NASPGHAN

North American Society for Pediatric Gastroenterology, Hepatology and Nutrition

Therapeutic Pediatric Endoscopy Hands On Course

June 29-30, 2012

ASGE Institute for Training and Technology
Oak Brook, Illinois

Course Directors:
Jenifer Lightdale, MD, MPH and Petar Mamula, MD

TABLE OF CONTENTS

Faculty List 1

Course information and Program Agenda 3

Treatment of Esophageal Strictures – Michael Manfredi 5

Advanced Imaging in GI Endoscopy – Charles Lightdale 41

Eosinophillic Esophagitis: Diagnosis – Christopher Liacouras 89

Endoscopic Hemostasis – Douglas Fishman 169

From Sward Swallowers to Buckyballs – Petar Mamula 259

Batteries and Magnets – Robert Kramer...317

Quality Sedation for Pediatric GI Endoscopy: Assessing, Monitoring and Using
Crisis Resource Management (CRM) – Jenifer Lightdale...347

Clips – Bradley Barth..399

FACULTY

Course Directors:

Jenifer Lightdale, MD, MPH
Attending Physician; Director, Patient Safety and Quality, Division of GI/Nutrition
Boston Children's Hospital
Boston, MA

Petar Mamula, MD
Attending Physician; Director, Endoscopy Suite; Associate Professor of Pediatrics, Perelman School of Medicine at the University of Pennsylvania
The Children's Hospital of Philadelphia
Philadelphia, PA

Bradley Barth, MD
Associate Professor of Pediatrics
University of Texas Southwestern Medical Center
Director of Endoscopy
Children's Medical Center - Dallas
Dallas, TX

Steven Erdman, MD
Gastroenterology Fellowship Program Director; Gastroenterology, Hepatology, & Nutrition Physician Team
Nationwide Children's Hospital
Columbus, OH

Douglas Fishman, MD
Assistant Professor, Pediatrics
Baylor College of Medicine
Director, Gastrointestinal Procedures Unit; Interim-Director Liver Center
Texas Children's Hospital
Houston, TX

Marsha Kay, MD
Department Chair; Director Pediatric Endoscopy
Cleveland Clinic
Cleveland, OH

Robert Kramer, MD
Associate Professor of Pediatrics; Director of Endoscopy; Medical Director, GoodLife2 Adolescent Obesity Clinic
Children's Hospital Colorado
Aurora, CO

Christopher Liacouras, MD
Attending Physician; Co-director, Center for Pediatric Eosinophilic Disorders; Professor of Pediatrics, Perelman School of Medicine at the University of Pennsylvania
The Children's Hospital of Philadelphia
Philadelphia, PA

Charles Lightdale, MD
Professor of Clinical Medicine; Director of Clinical Research; Chair, Clinical Research Committee
Division of Digestive and Liver Diseases
Columbia University Medical Center
New York, NY

Michael Manfredi, MD
Associate Director, Esophageal Atresia Treatment Program; Associate Director, Gastrointestinal Procedure Unit; Attending Physician
Boston Children's Hospital
Boston, MA

Bryan Sauer, MD, MS
Assistant Professor of Medicine
University of Virginia Health System
Charlottesville, VA

The following companies have provided in-kind support for this course:
ERBE USA, Inc.
FujiFilm Medical Systems USA, Inc.
Olympus Corporation of the Americas

This course is supported by a restricted educational grant from the Olympus Corporation of the Americas

Faculty Disclosures:
Brad Barth: nothing to disclose
Steve Erdman: nothing to disclose
Doug Fishman: nothing to disclose
Marsha Kay: nothing to disclose
Rob Kramer: nothing to disclose
Chris Liacouras: Nutricia, Speakers Bureau and Abbott, Speakers Bureau
Charles Lightdale: nothing to disclose
Jenifer Lightdale: nothing to disclose
Petar Mamula: nothing to disclose
Michael Manfredi: nothing to disclose
Bryan Sauer: nothing to disclose

Course Description:
This course is intended to address the needs of pediatric gastroenterologists and fellows in training who are interested in improving their knowledge of familiar and new endoscopic techniques. Emphasis will be placed on the specialized use of therapeutic endoscopic techniques and instruments in infants and children.

Topics include:
Hemostasis- Heater/Bipolar probes, clipping techniques, argon plasma coagulation, variceal banding and sclerotherapy
Saline assisted polypectomy
Balloon Dilation (stricture and achalasia)
Video capsule deployment/Wireless pH probe placement/Foreign body removal

Course Objectives:
At the conclusion of this course, participants will be able to:

- Understand basic principles and practice of therapeutic endoscopy in children
- Identify and properly use endoscopic therapeutic equipment key to each procedure
- Employ basic skills to perform effective and safe therapeutic pediatric endoscopy

Program Agenda:

Friday, June 29th

5:30-5:45pm Welcome and Course Objectives

5:45-6:15pm Treatment of strictures- Mike Manfredi

6:15-6:35pm New Advances in Endoscopic Imaging – Charles Lightdale

6:35-7:00pm Challenging Cases – Faculty

7:00-7:30pm Eosinophillic Esophagitis: Guideline update – Chris Liacouras

7:30-9:00pm Buffet Dinner Reception

Saturday, June 30th

07:00-07:45am Breakfast/Checkout

07:45-08:00am Travel to IT & T Center

08:00-08:15am Introduction and Orientation to IT & T Center

08:15am-12:30pm Small groups of 4-5 people rotate every 30 minutes between 8 stations, with 15 minute break from 10:15-10:30am

- Clips
- Heater/Bipolar probes/Injection therapy
- Argon plasma coagulation
- Multiple banding/Polypectomy
- Balloon dilation/Stent placement
- Enteroscopy/Video capsule deployment/Wireless pH probe placement
- Foreign body removal
- PEG placement

012:30-1:00pm Lunch

01:00-1:45pm Free time at hands-on stations

01:45-2:00pm Travel to hotel

02:00-2:15pm Break

02:15-2:45pm Hemostasis – Doug Fishman

02:45-3:15pm New Technologies – Petar Mamula

03:15-3:45pm Batteries and Magnets – Rob Kramer

03:45-4:00pm Break

04:00-4:25pm Sedation/Crisis Resource Management – Jenifer Lightdale

04:25-4:50pm Clips – Brad Barth

04:50-5:00pm Wrap-up and Adjourn

Treatment of Esophageal Strictures

Michael Manfredi, MD

Children's Hospital Boston

Disclosures: I have no financial relationships with a commercial entity to disclose.

Learning Objectives

- Describe and classify esophageal strictures
- Define refractory esophageal strictures
- Learn the various treatment options for esophageal strictures
- Understand treatment algorithm for strictures

Stricture Classification

Simple Stricture

- diameter that allows scope passage before dilation
- Short (<2cm in length)
- straight

Complex Stricture

- diameter that does not allow scope passage
- long (>2cm in length)
- tortuous

Predictors of Refractory Stricture

Complex Stricture

- Chiu et al: Showed higher rate of dilation failure with strictures > 8cm long and/or diameter <4mm

Stricture Etiology

- Anastomotic Stricture
- Caustic Ingestion
- Radiation therapy induced

Chiu YC, et al. Factors influencing clinical applications of endoscopic balloon dilation for benign esophageal strictures. Endoscopy 2004;36(7):595-600.

Refractory Strictures

- No uniform definition
- Definition is important to truly evaluate new treatment techniques
- Proposed definition:
  - Inability to successfully remediate the lumen to a diameter of 14mm over 5 session at two week intervals.

Types of Dilation

Balloon Dilation

Mechanical:

- Savary-Gilliard
- Maloney

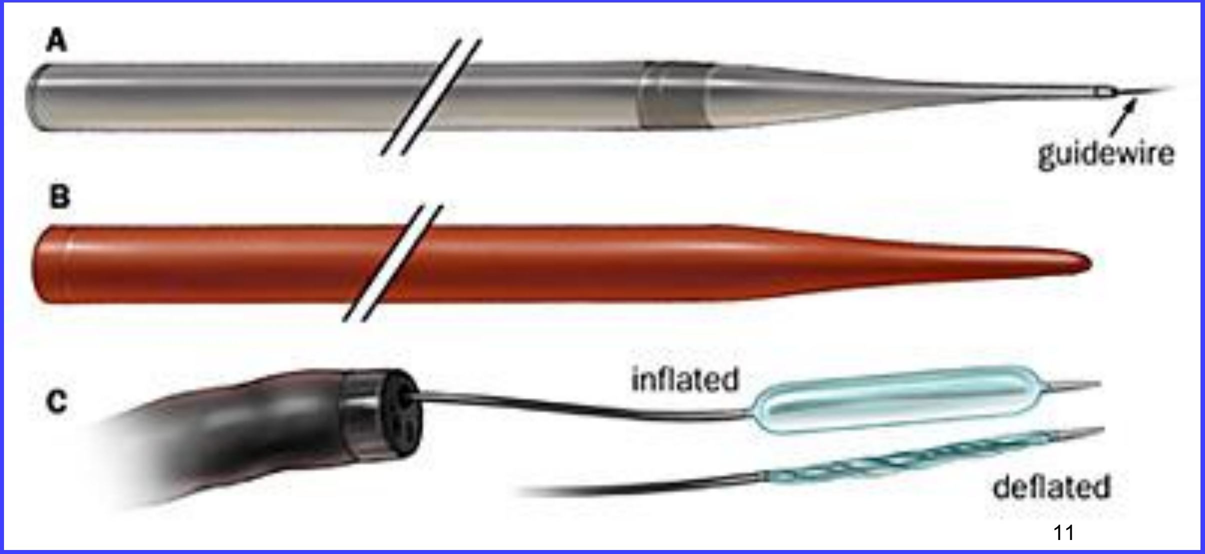


Image copied from http://www.hopkins-gi.org

Mechanical Dilation

- Delivers both radial and longitudinal force from proximal to distal portion of the stricture
- Can be passed over a guidewire or freely into the esophagus

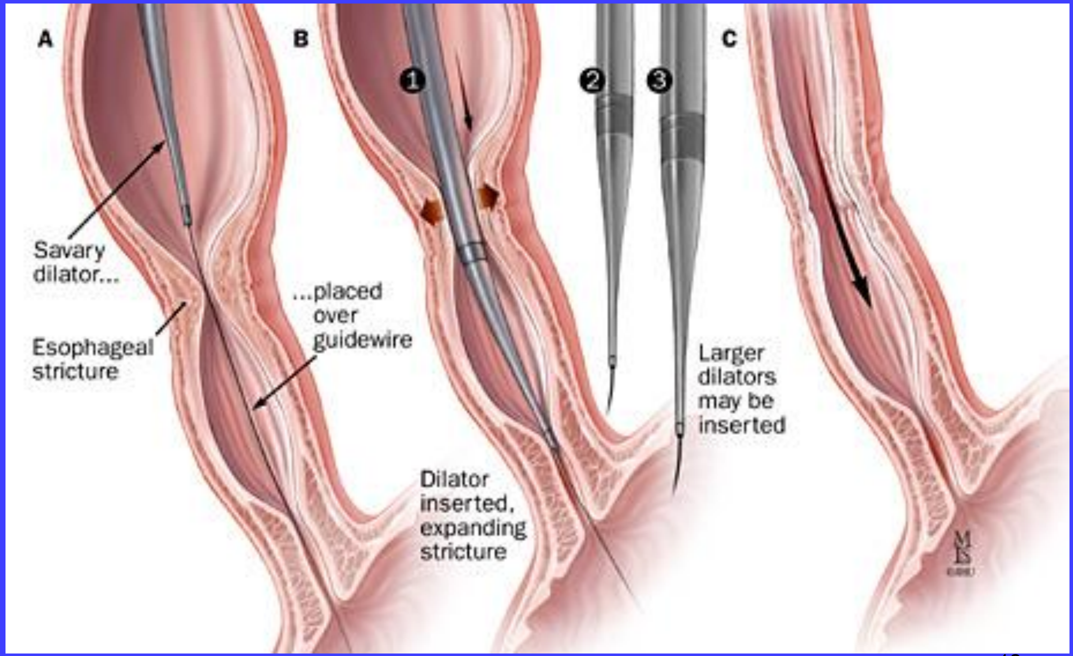
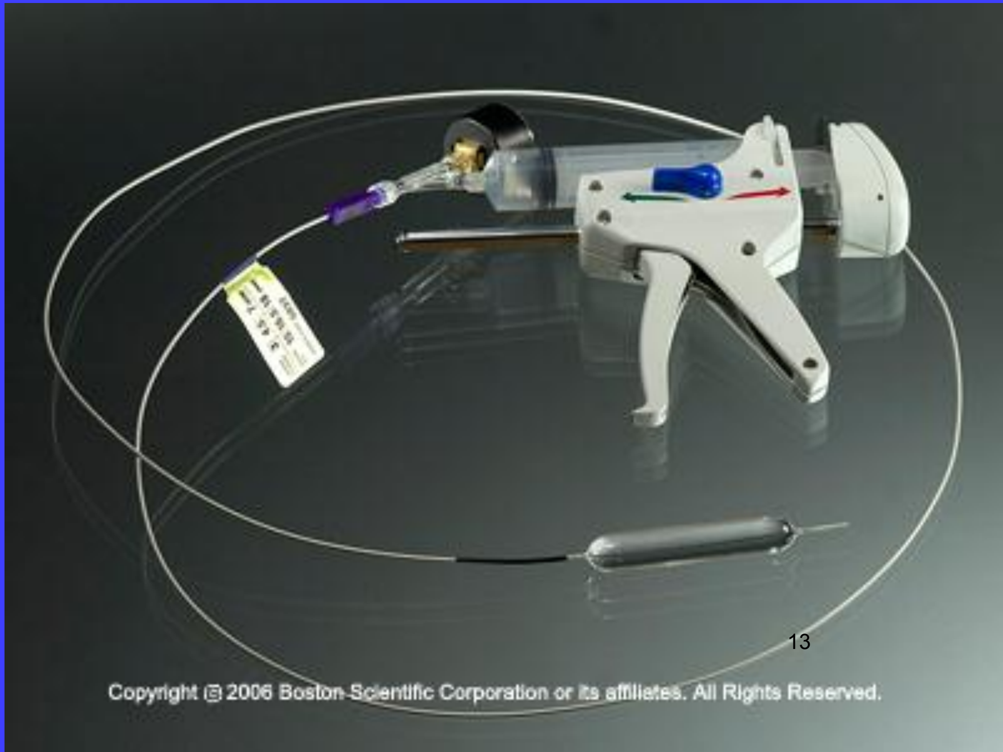


Image copied from http://www.hopkins-gi.org

Balloon Dilation

- Delivers equal radial force *simultaneously* across the *entire length* of the stricture
- Can be done through the scope or over a wire



Which Method is Superior?

- No clear difference in effectiveness and safety has been reported
  - Perforation 0.1%-0.4%
  - Hemorrhage <0.4%
  - Bacteremia ?
- Balloon dilation has a clear advantage in patients with epidermolysis bullosa
- The method of choice depends on operator comfort with the equipment

Siersema PD. Treatment options for esophageal strictures. Nature clinical practice 2008;5(3):142-52.

How Big Can You Dilate?

"The Rule of Three":

- No more than three dilators in 1mm increments should be passed in a single session for a total of 3mm
- Developed for bougie dilations

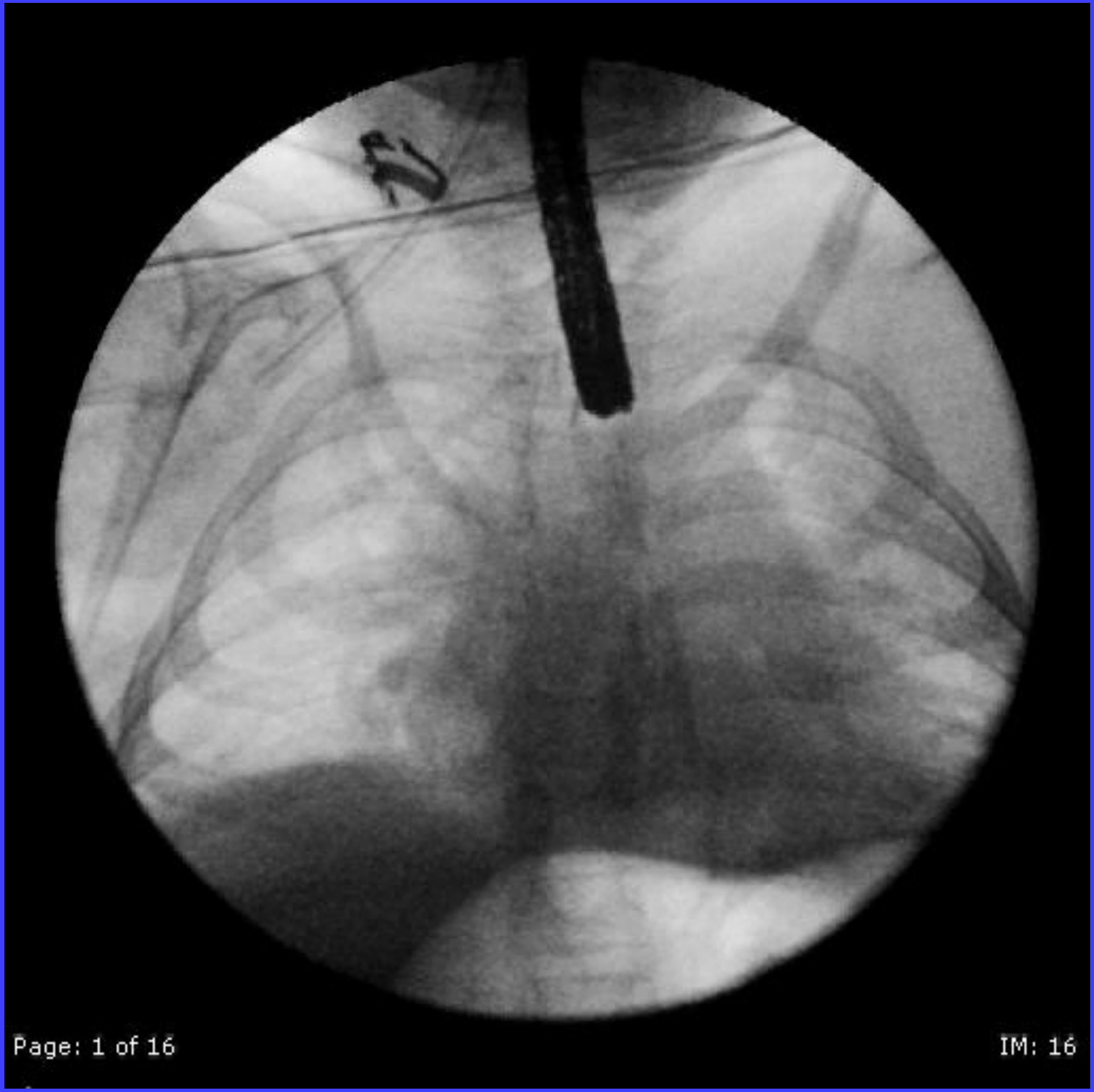
  and applied to balloon dilations
  - No clinical study has demonstrated safety or efficacy
  - Good guideline to follow

Fluoroscopy or not to Fluoroscopy

- Efficacy and safety of endoscopic dilation without fluoro has been shown

- Fluoroscopy allows:
  - direct placement of the balloon or bougie catheter (decreasing the risk of perforation)
  - observe severity of stenosis (“waist”)
- Fluoro generally recommended for complex strictures

Esophageal Stricture Waist



Treatments of Refractory Strictures

- Intralesional Corticosteroid Therapy
- Stent Placement
- Mitomycin C
- Incisional therapy

Intralesional Corticosteroid Therapy

- Proposed mechanism: local inhibition of inflammatory response resulting in reduced collagen formation
- Multiple studies have shown effect in reducing recurrent stricture formation
  - Most small uncontrolled studies
  - Strictures of diverse etiology
  - One randomized controlled trial which showed effectiveness in peptic strictures *

*Ramage JL, et al. A prospective, randomized double blind…Am J Gastroenterol 2005;100:1388-91

Intralesional Corticosteroid Therapy

Questions:

- Type of Steroid
  - triamcinolone acetate
- Dose of Steroid
  - 40mg/ml diluted one to one and administered in four quadrants in 0.5ml aliquots
  - No standard pediatric dosing (1-2mg/kg)
- Frequency of dilations
- Injection technique
  - Pre or Post dilation

