUNG,* BROOKS CASH,¶ DAVID A. LIEBERMAN,§ RICHARD E. SAMPLINER,‖ and PRATEEK SHARMA*

*Division of Gastroenterology and Hepatology, Veterans Affairs Medical Center and University of Kansas School of Medicine, Kansas City, Missouri; ‡Department of Gastroenterology and Hepatology, Cleveland Clinic Foundation, Cleveland, Ohio; §Division of Gastroenterology and Hepatology, Veterans Affairs Medical Center and Oregon Health and Science University, Portland, Oregon; ‖Department of Gastroenterology and Hepatology, Southern Arizona Veterans Affairs Health Care System and University of Arizona Health Science Center, Tucson, Arizona; ¶Division of Gastroenterology and Hepatology, National Naval Medical Center, Bethesda, Maryland

This article has an accompanying continuing medical education activity on page e26. Learning Objectives—At the end of this activity, the learner will appreciate that the rate of progression to low-grade dysplasia is much higher than the incident rate per year for esophageal cancer for Barrett's esophagus; appreciate the risk factors for progression to esophageal cancer in patients with Barrett's esophagus; and recognize the wide variability in the previous reporting of progression of Barrett's esophagus to cancer.

See editorial on page 194.

BACKGROUND & AIMS: The risks of dysplasia and esophageal adenocarcinoma (EAC) are not clear for patients with nondysplastic Barrett's esophagus (NDBE); the rate of progression has been overestimated in previous studies. We studied the incidences of dysplasia and EAC and investigated factors associated with progression of BE. **METHODS:** The BE study is a multicenter outcomes project of a large cohort of patients with BE. Neoplasia was graded as low-grade dysplasia, high-grade dysplasia (HGD), or EAC. Patients followed up for at least 1 year after the index endoscopy examination were included, whereas those diagnosed with dysplasia and EAC within 1 year of diagnosis with BE (prevalent cases) were excluded. Of 3334 patients with BE, 1204 met the inclusion criteria (93.7% Caucasian; 88% male; mean age, 59.3 y) and were followed up for a mean of 5.52 years (6644.5 patient-years). **RESULTS:** Eighteen patients developed EAC (incidence, 0.27%/y; 95% confidence interval [CI], 0.17–0.43) and 32 developed HGD (incidence, 0.48%/y; 95% CI, 0.34–0.68). The incidence of HGD and EAC was 0.63%/y (95% CI, 0.47–0.86). There were 217 cases of low-grade dysplasia (incidence, 3.6%/y; 95% CI, 3.2–4.1). Five and 10 years after diagnosis, 98.6% (n = 540) and 97.1% (n = 155) of patients with NDBE were cancer free, respectively. The length of the BE was associated significantly with progression (EAC <6 cm, 0.09%/y vs EAC ≥6 cm, 0.65%/y; $P = 0.001$). **CONCLUSIONS: There is a lower incidence of dysplasia and EAC among patients with NDBE than previously reported. Because most patients are cancer free after a long-term follow-up period, surveillance intervals might be lengthened, especially for patients with shorter segments of BE.**

Keywords: Barrett's Esophagus; Dysplasia; Esophageal Adenocarcinoma; Esophageal Cancer; Screening; Surveillance; Prevention.

Barrett's esophagus (BE), a known complication of chronic gastroesophageal reflux disease, is a well established premalignant lesion for esophageal and gastroesophageal adenocarcinoma.[1,2] Approximately 10% to 15% of patients with chronic gastroesophageal reflux disease are diagnosed with BE. In addition, BE has been reported in patients with no reflux symptoms.[3] The risk of esophageal adenocarcinoma (EAC) is increased 30 to 40 times among patients with BE compared with those without this condition. EAC continues to increase at a rate greater than any other cancer in the Western world (>500% since the 1970s), exceeding that of other more common cancers such as breast, colon, lung, and prostate cancer.[4] In 2009, it is estimated that 16,470 new cases of esophageal cancer will be diagnosed in the United States, of which close to 60% will be adenocarcinomas.[5] Despite all the recent advances in the diagnosis and management of this lethal cancer, the overall 5-year survival rate remains dismal (15%–20%).[6]

Although not evaluated in randomized controlled trials, surveillance of patients with BE is recommended by all major gastroenterology societies and published guidelines.[1,7] Multiple observational studies suggest that endoscopic surveillance is associated with detection of EAC at an earlier stage along with improved survival.[8,9] However, the burden of endoscopic surveillance of BE patients is significant and continues to generate a great deal of controversy.[10,11] In addition, there has been a lot of interest in the endoscopic ablation of nondysplastic BE (NDBE). The true incidence of EAC in patients with BE is central to determining the effectiveness of surveillance endoscopy or any intervention strategy. The exact incidence of EAC

Abbreviations used in this paper: BE, Barrett's esophagus; CI, confidence interval; EAC, esophageal adenocarcinoma; HGD, high-grade dysplasia; LGD, low-grade dysplasia; NDBE, nondysplastic Barrett's esophagus; NSAID, nonsteroidal anti-inflammatory drug; PPI, proton pump inhibitor; SD, standard deviation.

1542-3565/$36.00
doi:10.1016/j.cgh.2010.11.008

LGD Progression to EAC

(Curvers, Am J Gastro, 2010)

- Population-based study (Amsterdam Gastroenterological Association Barrett's Registry) from 2000 to 2006
- Histology reports from six community hospitals were reviewed by two expert GI pathologists
- 1,198 pts diagnosed with BE
- 121 pts diagnosed with LGD & had f/u bxs
- 19 pts had a consensus dx of LGD
- LGD pts had a 13.4% annual progression risk for HGD or EAC
- 10.5% LGD pts developed cancer in an average f/u of just over 3 yrs

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], Brenda Elzer, MSc[1], Lubertus C. Baak, MD, PhD[3,12], Clarisse Bohmer, MD, PhD[4,12], Rosalie C. Mallant-Hent, MD, PhD[5,12], Arnout van Oijen, MD[6,12], Anton H. Naber, MD, PhD[7,12], Pieter Scholten, MD[8,12], Olivier R. Busch, MD, PhD[9,13], Harriët G.T. Blaauwgeers, MD, PhD[10,13], Gerrit A. Meijer, MD, PhD[11,13] and Jacques J.G.H.M. Bergman, MD, PhD[1,12,13]

OBJECTIVES: **Published data on the natural history of low-grade dysplasia (LGD) in Barrett's esophagus (BE) are inconsistent and difficult to interpret. We investigated the natural history of LGD in a large community-based cohort of BE patients after reviewing the original histological diagnosis by an expert panel of pathologists.**

METHODS: **Histopathology reports of all patients diagnosed with LGD between 2000 and 2006 in six non-university hospitals were reviewed by two expert pathologists. This panel diagnosis was subsequently compared with the histological outcome during prospective endoscopic follow-up.**

RESULTS: **A diagnosis of LGD was made in 147 patients. After pathology review, 85% of the patients were downstaged to non-dysplastic BE (NDBE) or to indefinite for dysplasia. In only 15% of the patients was the initial diagnosis LGD. Endoscopic follow-up was carried out in 83.6% of patients, with a mean follow-up of 51.1 months. For patients with a consensus diagnosis of LGD, the cumulative risk of progressing to high-grade dysplasia or carcinoma (HGD or Ca) was 85.0% in 109.1 months compared with 4.6% in 107.4 months for patients downstaged to NDBE ($P<0.0001$). The incidence rate of HGD or Ca was 13.4% per patient per year for patients in whom the diagnosis of LGD was confirmed. For patients downstaged to NDBE, the corresponding incidence rate was 0.49%.**

CONCLUSIONS: **LGD in BE is an overdiagnosed and yet underestimated entity in general practice. Patients diagnosed with LGD should undergo an expert pathology review to purify this group. In case the diagnosis of LGD is confirmed, patients should undergo strict endoscopic follow-up or should be considered for endoscopic ablation therapy.**

Am J Gastroenterol advance online publication, 11 May 2010; doi:10.1038/ajg.2010.171

INTRODUCTION

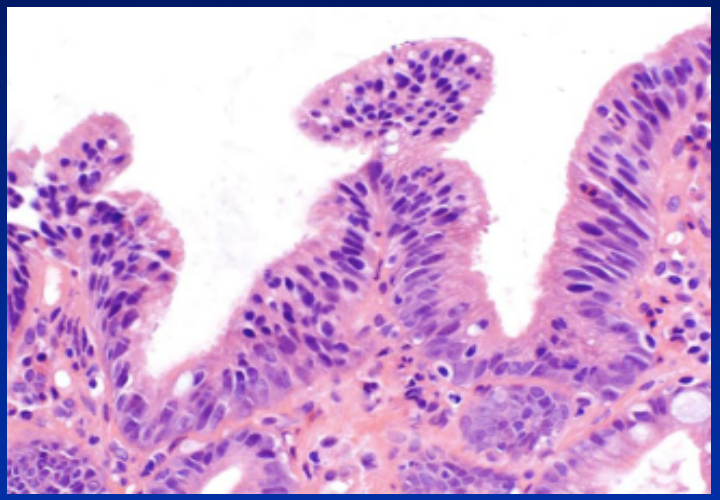
Barrett's esophagus (BE) is a condition that is induced by chronic tissue injury and inflammation due to gastroesophageal reflux. The clinical finding of BE is replacement of the squamous epithelial lining of the distal esophagus with a columnar epithelium containing goblet cells (specialized intestinal metaplasia). Patients with BE have a significantly increased risk for developing esophageal adenocarcinoma over that of the general population (~100×) (1). This malignancy has a dismal prognosis with an all-stage 5-year survival of ~15% (2,3). Neoplastic progression from non-dysplastic BE (NDBE) to esophageal adenocarcinoma is considered to be a multistep process that is associated with increasing (epi)genetic abnormalities, which are accompanied by morphological changes including atypia, loss of cellular differentiation, distributed loss of tissue architecture, and ultimately invasion (4–7). This continuous spectrum of changes is stratified

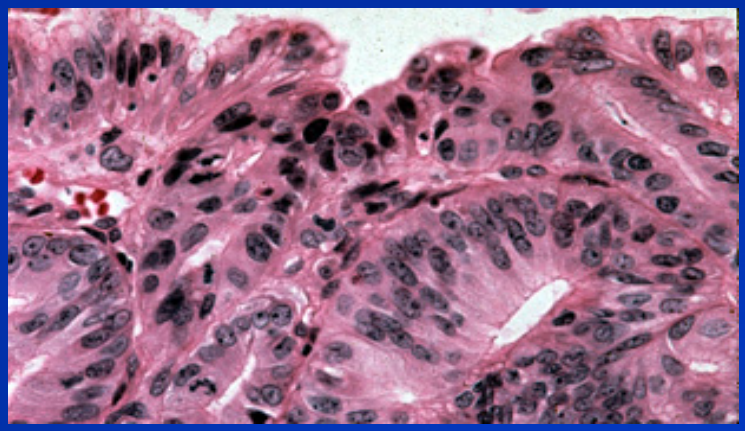
[1]Department of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands; [2]Department of Pathology, Academic Medical Center, Amsterdam, The Netherlands; [3]Department of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands; [4]Department of Gastroenterology and Hepatology, Spaarne Hospital, Hoofddorp, The Netherlands; [5]Department of Internal Medicine, Flevohospital, Almere, The Netherlands; [6]Department of Gastroenterology and Hepatology, Medical Center Alkmaar, Alkmaar, The Netherlands; [7]Department of Internal Medicine, Tergooi Hospitals, Hilversum, The Netherlands; [8]Department of Gastroenterology and Hepatology, St Lucas Andreas Hospital, Amsterdam, The Netherlands; [9]Department of Surgery, Academic Medical Center, Amsterdam, The Netherlands; [10]Comprehensive Cancer Center Amsterdam, Amsterdam, The Netherlands; [11]Department of Pathology, Free University Hospital, Amsterdam, The Netherlands; [12]Amsterdam Gastroenterological Association, Amsterdam, The Netherlands; [13]Barrett Advisory Committee of the Comprehensive Cancer Centre Amsterdam, Amsterdam, The Netherlands. **Correspondence:** Jacques J.G.H.M. Bergman, MD, PhD, Department of Gastroenterology and Hepatology, Academic Medical Center, Meibergdreef 9, Amsterdam 1105 AZ, The Netherlands. E-mail: j.j.bergman@amc.uva.nl
Received 17 November 2009; accepted 22 March 2010

LGD in Barrett's Esophagus Has a High Risk of Progression When Confirmed by a Panel of Expert Pathologists

(Duits, Gut 2015)

- Prospective study with 293 LGD pts diagnosed in the community
- Pathology reviewed by expert GI panel
- 73 patients had confirmed LGD (27%)
- 9 patients upstaged to HGD/EAC (2%)
- When disease confirmed, 9.1% annual progression to HGD/EAC
- 5 year risk of HGD/EAC: 40%
- “The results indicate that patients with a confirmed diagnosis of LGD in BE have a markedly increased risk for progression to HGD/EAC.”





Confirmed LGD

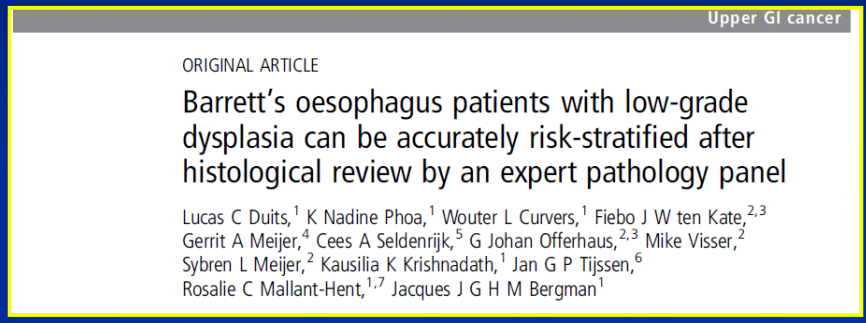
INCREASED RISK OF PROGRESSION

N	STUDY TYPE	PROGRESSION TO HGD/EAC[1]	STUDY
127	RCT	13.6% (annual rate of progression)	Shaheen et al. 2009
147	Prospective	13.4% (per patient-year)	Curvers et al. 2010
293	Retrospective	9.1% (per-patient year)	Duits et al. 2014
85	Prospective	9% (annual rate of progression	Clark et al. 2014
136	RCT	11.8% (per patient-year)	Phoa et al. 2014
125	Retrospective	6.6% (annual rate of progression per Kaplan-Meier method), 14.8% first year	Small et al. 2015

Radiofrequency Ablation vs Endoscopic Surveillance for Patients With Barrett Esophagus and Low-Grade Dysplasia

A Randomized Clinical Trial FREE

K. Nadine Phoa, MD[1]; Frederike G. I. van Vilsteren, MD[1]; Bas L. A. M. Weusten, MD[2]; Raf Bisschops, MD[3]; Erik J. Schoon, MD[4]; Krish Ragunath, MD[5]; Grant Fullarton, MD[6]; Massimiliano Di Pietro, MD[7]; Narayanasamy Ravi, MD[8]; Mike Visser, MD[9]; G. Johan Offerhaus, MD[9]; Cees A. Seldenrijk, MD[10]; Sybren L. Meijer, MD[9]; Fiebo J. W. ten Kate, MD[9]; Jan G. P. Tijssen, PhD[11]; Jacques J. G. H. M. Bergman, MD, PhD[1]

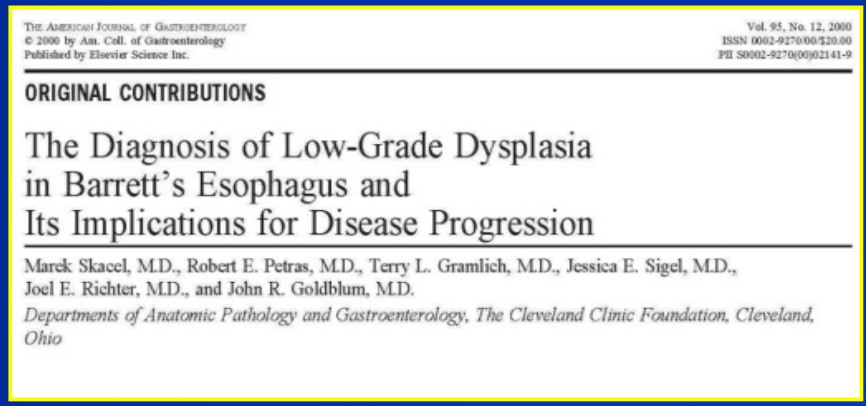


Upper GI cancer

ORIGINAL ARTICLE

Barrett's oesophagus patients with low-grade dysplasia can be accurately risk-stratified after histological review by an expert pathology panel

Lucas C Duits,[1] K Nadine Phoa,[1] Wouter L Curvers,[1] Fiebo J W ten Kate,[2,3] Gerrit A Meijer,[4] Cees A Seldenrijk,[5] G Johan Offerhaus,[2,3] Mike Visser,[2] Sybren L Meijer,[2] Kausilia K Krishnadath,[1] Jan G P Tijssen,[6] Rosalie C Mallant-Hent,[1,7] Jacques J G H M Bergman[1]



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ORIGINAL CONTRIBUTIONS

The Diagnosis of Low-Grade Dysplasia in Barrett's Esophagus and Its Implications for Disease Progression

Marek Skacel, M.D., Robert E. Petras, M.D., Terry L. Gramlich, M.D., Jessica E. Sigel, M.D., Joel E. Richter, M.D., and John R. Goldblum, M.D.

Departments of Anatomic Pathology and Gastroenterology, The Cleveland Clinic Foundation, Cleveland, Ohio

BADCAT Consensus Statement

(Bennett, Gastroenterology, 2012)

- An int'l, multidisciplinary, evidence-based review of BE management strategies using 80% agreement as a threshold for all consensus statements
- "Risk of progression from HGD to cancer is approximately 10% per year."

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 OGDE,[5] MICHAEL VIETH,[6] SCOTT SANDERS,[7] LAURA GAY,[8] OLIVER PECH,[9] GAUS LONGCROFT-WHEATON,[9] YVONNE ROMERO,[10] JOHN INADOMI,[11] JAN TACK,[12] DOUGLAS A. CORLEY,[13] HENDRIK MANNER,[14] SUSI GREEN,[8] 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,[27] JOHN GOLDBLUM,[27] CHARLES GORDON,[28] HEIKE GRABSCH,[29] CHRIS HAIGH,[21] MICHIO HONGO,[30] DAVID JOHNSTON,[31] RICKY FORBES-YOUNG,[32] ELAINE KAY,[33] PHILIP KAYE,[34] TONI LERUT,[12] LAURENCE B. LOVAT,[27] LARS LUNDELL,[35] PHILIP MARS,[33] TADAKUZA SHIMODA,[40] STUART SPECHLER,[41] STEPHEN SONTAG,[42] PETER MALFERTHEINER,[43] IAN MURRAY,[44] MANOJ NANU,[8] DAVID POLLER,[9] KRISH RAGUNATH,[36] JAROSLAW REGULA,[45] RENZO CESTARI,[46] NEIL SHEPHERD,[47] RAJVINDER SINGH,[27] HUBERT J. STEIN,[48] NICHOLAS J. TALLEY,[49] JEAN-PAUL GAUMOCHE,[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,[36] JUERGEN HOCHBERGER,[54] PETER KAHRILAS,[55] SEAN PRESTON,[56] RICHARD SAMPLINER,[57] PRATEEK SHARMA,[58] ROBERT STUART,[59] KENNETH WANG,[60] IRVING WAXMAN,[52] CHRIS ABLEY,[3] DUNCAN LOFT,[61] IAN PENMAN,[34] NICHOLAS J. SHAHEEN,[62] AMITABH CHAK,[52] GARETH DAVIES,[63] LORNA DUNN,[64] YNGVE FALCK-YTTER,[65] JOHN DECAESTECKER,[3] PRADEEP BHANDARI,[3] CHRISTIAN ELL,[6] S. MICHAEL GRIFFIN,[66] STEPHEN ATTWOOD,[67] HUGH BARR,[68] JOHN ALLEN,[17] MARK K. FERGUSON,[52] PAUL MOAYYEDI,[23] and JANUSZ A. Z. JANKOWSKI[1,2,3,69]

[1]Queens University, Belfast, UK; [2]University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin; [3]Amsterdam Medical Center, Amsterdam, The Netherlands; [4]University Hospitals of Leicester, Leicester, UK; [5]Harvard Medical School, Boston, Massachusetts; [6]Klinikum Bayreuth, Bayreuth, Germany; [7]Warwick Medical School, Coventry, UK; [8]Queen Mary University London, London, UK; [9]Queen Alexandra Hospital, Portsmouth, UK; [10]Mayo Clinic, Rochester, Minnesota; [11]Washington University, Seattle, Washington; [12]Leuven University, Leuven, Belgium; [13]Kaiser Permanente, San Francisco, California; [14]HSK Hospital, Wiesbaden, Germany; [15]Redditch General Hospital, Redditch, UK; [16]Maidstone and Tunbridge Wells NHS trust, Maidstone, UK; [17]Royal Marsden Hospital, London, UK; [18]City Hospital, Birmingham, UK and Sandwell Hospital, West Midlands, UK; [19]Queen Marys Hospital, Sidcup, UK; [20]University of Pennsylvania, Philadelphia, Pennsylvania; [21]Oregon Health & Science University, Portland, Oregon; [22]Royal Infirmary, Glasgow, UK; [23]The Johns Hopkins University School of Medicine, Baltimore, Maryland; [24]McMaster University, Hamilton, Ontario, Canada; [25]Bloomington Medical Centre, Bloomington, Minnesota; [26]University of Brescia, Brescia, Italy; [27]Anatomic Pathology, The Cleveland Clinic, Cleveland, Ohio; [28]The Royal Bournemouth Hospital, Bournemouth, UK; [29]University of Padova, Padua, Italy; [30]University of Leeds, Leeds, UK; [31]Wansbeck General Hospital, Northumbria, UK; [32]Tohoku University Hospital, Tohoku, Japan; [33]Ninewells Hospital, Dundee, UK; [34]Royal Infirmary, Edinburgh, UK; [35]Trinity College, Dublin, Ireland; [36]Digestive Diseases Centre, Nottingham University Hospital, Nottingham, UK; [37]University College London, London, UK; [38]Karolinska Institutet, CLINTEC, Stockholm, Sweden; [39]Darent Valley Hospital, Kent, UK; [40]National Cancer Center, Tokyo, Japan; [41]University of Dallas, Dallas, Texas; [42]Hines Veterans Affairs Hospital, Chicago, Illinois; [43]Magdeburg University, Magdeburg, Germany; [44]Royal Cornwall Hospitals, Truro, UK; [45]Institute of Oncology, Warsaw, Poland; [46]Gloucestershire Royal Hospitals, Gloucestershire, UK; [47]Lyell McEwin Hospital, University of Adelaide, Adelaide, Australia; [48]Polyclinic Klinikum München, München, Germany; [49]University of Newcastle, Newcastle, Australia; [50]Department of Gastroenterology, CHU and University of Nantes, Nantes, France; [51]Ulster Hospital, Belfast, UK; [52]University of Chicago, Chicago, Illinois; [53]ECD Solutions, PO Box 662, Bridgetown, St. Michael, Barbados; [54]St. Bernward Hospital, Hildesheim, Germany; [55]Northwestern University, Chicago, Illinois; [56]Barts Health NHS Trust, London, UK; [57]University of Arizona, Tucson, Arizona; [58]Veterans Affairs Medical Center and University of Kansas; [59]Oesophageal Cancer Fund, Dublin, Ireland; [60]Walsgrave Hospital, Coventry, UK; [61]University of North Carolina School of Medicine, Chapel Hill, North Carolina; [62]Case Western Reserve University School of Medicine, Cleveland, Ohio; [63]Harrogate District Hospital, Harrogate, UK; [64]Northern Oesophagogastric Cancer Unit Royal Victoria Infirmary, Newcastle upon Tyne, UK; [65]Louis Stokes Medical Center, Cleveland, Ohio; [66]Durham University, Durham, UK; [67]University of Minnesota School of Medicine, Minneapolis, Minnesota; [69]University of Oxford, Oxford, UK

Podcast interview: www.gastro.org/gastropodcast. Also available on iTunes. See Covering the Cover synopsis on page 275; see editorial on page 282.

BACKGROUND & AIMS: Esophageal adenocarcinoma (EA) is increasingly common among patients with Barrett's esophagus (BE). We aimed to provide consensus recommendations based on the medical literature that clinicians could use to manage patients with BE and low-grade dysplasia, high-grade dysplasia (HGD), or early-stage EA. **METHODS:** We performed an international, multidisciplinary, systematic, evidence-based review of different management strategies for patients with BE and dysplasia or early-stage EA. We used a Delphi process to develop consensus statements. The results of literature searches were screened using a unique, interactive, Web-based data-sifting platform; we used 11,904 papers to inform the choice of statements selected. An a priori threshold of 80% agreement was used to establish consensus for each statement. **RESULTS:** Eighty-one of the 91 statements achieved consensus despite generally low quality of evidence, including 8 clinical statements: (1) specimens from endoscopic resection are better than biopsies for staging lesions, (2) it is important to carefully map the size of the dysplastic areas, (3) patients that receive ablative or surgical therapy require endoscopic follow-up, (4) high-resolution endoscopy is necessary for accurate diagnosis, (5) endoscopic therapy for HGD is preferred to surveillance, (6) endoscopic therapy for HGD is preferred

Abbreviations used in this paper: BADCAT, Barrett's dysplasia and cancer task force; BE, Barrett's esophagus; EA, esophageal adenocarcinoma; EMR, endoscopic mucosal resection; HGD, high-grade dysplasia; LGD, low-grade dysplasia; RFA, radiofrequency ablation.

0016-5085/$36.00
http://dx.doi.org/10.1053/j.gastro.2012.04.052

Long Segment NDBE Progresses to HGD/EAC at a Significantly Elevated Rate

IM Progression to HGD/EAC by Length

(Anaparthy, Clin Gastroenterol Hepatol, 2013)

- Multi-center outcomes project
- 1175 NDBE pts were followed for a mean of 5.5 yrs
- 28% increase in risk of progression to HGD/EAC per 1 cm increase in length (p<0.001)
- Annual progression risk to HGD/EAC by length (p<0.0018):
  - 0.31%/year for length ≤3 cm
  - 0.97 %/year for length 4-6 cm
  - 1.26%/year for length 7-9 cm
  - 1.64%/year for length 10-12 cm
  - 2.41%/year for length ≥13 cm

CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2013;11:1430–1436

Association Between Length of Barrett's Esophagus and Risk of High-grade Dysplasia or Adenocarcinoma in Patients Without Dysplasia

RAJESWARI ANAPARTHY,* SRINIVAS GADDAM,* VIJAY KANAKADANDI,* BENJAMIN R. ALSOP,* NEIL GUPTA,* APRIL D. HIGBEE,* SACHIN B. WANI,* MANDEEP SINGH,* AMIT RASTOGI,* AJAY BANSAL,* BROOKS D. CASH,‡ PATRICK E. YOUNG,§ DAVID A. LIEBERMAN,§ GARY W. FALK,|| JOHN J. VARGO,¶ PRASHANTI THOTA,¶ RICHARD E. SAMPLINER,# and PRATEEK SHARMA*

*Department of Gastroenterology and Hepatology, Veterans Affairs Medical Center and University of Kansas School of Medicine, Kansas City, Missouri; †Department of Gastroenterology and Hepatology, National Naval Medical Center, Bethesda, Maryland; §Department of Gastroenterology and Hepatology, Oregon Health Sciences University, Portland, Oregon; ||Department of Gastroenterology and Hepatology, University of Pennsylvania, Perelman School of Medicine, Philadelphia, Pennsylvania; ¶Department of Gastroenterology and Hepatology, Cleveland Clinic Foundation, Cleveland, Ohio; and #Department of Gastroenterology and Hepatology, University of Arizona, Tucson, Arizona

BACKGROUND & AIMS: It is not clear whether length of Barrett's esophagus (BE) is a risk factor for high-grade dysplasia (HGD) or esophageal adenocarcinoma (EAC) in patients with nondysplastic BE. We studied the risk of progression to HGD or EAC in patients with nondysplastic BE, based on segment length.

METHODS: We analyzed data from a large cohort of patients participating in the BE Study—a multicenter outcomes project comprising 5 US tertiary care referral centers. Histologic changes were graded as low-grade dysplasia, HGD, or EAC. The study included patients with BE of documented length without dysplasia and at least 1 year of follow-up evaluation (n = 1175; 88% male), and excluded patients who developed HGD or EAC within 1 year of their BE diagnosis. The mean follow-up period was 5.5 y (6463 patient-years). The annual risk of HGD and EAC was plotted in 3-cm increments (≤3 cm, 4–6 cm, 7–9 cm, 10–12 cm, and ≥13 cm). We calculated the association between time to progression and length of BE.

RESULTS: The mean BE length was 3.6 cm; 44 patients developed HGD or EAC, with an annual incidence rate of 0.67%/y. Compared with nonprogressors, patients who developed HGD or EAC had longer BE segments (6.1 vs 3.5 cm; $P < .001$). Logistic regression analysis showed a 28% increase in risk of HGD or EAC for every 1-cm increase in BE length ($P = .01$). Patients with BE segment lengths of 3 cm or shorter took longer to develop HGD or EAC than those with lengths longer than 4 cm (6 vs 4 y; P = nonsignificant).

CONCLUSIONS: In patients with BE without dysplasia, length of BE was associated with progression to HGD or EAC. The results support the development of a risk stratification scheme for these patients based on length of BE segment.

Keywords: BEST Study; Esophageal Cancer; Screening; Surveillance; Intestinal Metaplasia.

Esophageal adenocarcinoma (EAC) is the most rapidly increasing incident cancer in the Western world, with a dismal 5-year survival rate of less than 20%.[1] Barrett's esophagus (BE), a well-established premalignant condition for EAC, is characterized by metaplastic transformation of squamous to columnar-type epithelium containing goblet cells (intestinal metaplasia) on histologic evaluation.[2,3] The progression to adenocarcinoma is believed to occur through a sequence of changes involving nondysplastic BE (NDBE), low-grade dysplasia (LGD), and high-grade dysplasia (HGD), before final progression to EAC.[3]

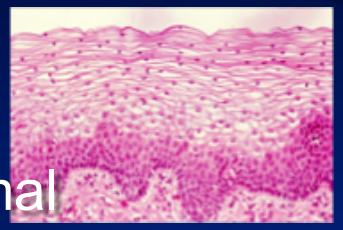
At present, the degree of dysplasia remains the most widely used risk-stratification tool for determining surveillance intervals and the management of patients with BE.[4] Upper-gastrointestinal endoscopy with random 4-quadrant biopsy specimens every 1 to 2 cm is endorsed by various gastroenterology societies for surveillance of patients with BE because there is evidence from retrospective studies suggesting that endoscopic surveillance is associated with a diagnosis of EAC at an earlier stage along with improved survival.[2,3] According to the current guidelines for BE management, diagnosis of NDBE requires surveillance endoscopies every 3 to 5 years.[5] Nevertheless, the timing of endoscopic surveillance has implications on cost-effectiveness and resource use given the lack of clear data on cause-specific mortality related to BE and the low rate of

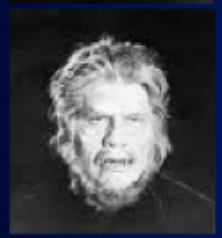
Abbreviations used in this paper: BE, Barrett's esophagus; CI, confidence interval; EAC, esophageal adenocarcinoma; HGD, high-grade dysplasia; LGD, low-grade dysplasia; NDBE, nondysplastic Barrett's esophagus; NSAID, nonsteroidal anti-inflammatory drug; PPI, proton pump inhibitor; SD, standard deviation.

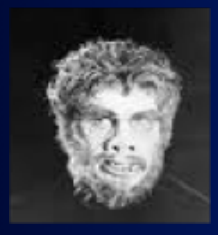
1542-3565/$36.00
http://dx.doi.org/10.1016/j.cgh.2013.05.007

3 stages of Barrett's

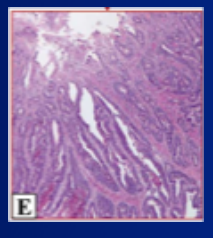
Normal

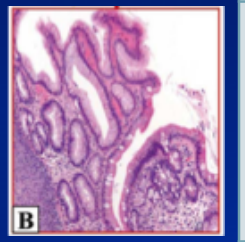


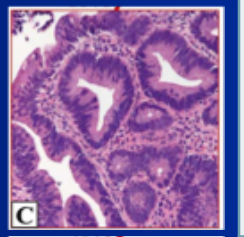


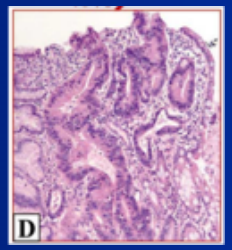


Cancer



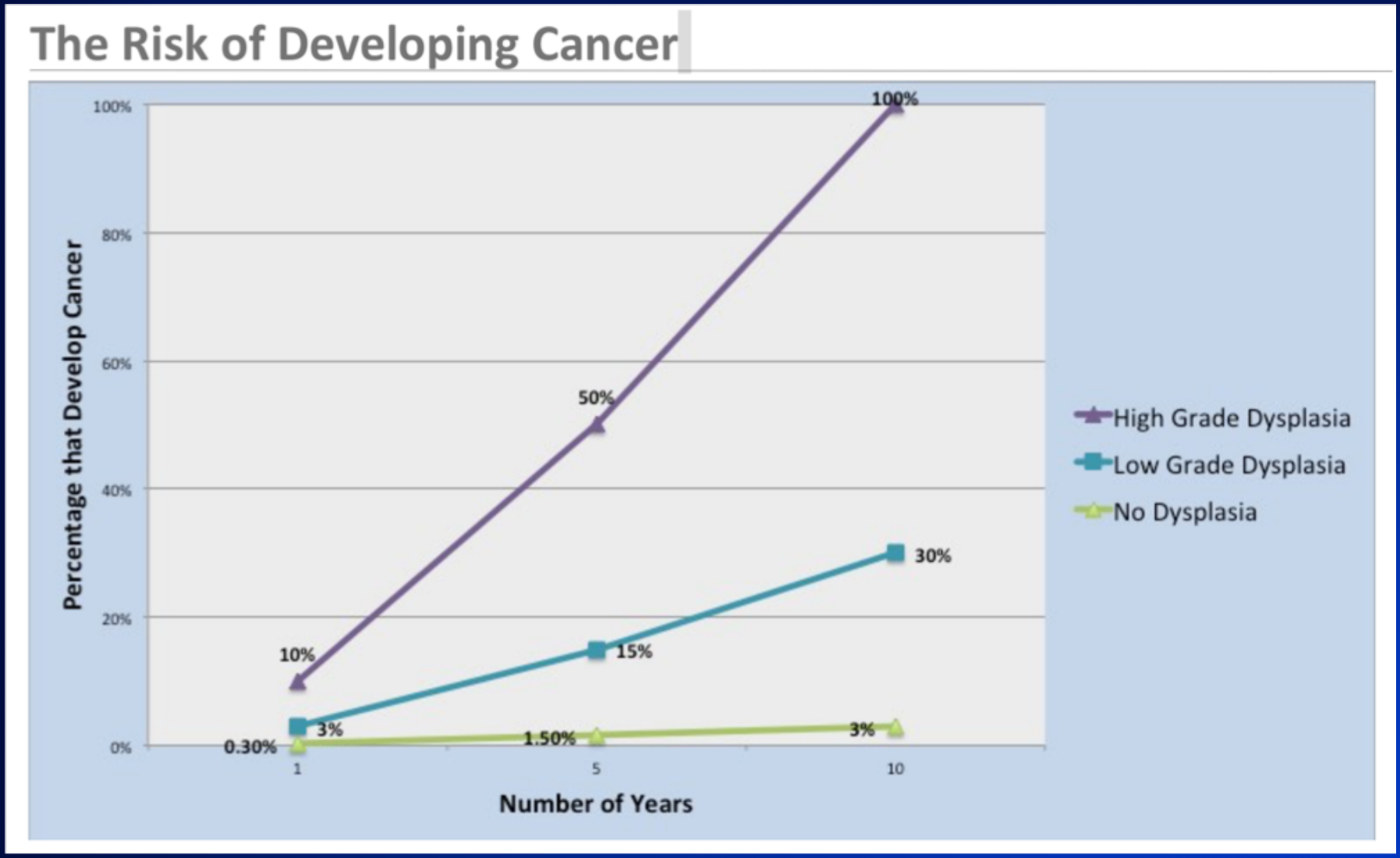






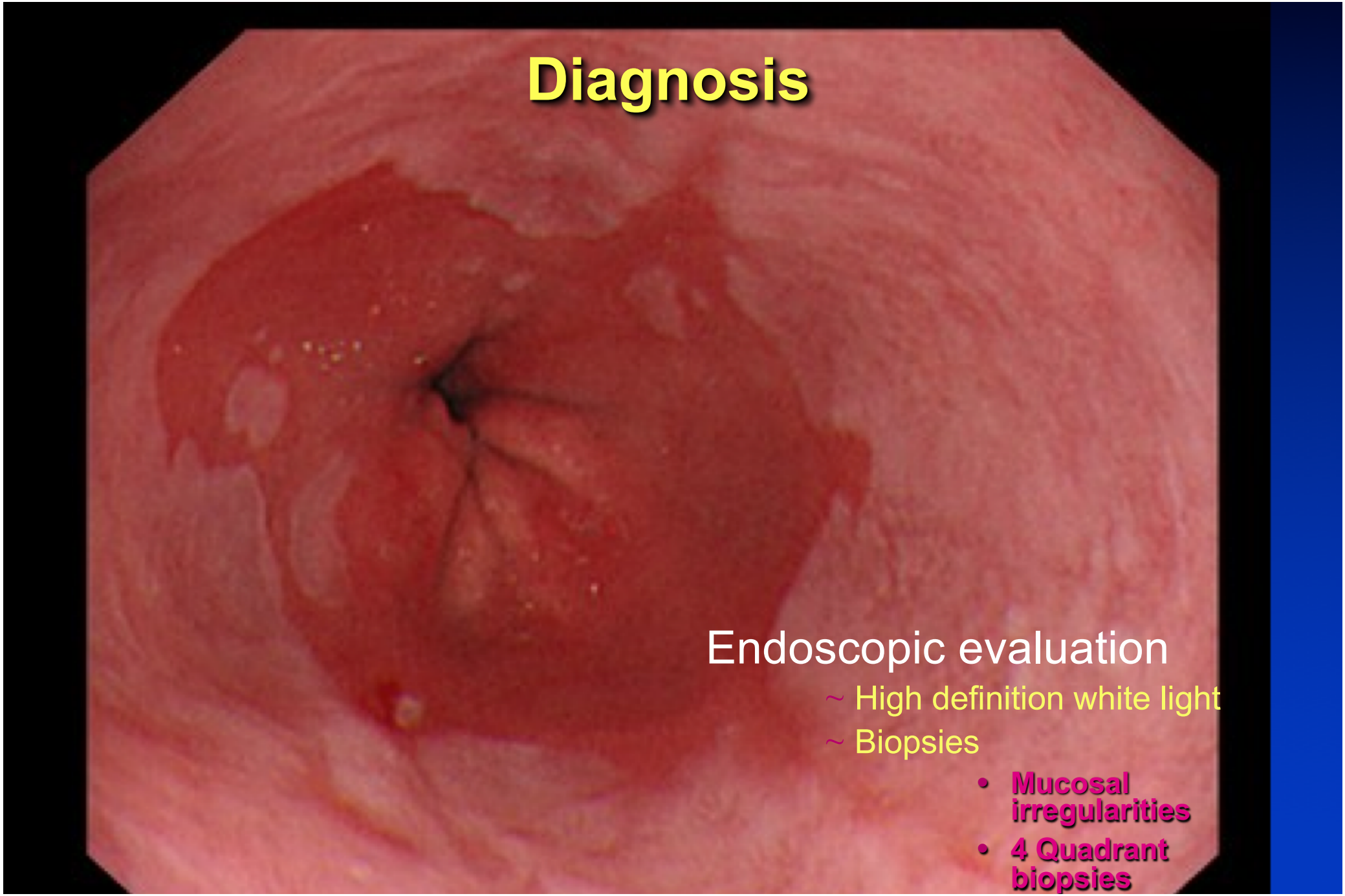
STAGE	Histology	% risk CA 1 year	% risk CA 10 year
1	Barrett's Without Dysplasia	0.3	3%
2	Barrett's Low Grade Dysplasia	3-5	50%
3	Barrett's High Grade Dysplasia	10	100%

iBook Graph


The Risk of Developing Cancer
Percentage that Develop Cancer
100%
80%
60%
40%
20%
0%
1
5
10
Number of Years
100%
50%
10%
30%
15%
3%
0.30%
1.50%
3%
High Grade Dysplasia
Low Grade Dysplasia
No Dysplasia

Recognition of BE & Dysplasia

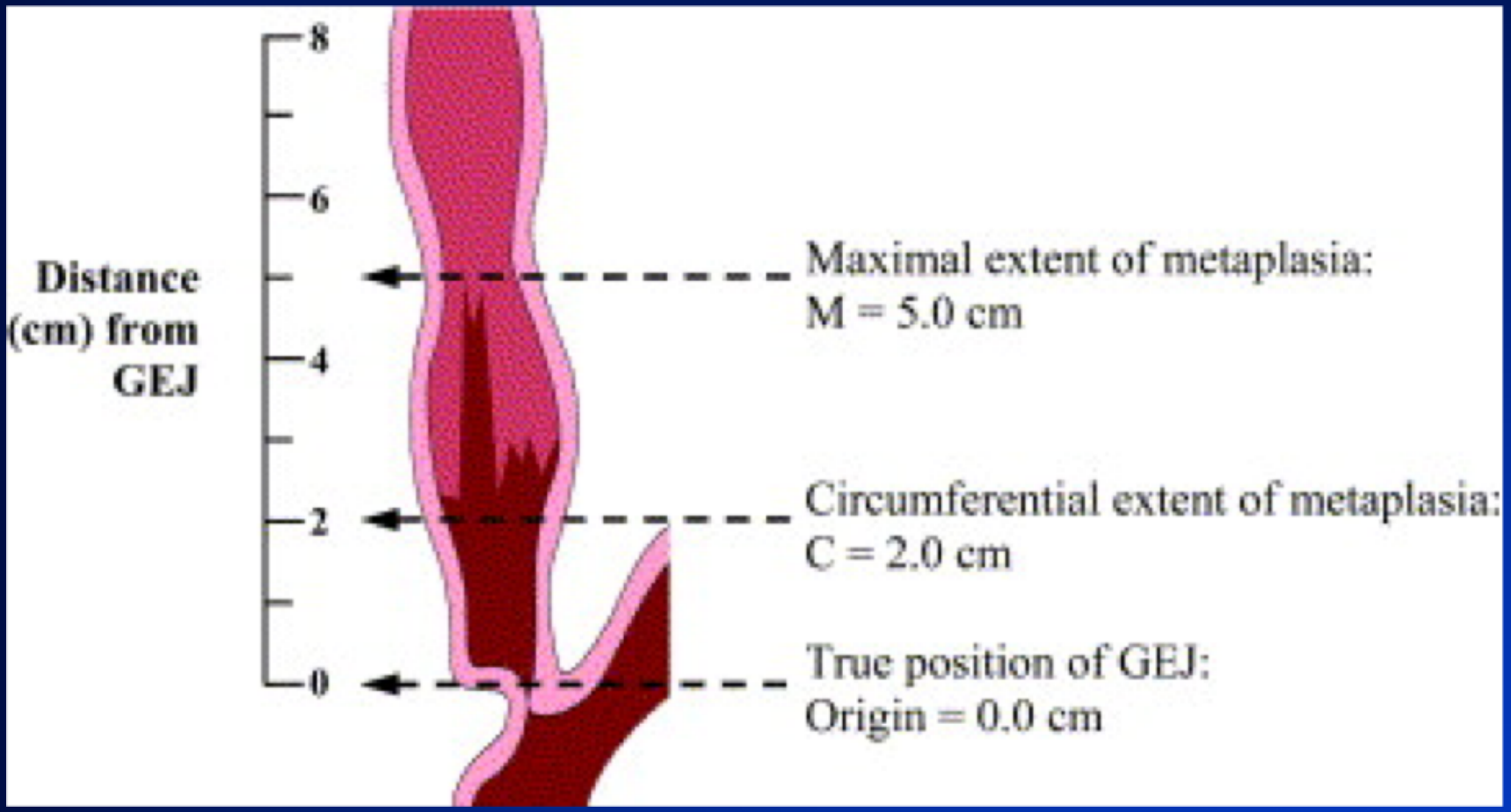
Diagnosis



Endoscopic evaluation

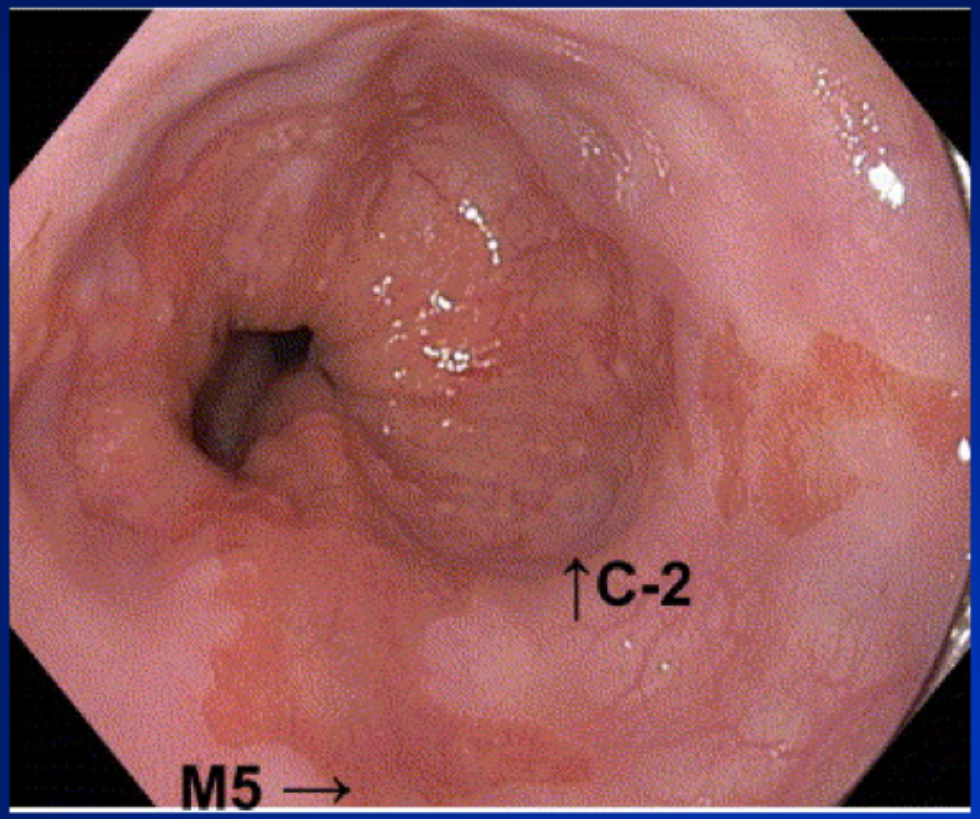
- ~ High definition white light
- ~ Biopsies
  - **Mucosal irregularities**
  - **4 Quadrant biopsies**