Esophageal Stenting

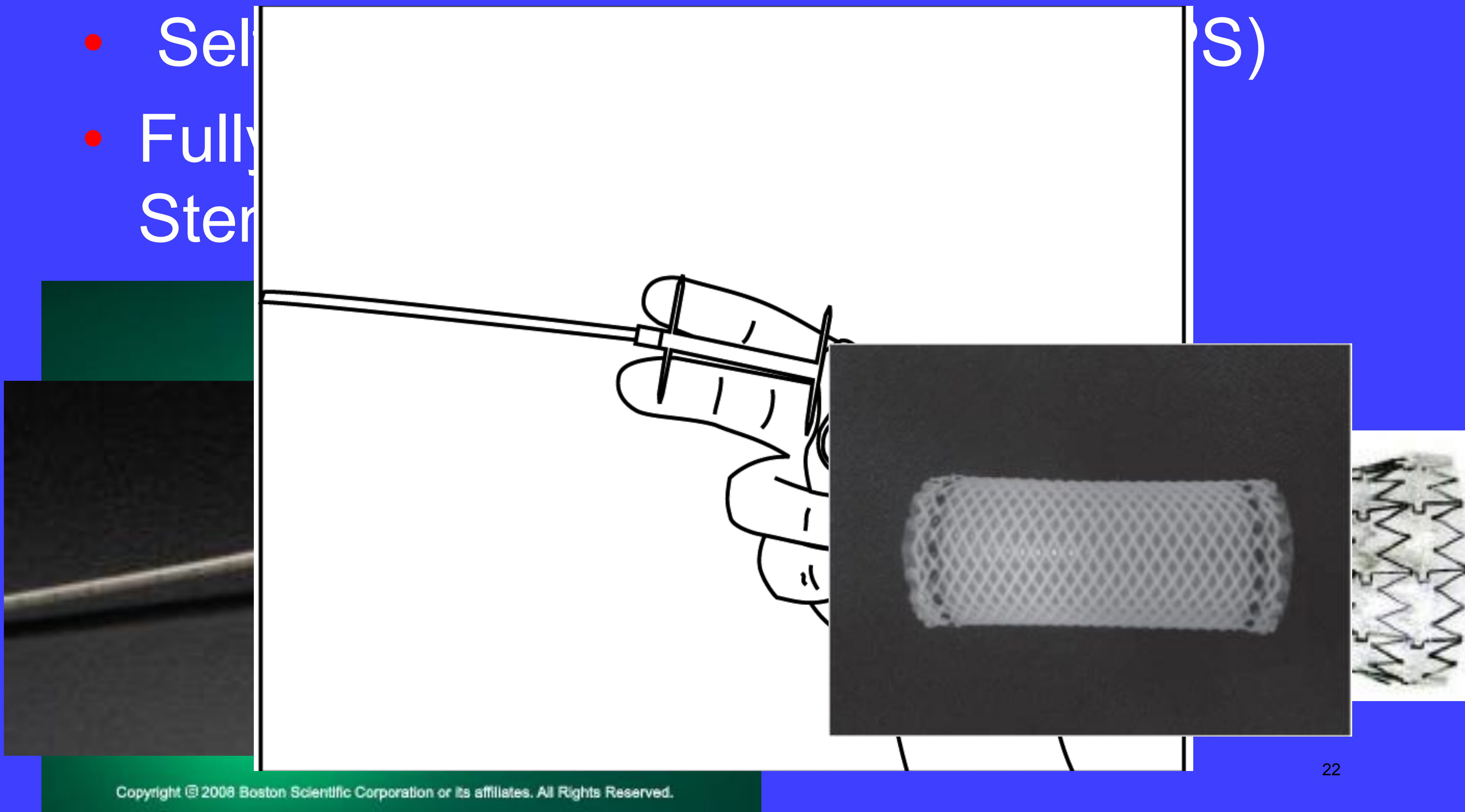
Dilating the esophagus for prolonged periods of time

- may reduce the risk of recurrent stricture formation
- may be an alternative treatment option to serial esophageal stricture dilations

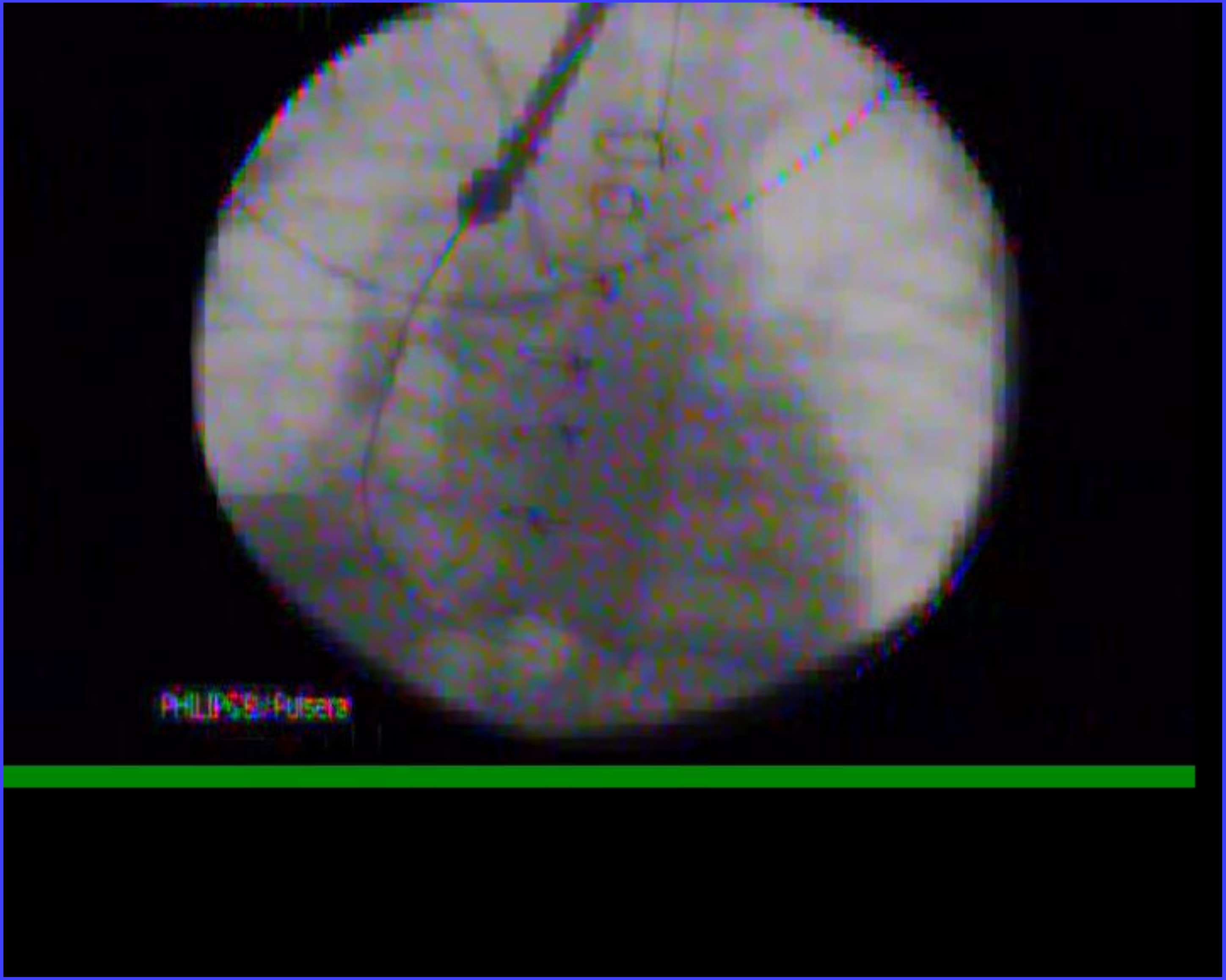
Two types of stents for temporary placement

Types of Stents

- Sel ... S)
- Fully ... Sten

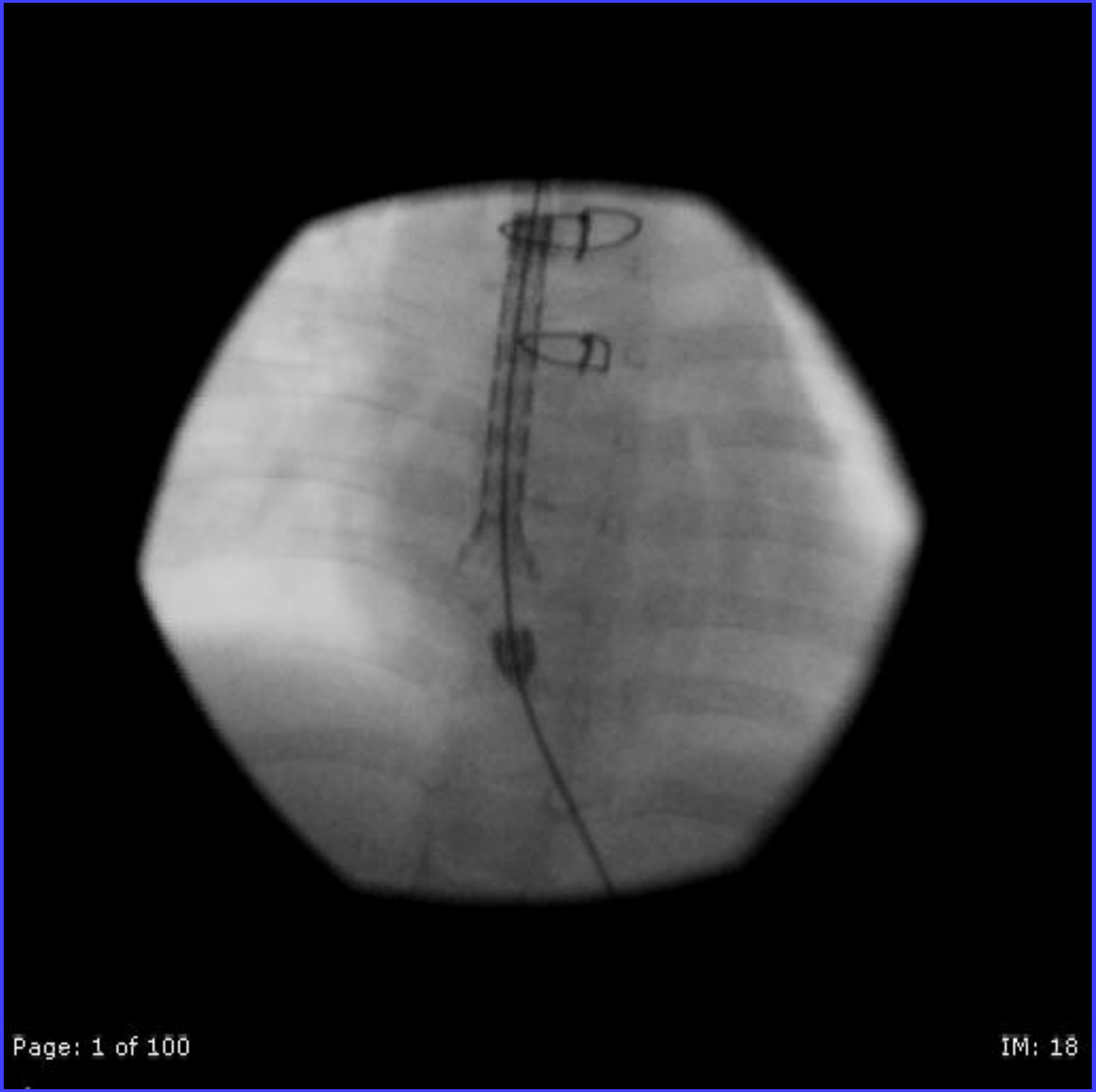


SEPS




PHILIPS BV Pulsera

FCSEMS Placement



Adult Stent Literature for Benign Strictures

Author	Stent Type	n	Reported Success*	Population
Repici (2004)	SEPS	15	80%	mixed
Dua (2008)	SEPS	38	32%	mixed
Barthel (2008)	SEPS	8	12%	anastomotic
Pennathur (2008)	SEPS	9	22%.	mixed
Fiorini (2001)	FCSEMS	10	50%	mixed
Kim (2008)	FCSEMS	55	33%	mixed
Bakken (2010)	FCSEMS	10	20%	mixed

* Reported success defined as no recurrent stricture

Pediatric Stent Literature

Author	Stent Type	n	Reported Success*	Population
Broto (2003)	SEPS	10	50%	caustic
Zhang (2005)	FCSEMS	8	75%	caustic
Best (2009)	FCSEMS	7	86%	mixed

* Reported success defined as no recurrent stricture

Mitomycin C

- Antineoplastic agent
  - disrupts base paring of DNA molecules
  - inhibits fibroblast proliferation and induces apoptosis in higher doses
- Has been used as an antiproliferative agent since the 1980’s in ophthalmology
- Long term effect on the esophagus is unknown

Topical Mitomycin C

- Questions:
  - Dose: range from .004mg/ml to 1mg/ml
    - .4mg/ml at our institution
  - Frequency of applications and limit
    - Unknown however it appears safe to have multiple applications
  - Technique
    - Topical with soaked pledget: care must be given to contact scar tissue only therefore placed with use of overtube, friction fit cap, rigid scope

Topical Mitomycin C

Technique

- Alternatively dripped on mucosa with sclerotherapy needle or placed with ERCP double lumen cytology brush

Length of time

- The drug is applied for 2 to 5 minutes

Irrigate or not Irrigate with saline

- No consensuses at our institution we irrigate the area after application to minimize any potential toxicity

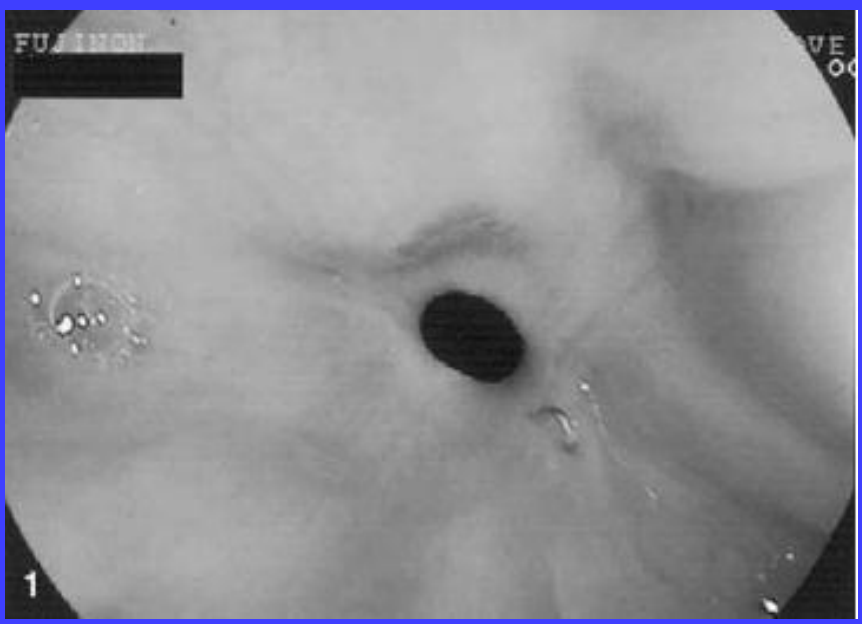
Mitomycin C

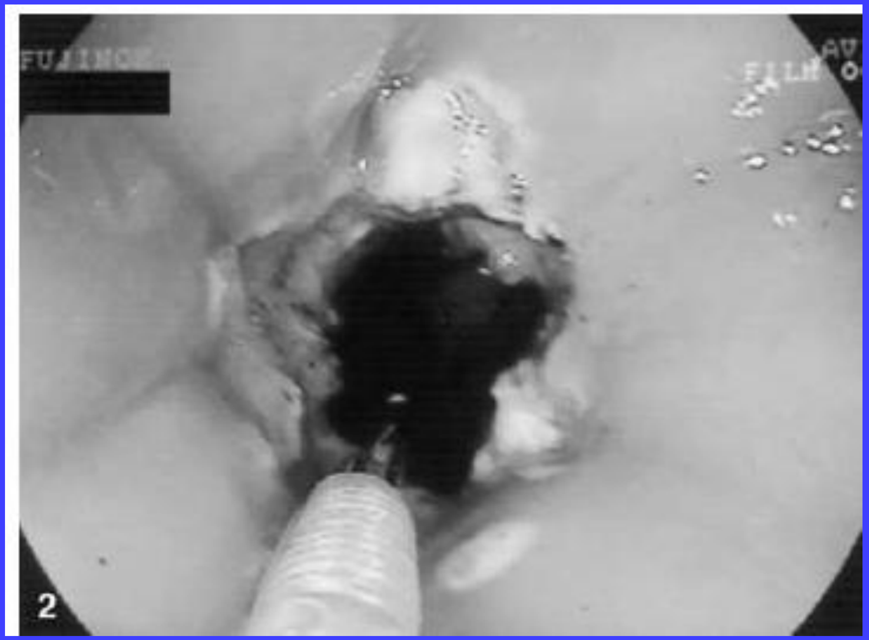
Author	# of patients	Conc of MMC used	Exposure time of MMC (min)	Success Rate**	Complications
Rosseneu et al, 2007	16	0.1 mg/ml - 0.3mg/ml	Range: 2-5	Major: 62.5 %; Partial: 18.7% None: 18.7%	None
Uhlen et al, 2006	4	1mg/ml	2	100 %	None
Heran et al, 2008	2	0.1mg/ml	1	100%	None
Chung et al, 2010	1	0.1mg/ml	3	100%	None
Olutoye et al, 2006	1	4 micro grams/ml	1	100%	None
Afzal et el, 2002	1	0.1 mg/ml	2	100%	None

**Defined as no recurrent stricture or decrease dilation frequency

Incisional Therapy

- Alternative to repeat dilations the use of electrocautery





Incisional Therapy

- Use needle knife cautery in order to make radial cuts into the stricture
- Use ERBE cut settings of 100 to 200W
- Considered in refractory *anastomotic* strictures

Incisional Therapy

Incisional Therapy

Surgery

- Esophageal resection with reanastomosis
- Esophagogastric anastomosis
- Colonic interposition
- Jejunal interposition

Refractory Stricture Algorithm

Balloon Dilation or Savory Dilation

Dilate up to 16-18mm	Up to 5 sessions

↓

Dilation combined with intralesional steroid injection (max 3 sessions)

↓

Anastomotic strictures consider Incisional Therapy (max 3 sessions)

Consider Mitomycin C (max 3 sessions)

↓

Stent Placement

↓

Surgery

Take Home Message

- Esophageal Dilation with balloon or savory dilators are equally safe and effective for the treatment of strictures
- Dilations should be performed every two weeks for 2-3 months before deeming a stricture refractory
- Intralesional Steroid therapy should be strongly considered as first line therapy for refractory strictures

Take Home Message

- Other therapies such as Mitomycin C, incisional therapy and stent placement have some reported benefit in small uncontrolled studies
- However, these therapies have more potential risks
- Surgical resection should be considered especially in short length strictures.

- Thank You

Advanced Imaging in GI Endoscopy

Charles J. Lightdale, MD
Columbia University
New York, NY

Advanced Imaging in Endoscopy Currently Available

- High resolution white light endoscopy
- Magnification and chromoendoscopy
- Digital chromoendoscopy
- Autofluorescence imaging
- Confocal laser endomicroscopy
- Endocytoscopy

High-Resolution Endoscopy

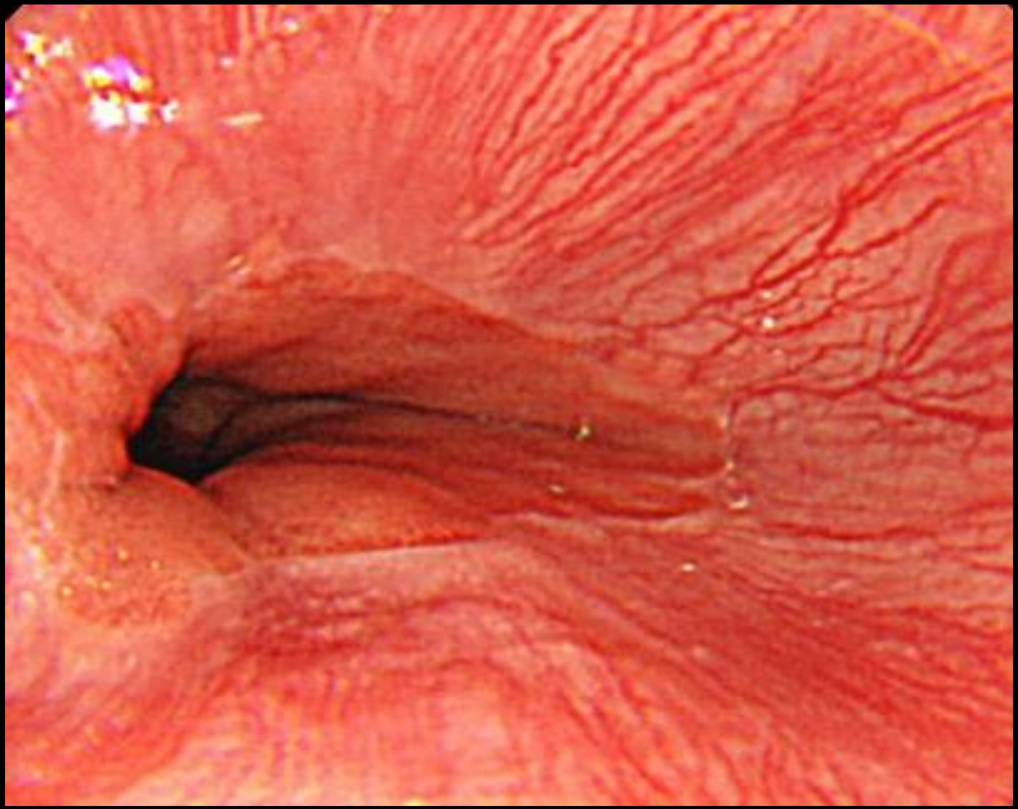
	CCD Pixels
Standard Endoscopy	300,000
High-Resolution	1,000,000

Kara, et al. Gastrointest Endosc 2005;61:671-678.

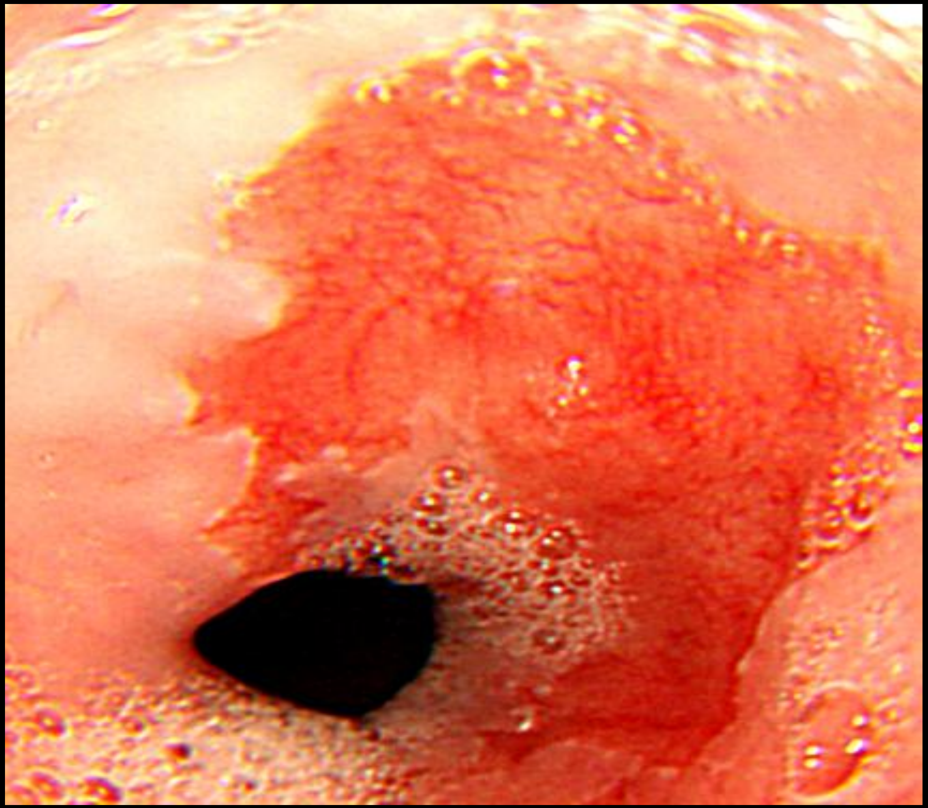
High-Definition Television

	Scanning Lines
Standard Analog	576
High-Definition TV	1080

Curvers, et al. Endoscopy 2008;40:1000-1007.



Normal



BE with HGD

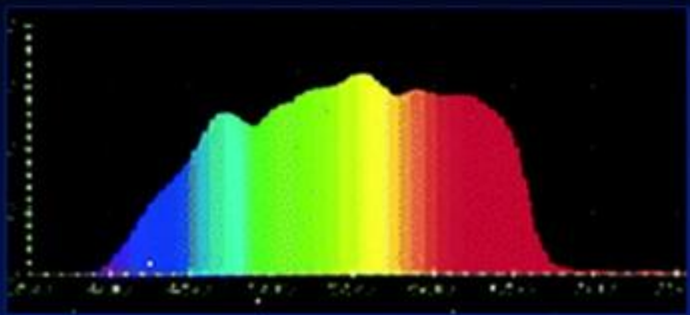
Optical Contrast Endoscopy [Virtual Image Enhanced Endoscopy]

- Reversible instant “virtual” contrast applied with the push of a button

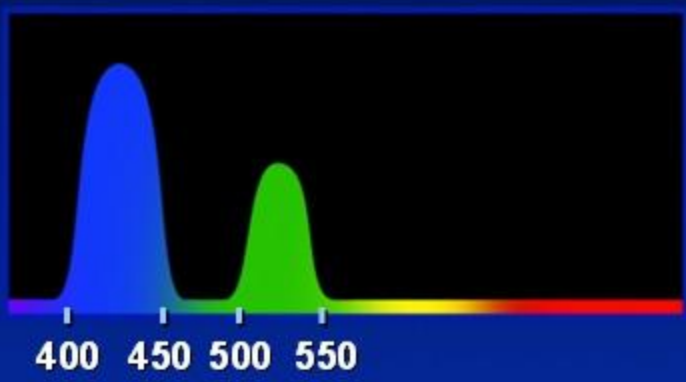
- Offers a fast and clean alternative to physical chromoendoscopy

- Olympus Narrow Band Imaging (NBI), Pentax i-Scan, Fujinon FICE

Narrow Band Imaging (NBI)



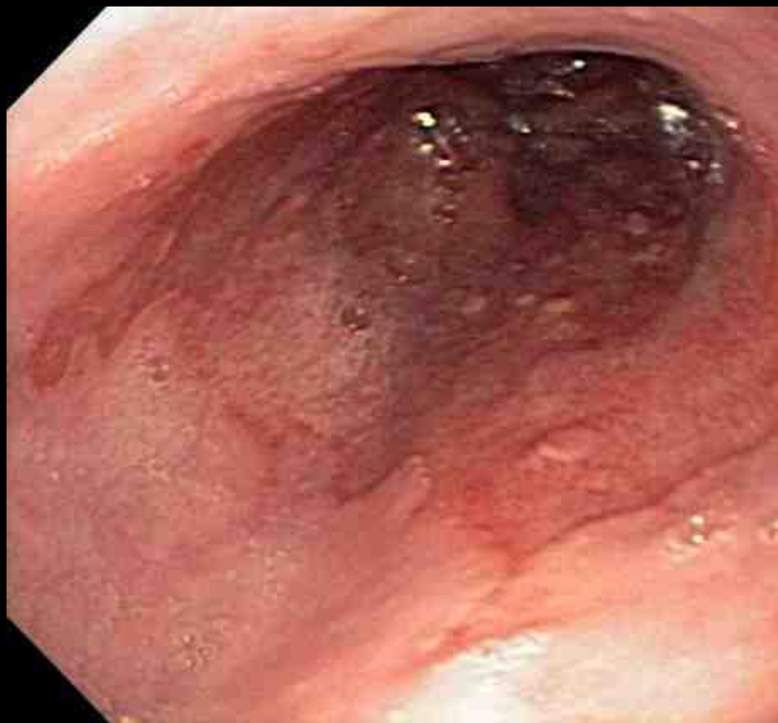
Conventional



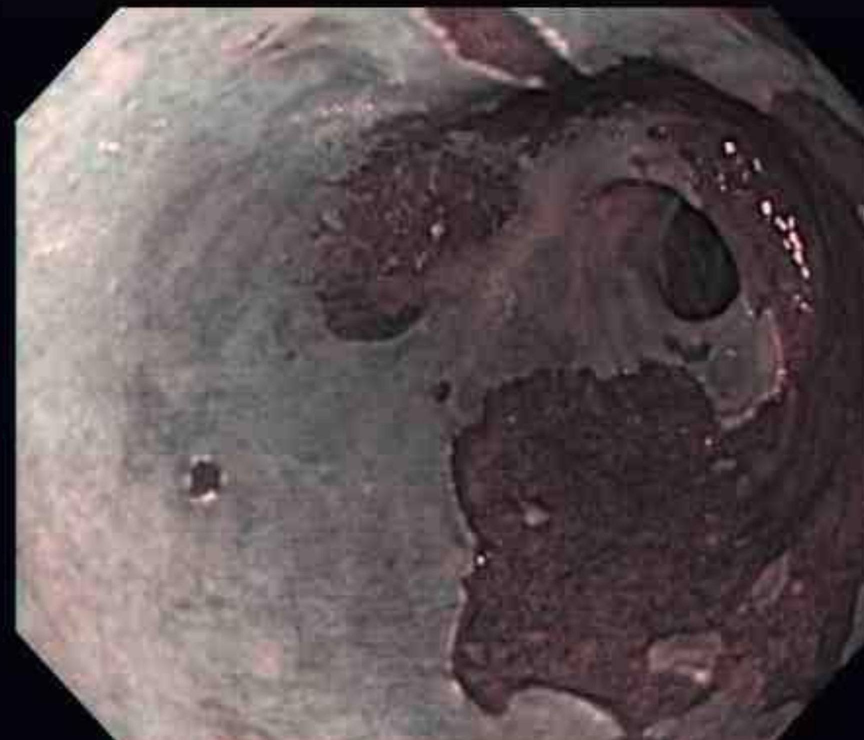
NBI

- Filters decrease the red light, allowing only narrow band of blue light and green light to illuminate the mucosal surface
- The system of NBI uses blue narrow band light (390-445 nm) and green narrow band light (530-550 nm)
- Blue light has a short wavelength that penetrates most superficially
- NBI improves the image of the mucosal surface patterns and highlights vasculature

Gono, K et al. J Biomed Opt 2004
Machida H et al. Endoscopy 2004

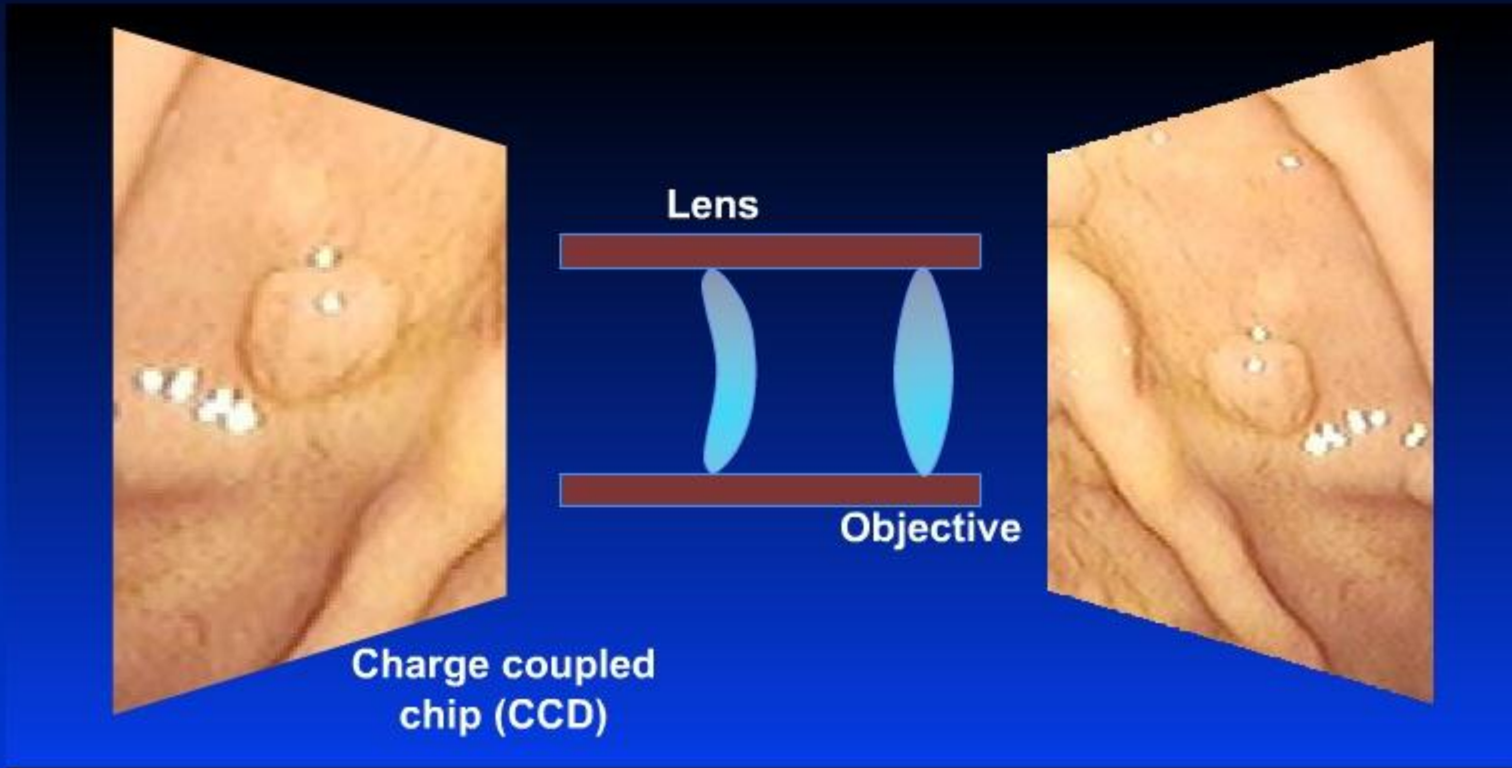


WLE



NBI

Magnification Endoscopy

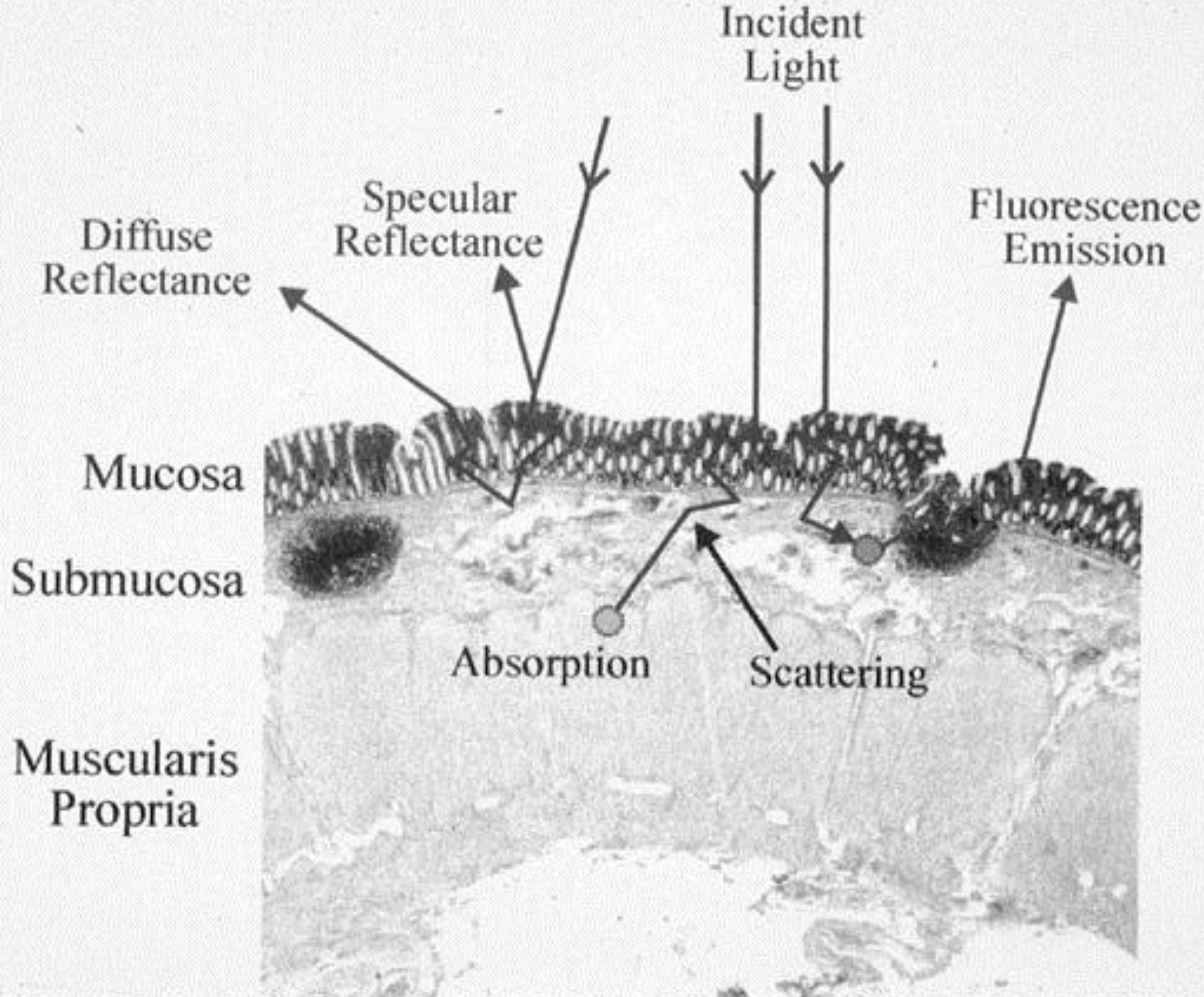


- Optical zoom does not reduce resolution
- Focal length after maximum optical zoom is short, the area covered is small
- Maximal efficiency is reached in combination with chromoendoscopy

No dysplasia vs. dysplasia in BE

Regular villous / gyriform patterns

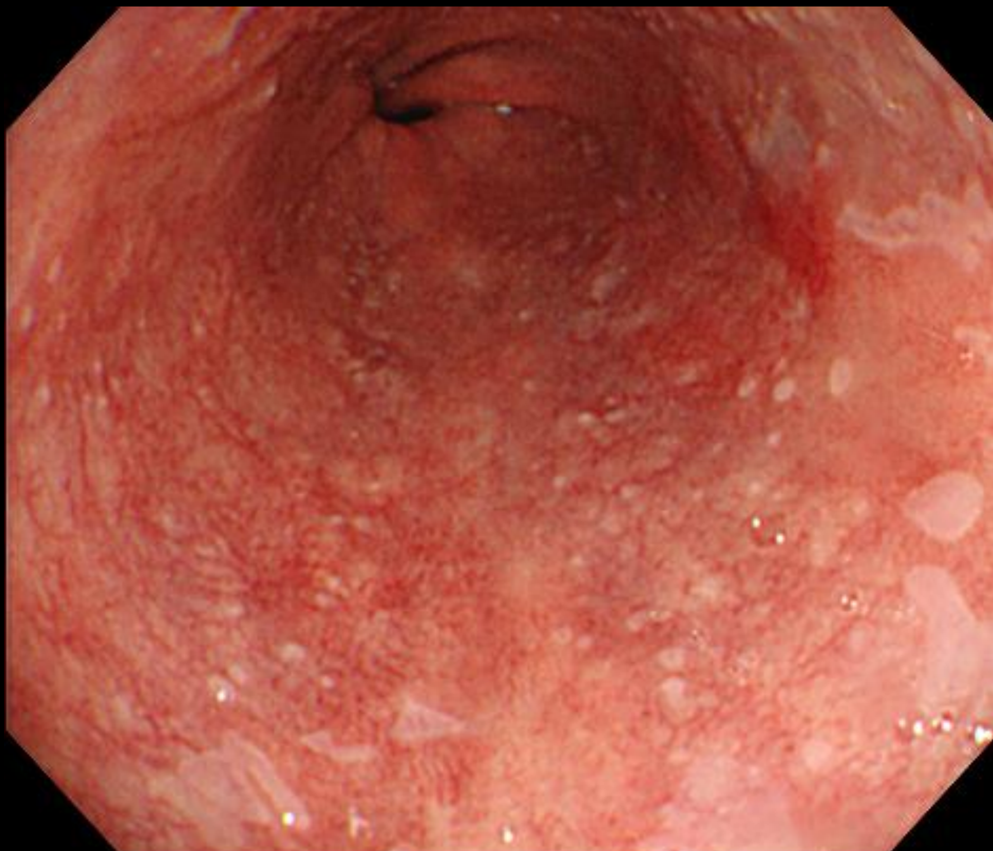
Irregular patterns or abnormal vessels


Incident
Light
Specular
Reflectance
Diffuse
Reflectance
Fluorescence
Emission
Mucosa
Submucosa
Absorption
Scattering
Muscularis
Propria

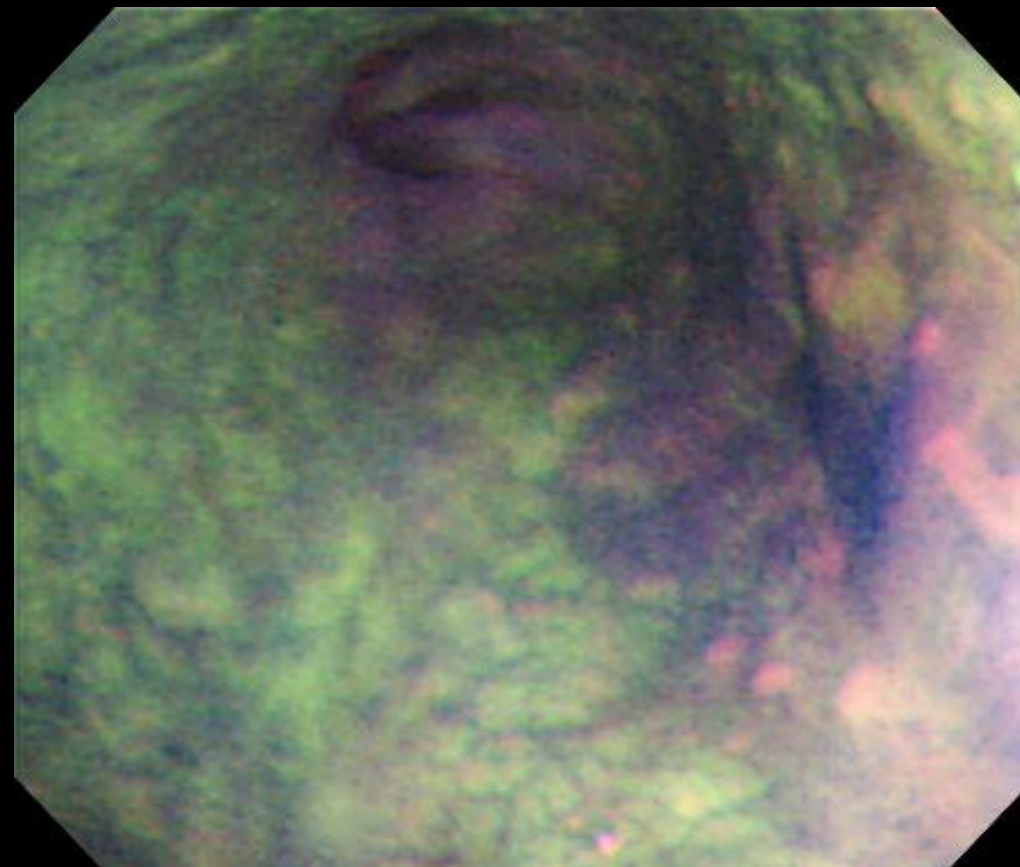
Autofluorescence Imaging (AFI)

- Endogenous substances fluoresce when excited with short wave-length light
- BE neoplasia different on AFI from BE
- Tri-modal Imaging: High Res+AFI+NBI
- Improves detection of BE neoplasia but has a high false positive rate.