Prague C and M Criteria

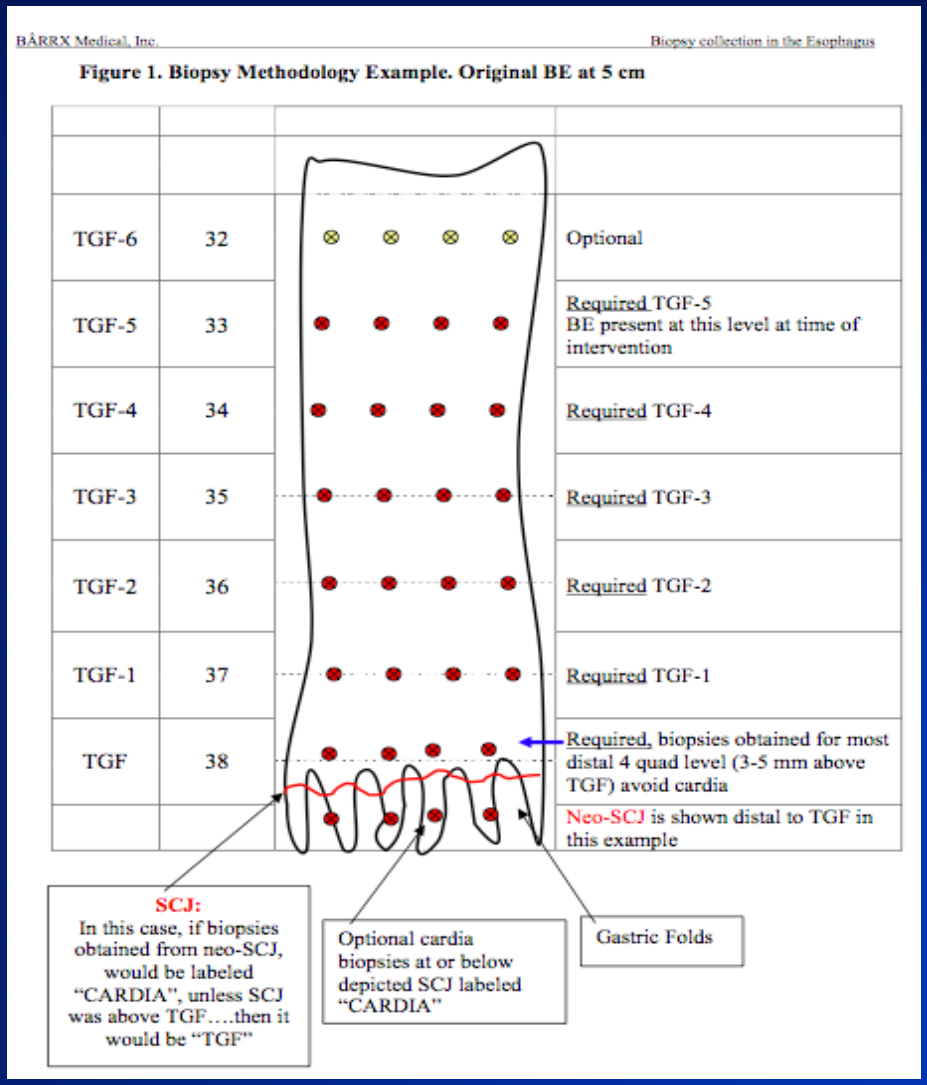


Sharma. Gastroenterology 2006

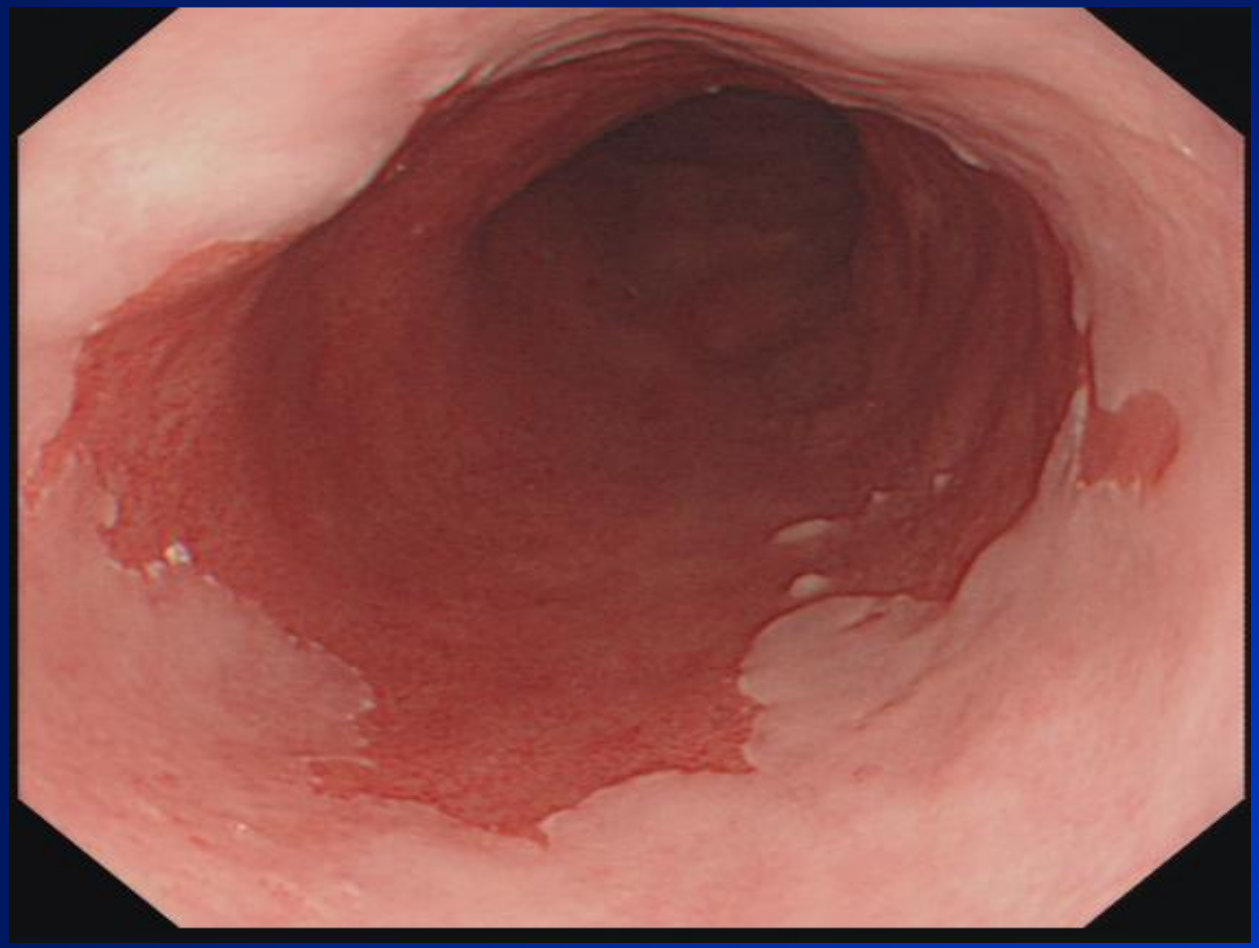
Prague C and M Criteria



Biopsy Regimen



BE Endoscopic Appearance



Narrow Band Imaging

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

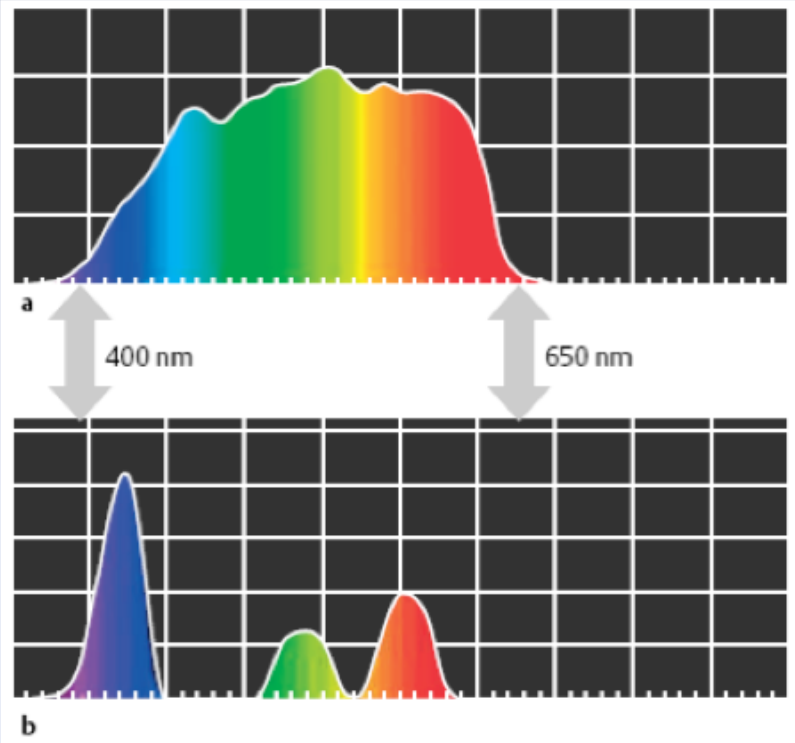
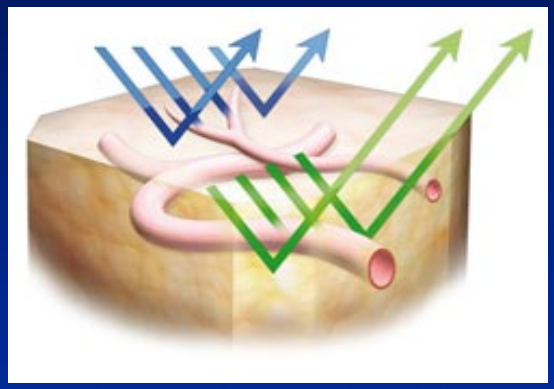
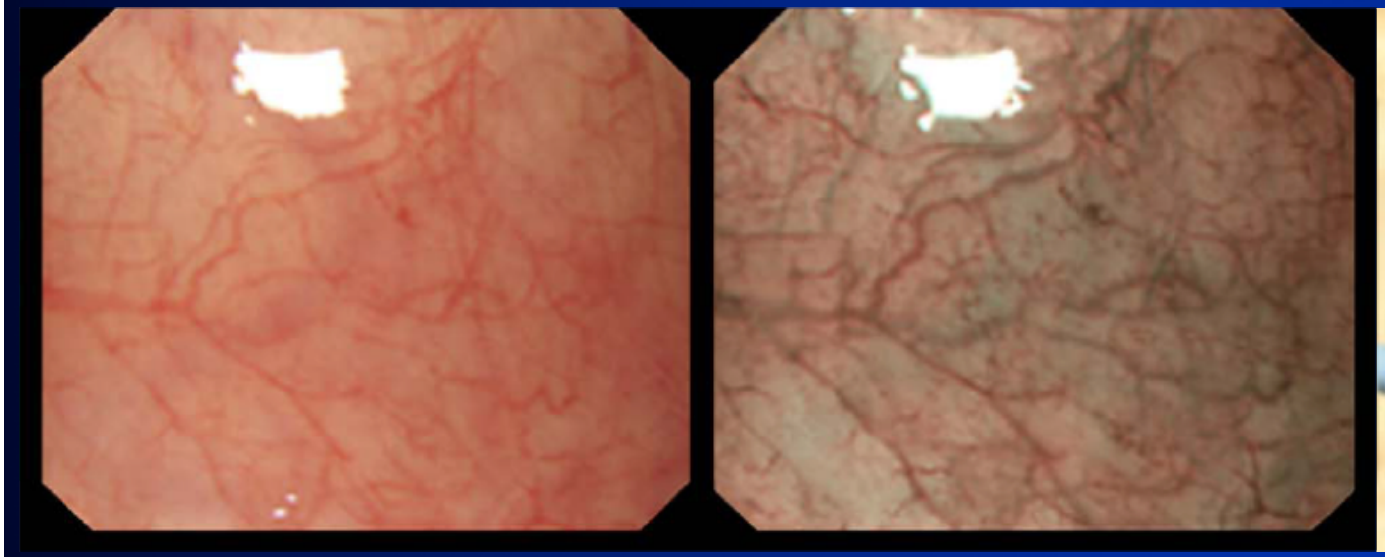


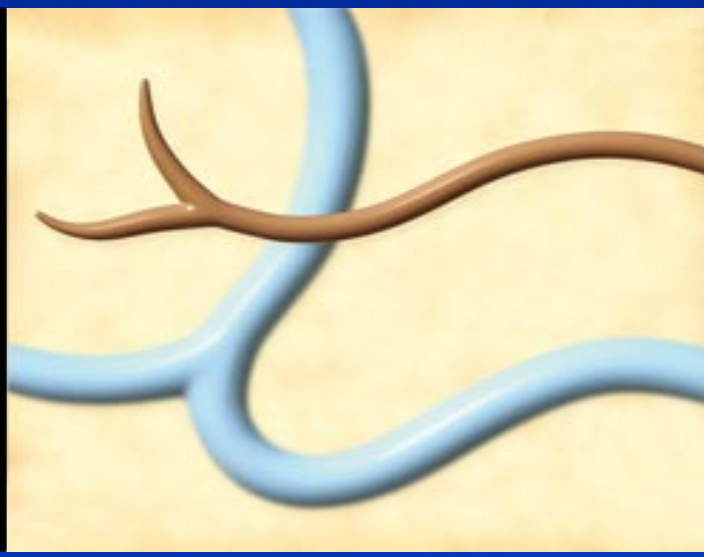
Figure 4 Reproduction of the radiance of the spectrum obtained with the broadband (**a**) or narrow-band (**b**) R/G/B interference filter, in the range 400 – 650 nm. The discontinuities in the radiance in image (**b**), with a higher value in the blue band, should be noted. Three filters were selected: for the B channel, a narrow band centered on 415 nm (width 30 nm), with an average penetration depth of 0.17 mm; for the G channel, a narrow band centered on 540 nm (width 20 nm), with an average penetration depth of 0.24 mm; and for the R channel, a narrow band centered on 600 nm (width 20 nm), with an average penetration depth of 0.28 mm. (Courtesy of Olympus Corporation, Japan.)

Narrow Band Imaging

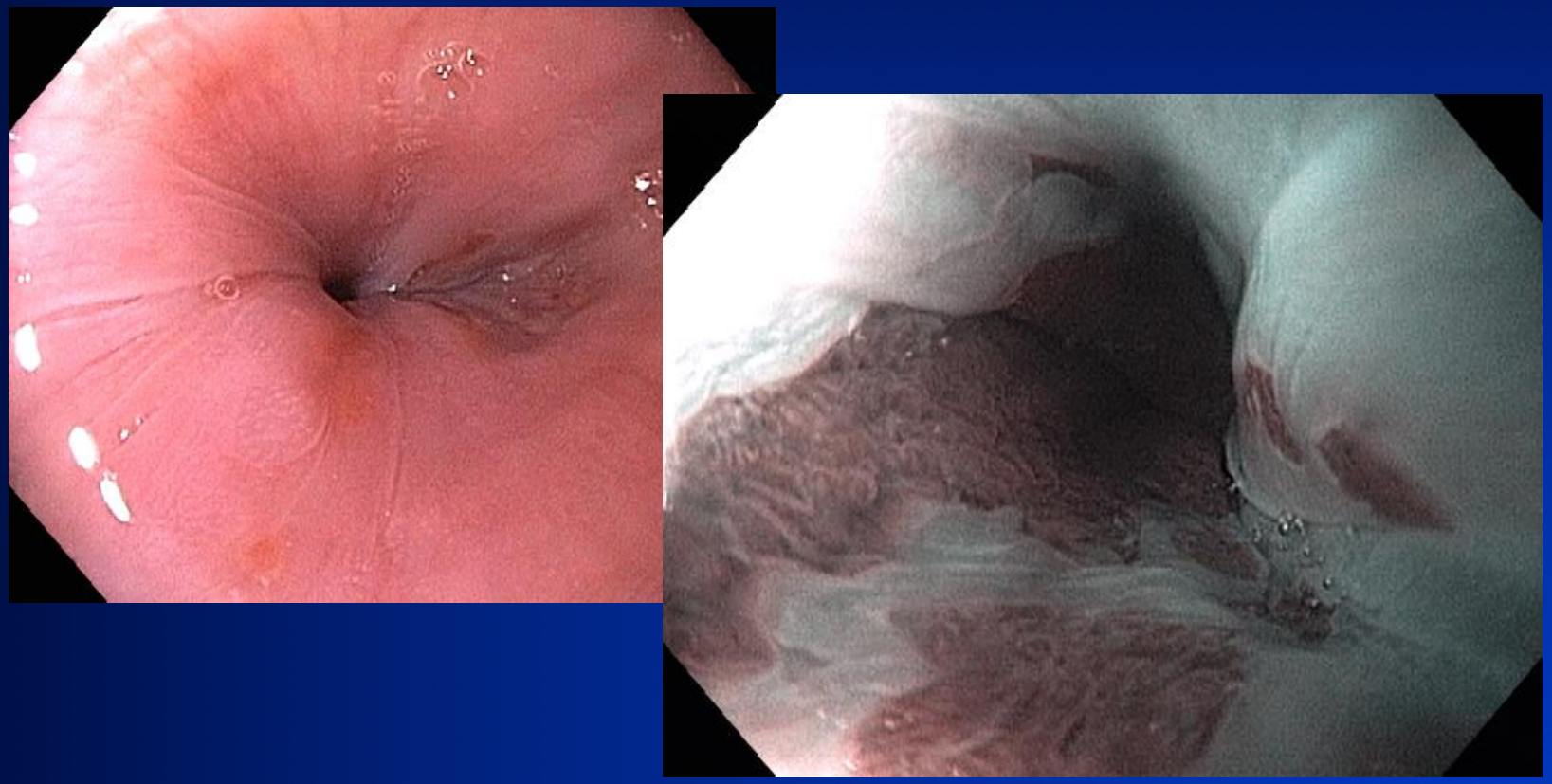
- NBI image on the monitor:
  Capillaries on the surface are displayed in brown and veins in the sub surface are displayed in cyan.







NBI for Detection of Barrett's Esophagus



NBI for Detecting Dysplasia within Barrett's

- Barrett's International NBI Group (BING)
- T
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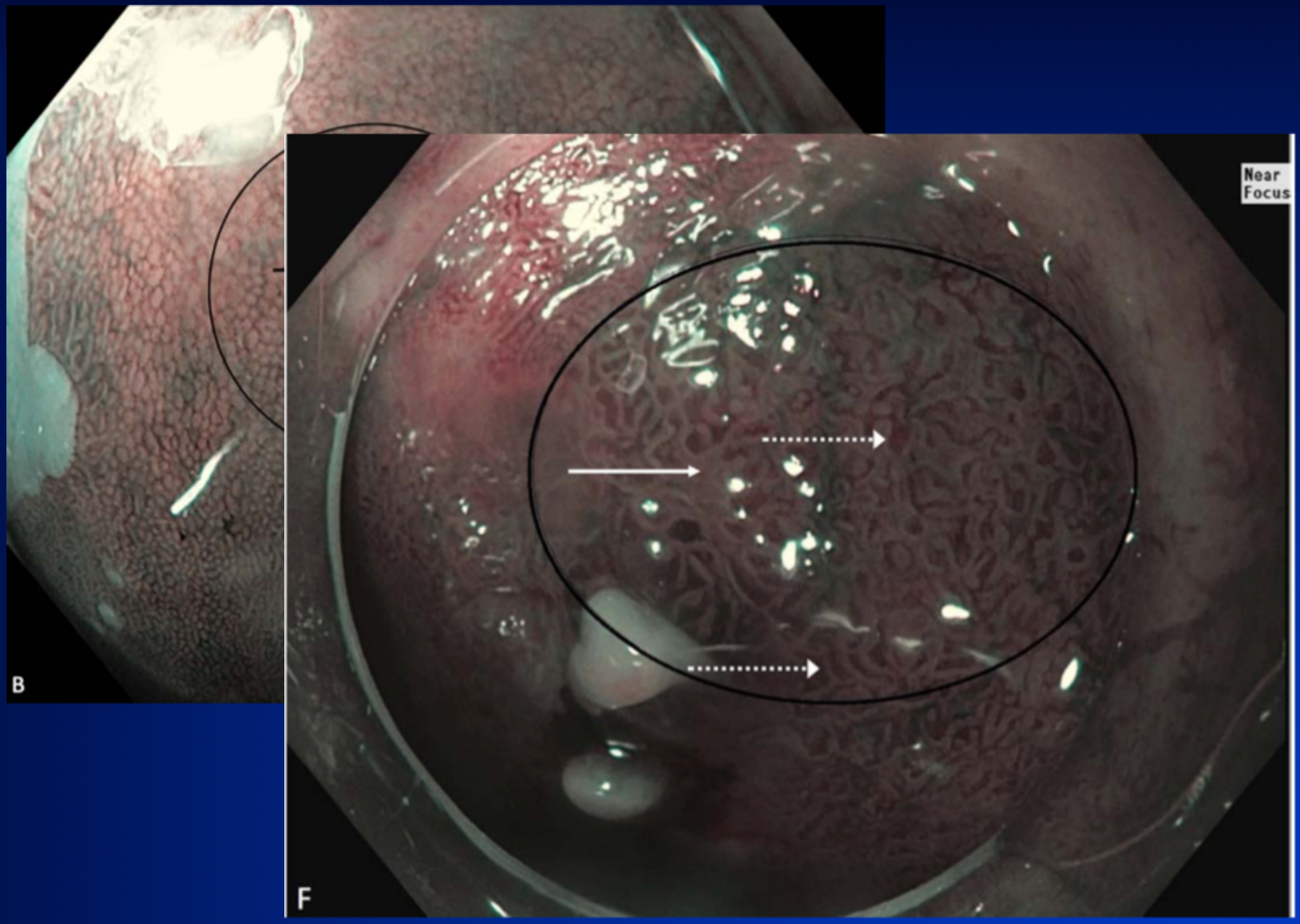
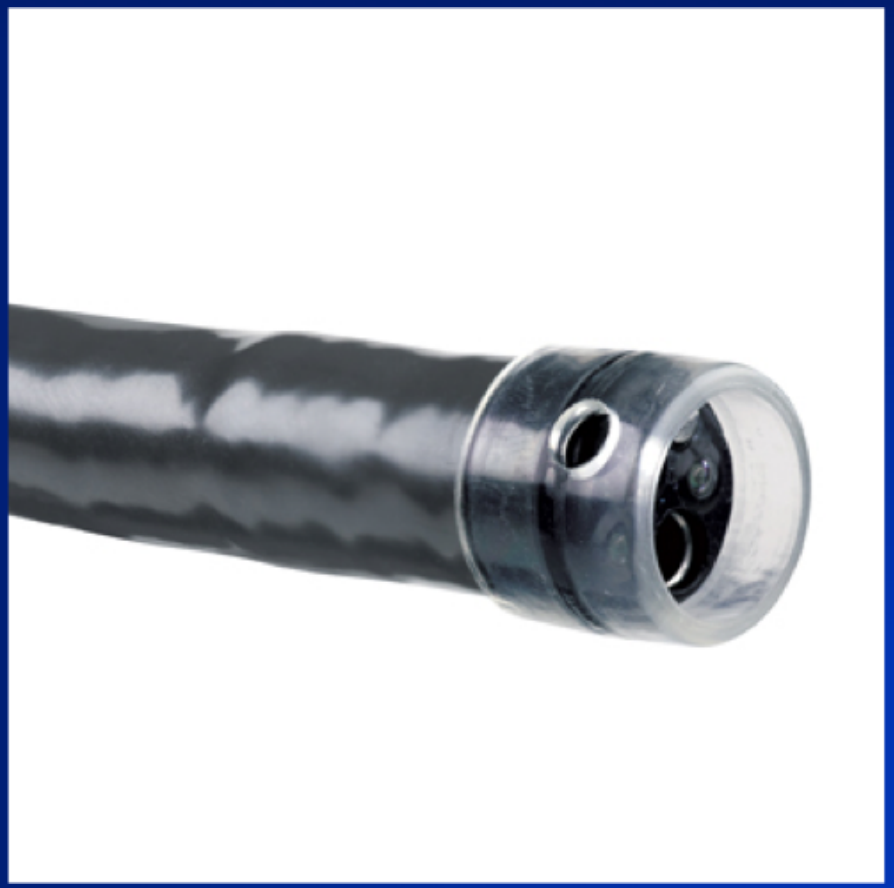
Morphologic Characteristics		Classification
Mucosal Pattern	Circular, Ridged, Villous, Tubular	Regular
	Absent or Irregular	Irregular
Vascular Pattern	Regularly situated along or between ridges Normal, long, branching patterns	Regular
	Focally or diffusely distributed vessels not following normal architecture	Irregular

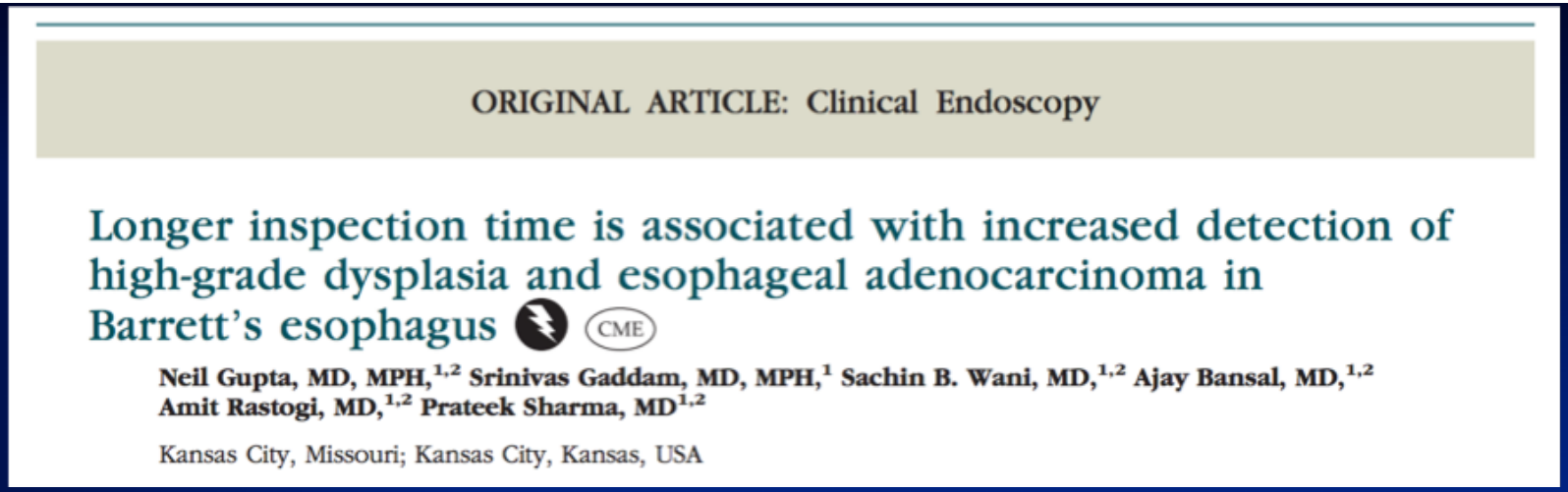
Sharma et al. Gastroenterology 2016;150:591–598



Sharma et al. Gastroenterology 2016;150:591–598

Distal Attachment Caps





ORIGINAL ARTICLE: Clinical Endoscopy

Longer inspection time is associated with increased detection of high-grade dysplasia and esophageal adenocarcinoma in Barrett's esophagus CME

Neil Gupta, MD, MPH,[1,2] Srinivas Gaddam, MD, MPH,[1] Sachin B. Wani, MD,[1,2] Ajay Bansal, MD,[1,2] Amit Rastogi, MD,[1,2] Prateek Sharma, MD[1,2]

Kansas City, Missouri; Kansas City, Kansas, USA

- 112 patients underwent endoscopic surveillance by 11 endoscopists.
- Patients with longer BITs were more likely to have an endoscopically suspicious lesion (P <.001)
- Direct correlation between the endoscopist's mean BIT per centimeter of BE and the detection of patients with HGD/EAC

Gastrointest Endosc 2012;76:531-8.

ORIGINAL ARTICLE: Clinical Endoscopy

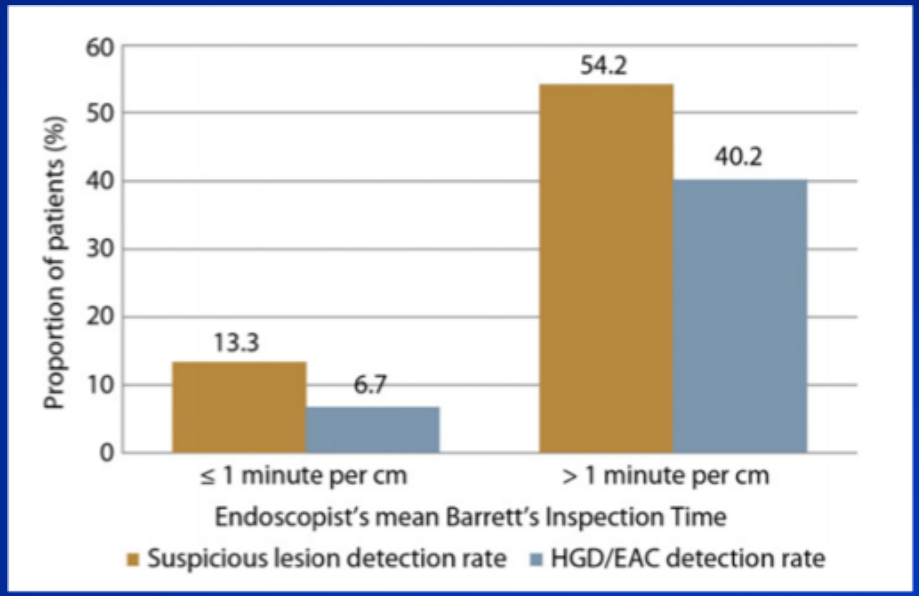
Longer inspection time is associated with increased detection of high-grade dysplasia and esophageal adenocarcinoma in Barrett's esophagus

CME

Neil Gupta, MD, MPH,[1,2] Srinivas Gaddam, MD, MPH,[1] Sachin B. Wani, MD,[1,2] Ajay Bansal, MD,[1,2] Amit Rastogi, MD,[1,2] Prateek Sharma, MD[1,2]

Kansas City, Missouri; Kansas City, Kansas, USA

- Endoscopists who had an average BIT longer than 1 minute per centimeter of BE detected more patients with endoscopically suspicious lesions (54.2% vs 13.3%, p .04)



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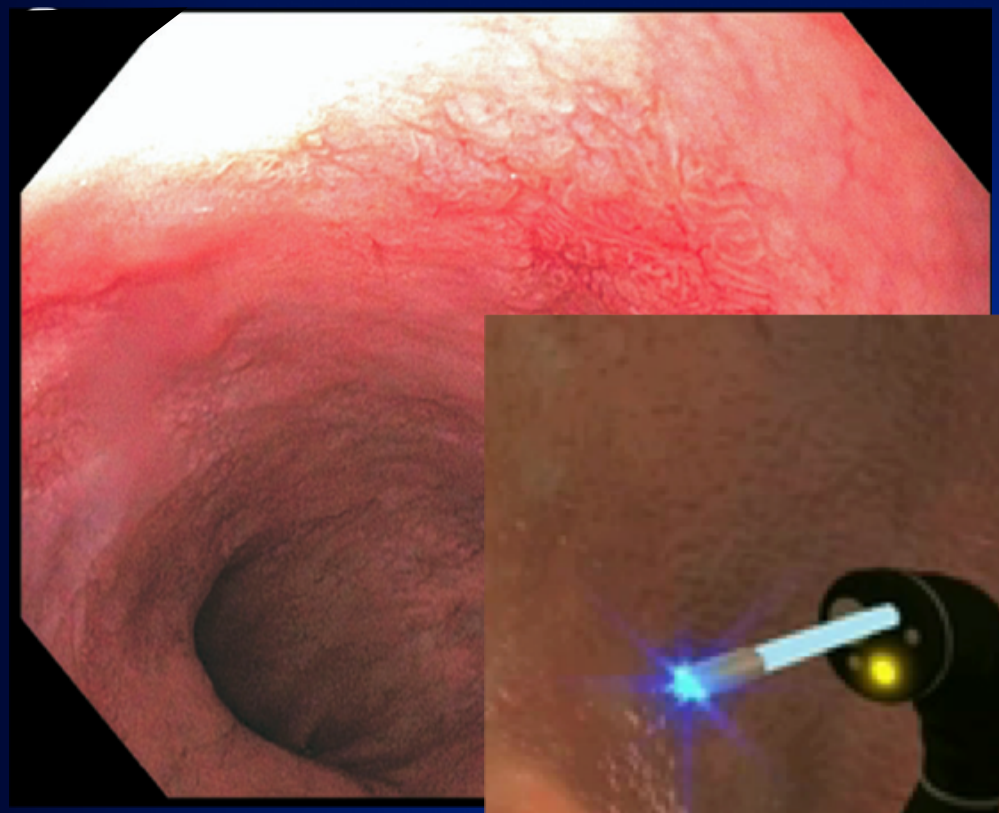
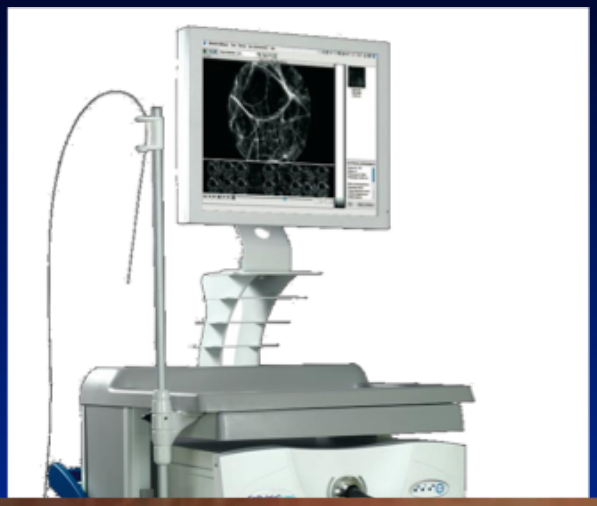
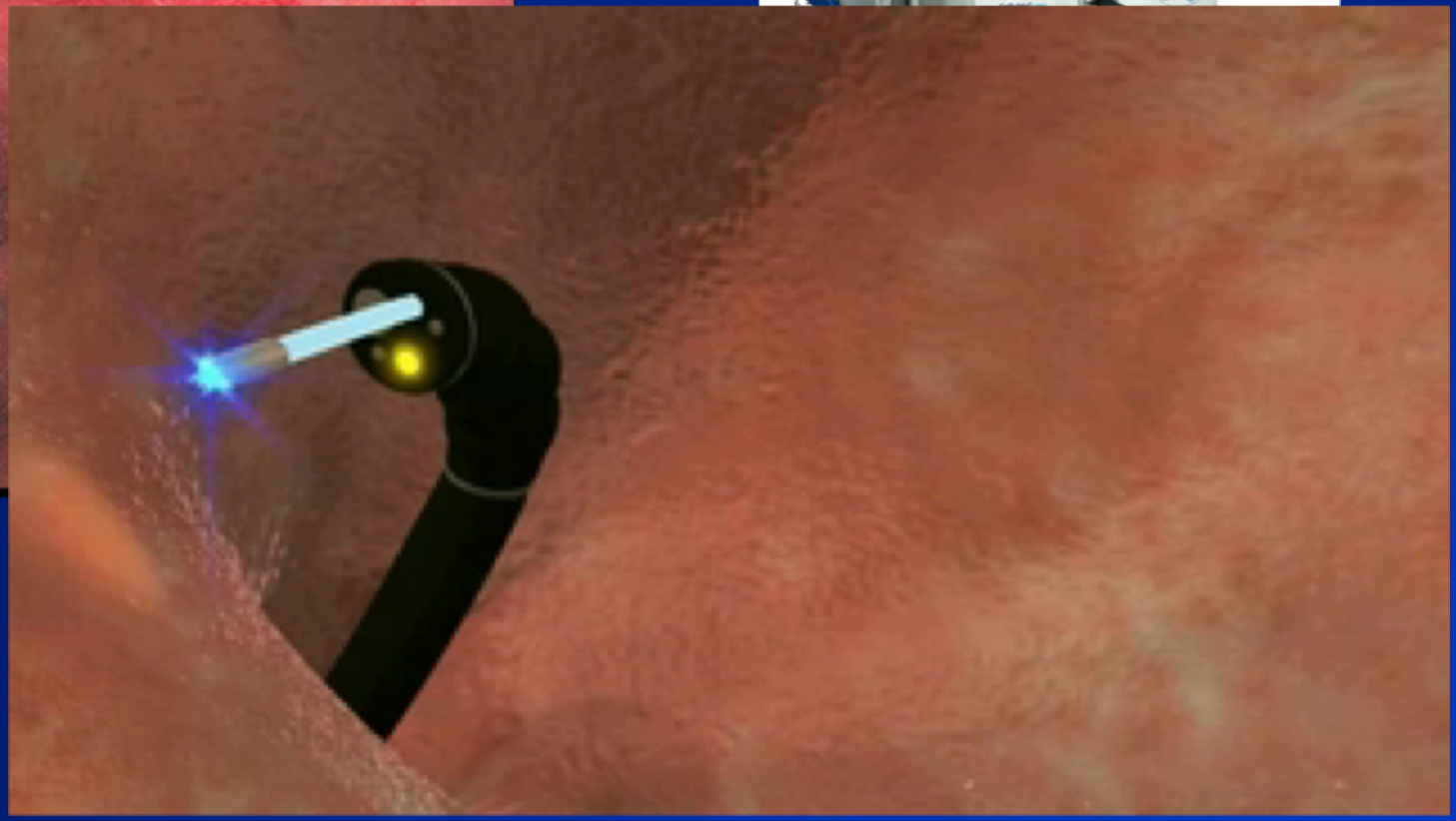
Endomicroscopy



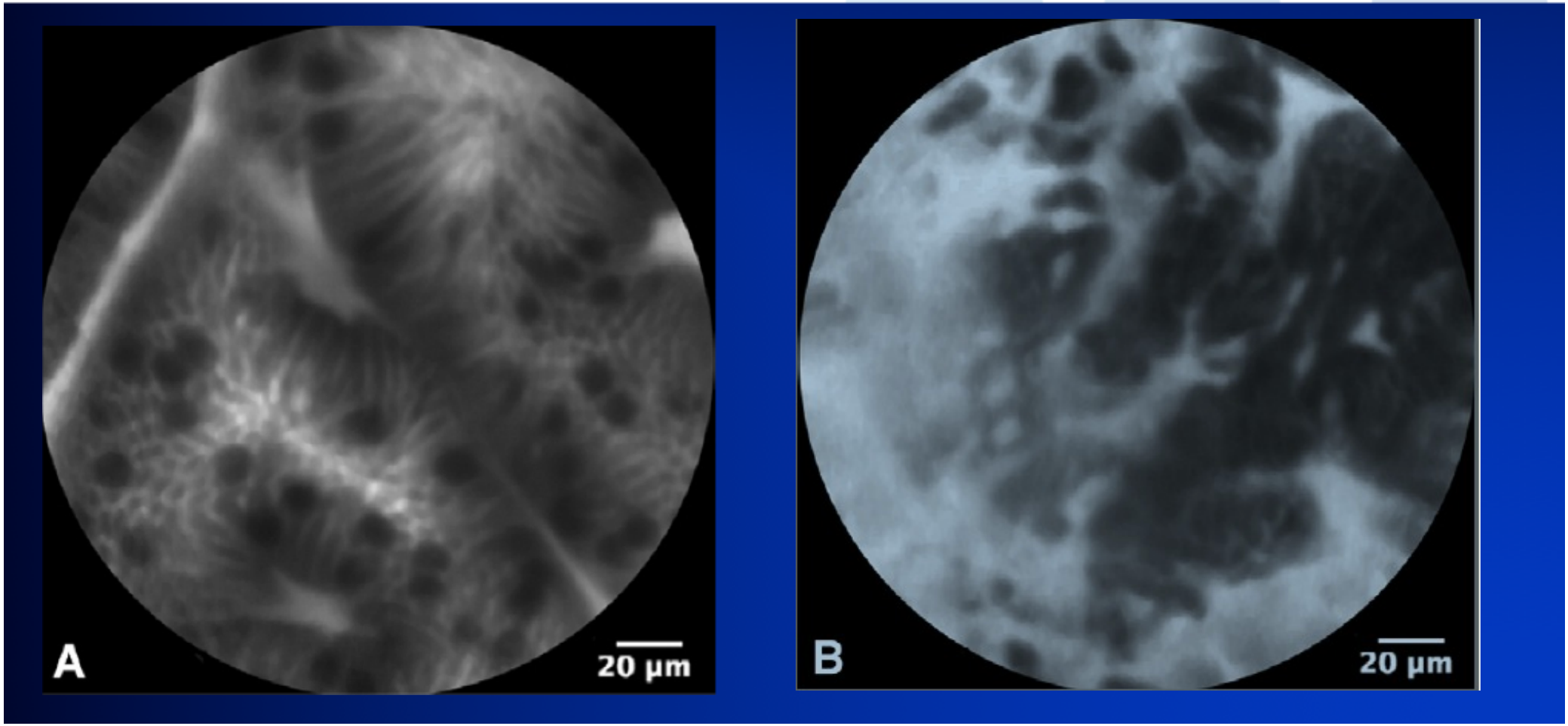




Real-time increased detection of neoplastic tissue in Barrett's esophagus with pCLE: final results of an international multicenter, prospective, randomized, controlled trial

P. Sharma, A. Meining, E. Coron, C. Lightdale, H. Wolfsen, A. Bansal, M. Bajbouj, J.-P. Galmiche, J. Abrams, A. Rastogi, N. Gupta, J. Michalek, G. Lauwers, M. Wallace

GASTROINTESTINAL ENDOSCOPY Vol. 74, Issue 3, Sep 2011, Pages 465-472



DONT BIOPCE TRIAL

Real-time increased detection of neoplastic tissue in Barrett's esophagus with pCLE: final results of an international multicenter, prospective, randomized, controlled trial

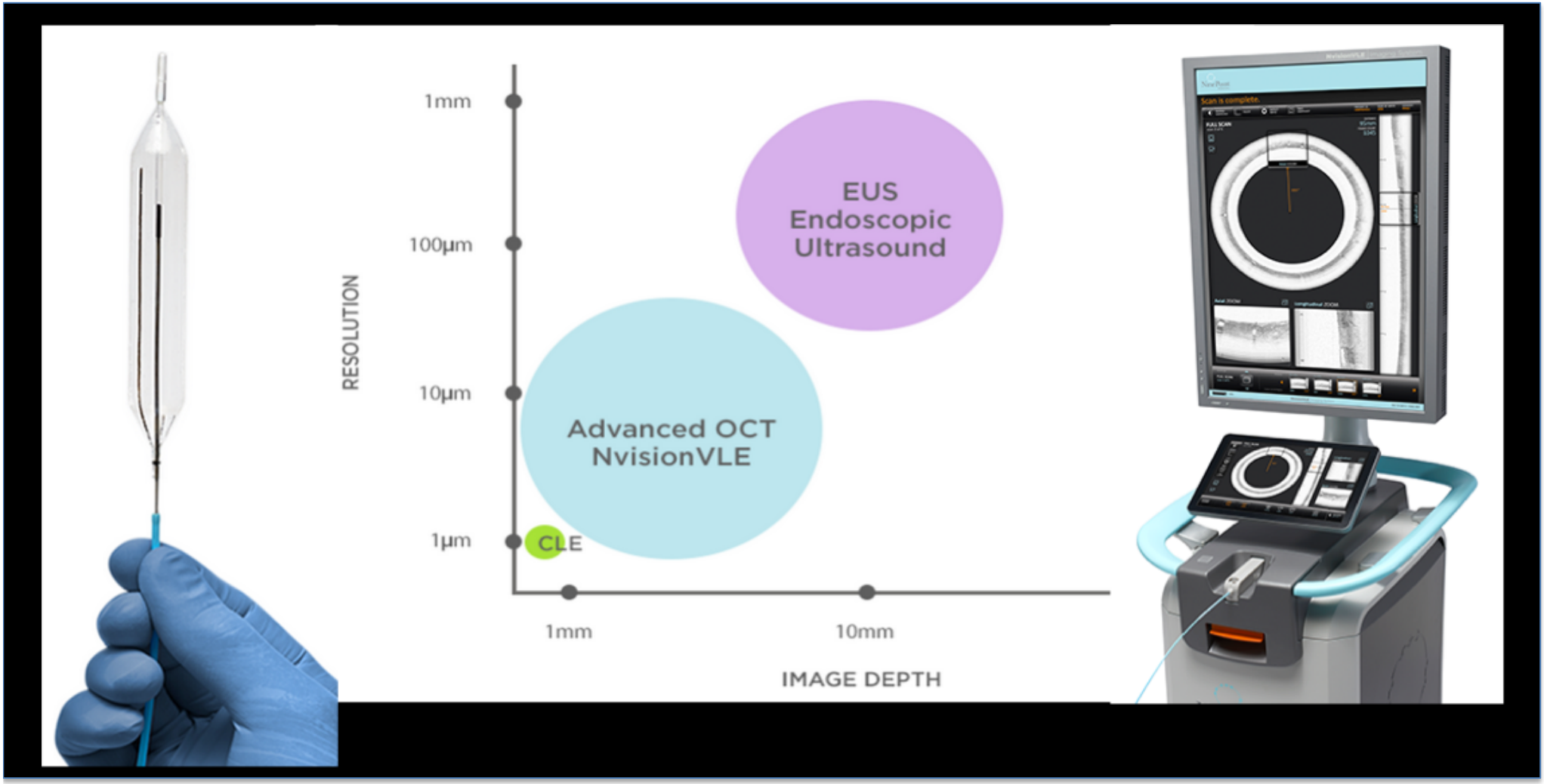
P. Sharma, A. Meining, E. Coron, C. Lightdale, H. Wolfsen, A. Bansal, M. Bajbouj, J.-P. Galmiche, J. Abrams, A. Rastogi, N. Gupta, J. Michalek, G. Lauwers, M. Wallace

GASTROINTESTINAL ENDOSCOPY Vol. 74, Issue 3, Sep 2011, Pages 465-472

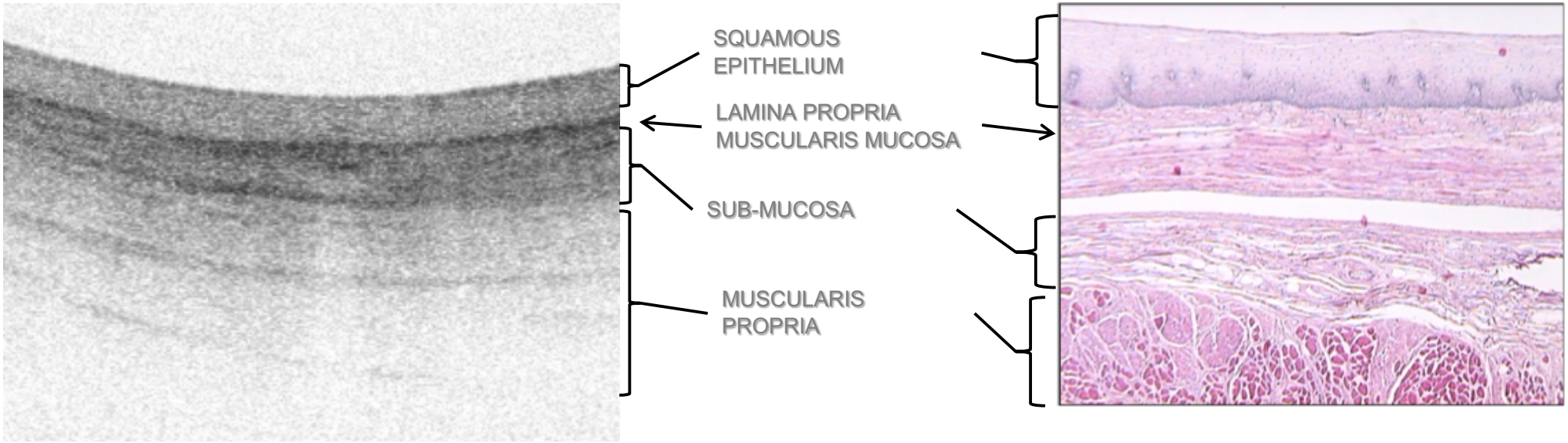
- Multicenter international trial (5 centers)
- Prospective, double blinded trial: WLE, NBI, pCLE
- 101 patients - 874 locations