AFI: High Grade Dysplasia



HD WLE



AFI

Combined Trimodal Imaging and Molecular Endpoints to Improve Risk Stratification in BE

- Targeted biopsies by AFI: 90 patients, 278 biopsies (AFI+ 178; AFI- 106)
- 3 biomarker panel correlated with dyplasia: aneuploidy, p53 IHC, Cyclin A ($p < 0.05$)
- Biomarkers ↑ in AFI+ areas ($p=0.003$)
- AFI- or < 2 biomarkers = low risk group: sensitivity 95%, specificity 80% for HGD/EC

Shariff et al. DDW 2012; Abstract 958.

Microscopy for the Endoscopist
Currently Available

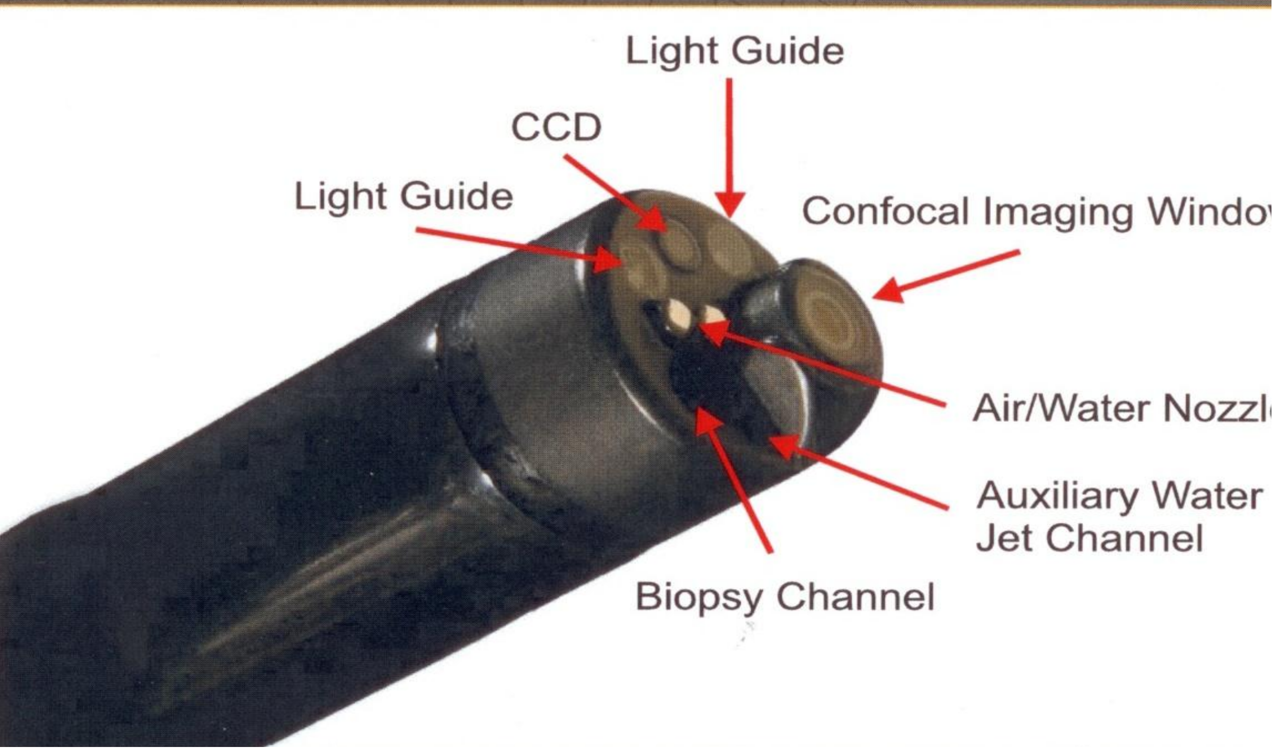
- Confocal laser endomicroscopy
- Endocytoscopy

Confocal Laser Endomicroscopy

- Optical biopsy; in vivo histology
- Magnification and resolution (~1 micron)
- Dedicated endoscope system (eCLE)
- Catheter-probe based system (pCLE)
- eCLE slightly better resolution
- pCLE faster image acquisition; flexible use
- IV Fluorescein used for contrast

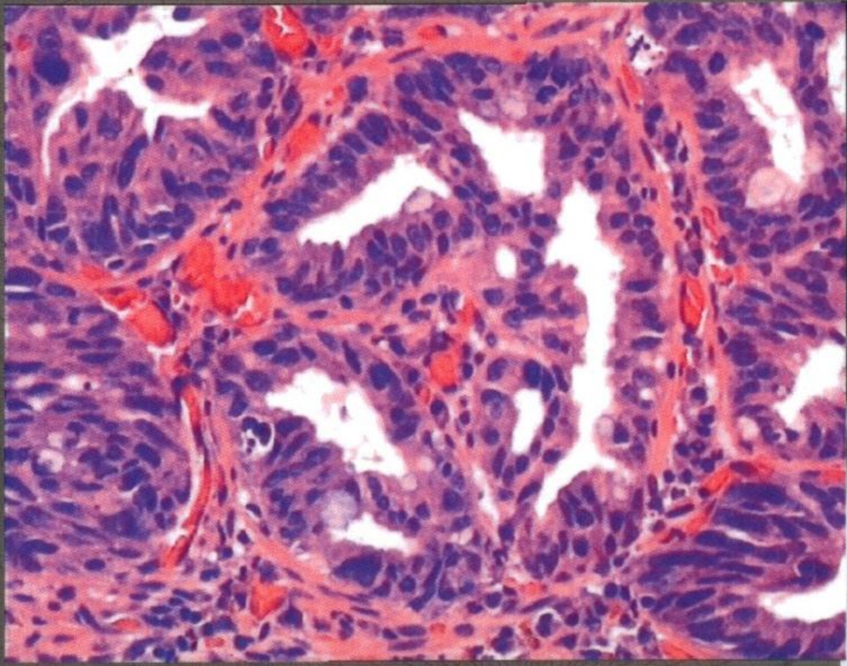
Kiesslich. Gastrointest Endosc Clin N Am. 2008;18(3):451-66.
Wallace. Aliment Pharmacol Ther 2010;31:548-52.