Negative Predictive Value of 94% for HGD/EC

Volumetric Laser Endomicroscopy



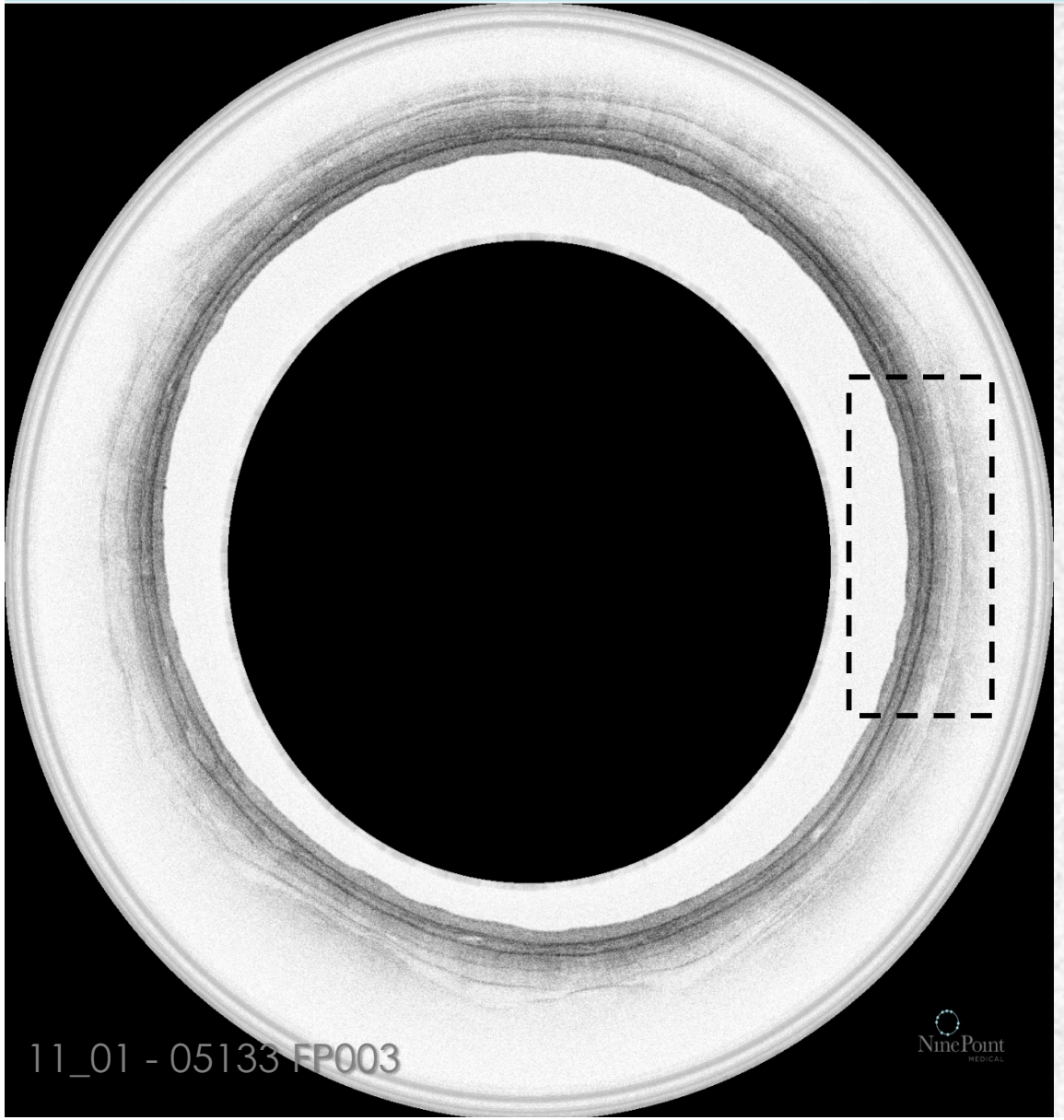
Normal Esophageal Mucosa*

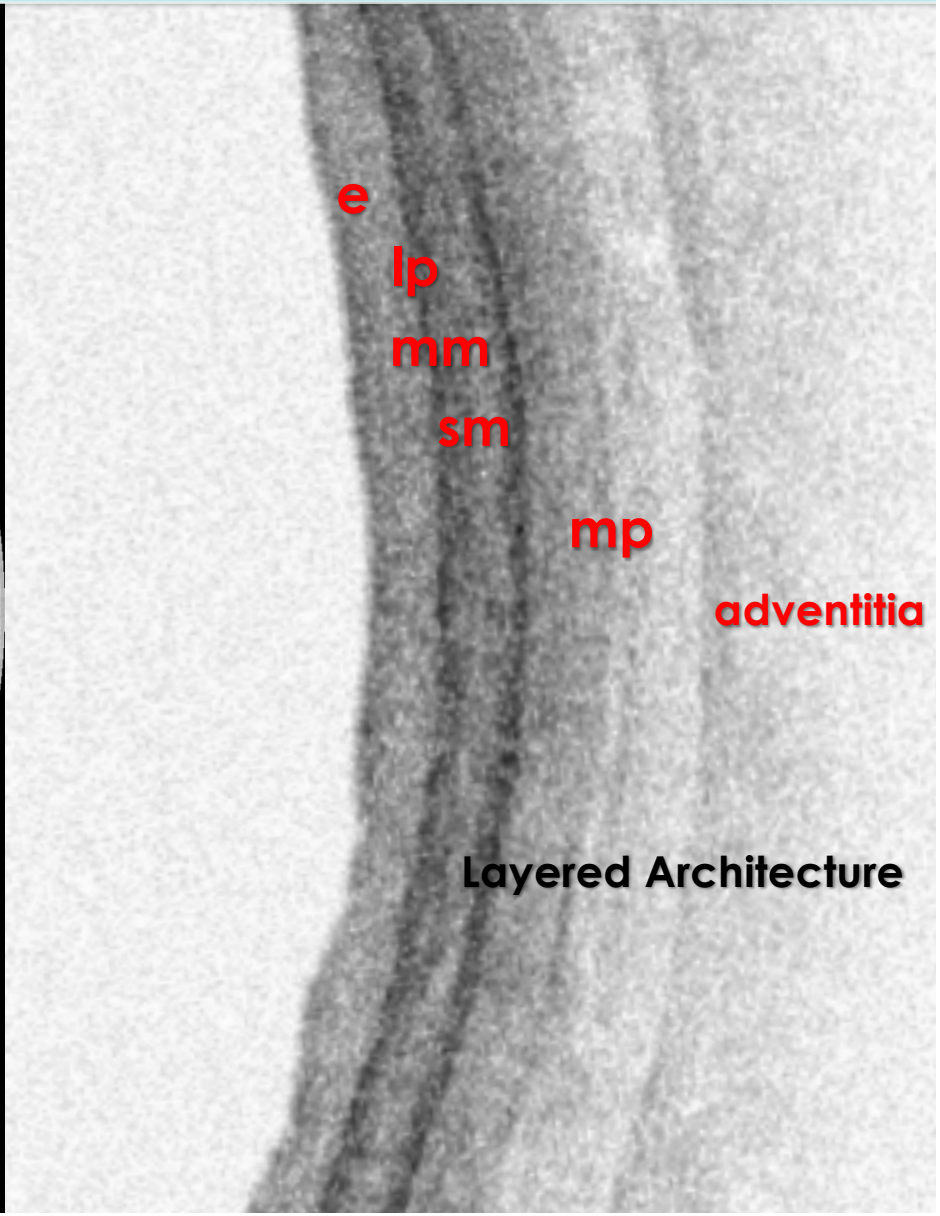


* Images are not of the same patient

Normal

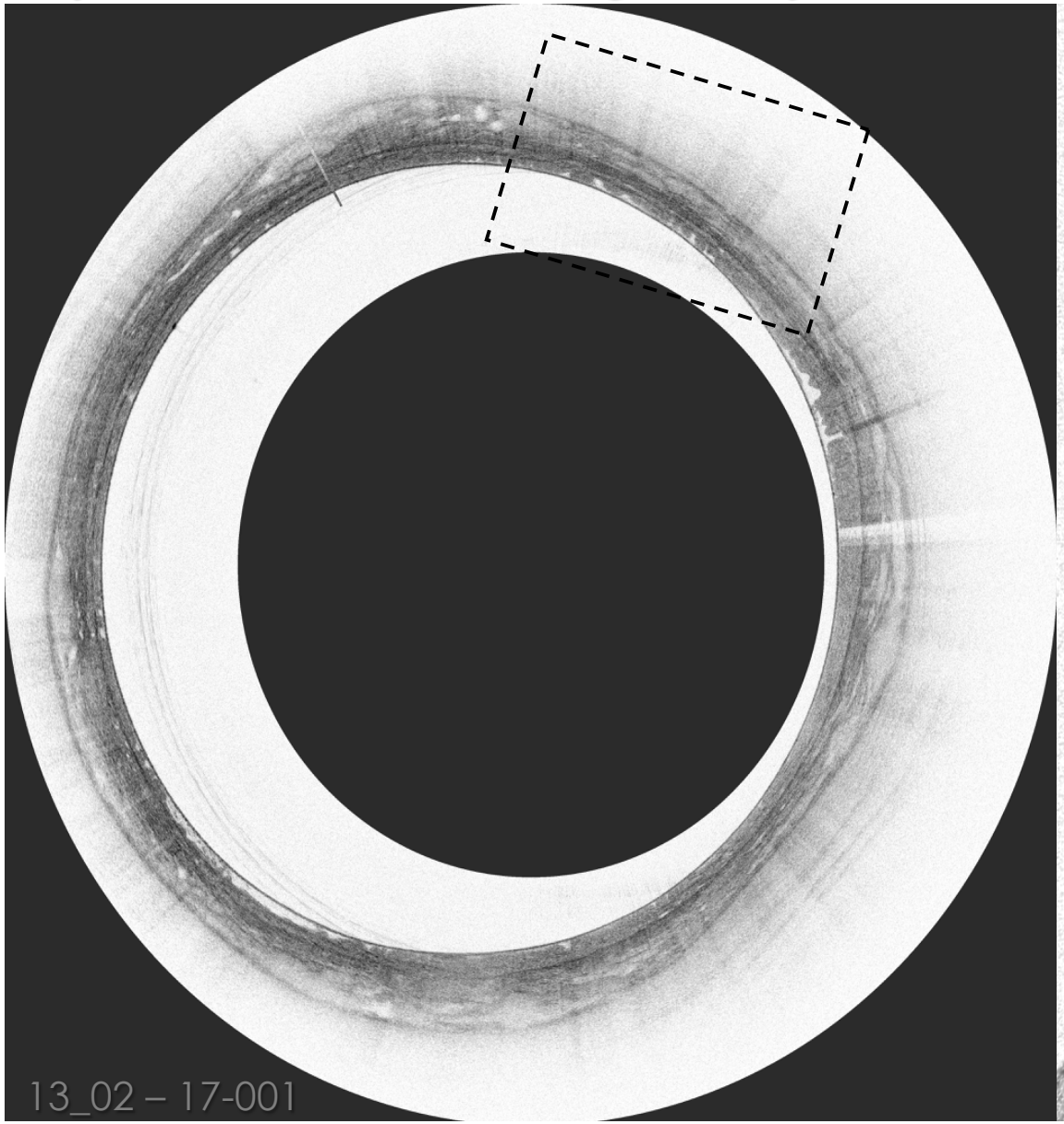
Esophageal Mucosa





Abnormal

Layered Architecture w/ Irregular Surface



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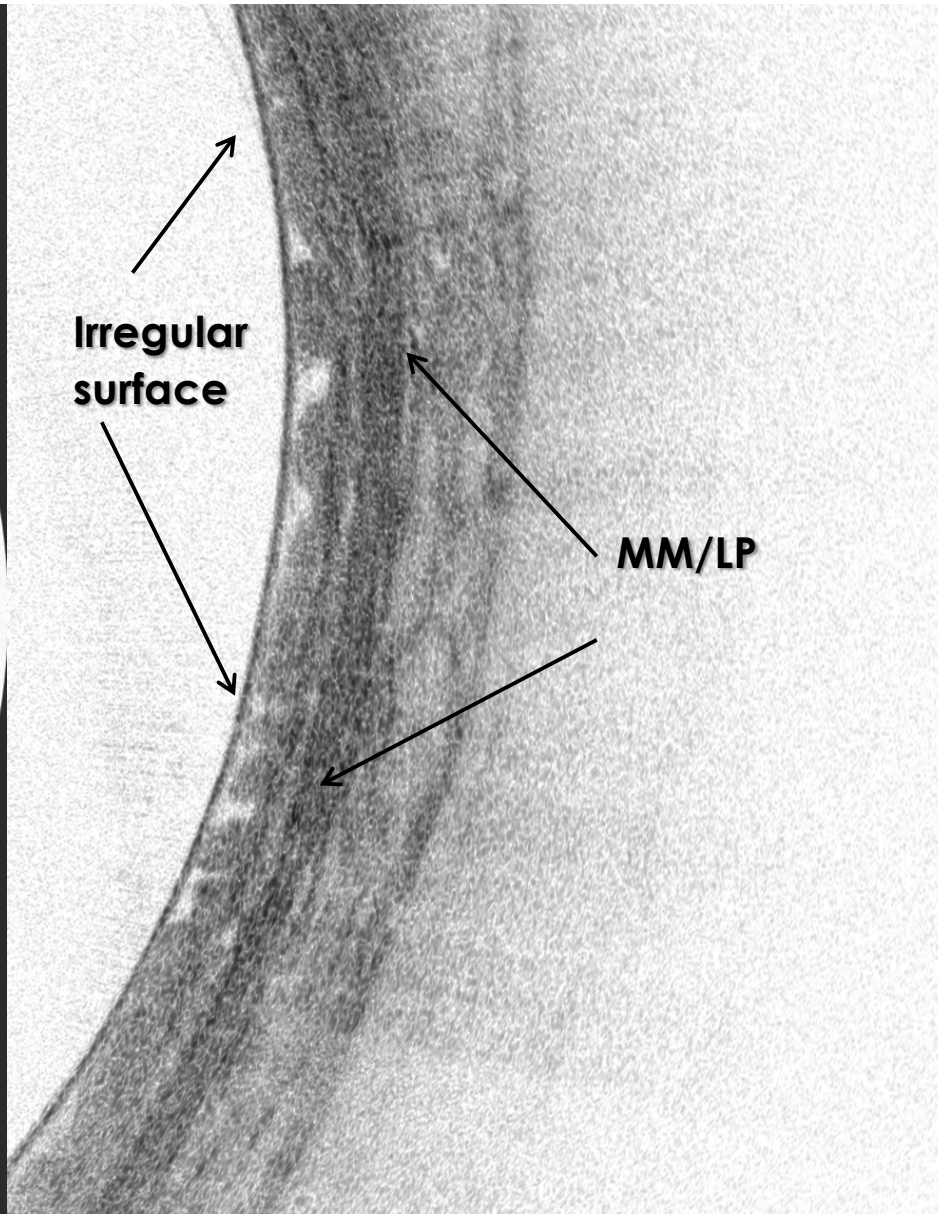
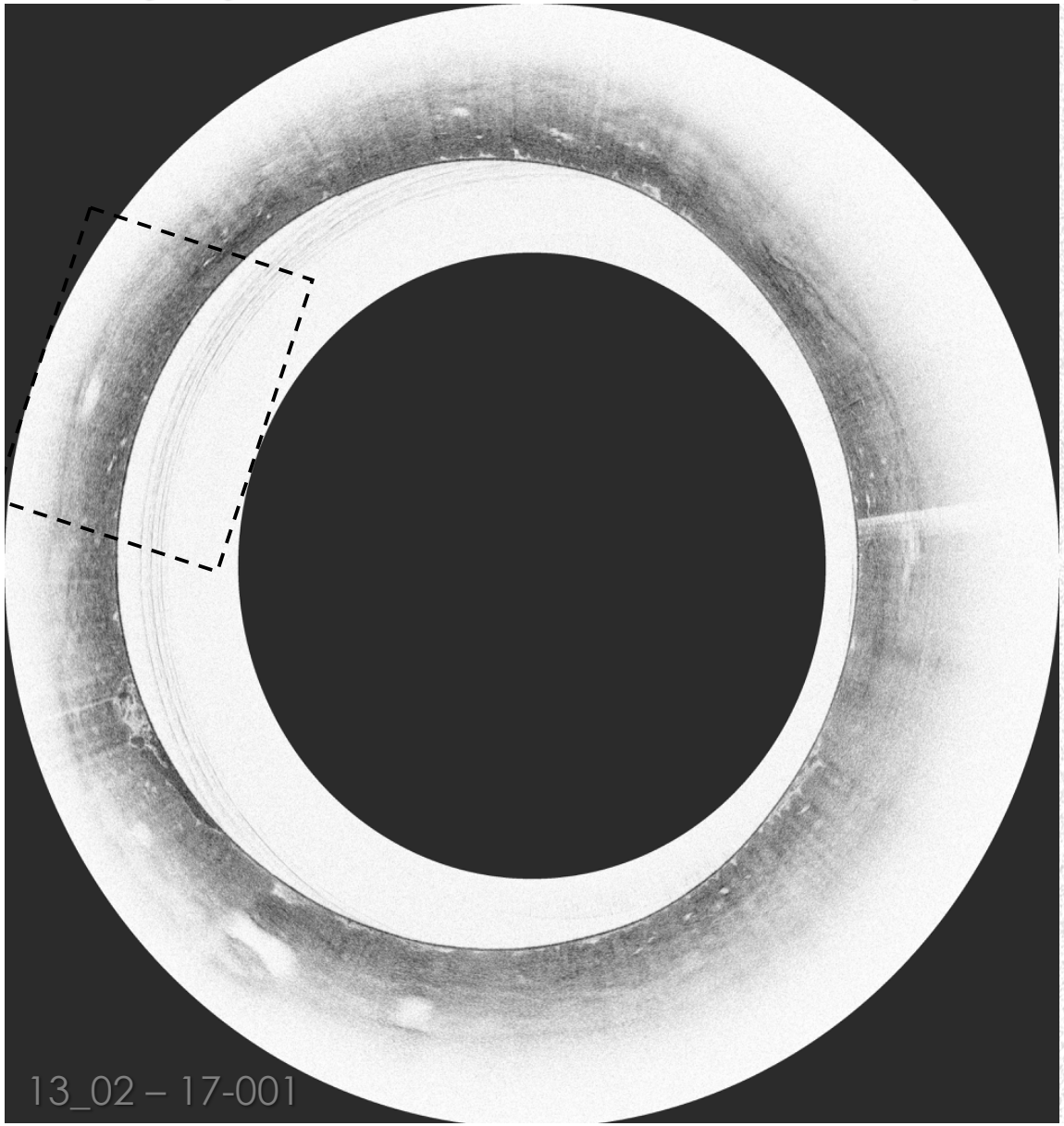


Abnormal

Loss of Layered Architecture w/ Glands in Epithelium



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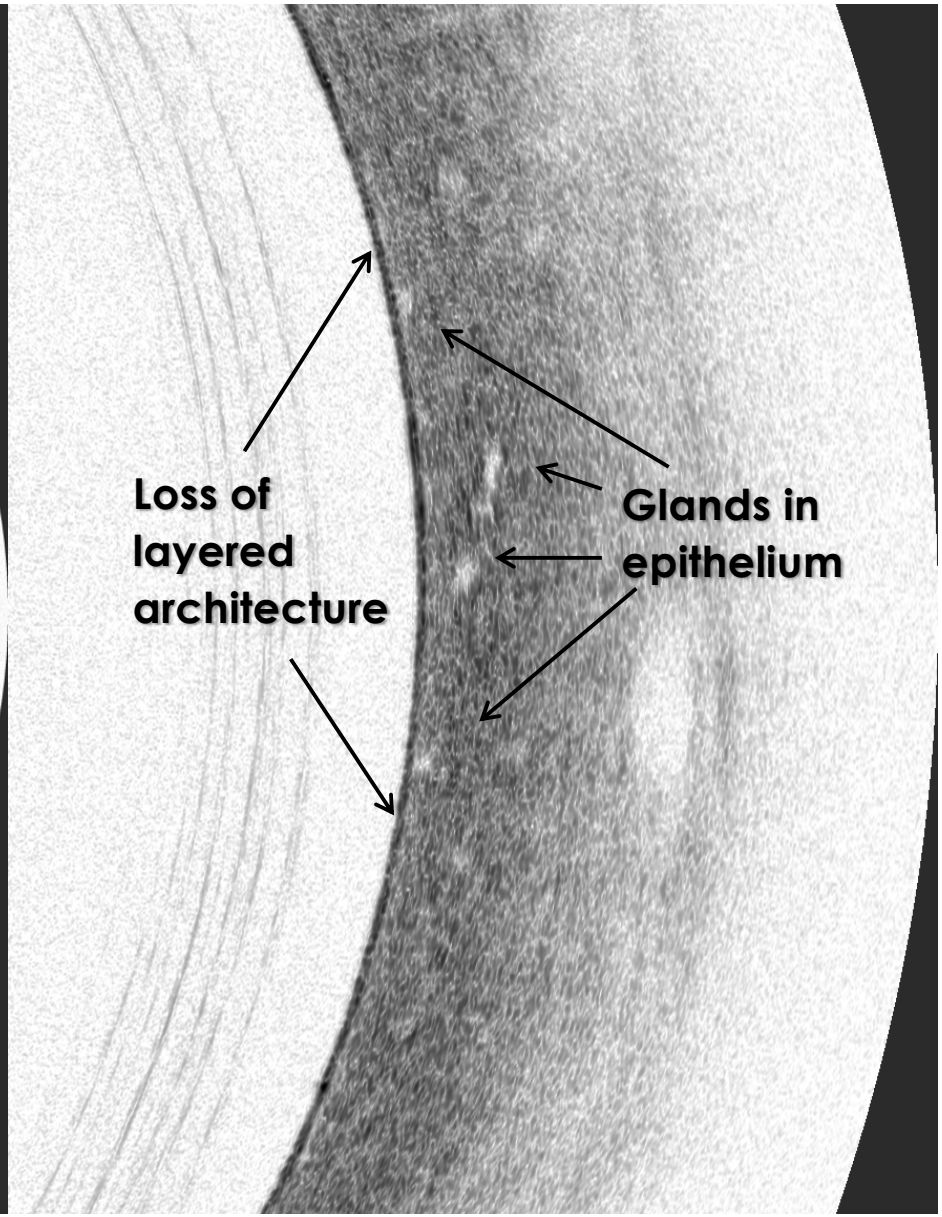
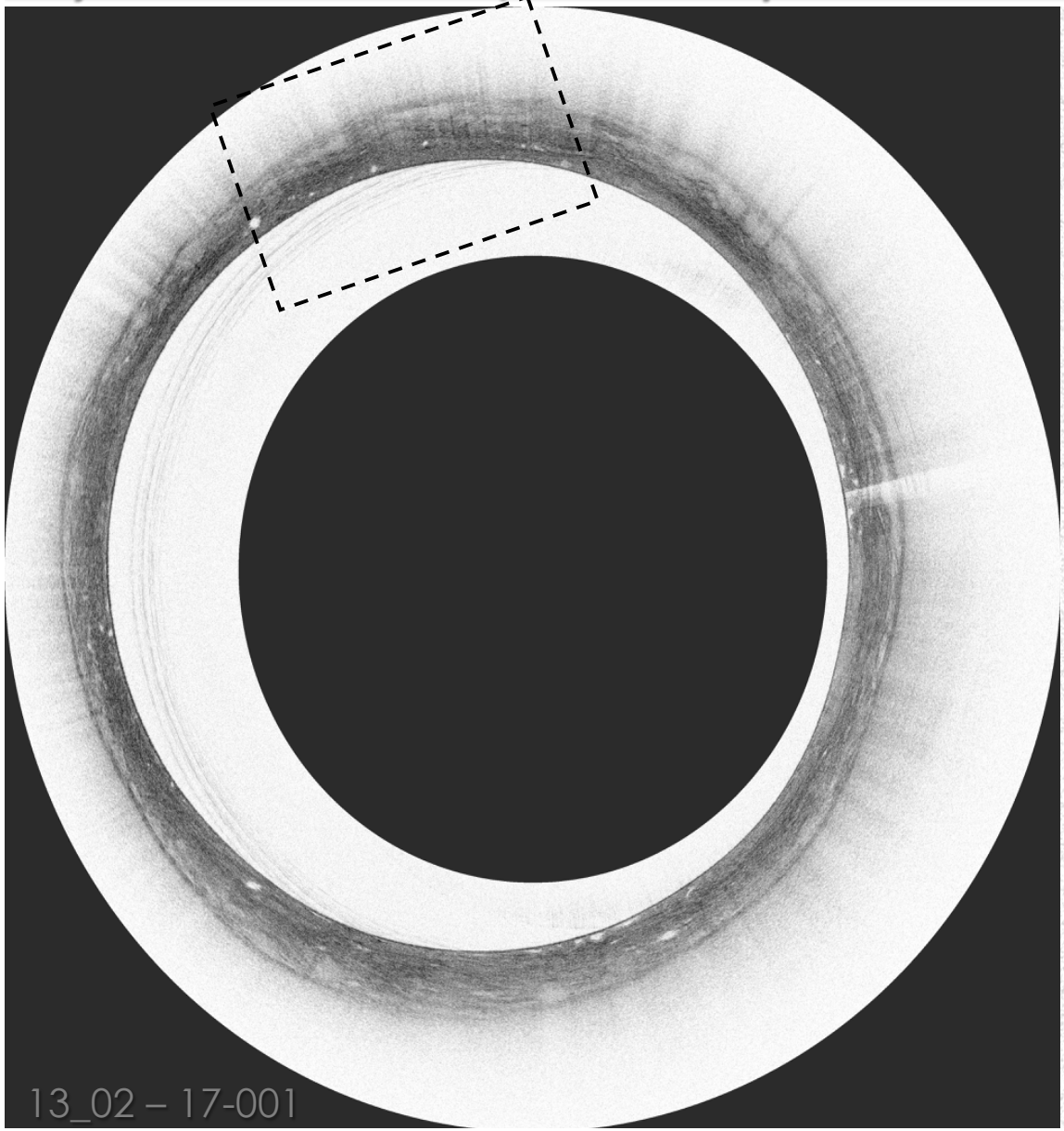
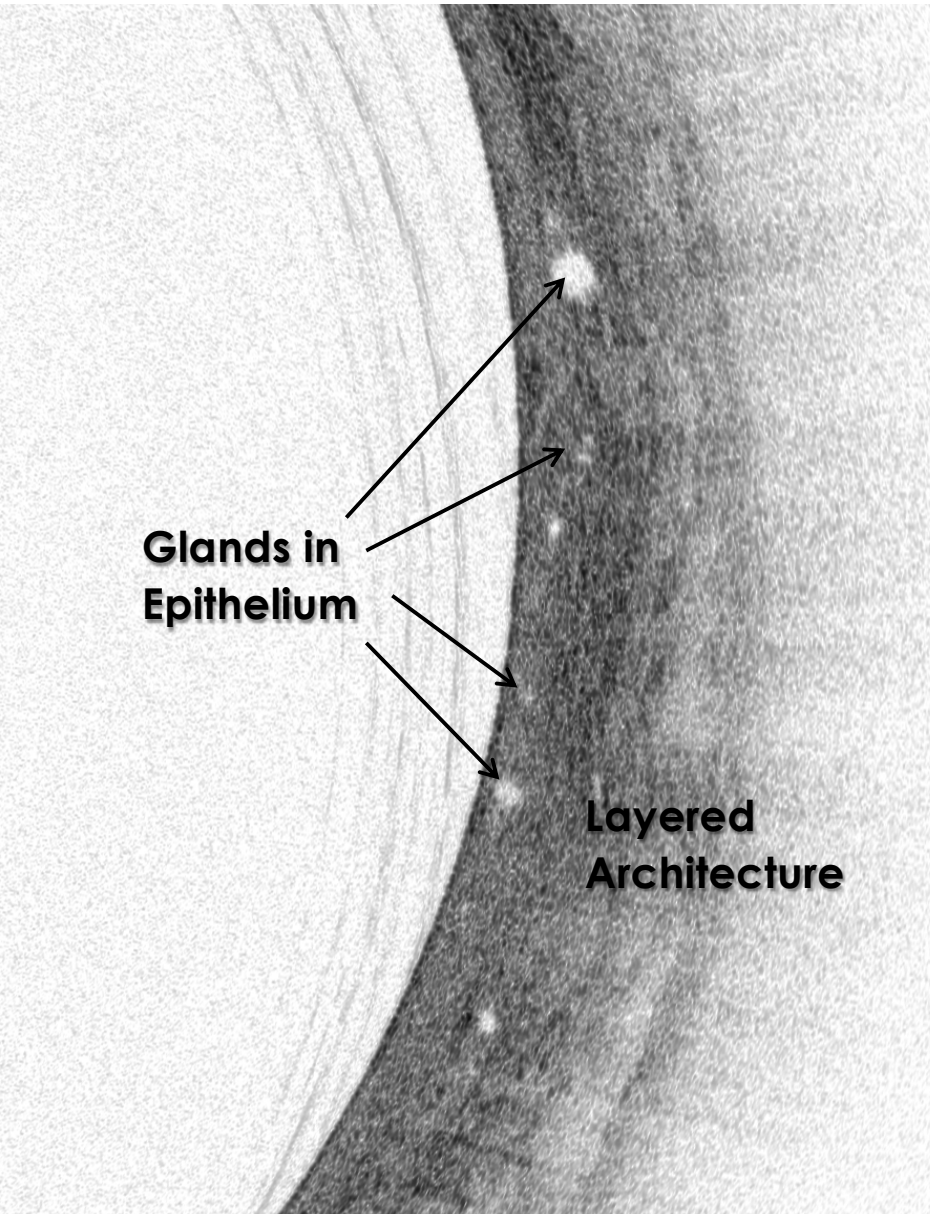


Abnormal

Layered Architecture w/ Glands in Epithelium

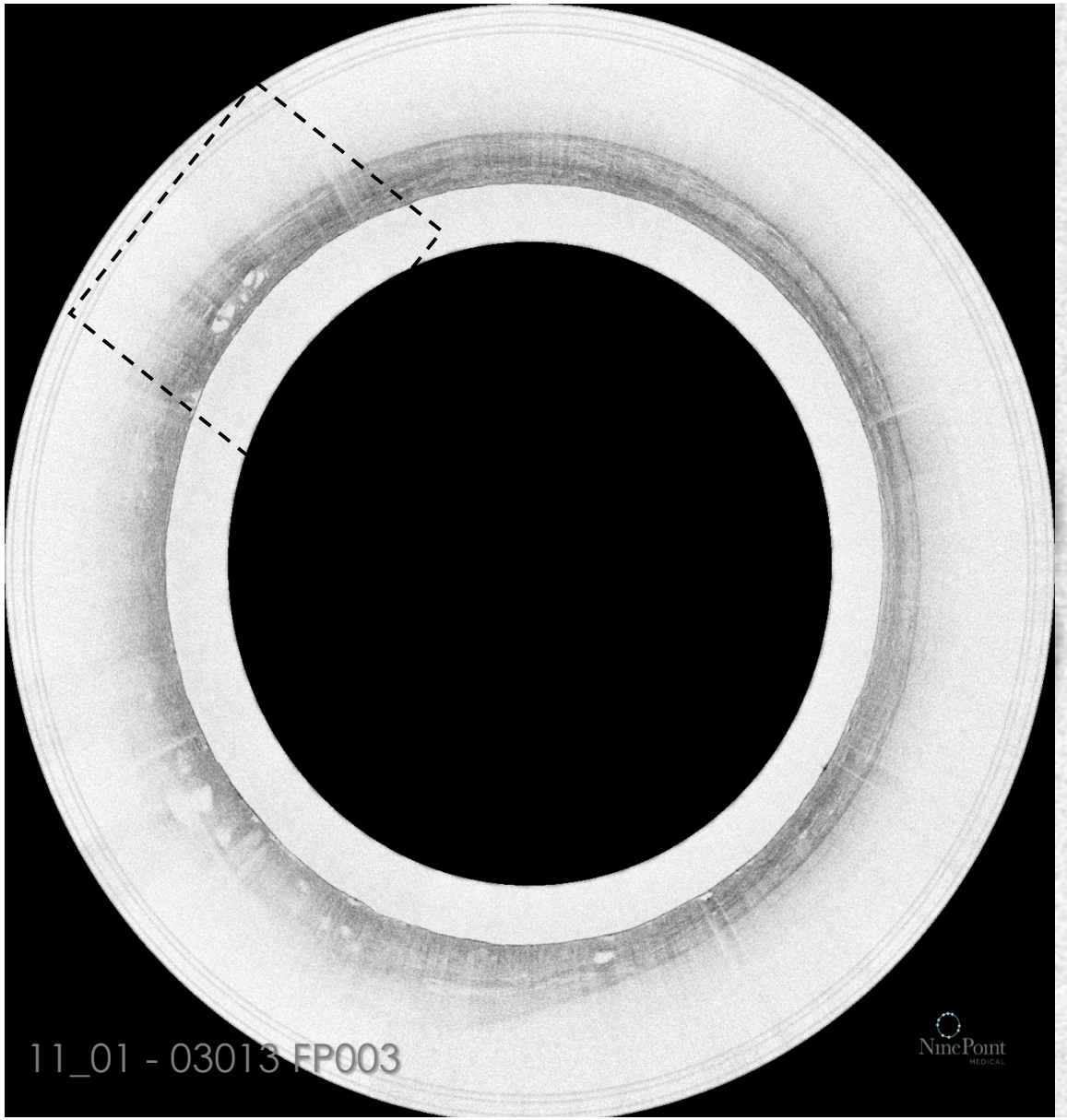


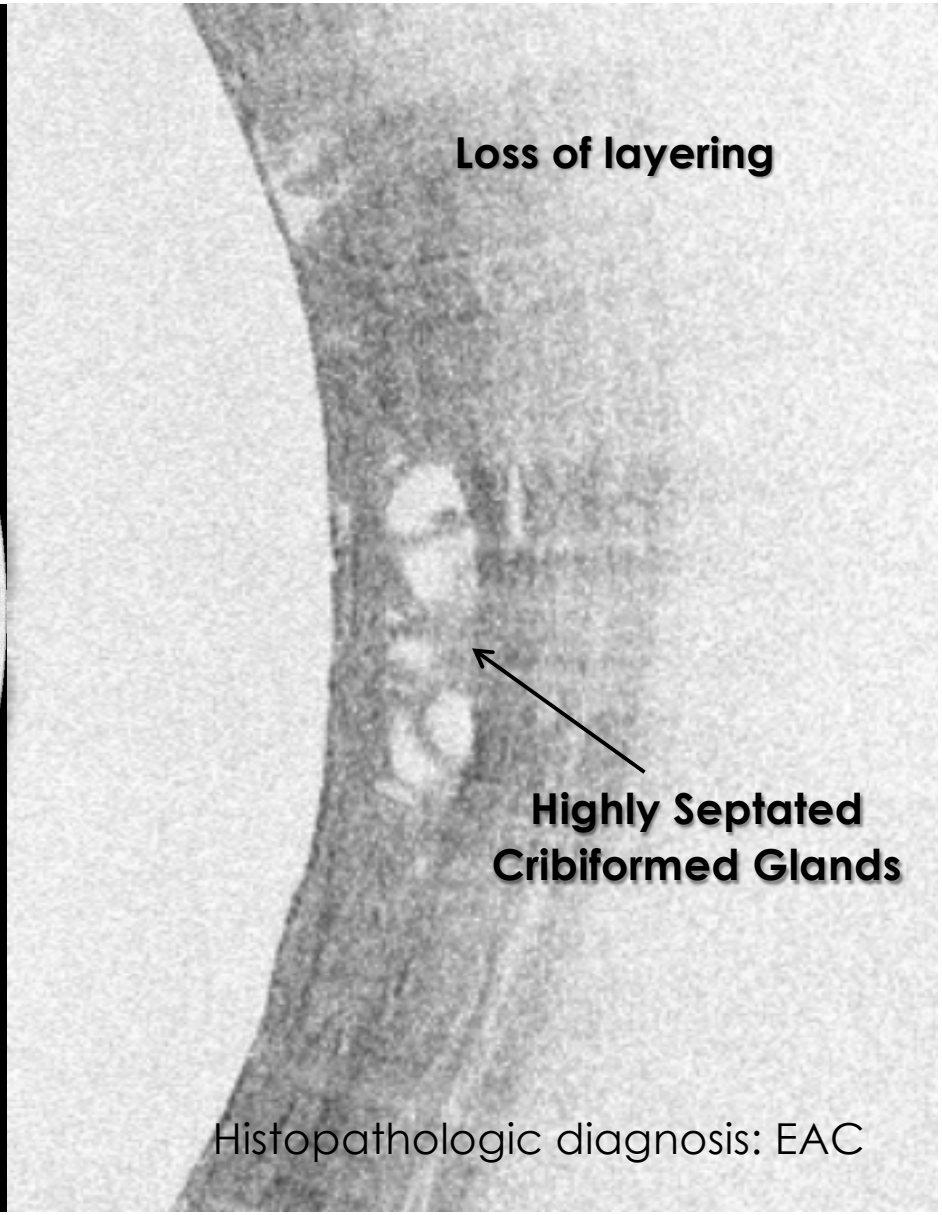
13_02 – 17-001



Abnormal

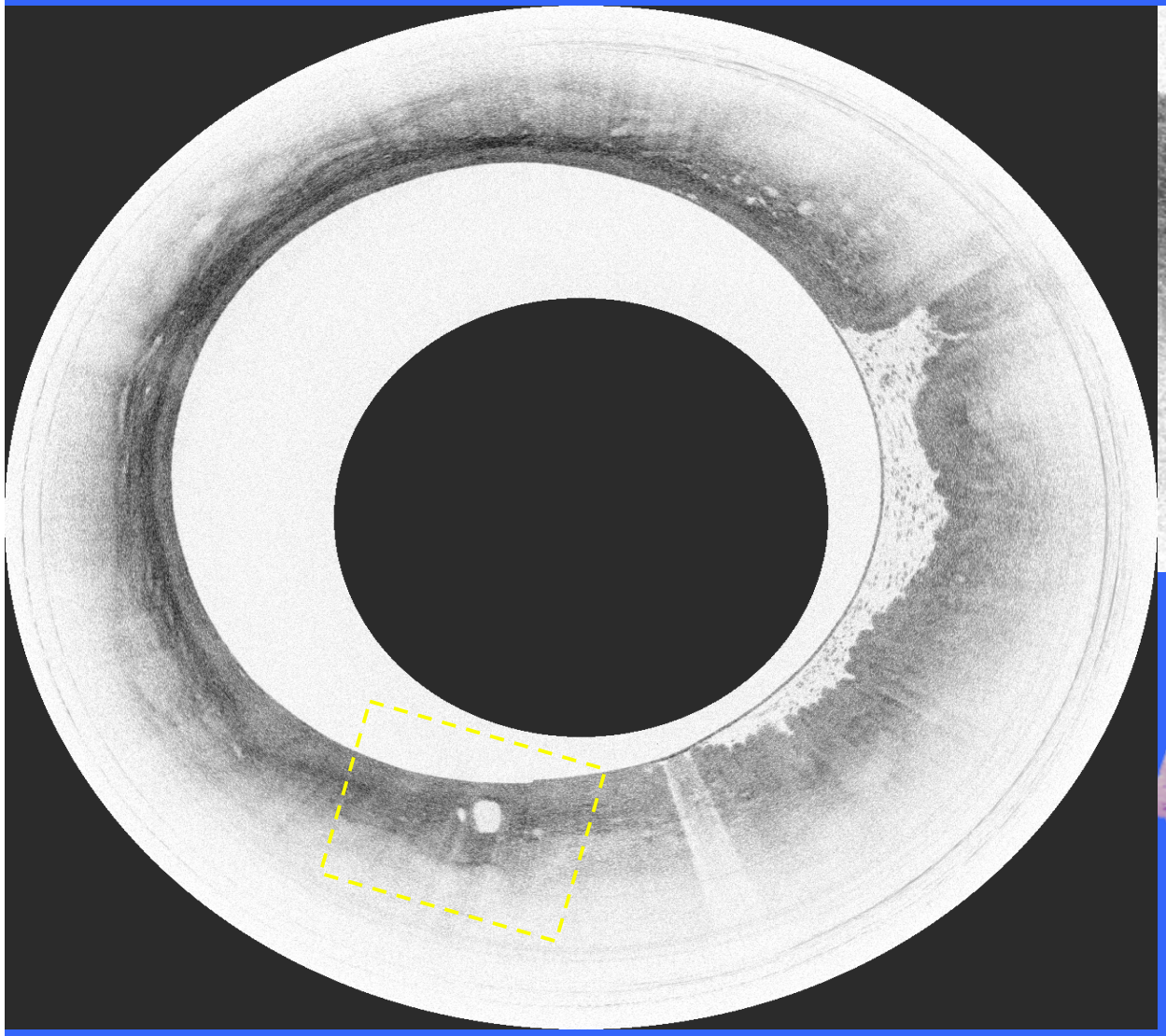
Atypical Glands

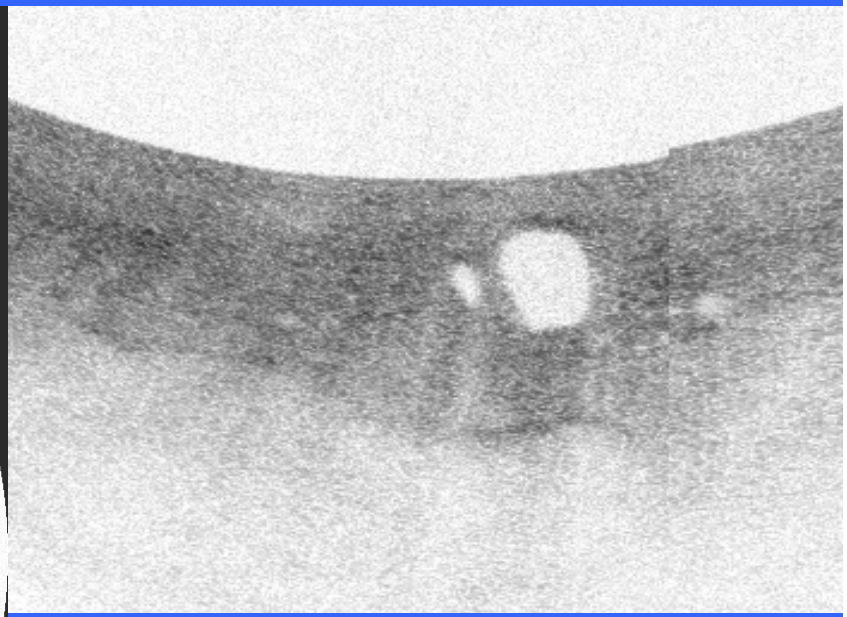


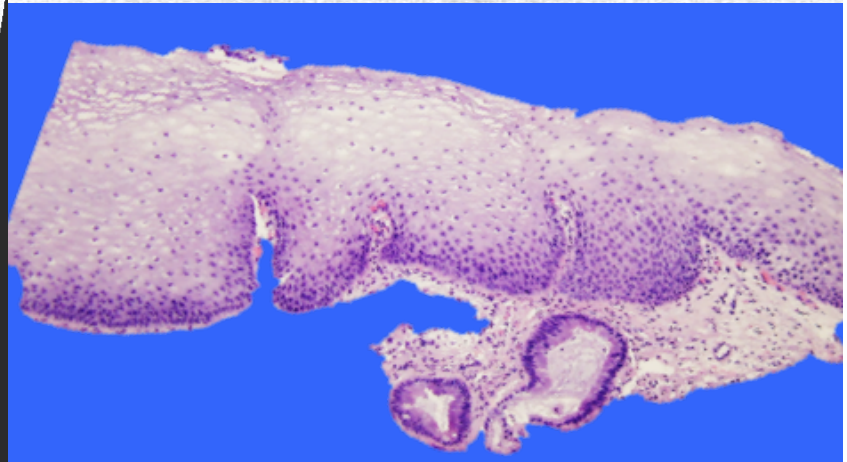


Histopathologic diagnosis: EAC

Buried BE







Courtesy of K. Chang, MD. UC Irvine Medical Center

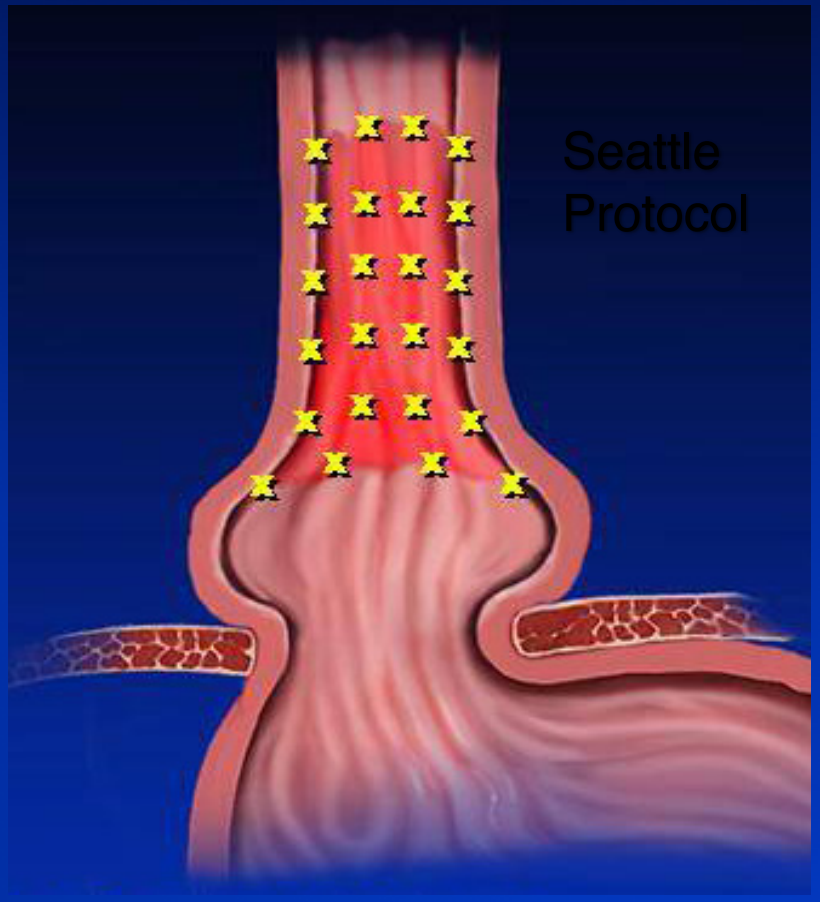
Endoscopic Surveillance

Endoscopic Surveillance in Patients With Barrett's Esophagus

We suggest that endoscopic surveillance be performed in patients with Barrett's esophagus (weak recommendation, moderate-quality evidence).

We suggest the following surveillance intervals (weak recommendation, low-quality evidence):

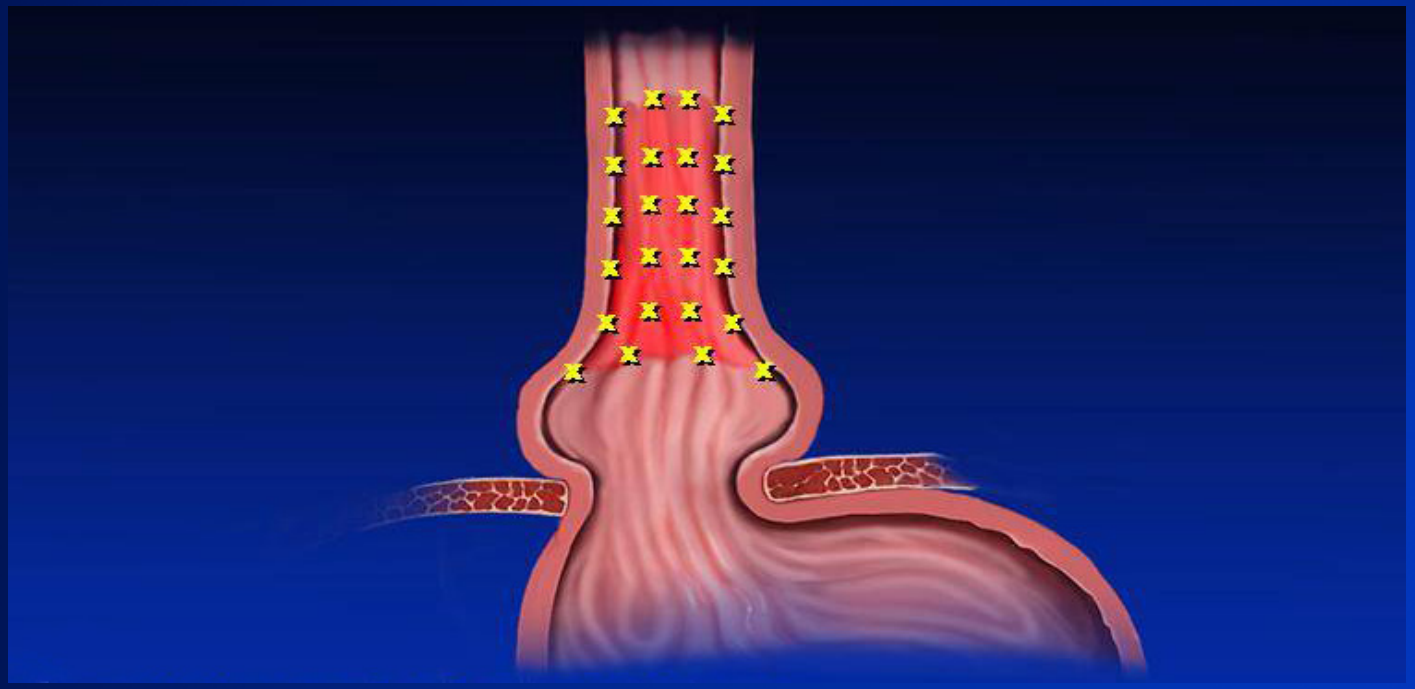
- No dysplasia: 3–5 years
- Low-grade dysplasia: 6–12 months
- High-grade dysplasia in the absence of eradication therapy: 3 months.



GASTROENTEROLOGY 2011;140:1084 –1091

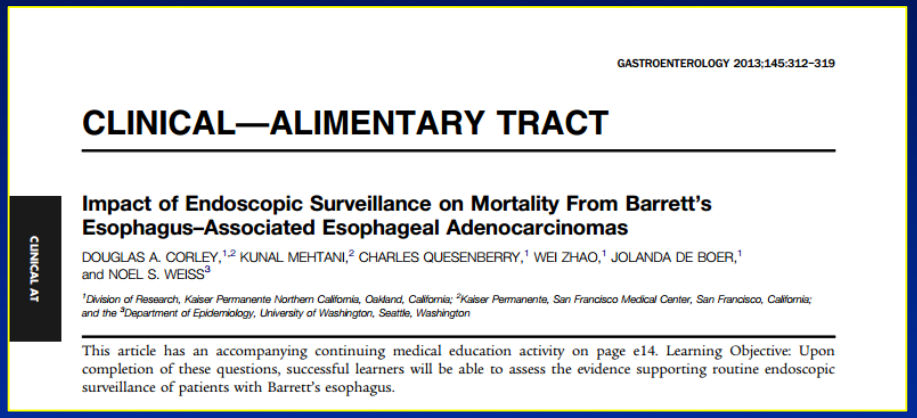
Endoscopic Surveillance of Barrett's

- Issues with surveillance
  - Sampling error
  - Pathologic discordance
  - Poor patient compliance
  - Cost-ineffective
- Surveillance does not prevent cancer
  - Over 50% of those who developed HGD or cancer while undergoing surveillance did not have findings of dysplasia (*Sharma, Clin Gastro Hep, 2006)*



Impact of Surveillance on Mortality

- Case-control study, community setting
- Among 8272 members with BE, 351 cases of EAC identified
- 70 EAC cases with prior dx of BE
- 38 of the pts. died due to EAC
- Surveillance histories of cases compared with 101 controls (pts. living with BE)
- Fatal cases almost as likely to receive surveillance (55.3%) as controls (60.4%)



GASTROENTEROLOGY 2013;145:312–319

CLINICAL—ALIMENTARY TRACT

CLINICAL AT

Impact of Endoscopic Surveillance on Mortality From Barrett's Esophagus–Associated Esophageal Adenocarcinomas

DOUGLAS A. CORLEY,[1,2] KUNAL MEHTANI,[2] CHARLES QUESENBERRY,[1] WEI ZHAO,[1] JOLANDA DE BOER,[1] and NOEL S. WEISS[3]

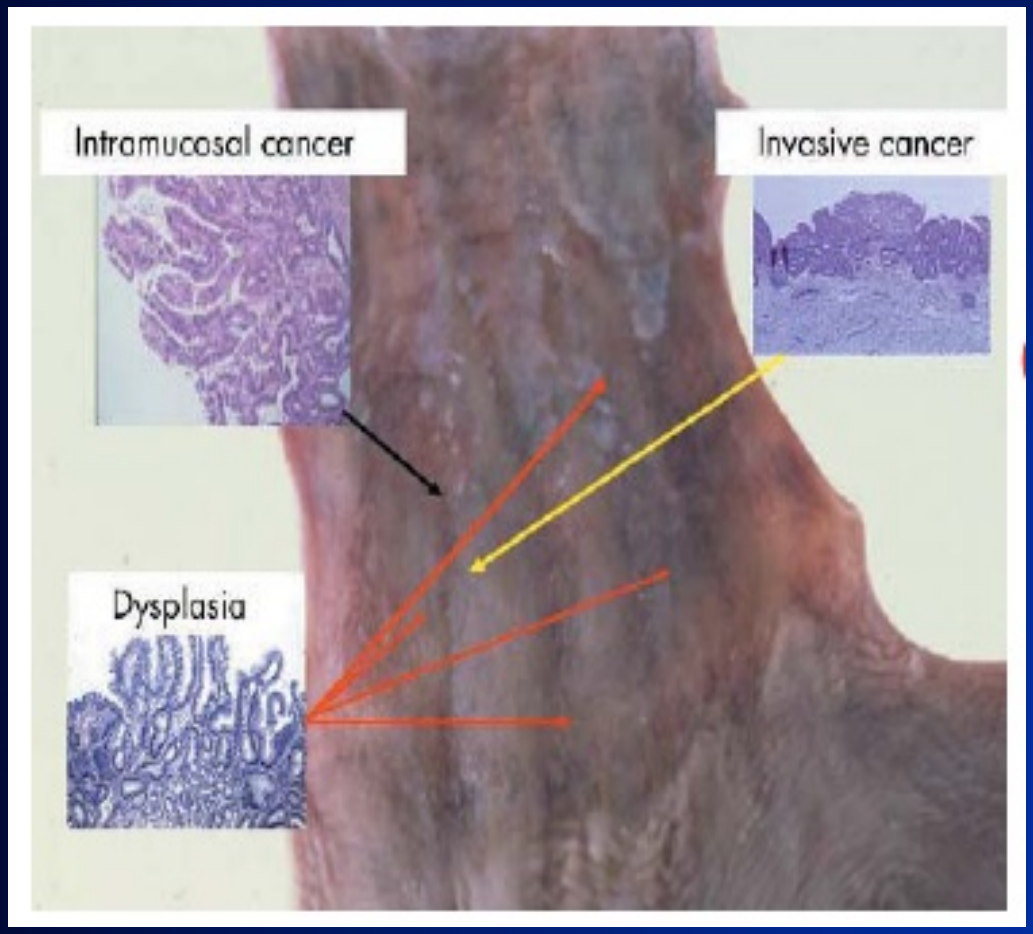
[1]Division of Research, Kaiser Permanente Northern California, Oakland, California; [2]Kaiser Permanente, San Francisco Medical Center, San Francisco, California; and the [3]Department of Epidemiology, University of Washington, Seattle, Washington

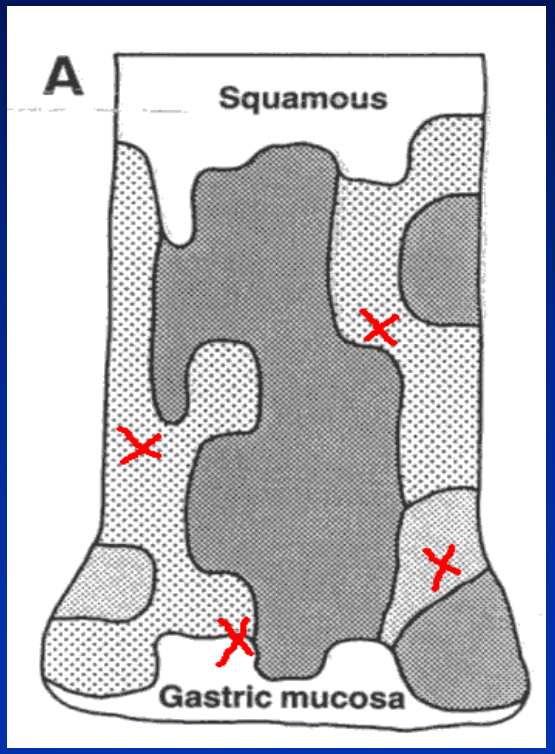
This article has an accompanying continuing medical education activity on page e14. Learning Objective: Upon completion of these questions, successful learners will be able to assess the evidence supporting routine endoscopic surveillance of patients with Barrett's esophagus.

Conclusion: Surveillance not associated with decreased risk of death due to EAC

1. Corley, DA, Mehtani K, Quesenberry C, et al. Impact of Endoscopic Surveillance on Mortality From Barrett's Esophagus-Associated Esophageal Adenocarcinomas. Gastroenterology. 2013 May 11;145(2):312-9

Sampling Error

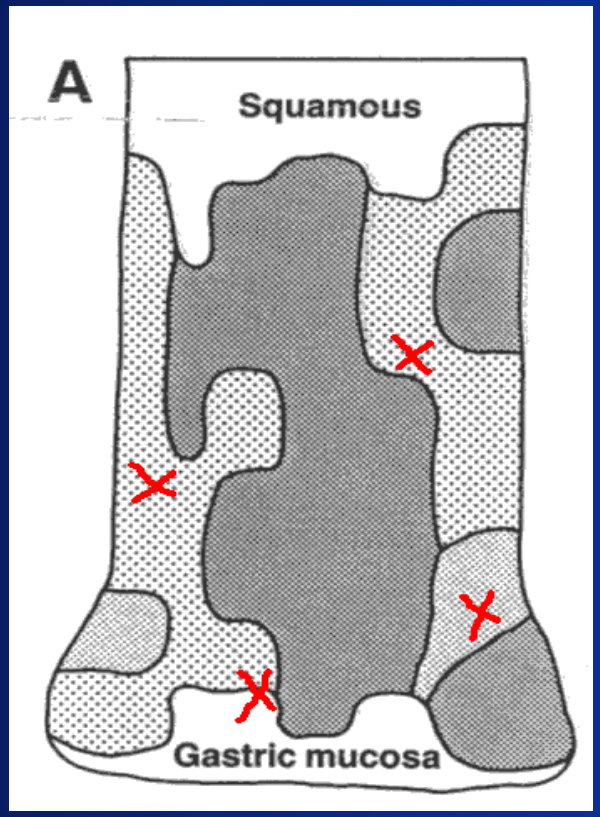




Metaplasia ("specialized")
Indefinite for Dysplasia/ Low Grade Dysplasia
High Grade Dysplasia
Cancer

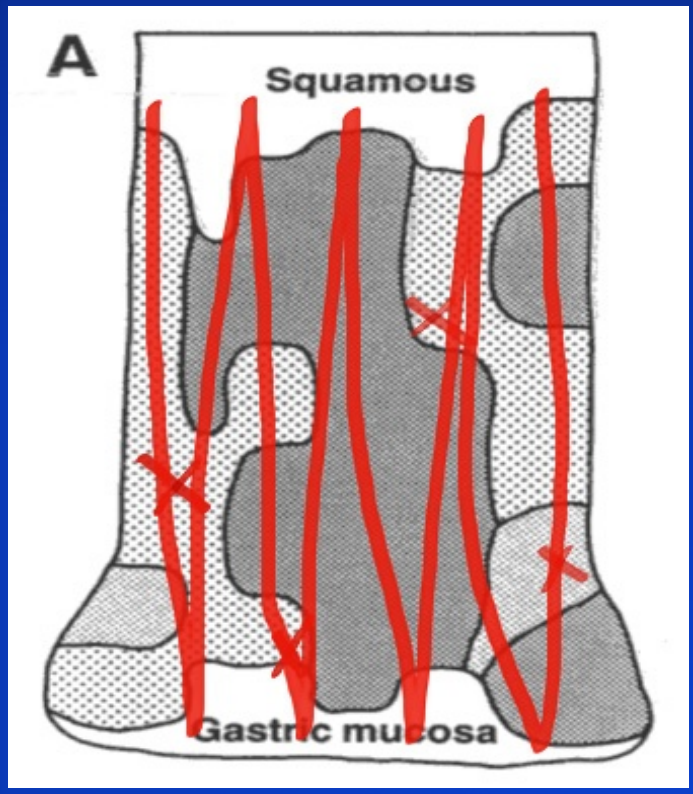
WATS^{3D}

Wide *A*rea Transepithelial Sample with 3-Dimensional Tissue Analysis



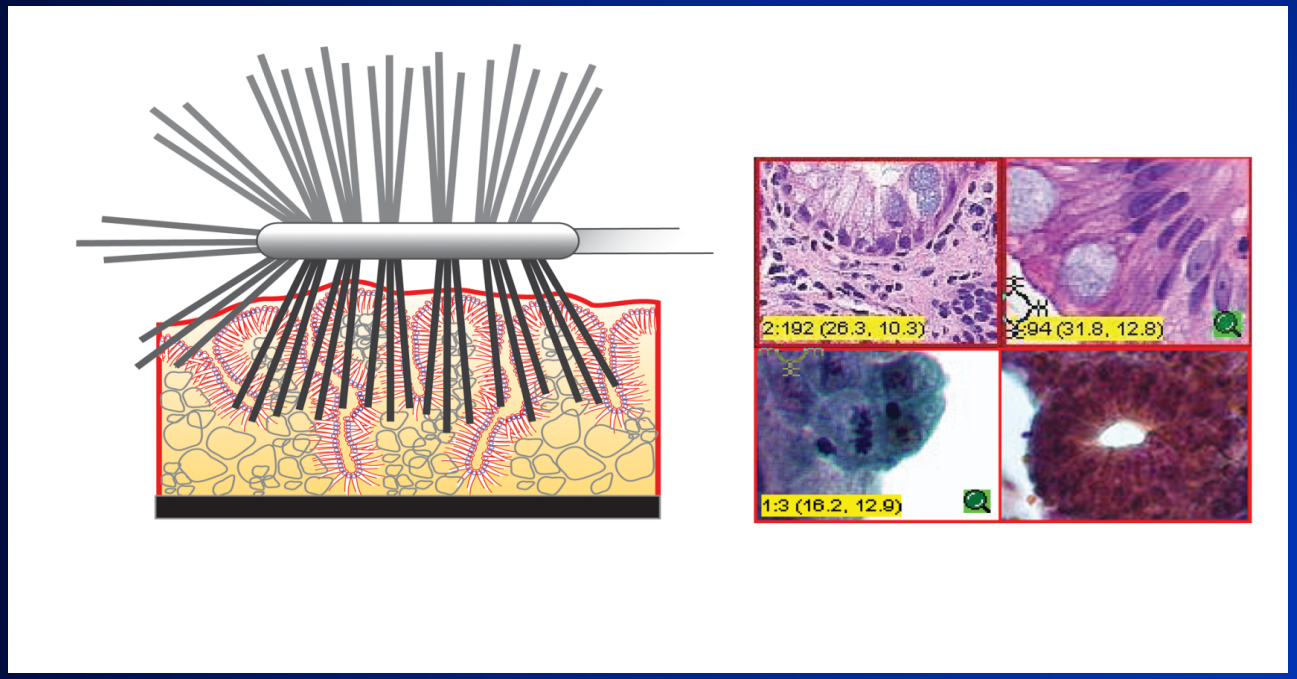
Forceps biopsy has a significant potential for sampling error

The wider surface area sampled by the transepithelial WATS biopsy addresses this problem

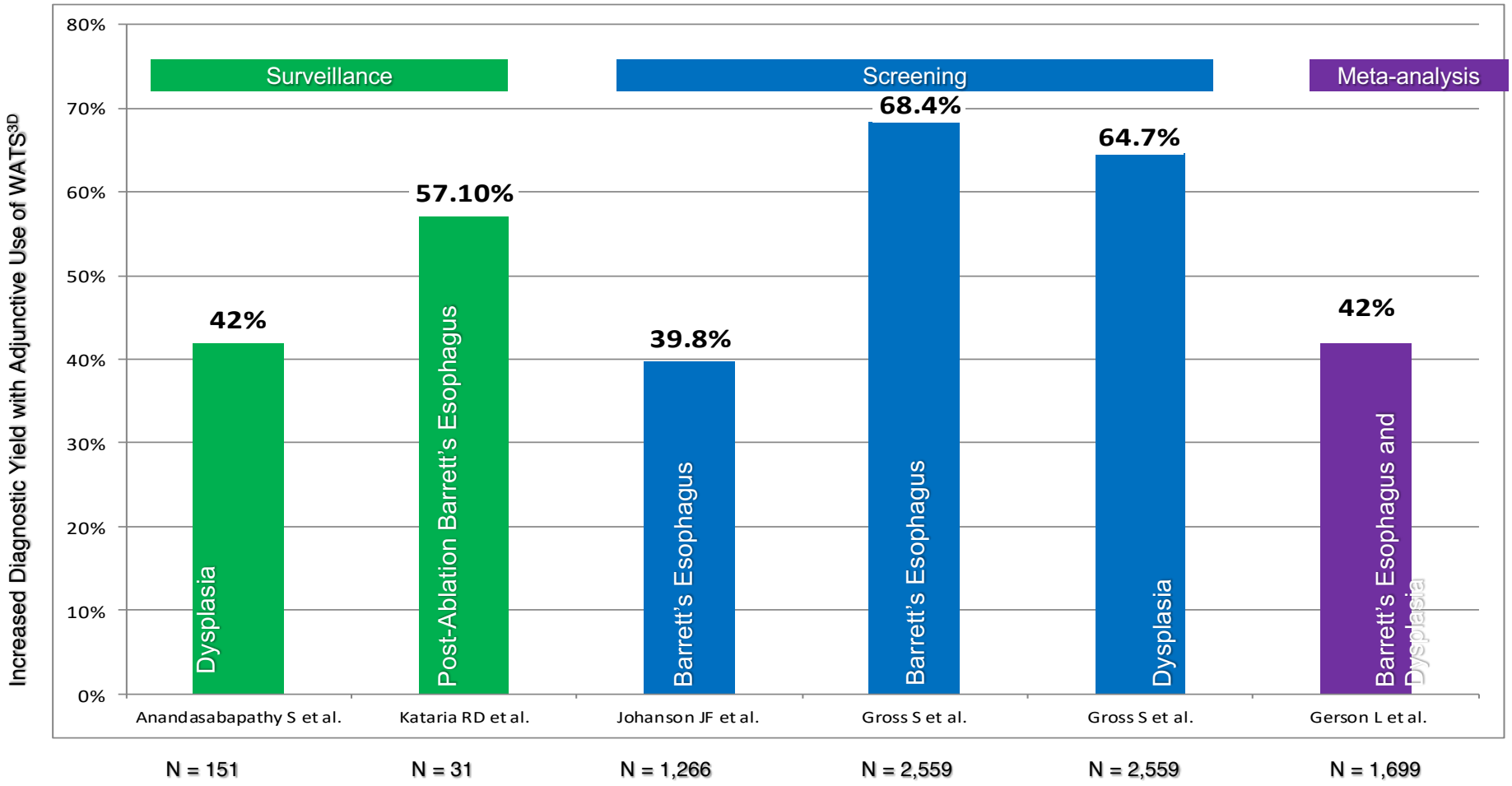


New Biopsy Brush

- EndoCDx WATS^{3D} Brush
  - ~More abrasive
  - ~Obtains transepithelial biopsy



Cross-Sectional Data - Added Yield of Barrett's Esophagus and Dysplasia



1. Anandasabapathy et al. *Dig Dis Sci*, e-pub
2. Kataria et al. American College of Gastroenterology Annual Meeting; October 11-16, 2013; San Diego, California. Abstract P23.
3. Johanson et al. *Dig Dis Sci*, e-pub
4. Gross et al. Digestive Disease Week; May 18-21, 2014; Chicago. Abstract Su1452.
5. Gerson et al. Digestive Disease Week; May 18-21, 2014; Chicago. Abstract Sa1833.