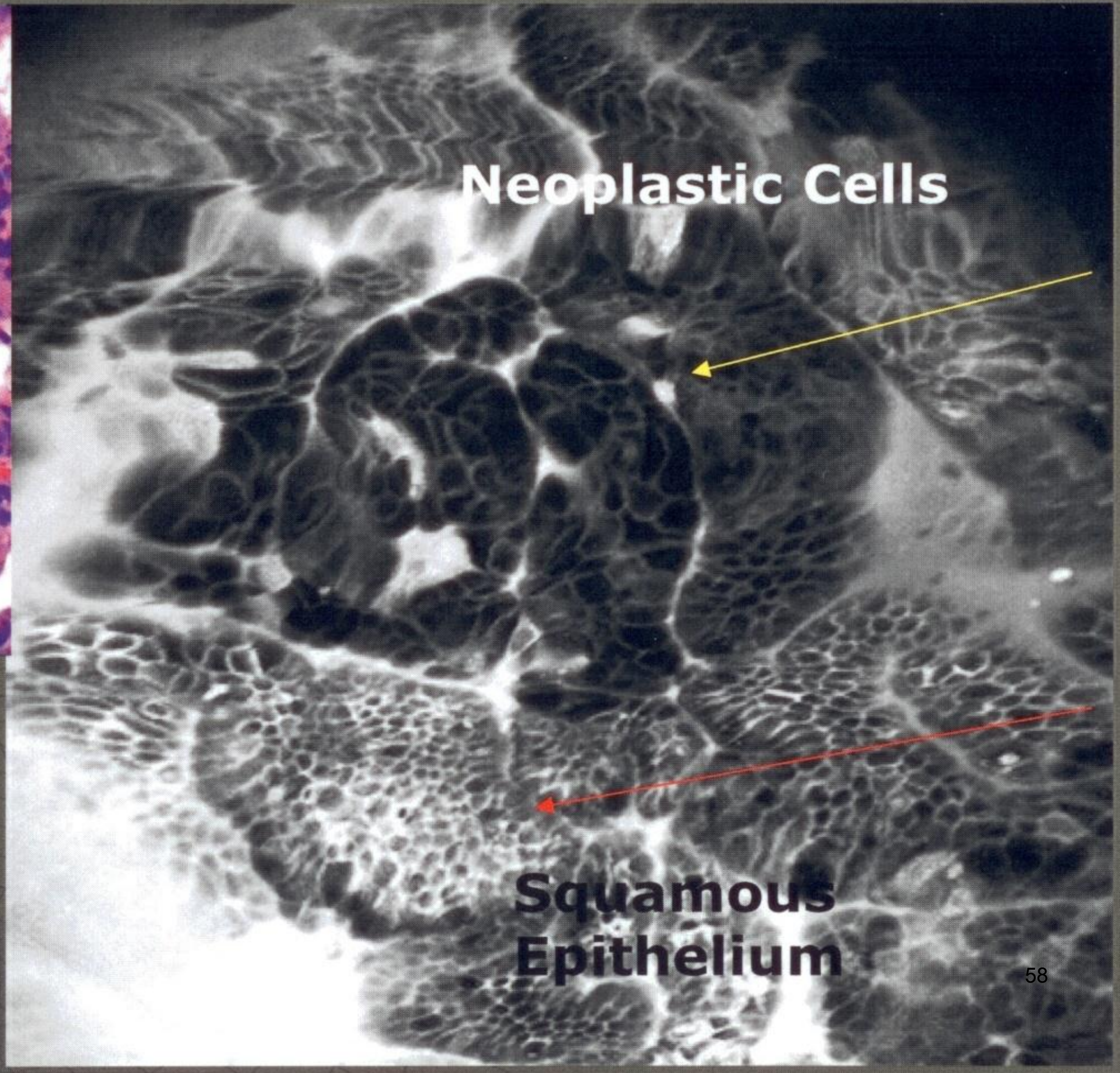
Confocal Endomicroscopy



eCLE
Pentax/Optiscan

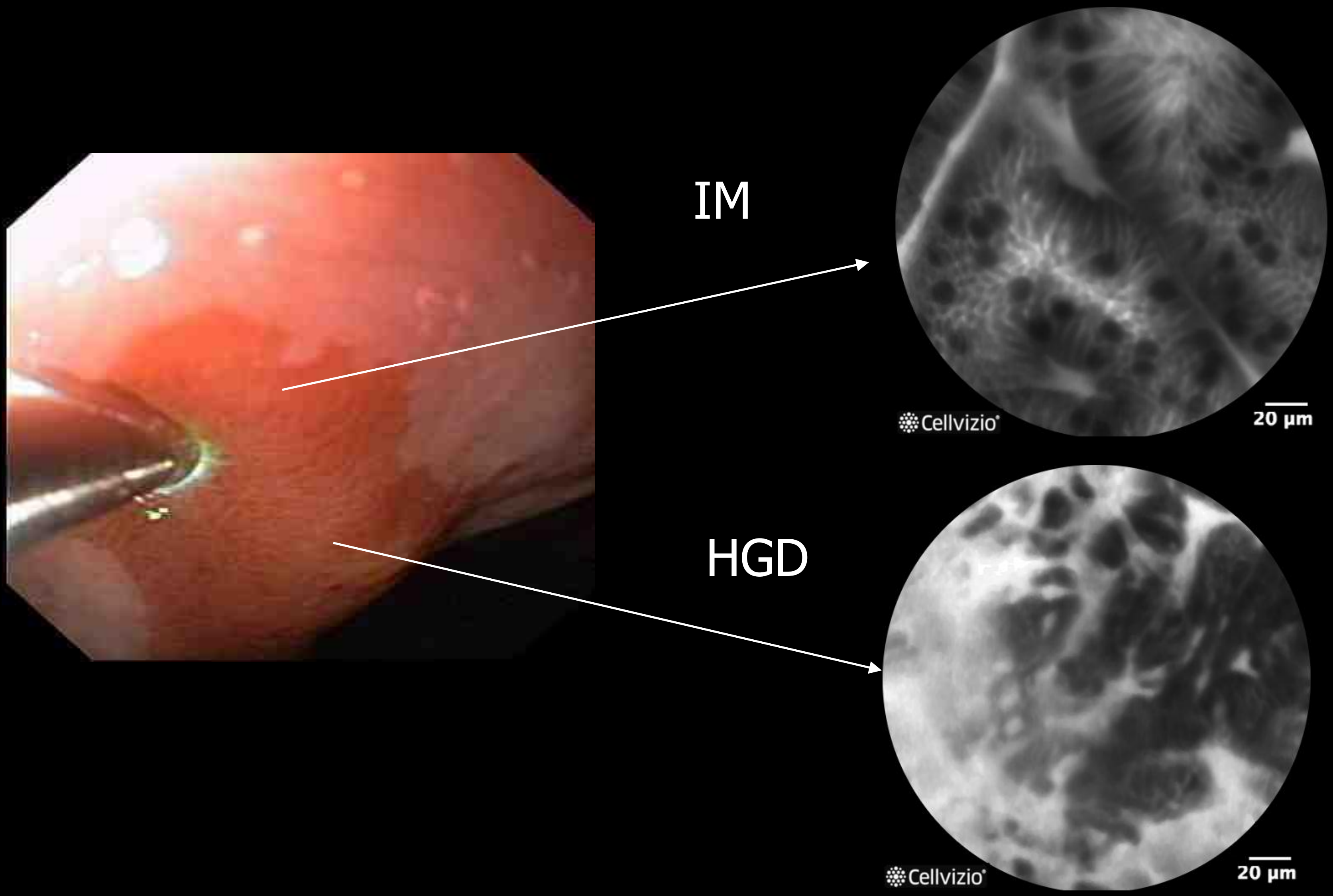
Confocal: Barrett's neoplasia

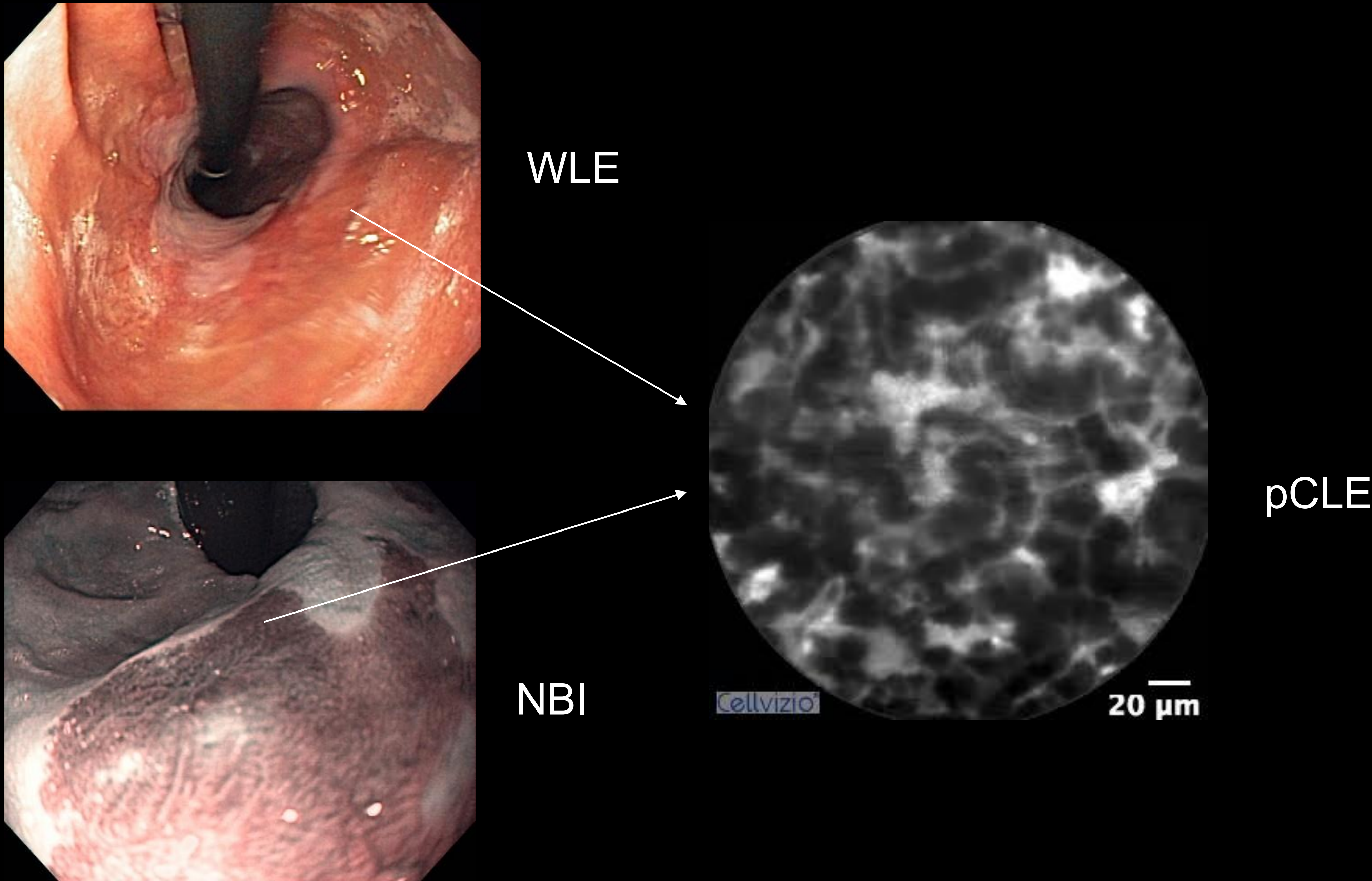


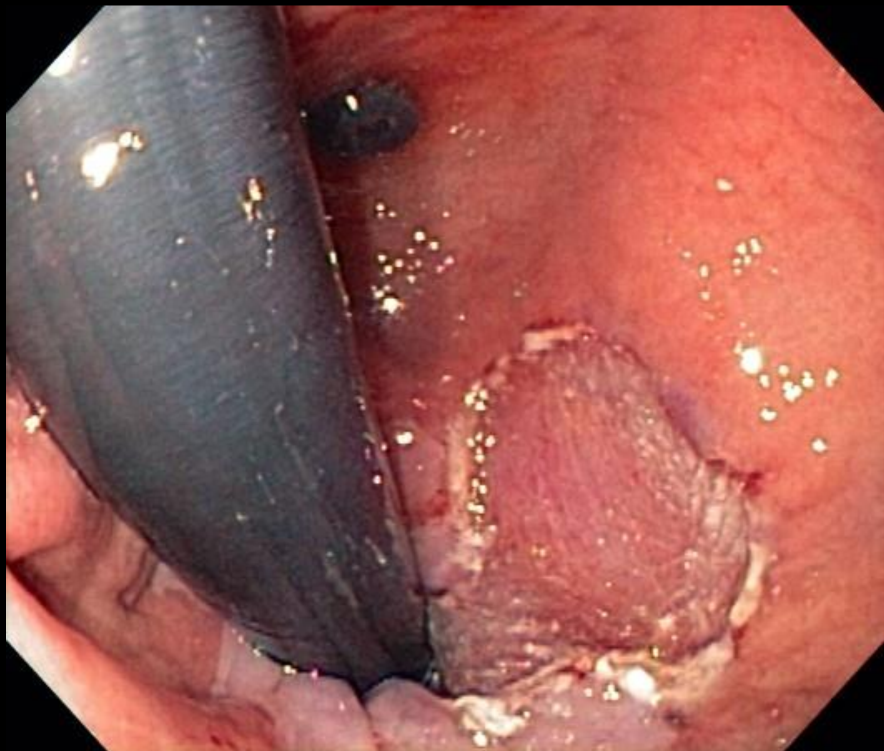


Kiesslich CGH,2006;4:979

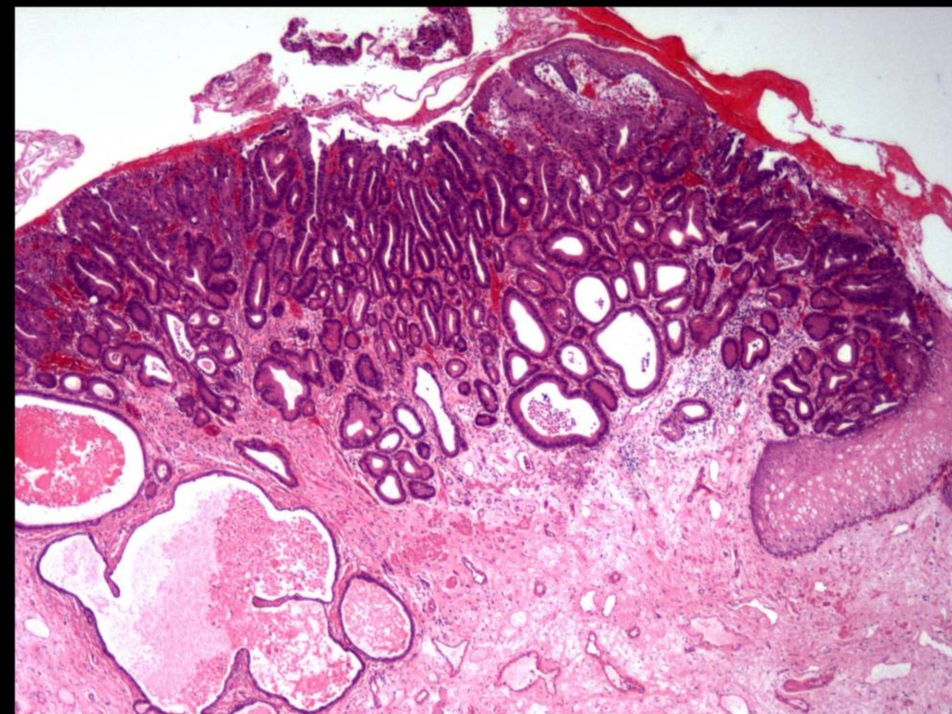
Confocal Probe BE




WLE
NBI
Cellvizio
20 µm
pCLE



EMR

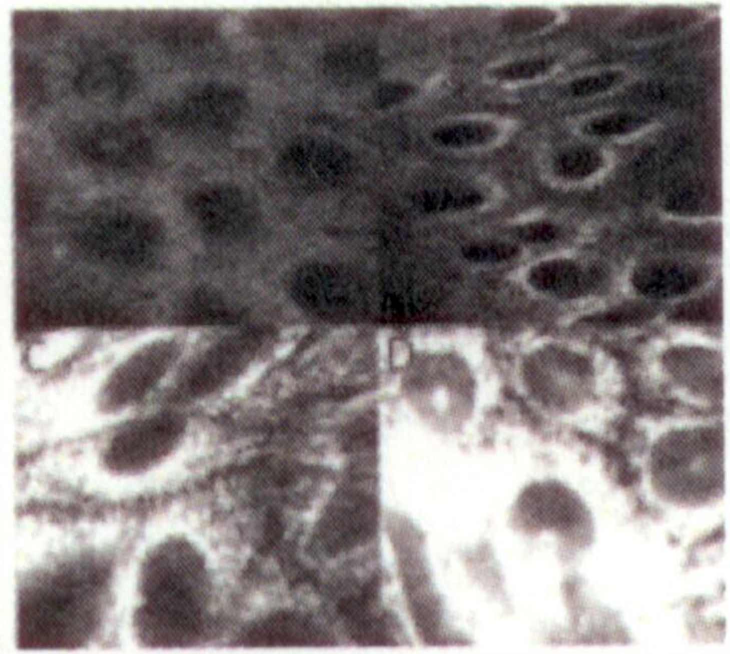
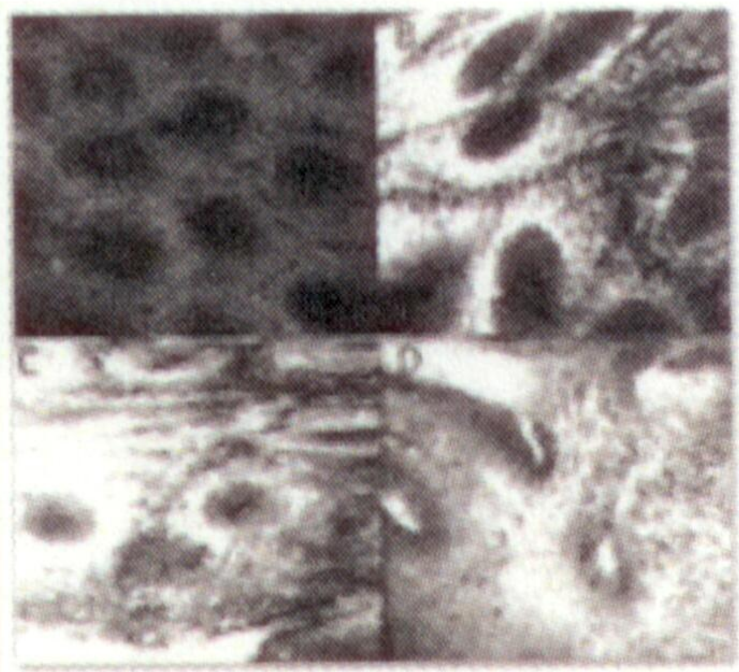


PATH = HGD

CLE in Inflammatory Bowel Disease

1. Grading severity of inflammation in UC based on crypt distortion and fluorescein leakage
2. Predicting relapse in CD and UC based on ↑ crypt lumen width and irregular vessels
3. Molecular imaging in CD using topical FITC-Adalimumab to predict anti-TNF response

1. Sauk et al. DDW 2012 #21
2. Moussata et al. DDW 2012 #22
3. Atreya et al. DDW 2012 #Su1915

Crypt Distortion: (A) Normal crypt architecture (B) Mild crypt distortion (C) Moderate crypt distortion with branching (D) Crypt dropout; crypt destruction	
Fluorescein Leakage: (A) No leakage (B) Mild leakage into lamina propria (C)Moderate leakage into lamina propria (D) Leakage into lamina propria and crypt lumen	

Per-Oral Cholangioscopy for Diagnosis of Malignant Biliary Strictures

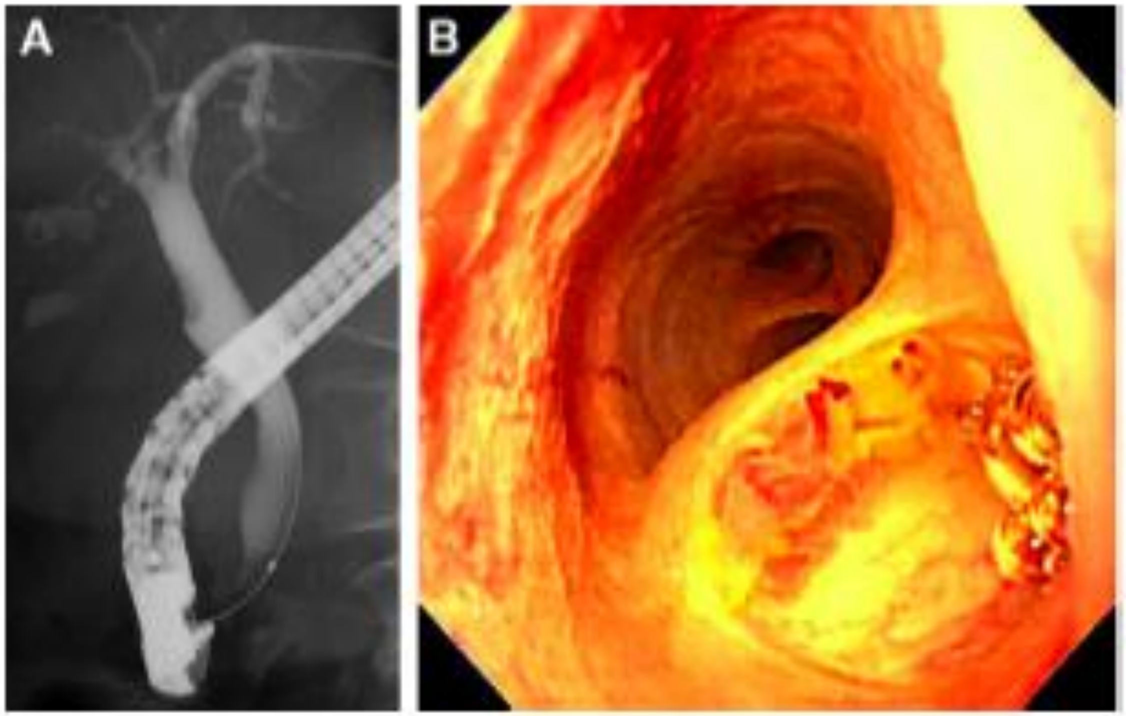
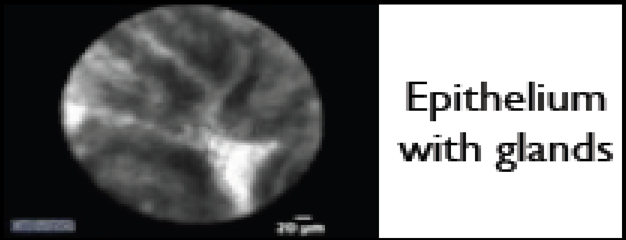
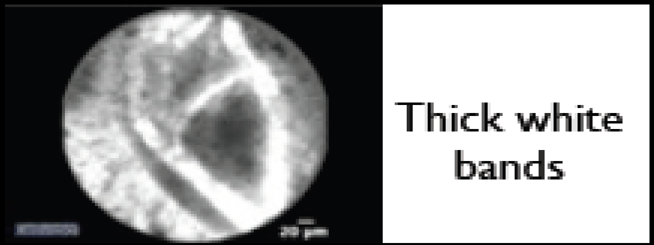


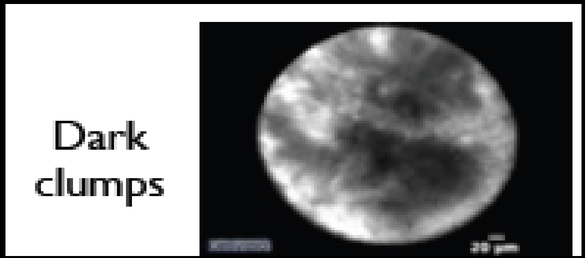
Figure 3. (A) Cholangiogram showed indeterminate filling defect. Biopsy specimens showed no malignancy. (B) Peroral video cholangioscopy (PVCS) showed tiny irregularly shaped papillary lesions from the cystic duct and diagnosed as malignancy.

Confocal Endomicroscopy for Diagnosis of Malignant Biliary Strictures

Miami Classification:
-Investigators from 6 centers reviewed videos of proven malignant and benign cases to develop descriptive classification and validate it

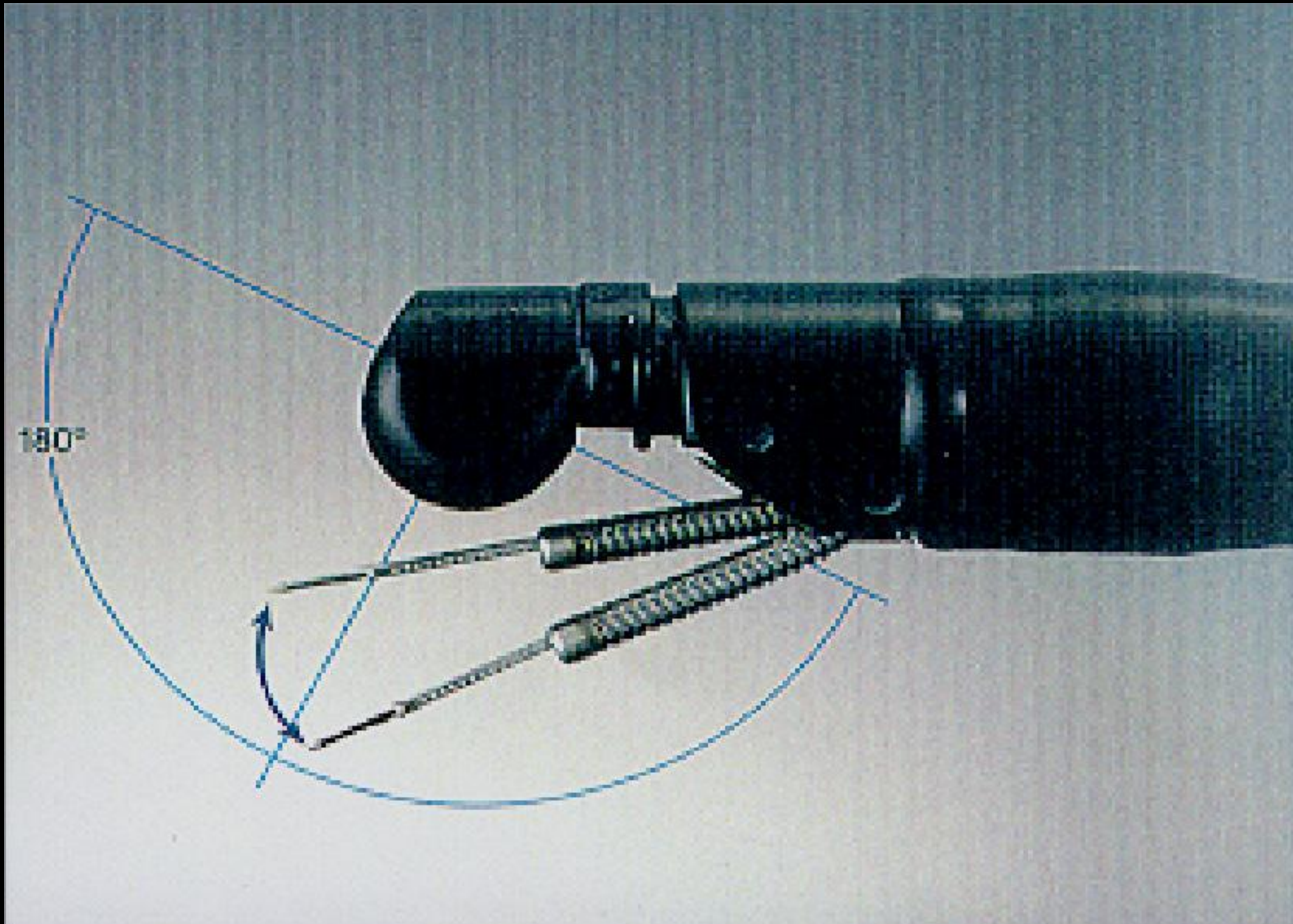






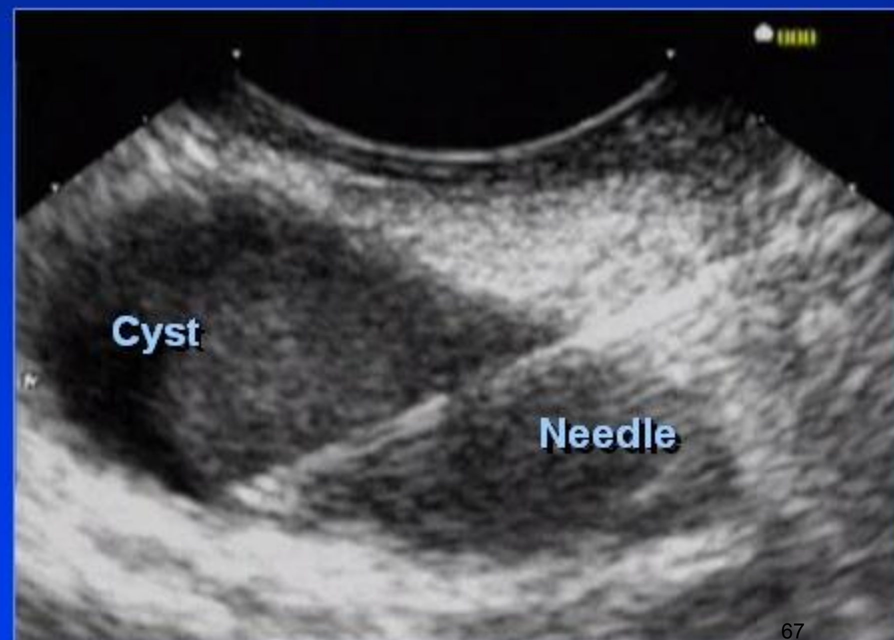
Combining 2 or more criteria: 96% sensitivity, 100% specificity for malignancy

Chen YK, et al. GIE 2010;71(5)AB788c

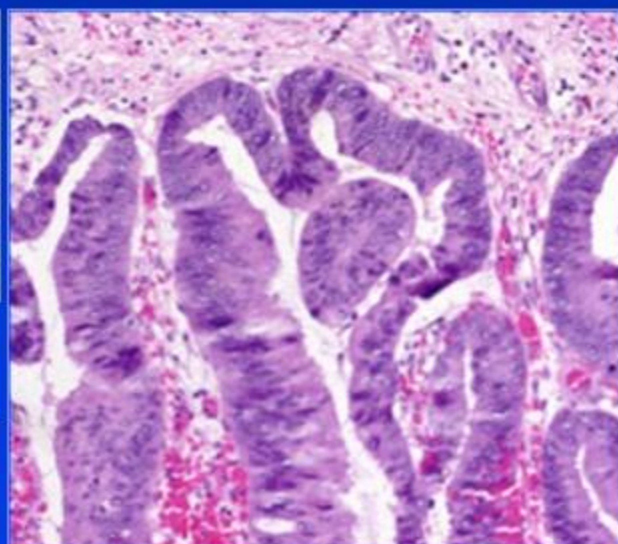

180°

Mucinous Cyst Neoplasm

- Macrocystic lesions
- Viscous, mucoid fluid
- Fluid analysis: CEA>200, low amylase
- Mucin-secreting epithelial cells
- Malignant potential