New Biopsy Brush

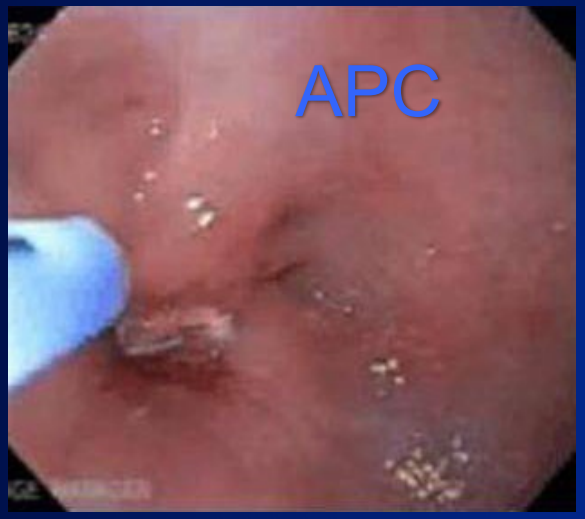
- EndoCDx WATS^{3D} Brush
  - ~A very valuable tool and will likely be in the guidelines very soon
  - ~Excellent service from the company
  - ~No cost to the patient… currently

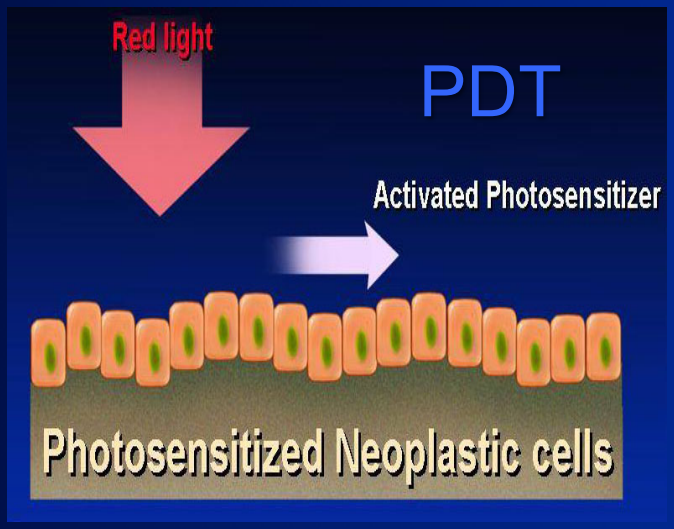
Therapy:
Endoscopic Mucosal Ablation

An ideal therapy would ...

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

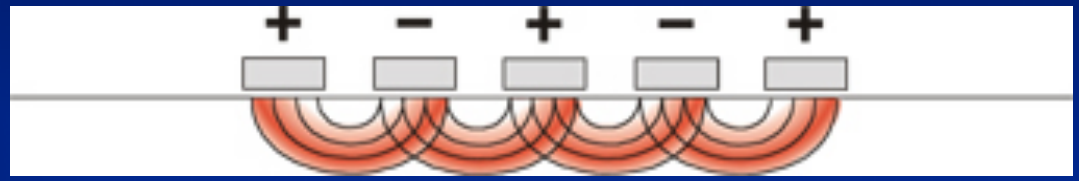
Mucosal Ablation





Radiofrequency Ablation

Proprietary Properties of RFA Lead to a Precise Ablation Depth (Mucosa-Submucosa Border)

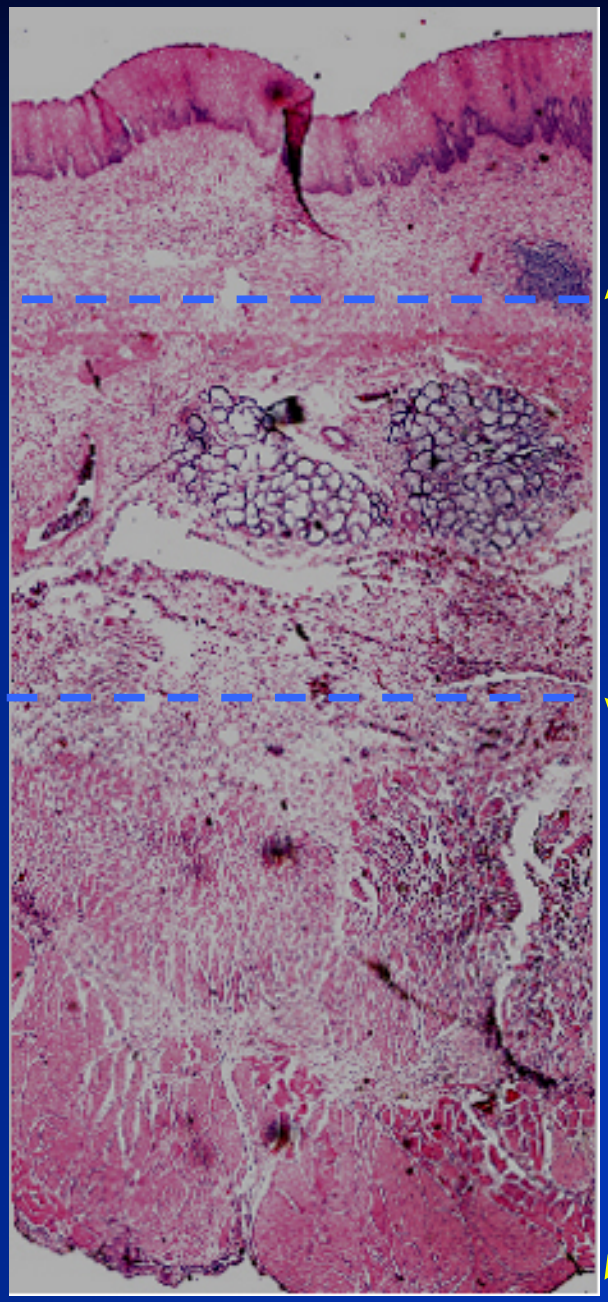


Mechanisms

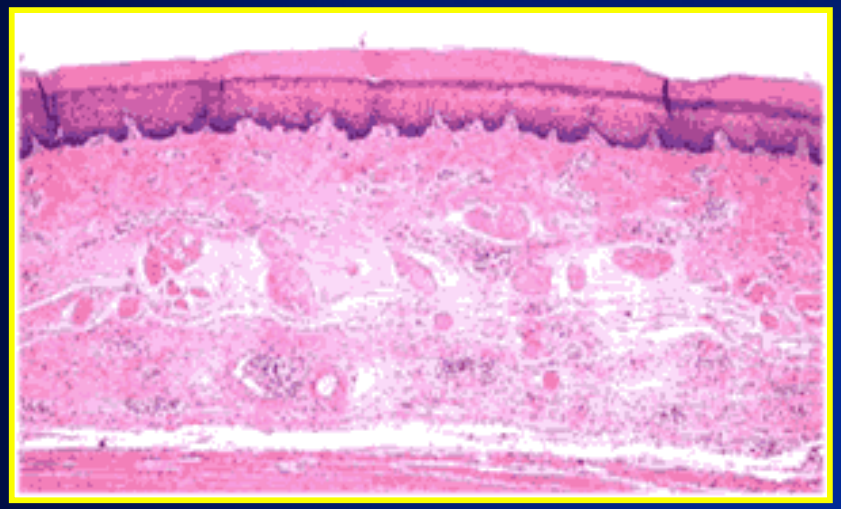
1. Tightly spaced electrodes (250 μm apart)
2. Proven pre-set energy & power densities
3. Generator turns off when a pre-determined resistance level in the ablated tissues is reached (mean of 0.3s)

Ganz, Gastrointest Endosc, 2004

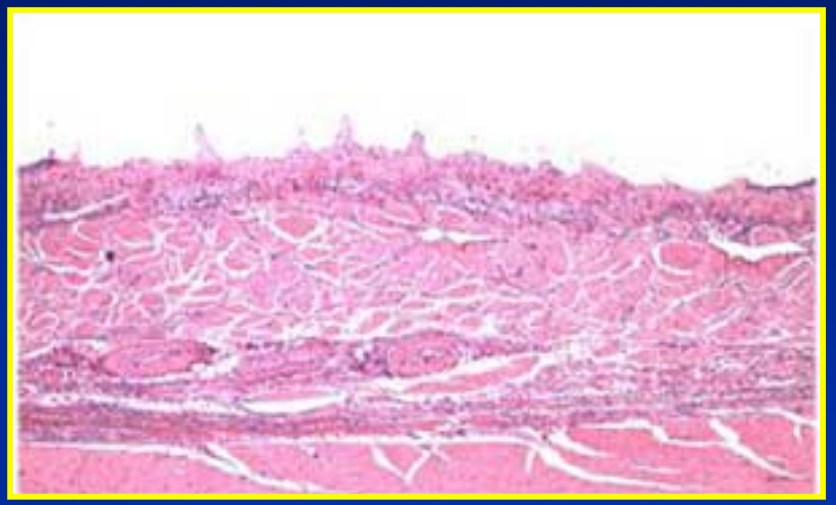
Human Esophagus



Histological Representation



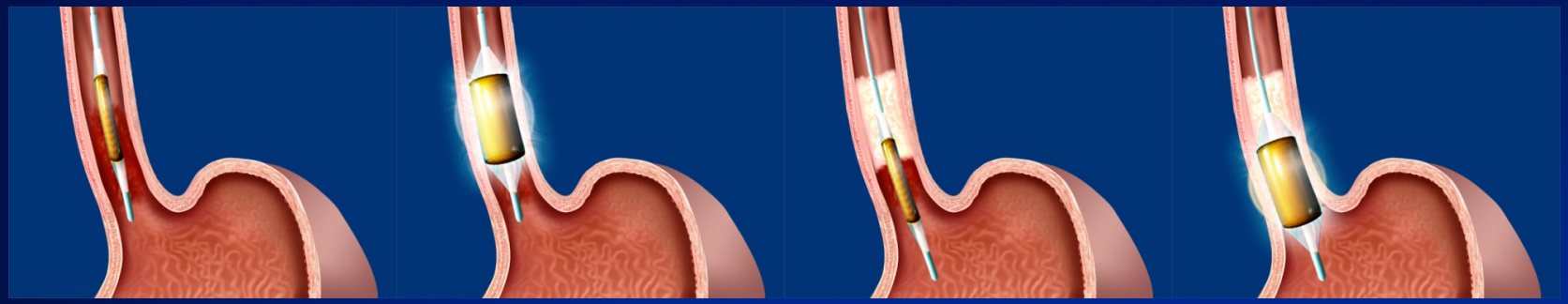
Normal



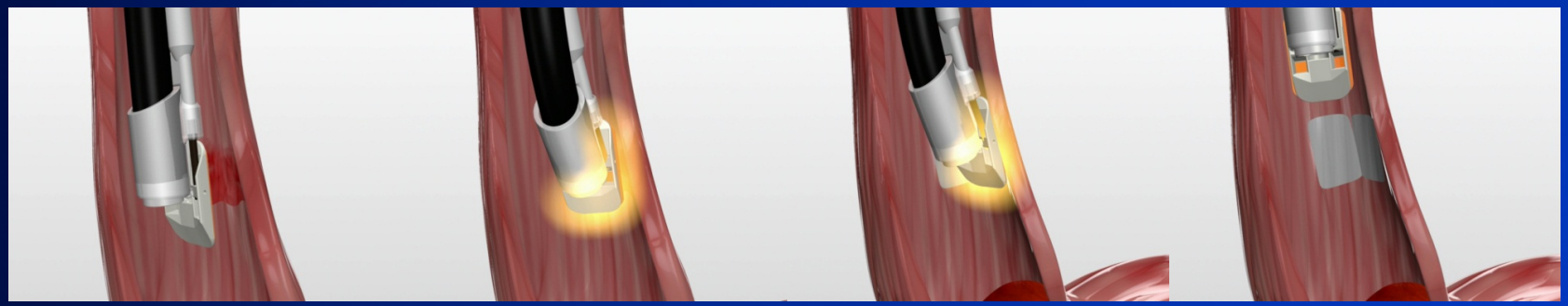
Post RF Ablation

Ablation Device Family

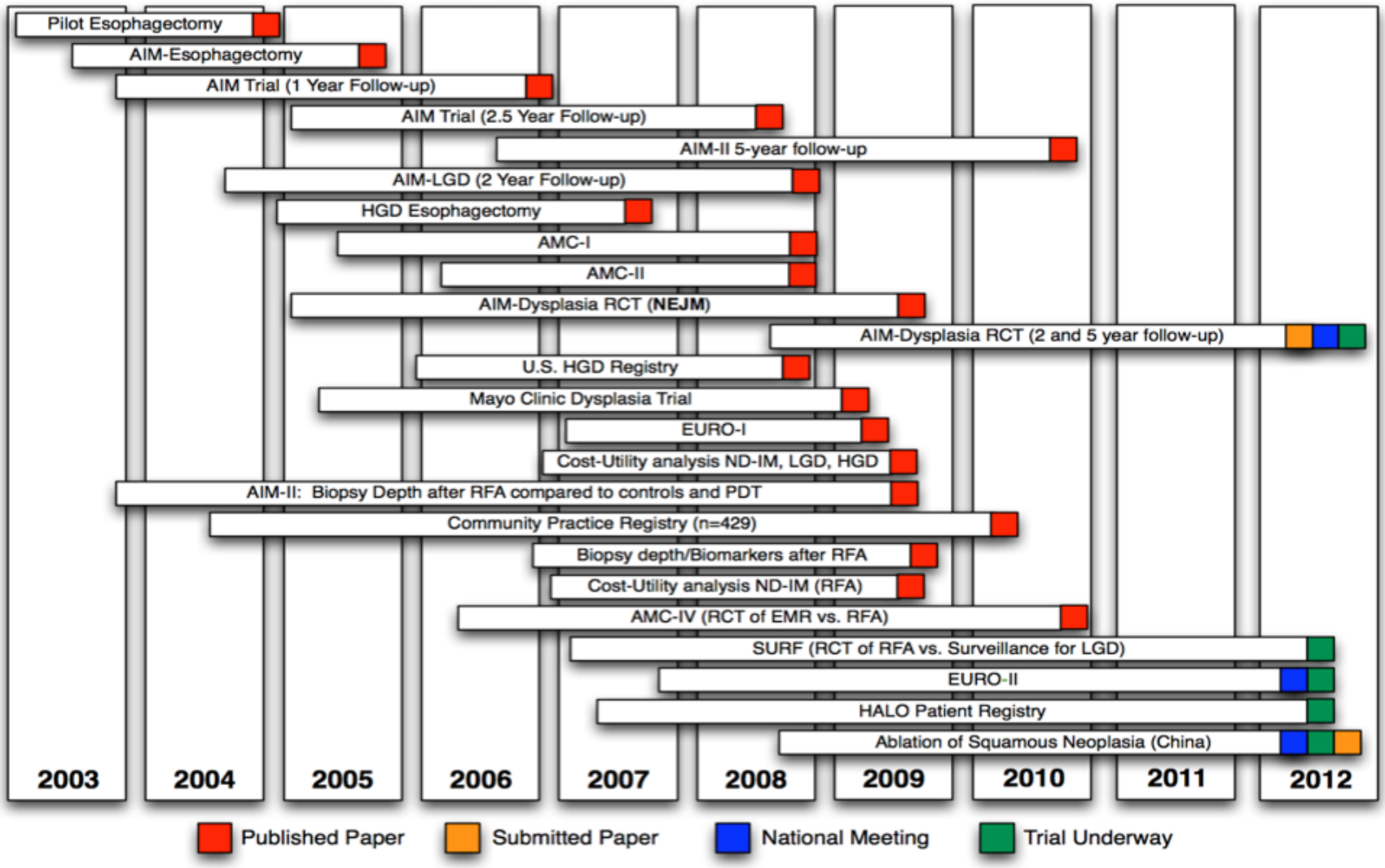
Circumferential Ablation



Focal Ablation



Clinical Trial Timeline
Studies Assessing the HALO^{90} and HALO^{360} Ablation Systems

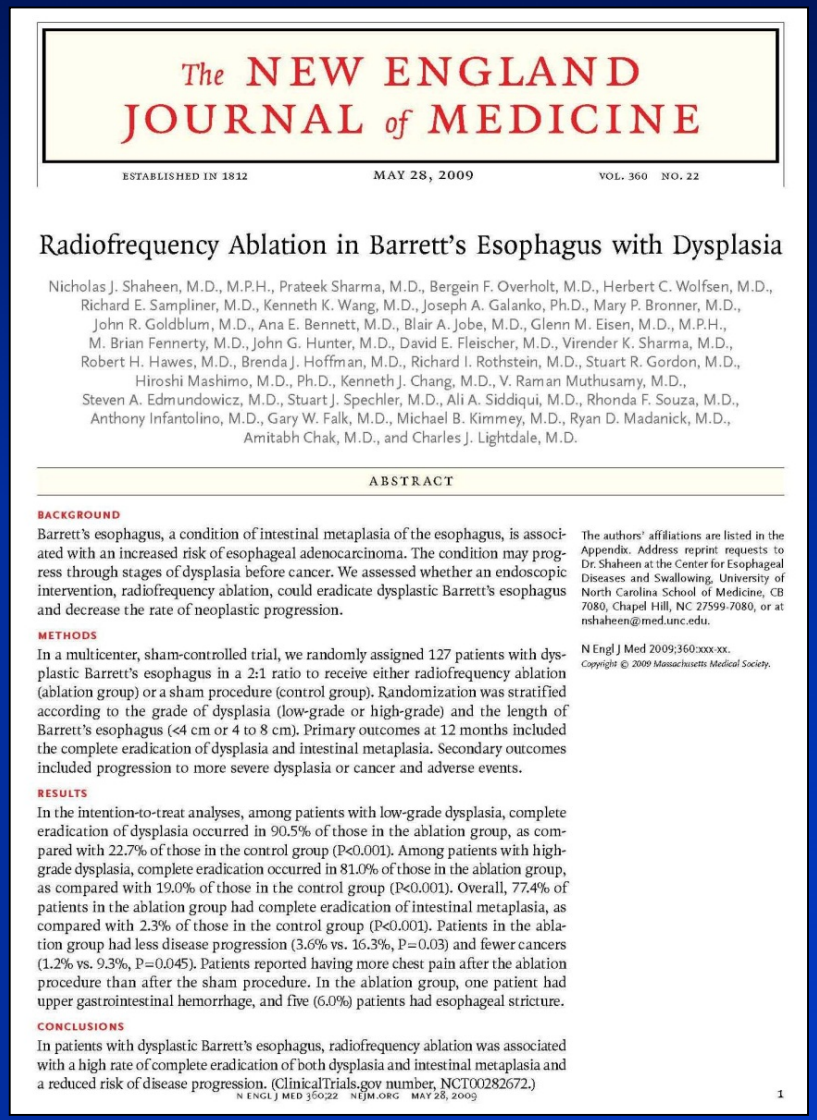


RFA for Barrett's Esophagus with Dysplasia

AIM Dysplasia Trial

(Shaheen, N Engl J Med, 2009)

- A RCT of 127 HGD & LGD pts
- 19 US medical centers
- Pts were randomized to treatment (RFA) & sham (surveillance) arms
- A statistically significant difference was demonstrated at 1 yr for both
  - Disease eradication (**P<0.001**)
  - Disease progression (**P<0.05**)



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 28, 2009 VOL. 360 NO. 22

Radiofrequency Ablation in Barrett's Esophagus with Dysplasia

Nicholas J. Shaheen, M.D., M.P.H., Prateek Sharma, M.D., Bergein F. Overholt, M.D., Herbert C. Wolfsen, M.D., Richard E. Sampliner, M.D., Kenneth K. Wang, M.D., Joseph A. Galanko, Ph.D., Mary P. Bronner, M.D., John R. Goldblum, M.D., Ana E. Bennett, M.D., Blair A. Jobe, M.D., Glenn M. Eisen, M.D., M.P.H., M. Brian Fennerty, M.D., John G. Hunter, M.D., David E. Fleischer, M.D., Virender K. Sharma, M.D., Robert H. Hawes, M.D., Brenda J. Hoffman, M.D., Richard I. Rothstein, M.D., Stuart R. Gordon, M.D., Hiroshi Mashimo, M.D., Ph.D., Kenneth J. Chang, M.D., V. Raman Muthusamy, M.D., Steven A. Edmundowicz, M.D., Stuart J. Spechler, M.D., Ali A. Siddiqui, M.D., Rhonda F. Souza, M.D., Anthony Infantolino, M.D., Gary W. Falk, M.D., Michael B. Kimmey, M.D., Ryan D. Madanick, M.D., Amitabh Chak, M.D., and Charles J. Lightdale, M.D.

ABSTRACT

BACKGROUND

Barrett's esophagus, a condition of intestinal metaplasia of the esophagus, is associated with an increased risk of esophageal adenocarcinoma. The condition may progress through stages of dysplasia before cancer. We assessed whether an endoscopic intervention, radiofrequency ablation, could eradicate dysplastic Barrett's esophagus and decrease the rate of neoplastic progression.

METHODS

In a multicenter, sham-controlled trial, we randomly assigned 127 patients with dysplastic Barrett's esophagus in a 2:1 ratio to receive either radiofrequency ablation (ablation group) or a sham procedure (control group). Randomization was stratified according to the grade of dysplasia (low-grade or high-grade) and the length of Barrett's esophagus (<4 cm or 4 to 8 cm). Primary outcomes at 12 months included the complete eradication of dysplasia and intestinal metaplasia. Secondary outcomes included progression to more severe dysplasia or cancer and adverse events.

RESULTS

In the intention-to-treat analyses, among patients with low-grade dysplasia, complete eradication of dysplasia occurred in 90.5% of those in the ablation group, as compared with 22.7% of those in the control group (P<0.001). Among patients with high-grade dysplasia, complete eradication occurred in 81.0% of those in the ablation group, as compared with 19.0% of those in the control group (P<0.001). Overall, 77.4% of patients in the ablation group had complete eradication of intestinal metaplasia, as compared with 2.3% of those in the control group (P<0.001). Patients in the ablation group had less disease progression (3.6% vs. 16.3%, P=0.03) and fewer cancers (1.2% vs. 9.3%, P=0.045). Patients reported having more chest pain after the ablation procedure than after the sham procedure. In the ablation group, one patient had upper gastrointestinal hemorrhage, and five (6.0%) patients had esophageal stricture.

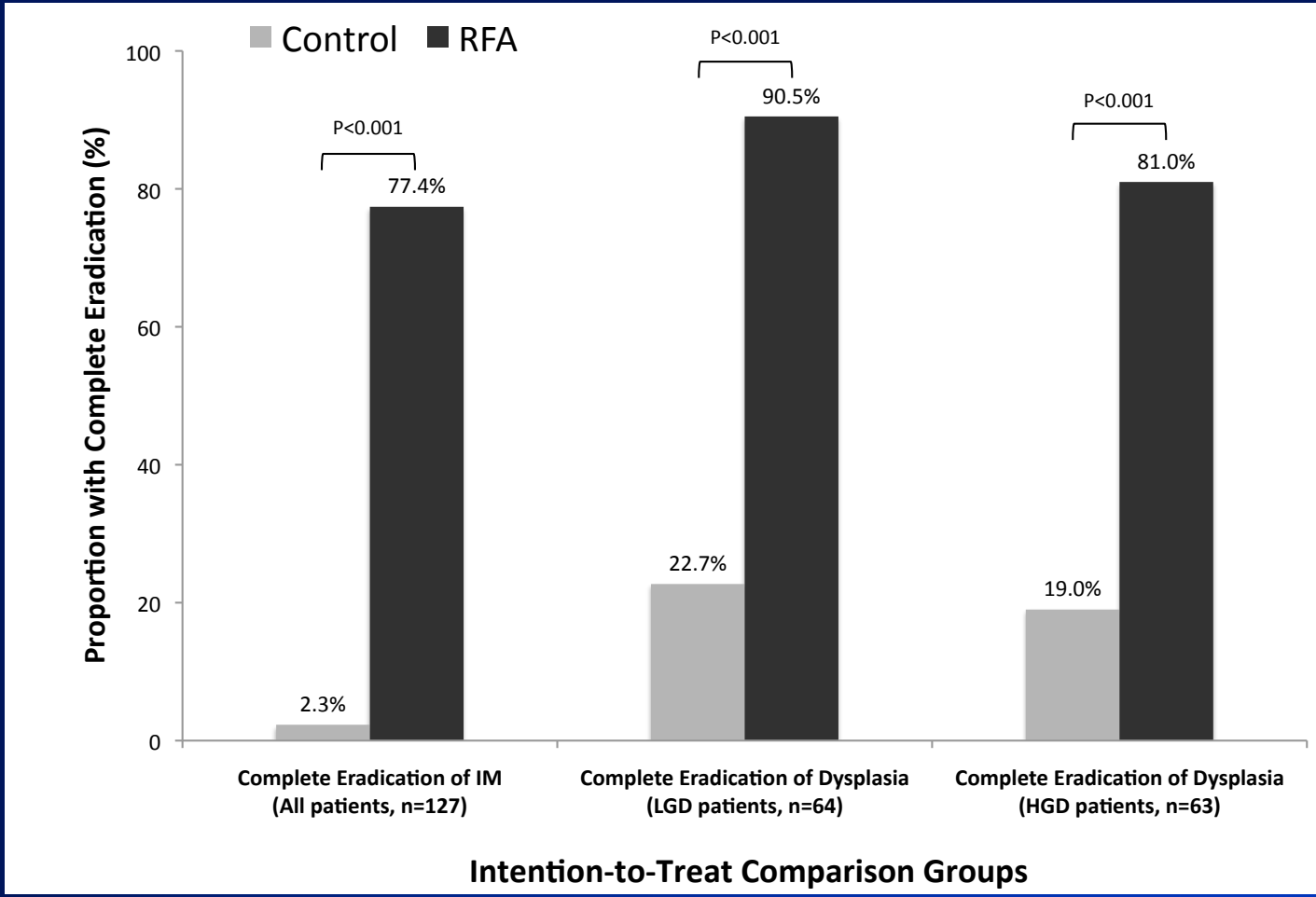
CONCLUSIONS

In patients with dysplastic Barrett's esophagus, radiofrequency ablation was associated with a high rate of complete eradication of both dysplasia and intestinal metaplasia and a reduced risk of disease progression. (ClinicalTrials.gov number, NCT00282672.)

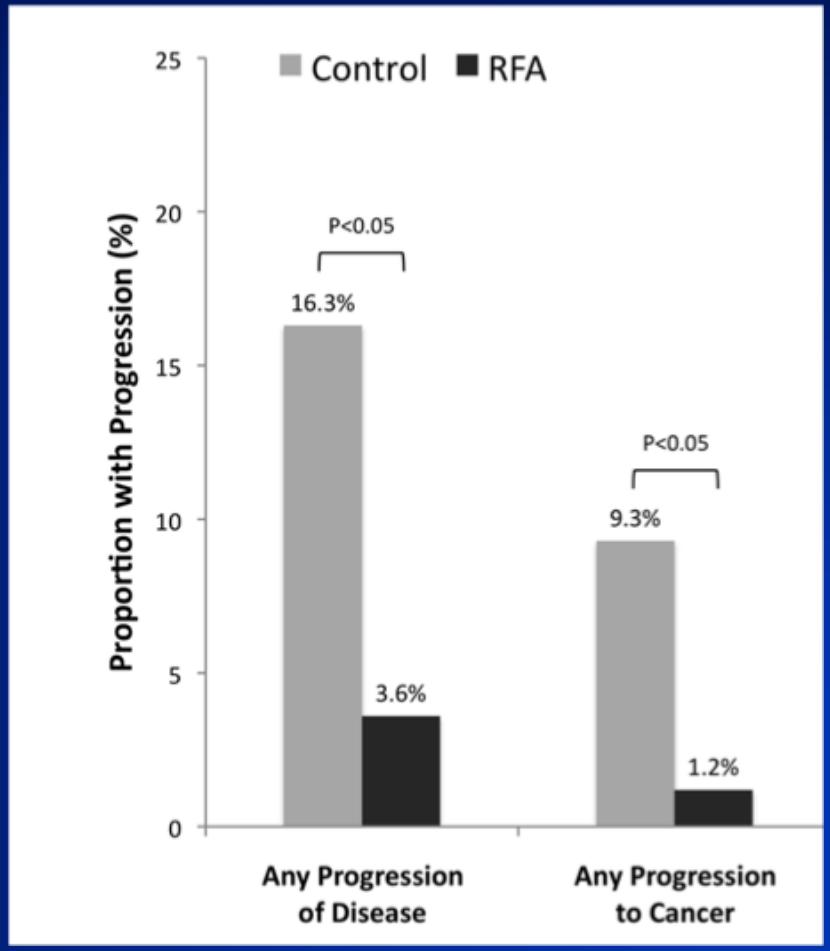
The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Shaheen at the Center for Esophageal Diseases and Swallowing, University of North Carolina School of Medicine, CB 7080, Chapel Hill, NC 27599-7080, or at nshaheen@med.unc.edu.

N Engl J Med 2009;360:xxx-xx.

Disease Eradication



Disease Progression



RFA Reduces Progression in Confirmed Low-Grade Dysplasia

SURF Trial, Phoa, JAMA, 2014

- European multicenter RCT of 136 confirmed LGD pts
- Pts randomized 1:1 to treatment (RFA) and control (surveillance) arms
- Complete eradication (CE) at 1 year:
  RFA: 88% CEIM, 93% CED
  Control: 0% CEIM, 28% CED (p<0.001)
- After median **36 mos** follow-up: **26.5%** of controls progressed to HGD/EAC vs. **1.5%** after RFA (p<0.001

  8.8% of controls progressed to EAC vs. **1.5%** after RFA (p<0.03
- Study terminated secondary to superiority of RFA and patient safety concerns should the trial continue

Research

Original Investigation

Radiofrequency Ablation vs Endoscopic Surveillance for Patients With Barrett Esophagus and Low-Grade Dysplasia
A Randomized Clinical Trial

K. Nadine Phoa, MD; Frederike G. I. van Vilsteren, MD; Bas L. A. M. Weusten, MD; Raf Bisschops, MD; Erik J. Schoon, MD; Krish Ragunath, MD; Grant Fullarton, MD; Massimiliano Di Pietro, MD; Narayanasamy Ravi, MD; Mike Visser, MD; G. Johan Offerhaus, MD; Cees A. Seldenrijk, MD; Sybren L. Meijer, MD; Flebo J. W. ten Kate, MD; Jan G. P. Tijssen, PhD; Jacques J. G. H. M. Bergman, MD, PhD

IMPORTANCE Barrett esophagus containing low-grade dysplasia is associated with an increased risk of developing esophageal adenocarcinoma, a cancer with a rapidly increasing incidence in the western world.

OBJECTIVE To investigate whether endoscopic radiofrequency ablation could decrease the rate of neoplastic progression.

DESIGN, SETTING, AND PARTICIPANTS Multicenter randomized clinical trial that enrolled 136 patients with a confirmed diagnosis of Barrett esophagus containing low-grade dysplasia at 9 European sites between June 2007 and June 2011. Patient follow-up ended May 2013.

INTERVENTIONS Eligible patients were randomly assigned in a 1:1 ratio to either endoscopic treatment with radiofrequency ablation (ablation) or endoscopic surveillance (control). Ablation was performed with the balloon device for circumferential ablation of the esophagus or the focal device for targeted ablation, with a maximum of 5 sessions allowed.

MAIN OUTCOMES AND MEASURES The primary outcome was neoplastic progression to high-grade dysplasia or adenocarcinoma during a 3-year follow-up since randomization. Secondary outcomes were complete eradication of dysplasia and intestinal metaplasia and adverse events.

RESULTS Sixty-eight patients were randomized to receive ablation and 68 to receive control. Ablation reduced the risk of progression to high-grade dysplasia or adenocarcinoma by 25.0% (1.5% for ablation vs 26.5% for control; 95% CI, 14.1%-35.9%; $P < .001$) and the risk of progression to adenocarcinoma by 7.4% (1.5% for ablation vs 8.8% for control; 95% CI, 0%-14.7%; $P = .03$). Among patients in the ablation group, complete eradication occurred in 92.6% for dysplasia and 88.2% for intestinal metaplasia compared with 27.9% for dysplasia and 0.0% for intestinal metaplasia among patients in the control group ($P < .001$). Treatment-related adverse events occurred in 19.1% of patients receiving ablation ($P < .001$). The most common adverse event was stricture, occurring in 8 patients receiving ablation (11.8%), all resolved by endoscopic dilation (median, 1 session). The data and safety monitoring board recommended early termination of the trial due to superiority of ablation for the primary outcome and the potential for patient safety issues if the trial continued.

CONCLUSIONS AND RELEVANCE In this randomized trial of patients with Barrett esophagus and a confirmed diagnosis of low-grade dysplasia, radiofrequency ablation resulted in a reduced risk of neoplastic progression over 3 years of follow-up.

TRIAL REGISTRATION trialregister.nl Identifier: NTR1198

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CME Quiz at jamanetworkcme.com and CME Questions page 1247

Author Affiliations: Author affiliations are listed at the end of this article.
Corresponding Author: Jacques J. G. H. M. Bergman, MD, PhD, Department of Gastroenterology and Hepatology, Academic Medical Center Amsterdam, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands (j.j.bergman@amc.uva.nl).

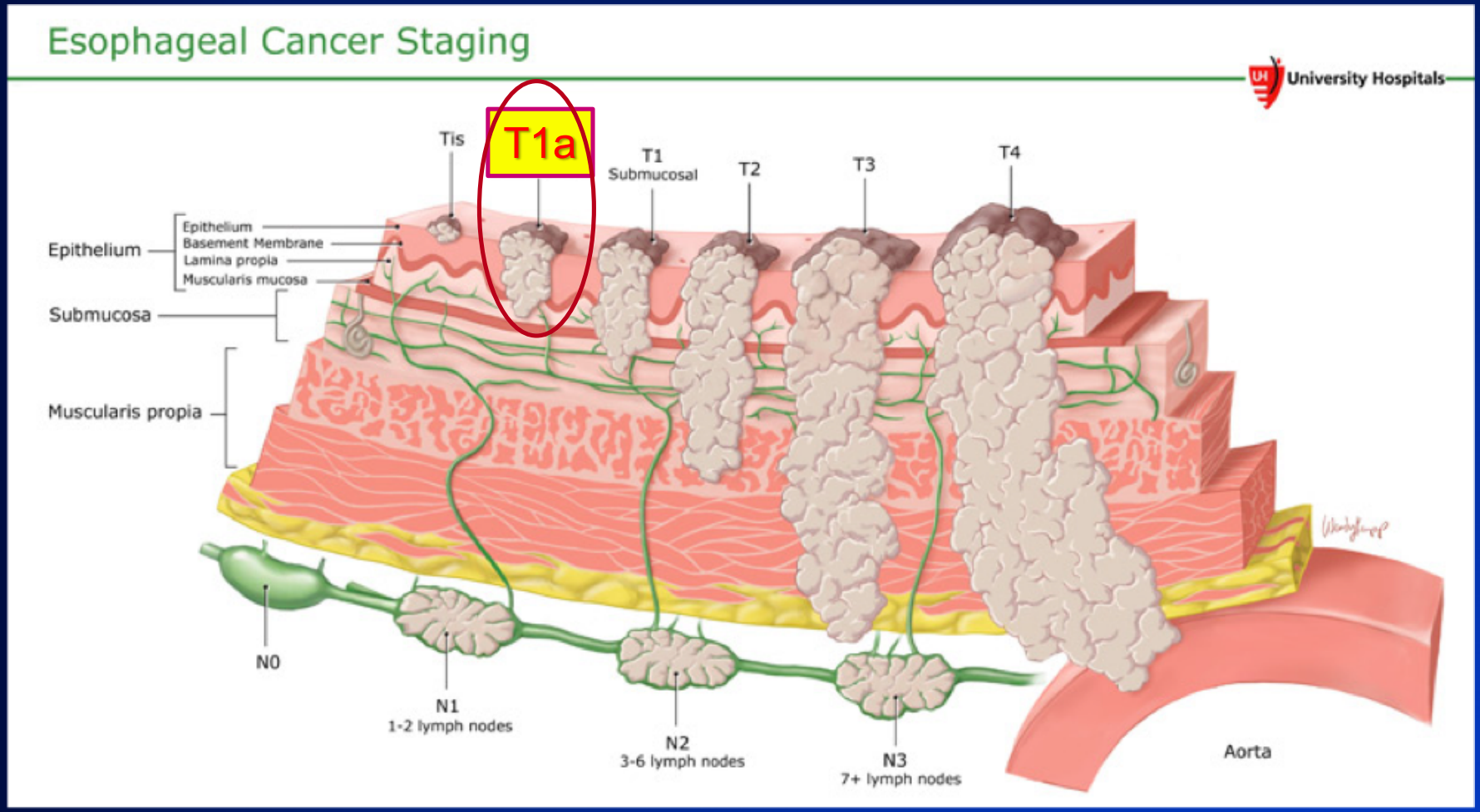
JAMA. 2014;311(12):1209-1217. doi:10.1001/jama.2014.2511

Phoa K, van Vilsteren F, Weusten BM, et al. Radiofrequency Ablation vs Endoscopic Surveillance for Patients With Barrett Esophagus and Low-Grade Dysplasia: A Randomized Clinical Trial. JAMA 2014;311:1209-1217.

Trial funded by Covidien, GI Solutions

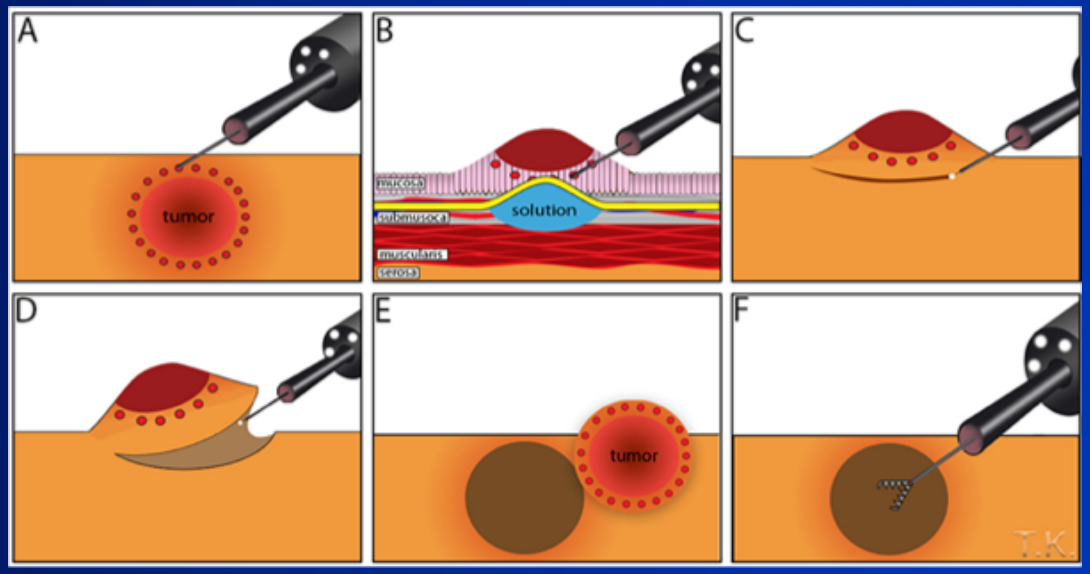
Endoscopic Management of Early Esophageal Cancer

Endoscopic Management of Early Esophageal Cancer

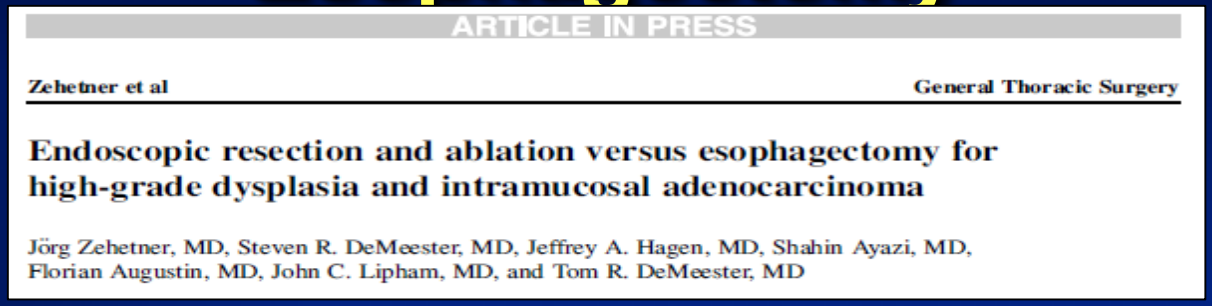


Endoscopic Management of Early Esophageal Cancer (EMR and ESD)

ESD



Endoscopic Resection vs Esophagectomy[1]



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Zehetner et al — General Thoracic Surgery

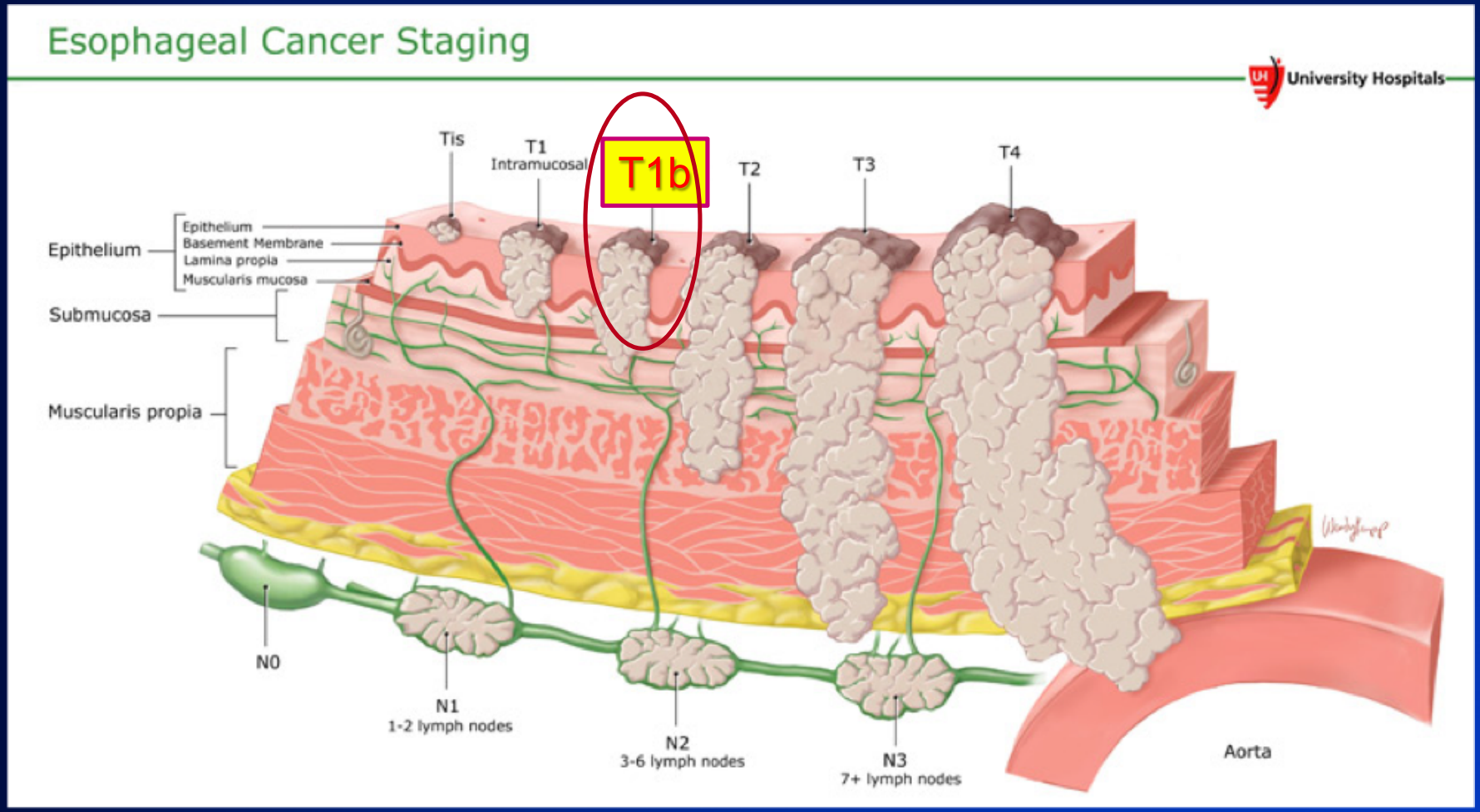
Endoscopic resection and ablation versus esophagectomy for high-grade dysplasia and intramucosal adenocarcinoma

Jörg Zehetner, MD, Steven R. DeMeester, MD, Jeffrey A. Hagen, MD, Shahin Ayazi, MD, Florian Augustin, MD, John C. Lipham, MD, and Tom R. DeMeester, MD

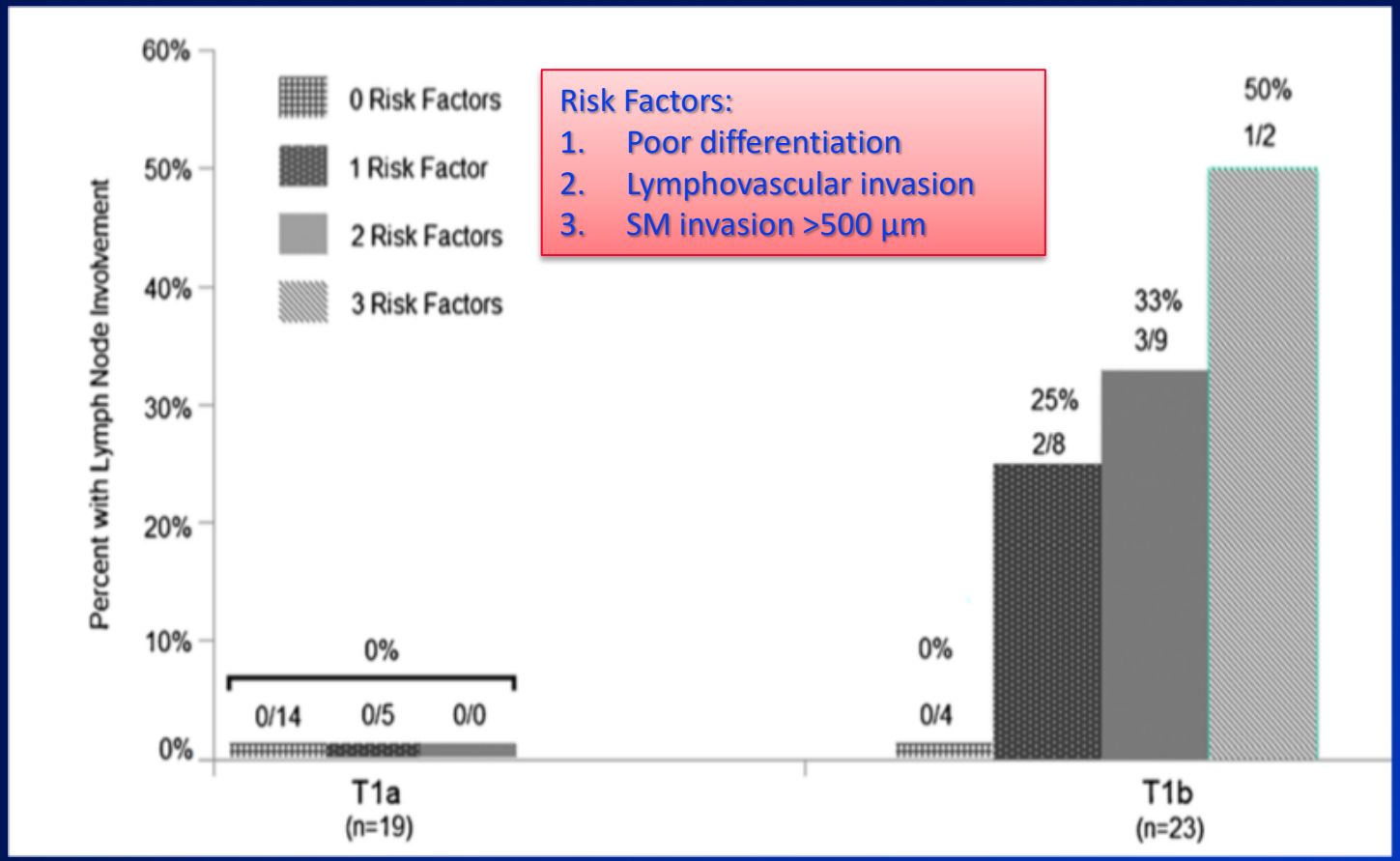
- Compares outcomes of endoscopic therapy (ER + RFA) vs esophagectomy in HGD and T1a
- Retrospective review 2001 – 2010
- Endotherapy: n = 40
- Esophagectomy: n = 61
- Compared with esophagectomy, endotherapy was associated with:
  - Lower morbidity (39% vs 0%, $p < .0001$)
  - Similar survival (94% at 3 years for both groups)
- Endotherapy for HGD/T1a has similar survival but decreased morbidity vs esophagectomy

1. Zehetner J, Demeester SR, Hagen JA, et al. Endoscopic resection and ablation versus esophagectomy for high-grade dysplasia and intramucosal adenocarcinoma. J Thorac Cardiovasc Surg 2011;141:39-47.

Endoscopic Management of Early Esophageal Cancer



Risk of Lymph Node Mets for T1a and T1b Cancer



Boys, Chandrasoma,Vallone, Demeester et al. J Gastrointest Surg (2016) 20:6–12

Disease Treatment Summary

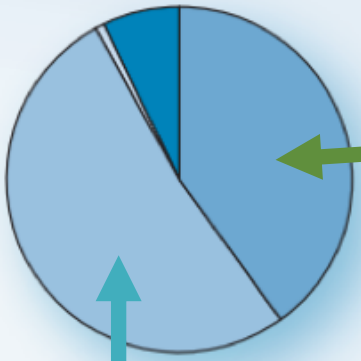
Stage of Disease	Recommendations
Non-dysplastic Barrett's	Surveillance* (or Ablation in select individuals)
Low Grade Dysplasia (confirmed)	Endoscopic Ablation*
High Grade Dysplasia	Endoscopic Eradication*
T1a, some T1b	Endoscopic Resection (EMR and ESD)
T1b, T2, T3	Surgery

*AGA 2011 Guidelines, ACG 2015 Guidelines

Endoscopy is missing the BIG PICTURE

~10,000 per year

Of ~10,000 oesophageal adenocarcinomas diagnosed each year in the USA, only 7% are identifed through current approaches to cancer control



40%
Without GERD
No Endoscopy

52%
Some GERD Hx
No Endoscopy

Diagnosed after Alarm symptoms developed

> 50% Advanced Disease that will need Surgery

Vaughan, T. L. & Fitzgerald, R. C. Nat. Rev. Gastroenterol Hepatol. 12, 243–248 (2015)

Non-invasive screening coming soon

Acceptability and accuracy of a non-endoscopic screening test for Barrett's oesophagus in primary care: cohort study

Cytosponge

BMJ. 2010 Sep 10;341:c4372

Cytosponge Screening

Thank you!

jsamaras@uci.edu