CEA staining


Histology of the epithelium

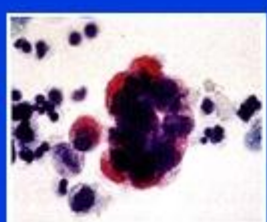
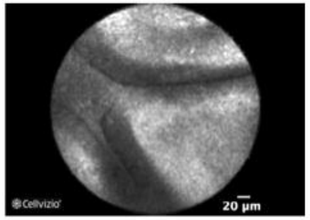
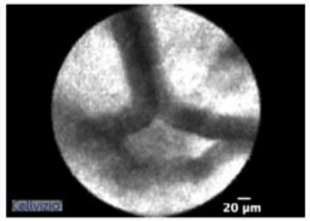
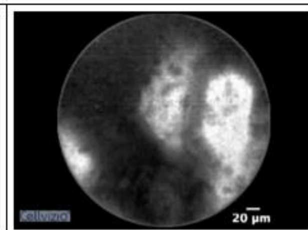
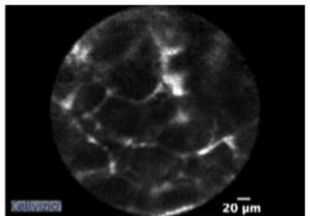
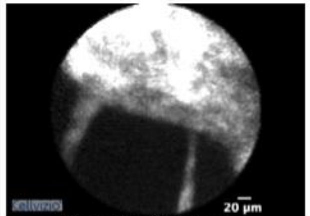
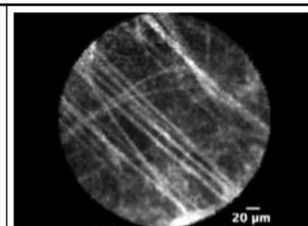
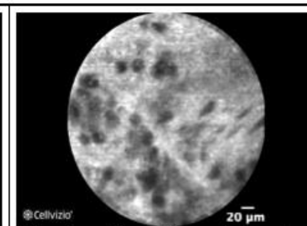
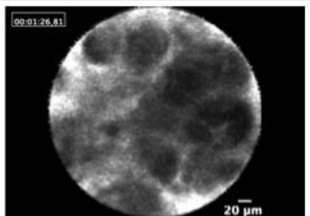
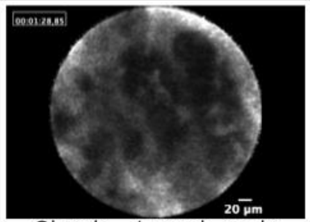
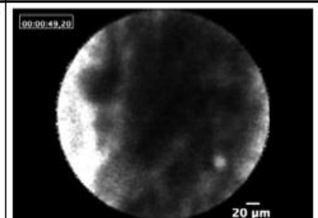
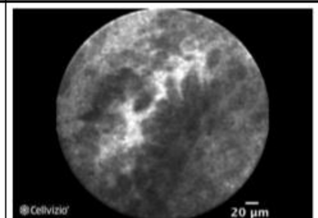
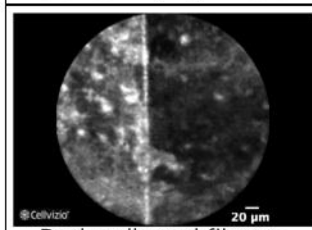
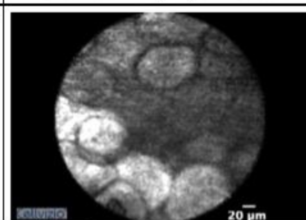
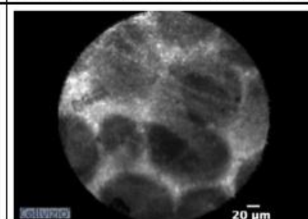
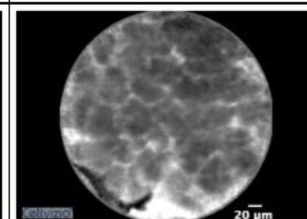
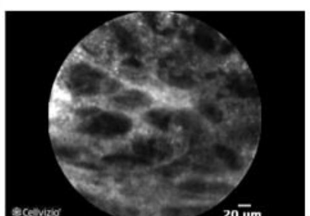
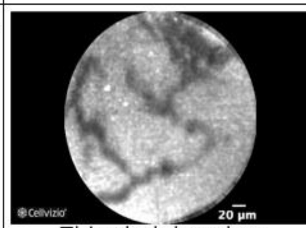
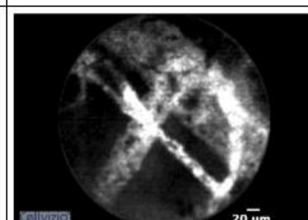
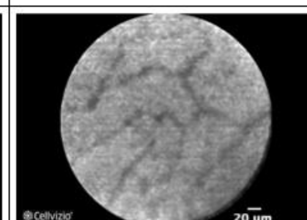
Cytology


Table 6: Images obtained during the first nCLE clinical study

<table>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td colspan="4">Papillary projections identified in IPMN cases</td>
</tr>
<tr>
<td>
Acini – IPMN</td>
<td>
Vascularization – Neuroendocrine Tumor</td>
<td>
Fibers - GIST</td>
<td>
Black cells - Pseudocyst</td>
</tr>
<tr>
<td>
Glands – Lymph node</td>
<td>
Glands – Lymph node</td>
<td>
Dark clump – Lymph node</td>
<td>
Dark cells - Sarcoma</td>
</tr>
<tr>
<td>
Dark cells and fibers - Sarcoma</td>
<td>
Thin circular structures - IPMN</td>
<td>
Thin circular structures - IPMN</td>
<td>
Acini – IPMN</td>
</tr>
<tr>
<td>
Acini – IPMN</td>
<td>
Thin dark bands – Pseudocyst</td>
<td>
Vascularization – Serous cystadenoma</td>
<td>
Thin dark bands – IPMN</td>
</tr>
</table>

Endocytoscopy

- The tip of the endoscope is equipped with a microscope-level objective optical system
- Allows cellular- level observation of the mucosal surface during endoscopy

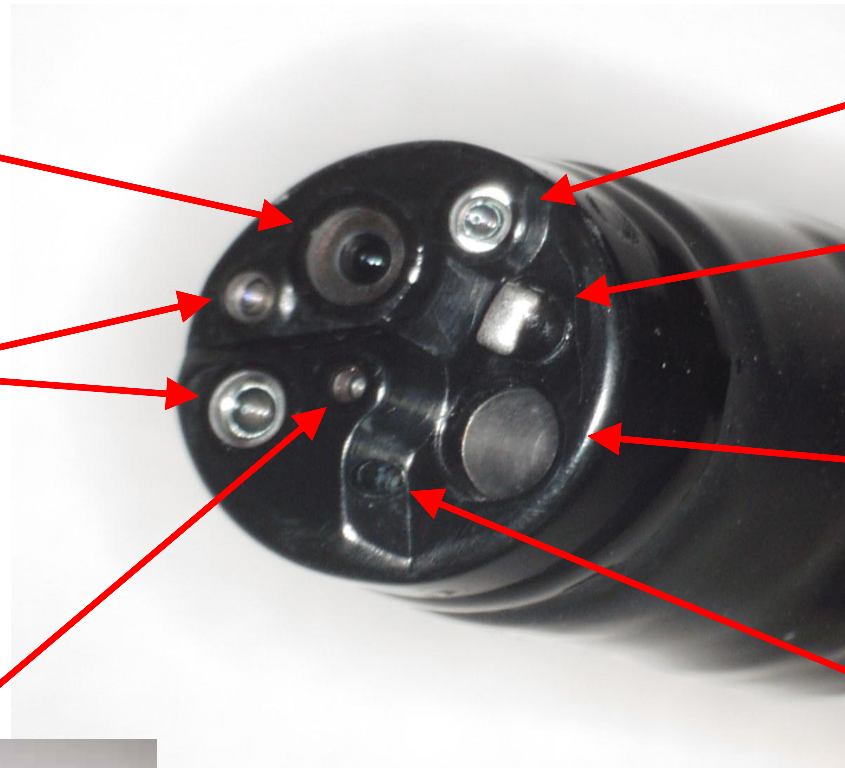
Endocytoscopy images courtesy of H. Inoue, MD.

Endocytoscopy: Dual CCD Integrated Scope type

Objective lens for conventional imaging

Light guide

Objective lens for cellular imaging



Light guide

Air/water nozzle

Instrument channel

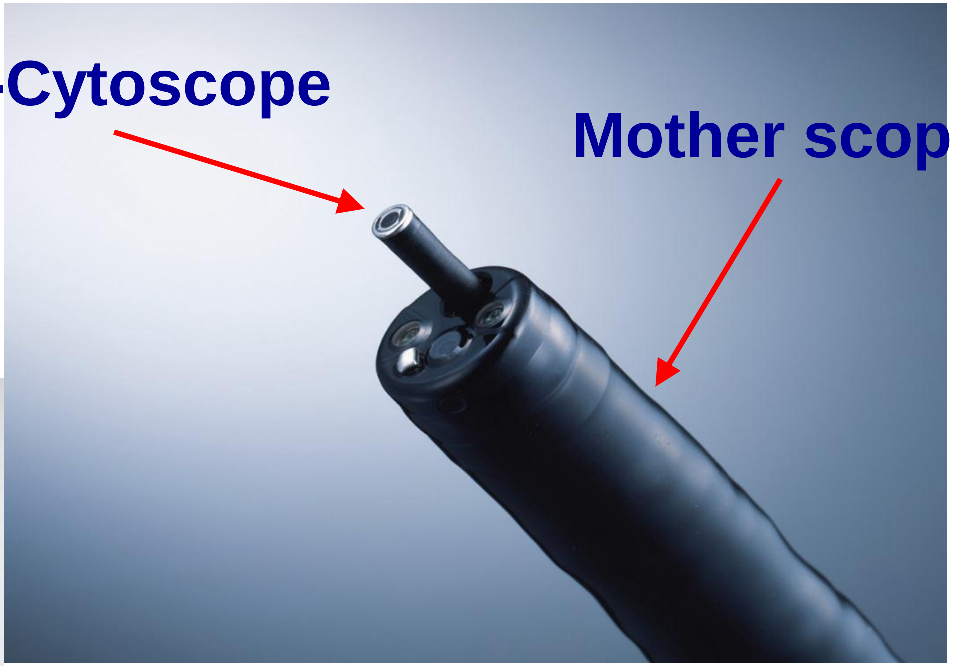
Auxiliary water channel

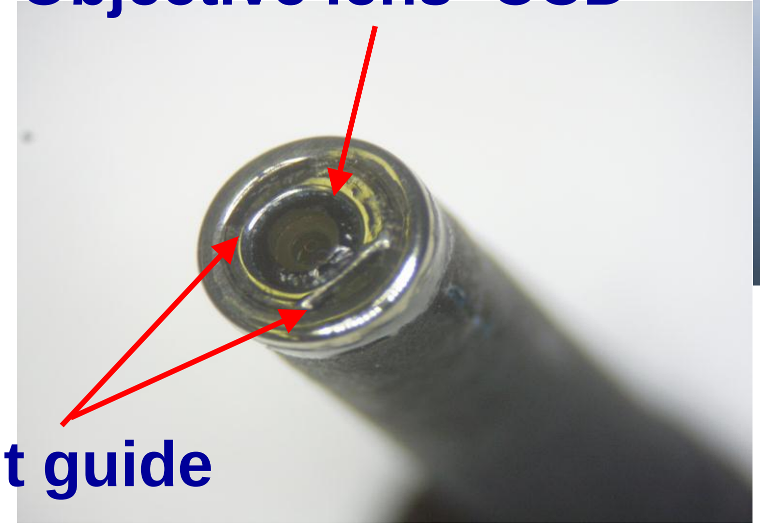
GIF-Y0001

Spec. of Dual CCD Integrated Scope type

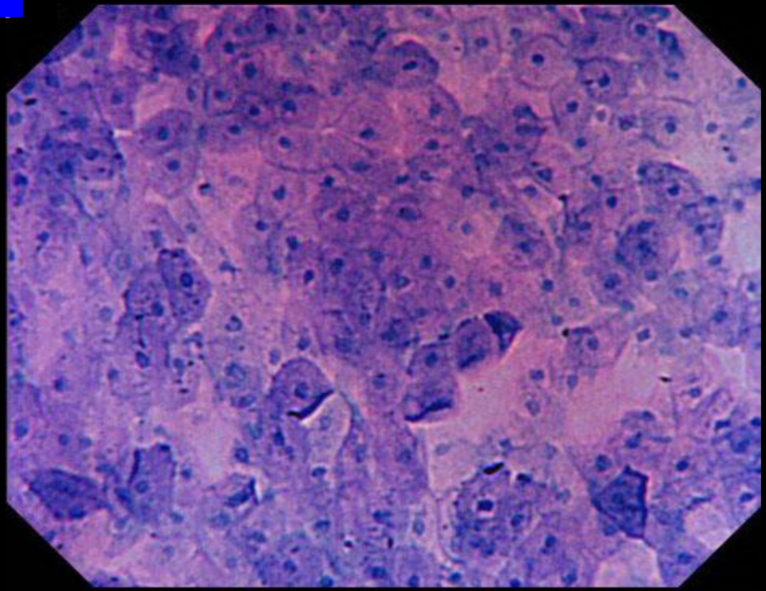
		GIF-Y0001
Conven-tional	Image Quality	Q-Image
	Magnification	Max x80
Cellular Imaging	Magnification	x580 on 19 inch monitor
	Field of view	400 x 400 μm
	Horizontal res.	4.0 μm
	Depth of field	0-50 μm
Distal end outer diameter		φ11.6 mm
Insertion tube outer diameter		φ11.3 mm
Channel diameter		φ2.8 mm

Probe type


Endo-Cytoscope
Mother scope


Objective lens+CCD
Light guide

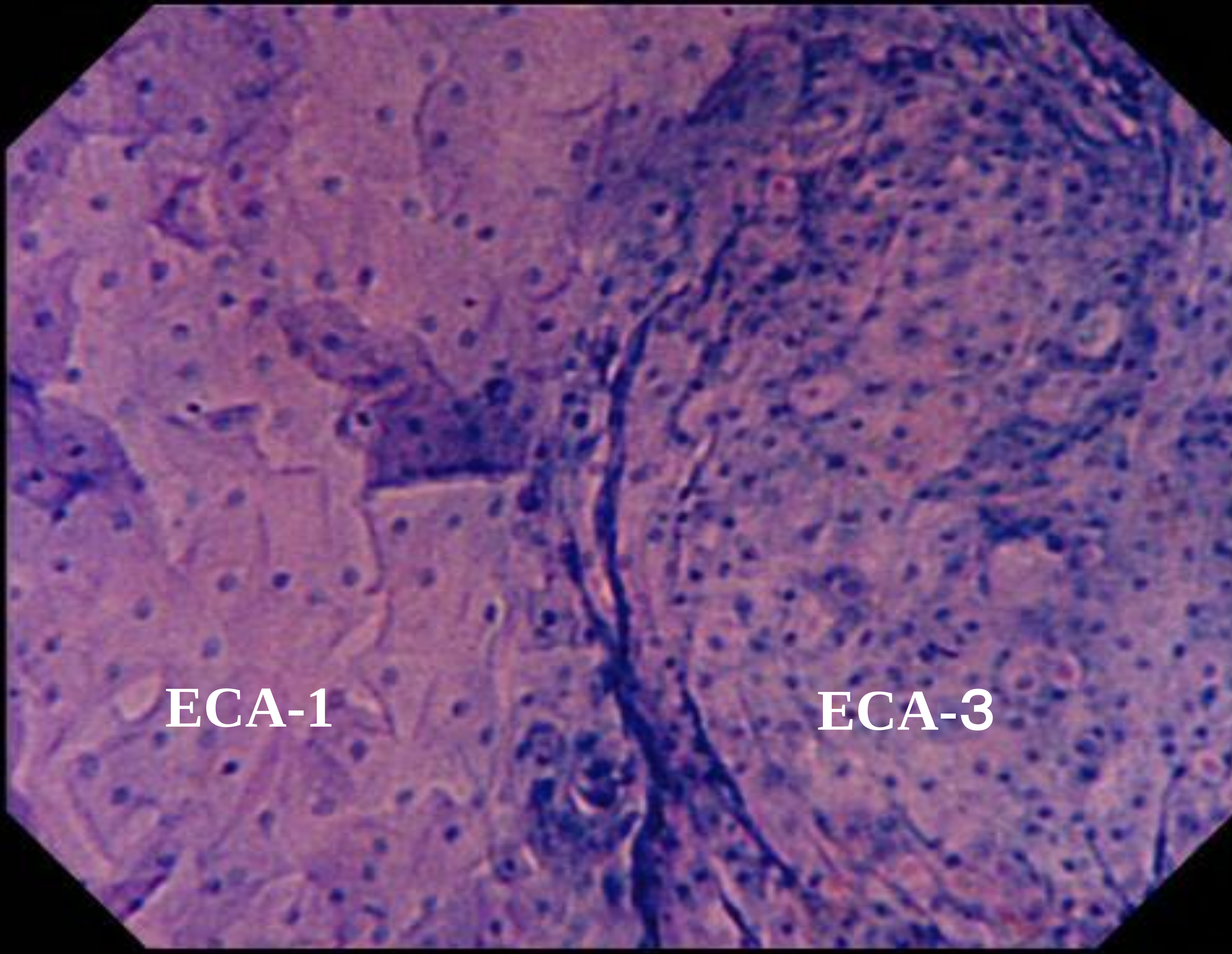
CM solution
Crystal violet and methylene blue solution

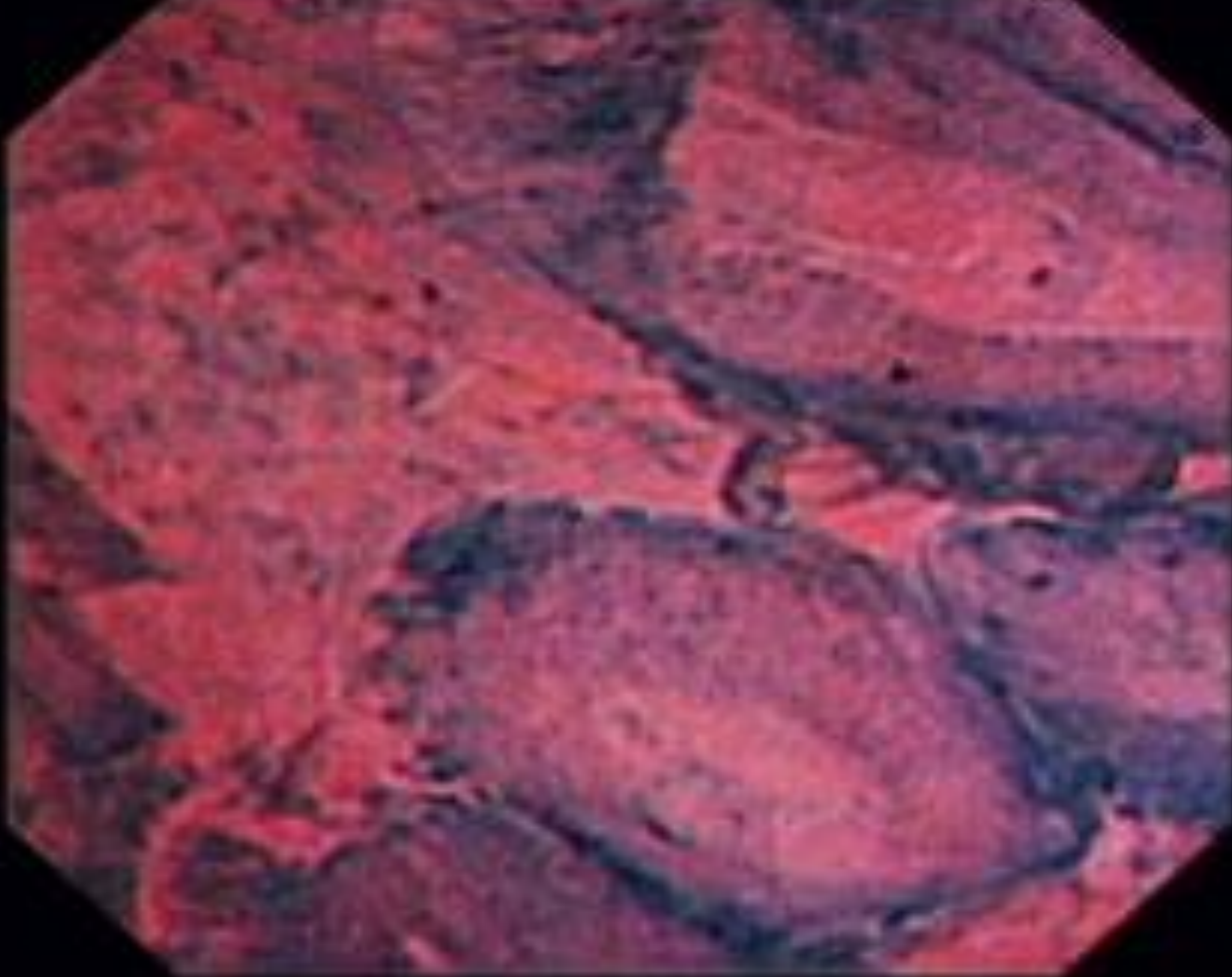


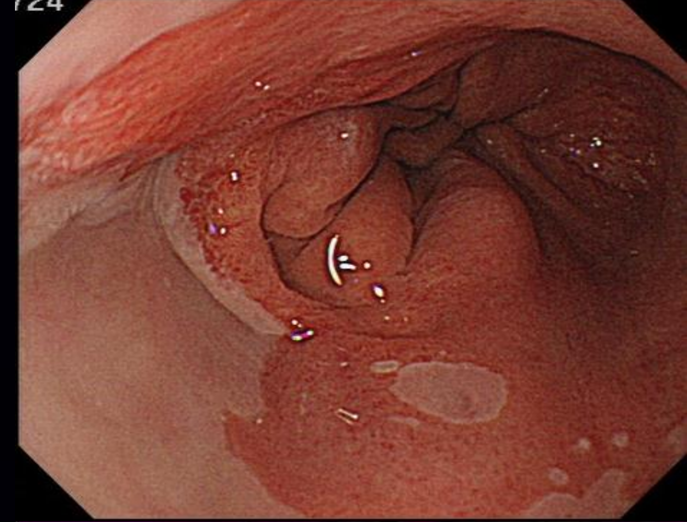
Crystal violet : methylene blue
0.025% : 0.05%

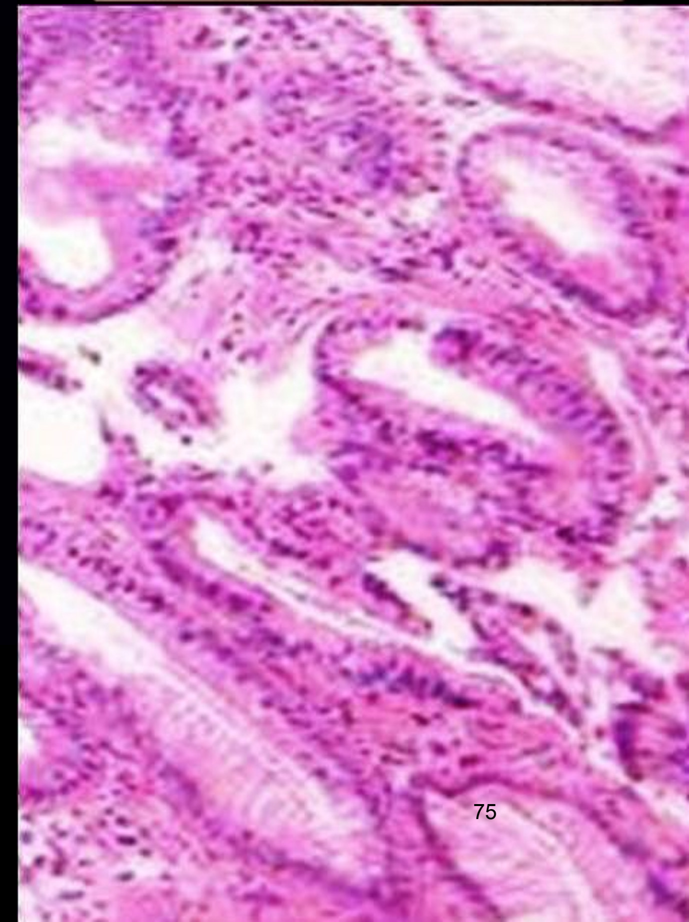
※ 1 10 times diluted methylene blue concentration
Olliver, J. R., C. P. Wild, et al. (2003). "Chromoendoscopy with methylene blue and associated DNA damage in Barrett's oesophagus." Lancet **362**(9381): 373-4.

CM2重染色









Endocytoscopy

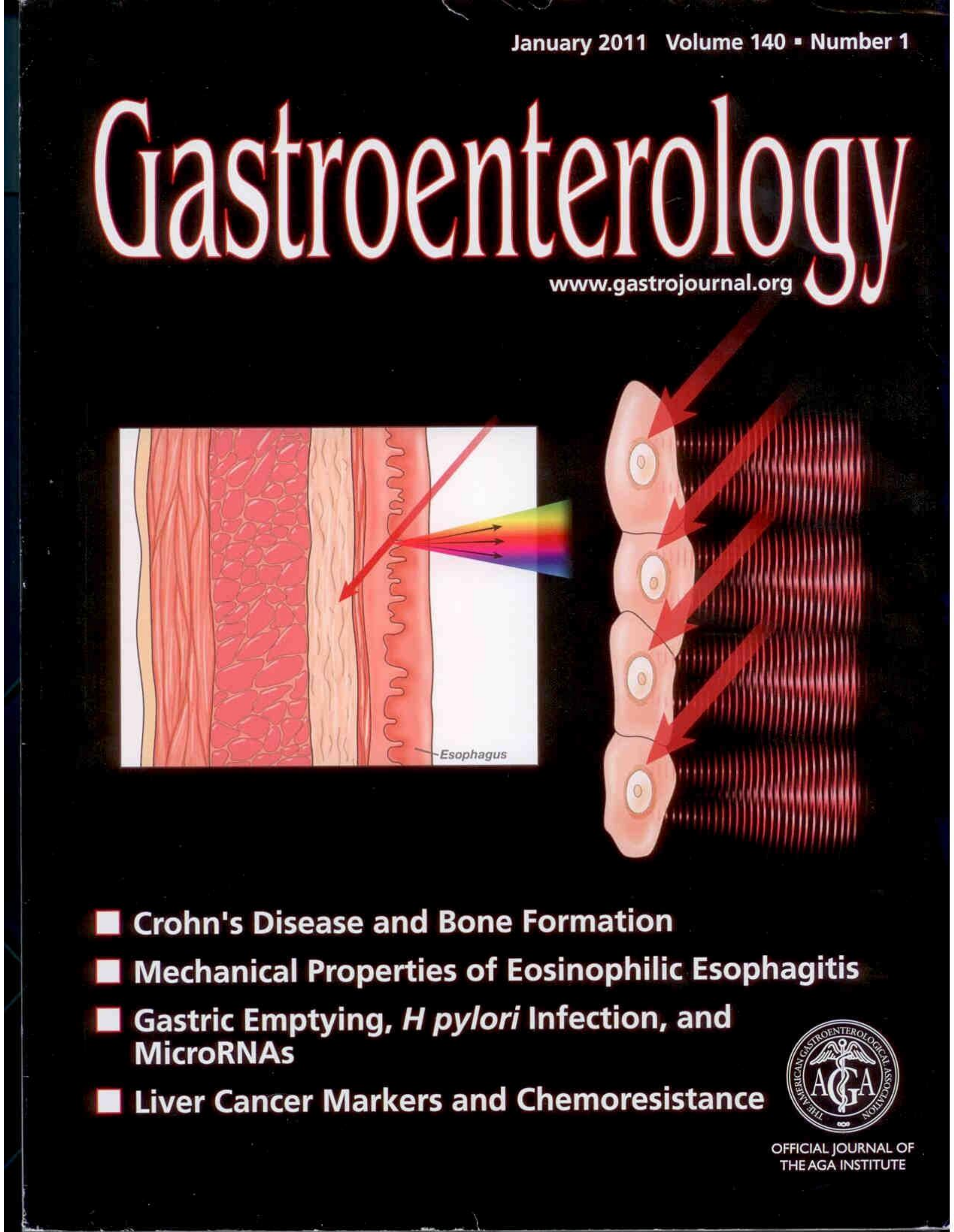
Background, ECA-2

Advanced Imaging in Endoscopy Currently Available

- High resolution white light endoscopy
- Magnification and chromoendoscopy
- Digital chromoendoscopy
- Autofluorescence imaging
- Confocal laser endomicroscopy
- Endocytoscopy

Advanced Imaging in Endoscopy
Under development

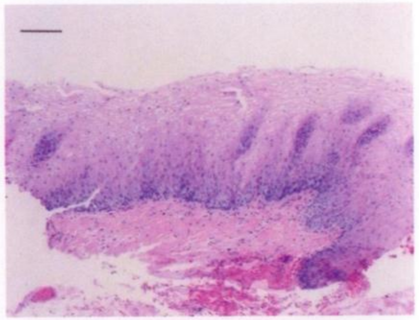
- Angle-Resolved Low-Coherence Interferometry (a/LCI)
- Optical Coherence Tomography
- Volumetric Laser Endomicroscopy
- Light Scattering Spectroscopy
- Raman Spectroscopy
- Reflectance Spectroscopy
- Molecular Imaging with fluorescent probes


January 2011 Volume 140 ▪ Number 1
Gastroenterology
www.gastrojournal.org
Esophagus
Crohn's Disease and Bone Formation
Mechanical Properties of Eosinophilic Esophagitis
Gastric Emptying, *H pylori* Infection, and MicroRNAs
Liver Cancer Markers and Chemoresistance
AGA
THE AMERICAN GASTROENTEROLOGICAL ASSOCIATION
OFFICIAL JOURNAL OF THE AGA INSTITUTE

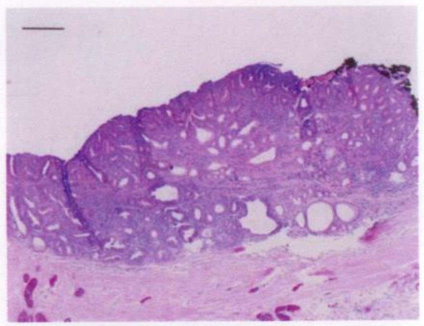
Detecting the Primary Marker for Cancer

Pathologist View

Normal tissue

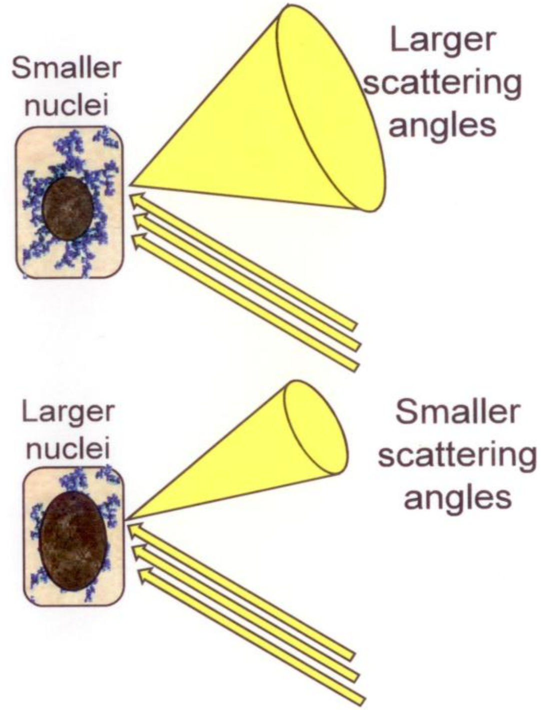


Precancerous tissue

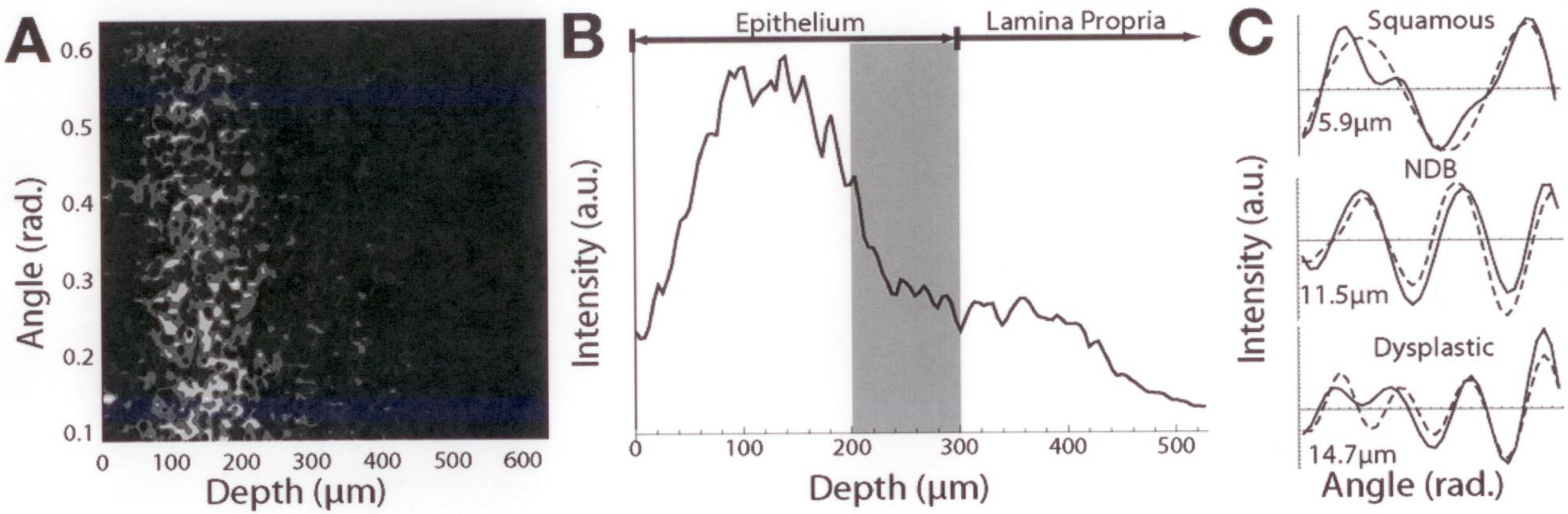


65% agreement between pathologists

Oncoscope View

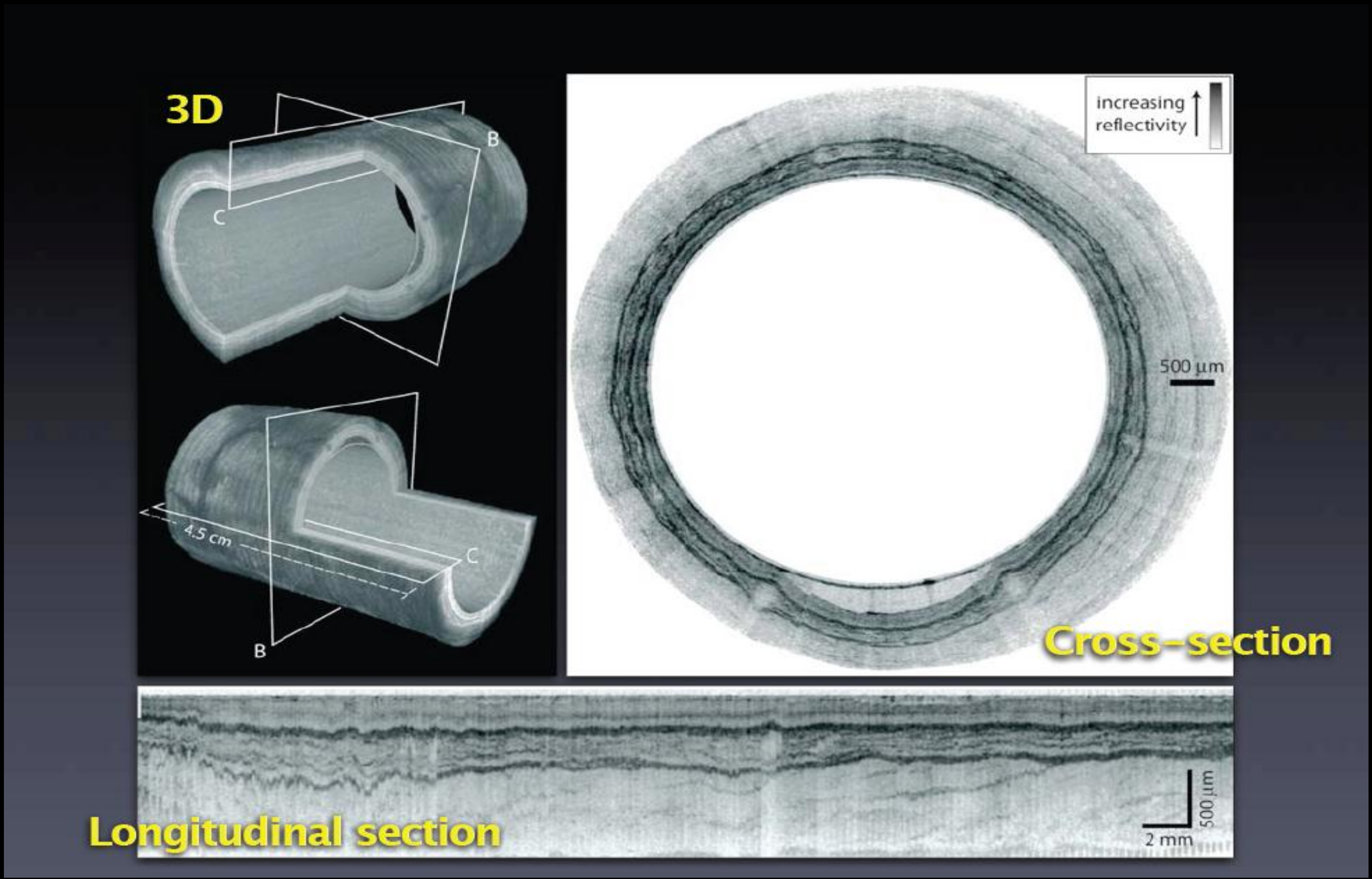


Oncoscope



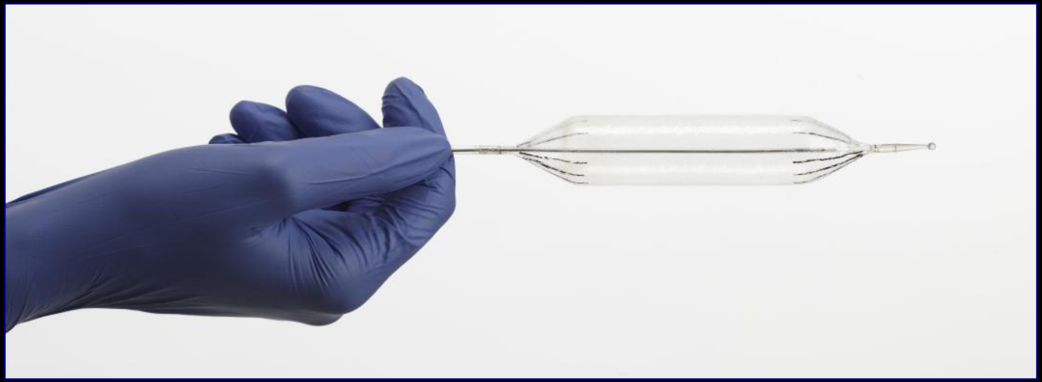
Terry, et al. Gastroenterology 2011;140:42-50.

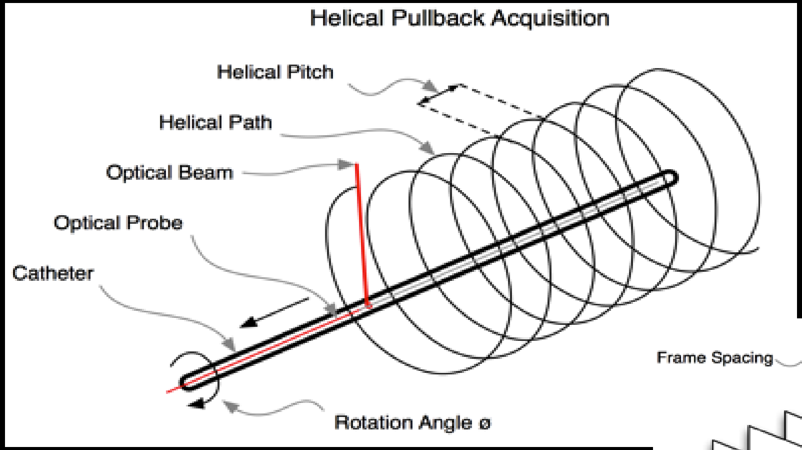
Volumetric Laser Endomicroscopy
Longitudinal Whole-Organ Views

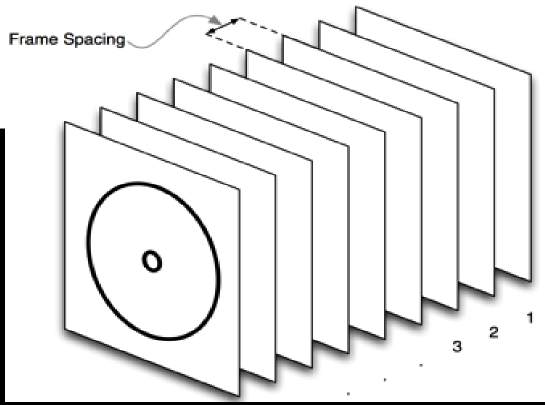


VLE Optical Probe

- Optical fiber rotates within center lumen of catheter sheath

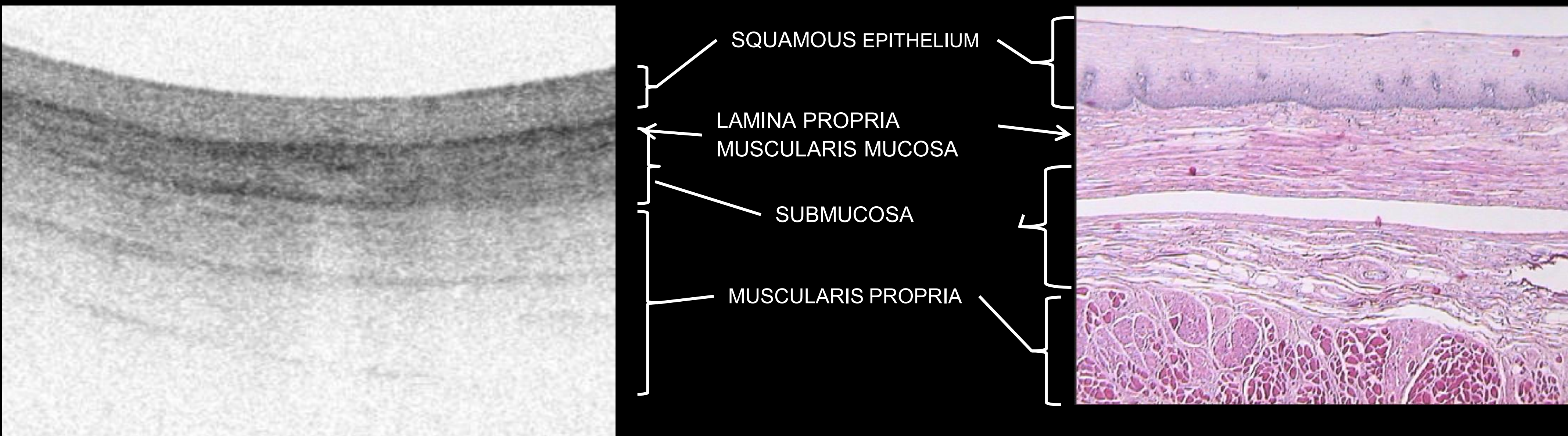






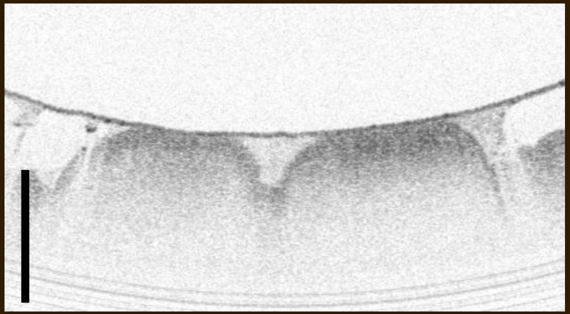
- Helical pullback of the probe creates a series of transverse images

NORMAL SQUAMOUS MUCOSA

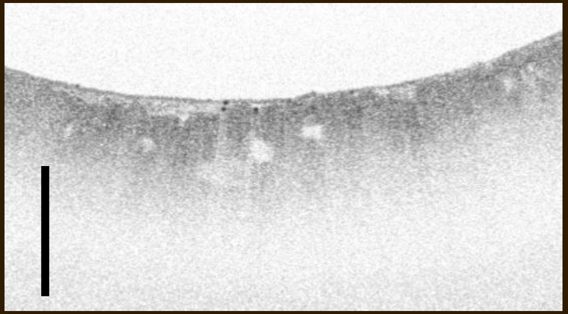


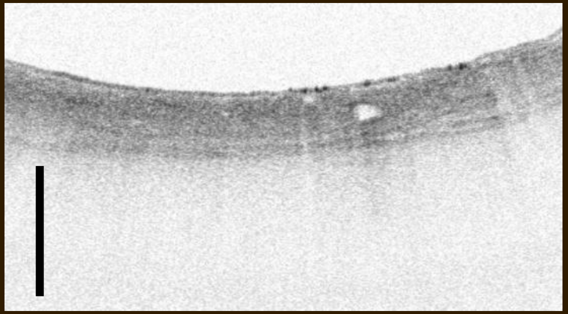
Cardia, BE, Squamous

NORMAL CARDIA
-PIT & CRYPT ARCHITECTURE
-HIGHLY REFELECTIVE SURFACE
-REDUCED IMAGE PENETRATION

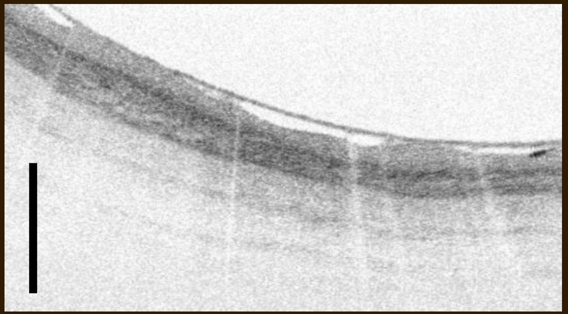


BARRETT'S
-IRREGULAR SURFACE
-LOSS OF LAYERED ARCHITECTURE
-IRREGULAR CRIBIFORMED GLANDS
-GLANDS OR DUCTS IN MUCOSA





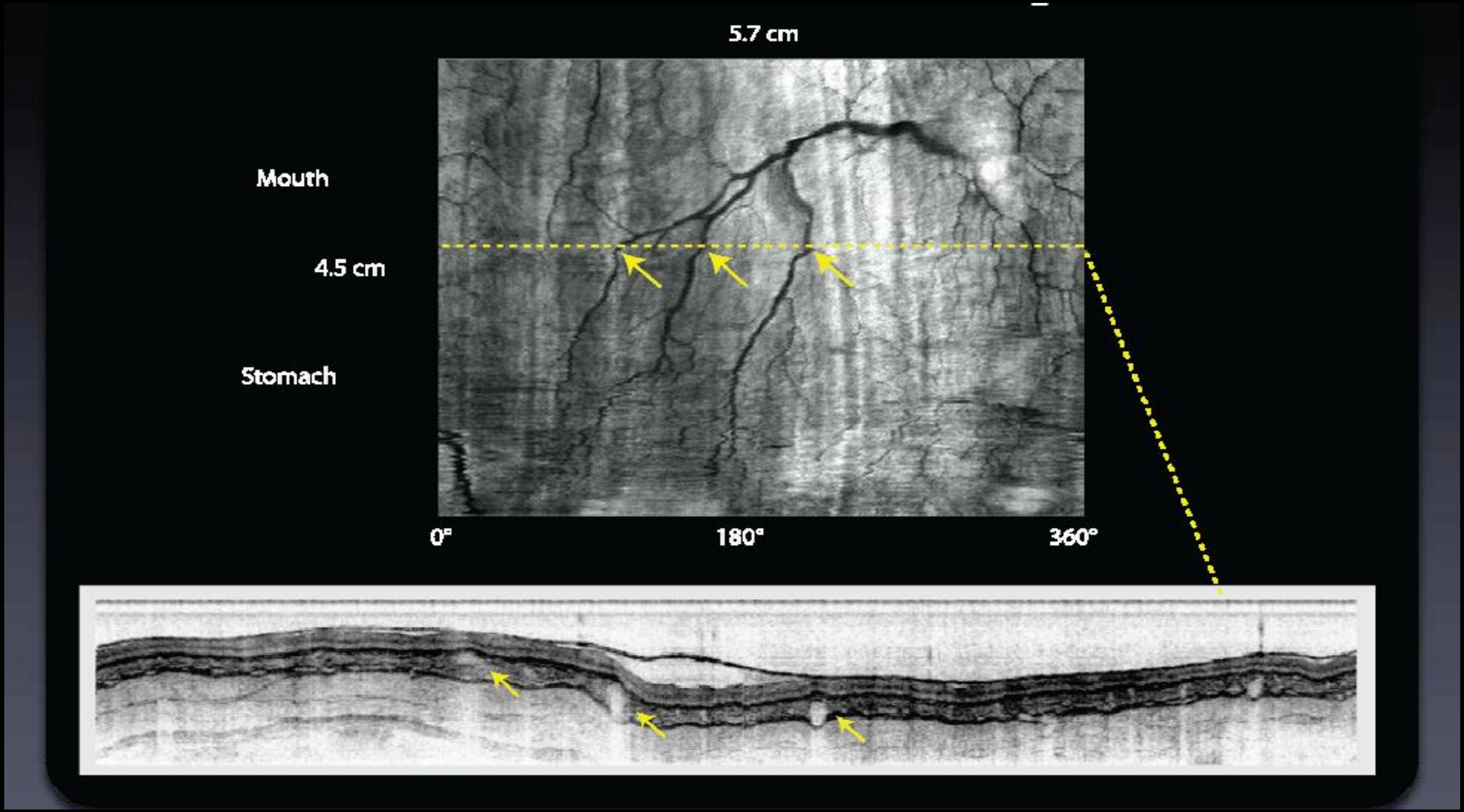
NORMAL SQUAMOUS
-LAYERED ARCHITECTURE



SCALE BAR = 2MM

Suspected Intramucosal Carcinoma

Vascular View



Endoscopic Optical Biopsy: *In Vivo* Histology

- Potential for improved diagnosis in many diseases, inflammatory, vascular, and neoplastic.
- Improve cost effectiveness with fewer biopsies
- Provide more accurate diagnosis with a targeted rather than random approach.
- Guide endoscopic therapy “on the spot” in “real-time” to avoid delay and promote efficient management.

Eosinophilic Esophagitis: Diagnosis

Chris A. Liacouras, MD
Professor of Pediatric Gastroenterology
University of Pennsylvania
The Children's Hospital of Philadelphia

AIMS

- To provide history behind the diagnosis of EoE
- To define EoE and explain the EoE Diagnostic Guidelines
- To provide information on the clinical presentation, endoscopic evaluation and histologic findings required to make a diagnosis of EoE
- To briefly update the available treatment options for EoE

History & Definition

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Distribution of EoE

CA Liacouras

Children's Hospital of Philadelphia

University of Pennsylvania

Eosinophilic Esophagitis History

Pre - 1982

Rare reports of esophageal eosinophila

Winter, et al, - 1982

“Eosinophils as a diagnostic criterion for GERD”

1982 – 1995

Pathologists reported “almost all” esophageal biopsies that had eosinophils as “reflux esophagitis” with no other description

Landmark Article

Eosinophilic Esophagitis Attributed to Gastroesophageal Reflux: Improvement With an Amino Acid–Based Formula

KEVIN J. KELLY,*,† AUDREY J. LAZENBY,§ PETER C. ROWE,* JOHN H. YARDLEY,||
JAY A. PERMAN,*,† and HUGH A. SAMPSON*,¶
Divisions of †Pediatric Gastroenterology/Nutrition and ¶Pediatric Allergy/Immunology and Departments of *Pediatrics and ||Pathology, The Johns Hopkins University School of Medicine, Baltimore, Maryland; and §Department of Pathology, University of Alabama at Birmingham, Birmingham, Alabama

EoE Definition
1995 – 2007

- 1995 – 2002
  - Thought to primarily a rare pediatric disease; ? food allergy
  - ? Pathognomonic endoscopic/histologic features
- 2002 – 2005
  - Adult involvement – dysphagia a predominant symptom
  - EoE becoming more prevalent; confusion between children and adults
  - Realized no pathognomonic features
- 2006 – FIGERS (60+ physicians @ AAAAI)
- 2007 – 1st EoE Guideline

2007 Consensus Recommendations

- Significant increase in number of pediatric and adult patients identified with EoE across specialties
- Few controlled trials = controversies in management
- Summary of information from FIGERS meeting
  - Systematic review of literature performed up to 2006
  - Expert opinion to fill in knowledge gaps
- Recommendations included
  - Current state of knowledge on EoE
  - Strategies to advance field and future research

Furuta, GT. et al; Gastroenterology 2007; 133:1342-63.

2007 Consensus Recommendations

- **Clinicopathologic diagnosis**
  - **Presence of clinical symptoms related to esophageal dysfunction**
    - Vomiting, Abdominal pain, Heartburn, Dysphagia, Reflux sympyoms, Feeding difficulty, etc.
  - **Isolated esophageal eosinophilia**
    - > 15 eos per 40X HPF
    - Histology of remainder of GI tract normal
  - **Exclusion of other GI disorders**
    - Absence of pathologic GERD
      - Lack of response to PPI therapy or normal pH probe
    - Infection, Crohn's disease, hypereosinophilic syndrome

Furuta, GT. et al; Gastroenterology 2007; 133:1342-63.

2007 -2011

- Scientific publications on EoE doubled
- Increasing recognition of patients with EoE
  - Poor use of the 2007 Recommendations
  - Survey by AAAAI and NASPGHAN revealed only 1/3 of physicians followed 2007 guidelines to make diagnosis
  - Many investigators still not using clinico-pathologic diagnosis - any patient with esophageal eosinophilia or food impaction and endoscopic findings = EoE

CLINICAL REVIEW

Variability in Diagnostic Criteria for Eosinophilic Esophagitis: A Systematic Review

Evan S. Dellon, M.D.,[1,2] Ademola Aderoju, M.D.,[2] John T. Woosley, M.D., Ph.D.,[3] Robert S. Sandler, M.D., M.P.H.,[2] and Nicholas J. Shaheen, M.D., M.P.H.[1,2]

2011 Consensus Report

- Panel of 33 physicians (6 months)
- **Conceptual Definition**
  - ***"Eosinophilic esophagitis represents a chronic, immune/antigen mediated, esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation"***
- Pediatric and Adult EoE likely the same disease

Liacouras et al, JACI, 2011

2011 Updated Consensus Report

- Diagnostic Guideline
  - EoE is a clinico-pathologic disease
  - Clinically characterized by esophageal dysfunction
  - Pathologically 1 or more biopsies show eosinophil predominant inflammation (15+ eos in peak hpf)
  - Isolated to esophagus (need for other GI biopsies)
  - Other causes need to be excluded
    - “PPI responsive esophageal eosinophilia”
    - Distinguish between “EoE” and “esophageal eosinophila”
  - EoE diagnosis made by clinicians
  - Rarely < 15 eos/hpf (if other path features are present)

CA Liacouras
Children’s Hospital of Philadelphia
University of Pennsylvania

Esophageal Eosinophilia

- Histologic Finding
  - Eosinophilic Esophagitis
  - Gastroesophageal Reflux Disease
  - PPI-responsive esophageal eosinophilia
  - Celiac Disease
  - Eosinophilic gastroenteritis
  - Crohn’s Disease
  - Hypereosinophilic syndrome
  - Achalasia
  - Vasculitis, pemphigus, connective tissue disease
  - Infection
  - GVHD
  - Others

CA Liacouras
Children’s Hospital of Philadelphia
University of Pennsylvania

PPI-responsive esophageal eosinophilia

	Patient 1	Patient 2	Patient 3
Age (yr)/sex	14/M	25/M	13/F
Presentation	Pain	Food impaction	Dysphagia
Environmental Allergies	Yes	Yes	No
Treatment	Omeprazole 10 mg BID	Omeprazole 20 mg BID	Omeprazole 20 mg QD
Eosinophils/HPF			
Before treatment	37	21	59
After treatment	1	3	0

Many other publications since 2006 have corroborated results

Ngo, et al. *Am J Gastroenterol* 2006;101:1666–1670.

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

PPI-responsive esophageal eosinophilia

- Considered to be "distinct" from EoE
- Etiology
  - Gastroesophageal Reflux responsive to acid suppression
  - Anti-inflammatory effect of PPI
    - ? etiology
    - ? Peptic, ?Allergic, ?Subset of EoE
    - ? Combination of GERD and EoE
- Important to make distinction
- Further research needed

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Epidemiology and Incidence of Eosinophilic Esophagitis

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

EoE Incidence/Prevalence

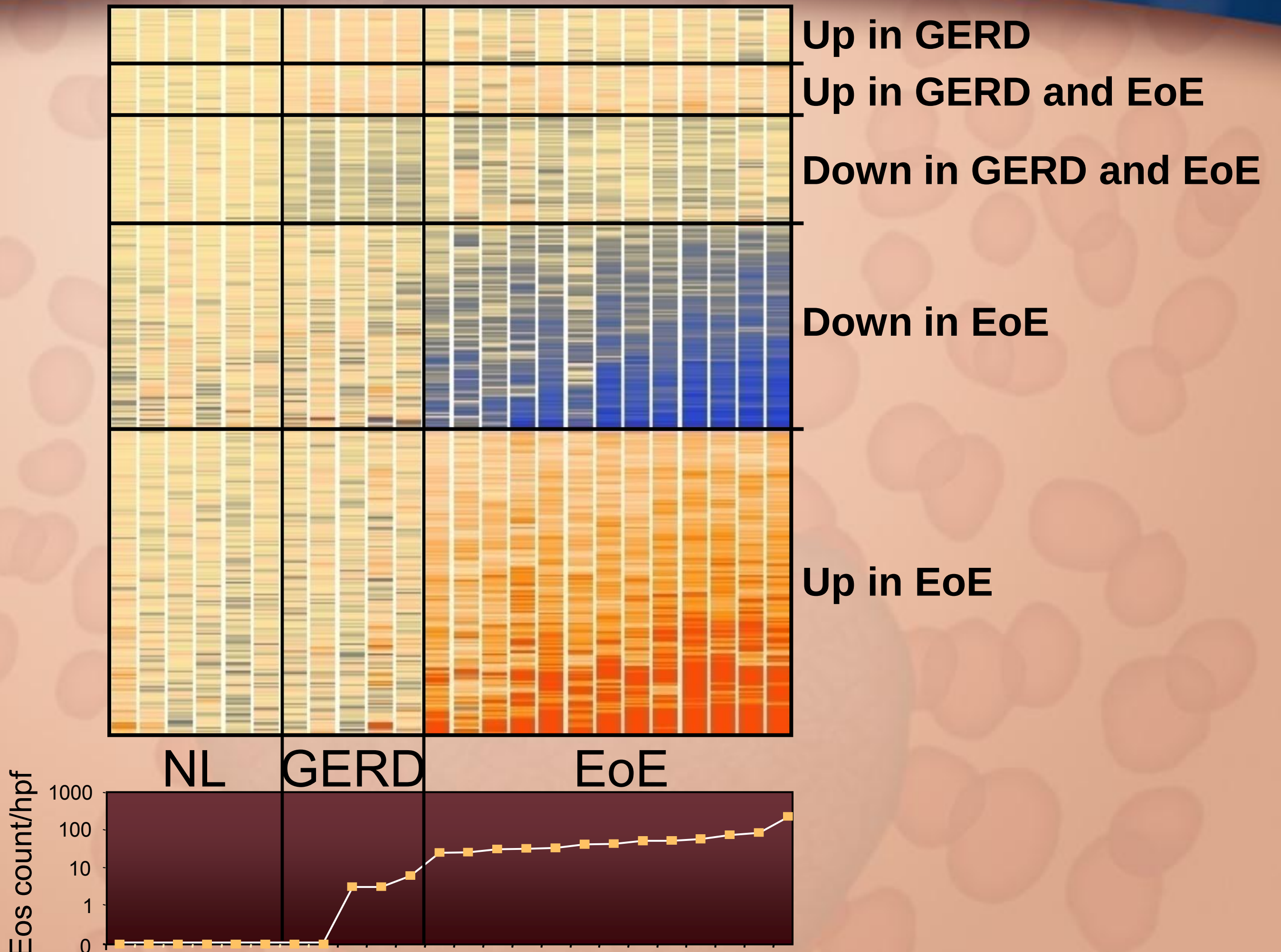
- Children
  - Incidence 1-2/10,000 (Noel et al 2004)
  - Incidence 4-5/10,000 (Liacouras 2012 in press)
  - Prevalence significantly increasing
- Adults
  - Olten County, Switzerland – Hruz et al 2011
  - Increase in incidence from 1/100,000 in the 1990’s to close to 10/100,000 by 2009
  - Prevalence also significantly increased

CA Liacouras
Children’s Hospital of Philadelphia
University of Pennsylvania

Genetics

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

EoE Vs Reflux Esophagitis (GERD)



EoE has a gene expression profile different from GERD

Blanchard, et al; J Clin Invest 2006.

EoE - Genetics

- Increased incidence in siblings and 1st degree relatives
- Collaboration between CHOP and Cincinnati Children's Hospital – 2010
- Nature Genetics 42:289-10, 2010
- Identified gene locus at chromosome 5q22
- TSLP gene (Thymic Stromal Lymphopoetin Protein)
- Future – genetic markers may help differentiate causes of esophageal eosinophilia and identify specific genotypes/phenotypes which identify severity of disease (fibrosis) or which treatment may be effective

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Clinical Symptoms

Clinical Features

- Male predominance (about 3:1)
- Multiple reports of familial clustering (within and across generations)
- Strong association with other atopic disorders: asthma, allergic rhinitis, eczema other food allergies
- Chronic condition in children and adults

Furuta, GT. Gastroenterology 2007; 133:1342.

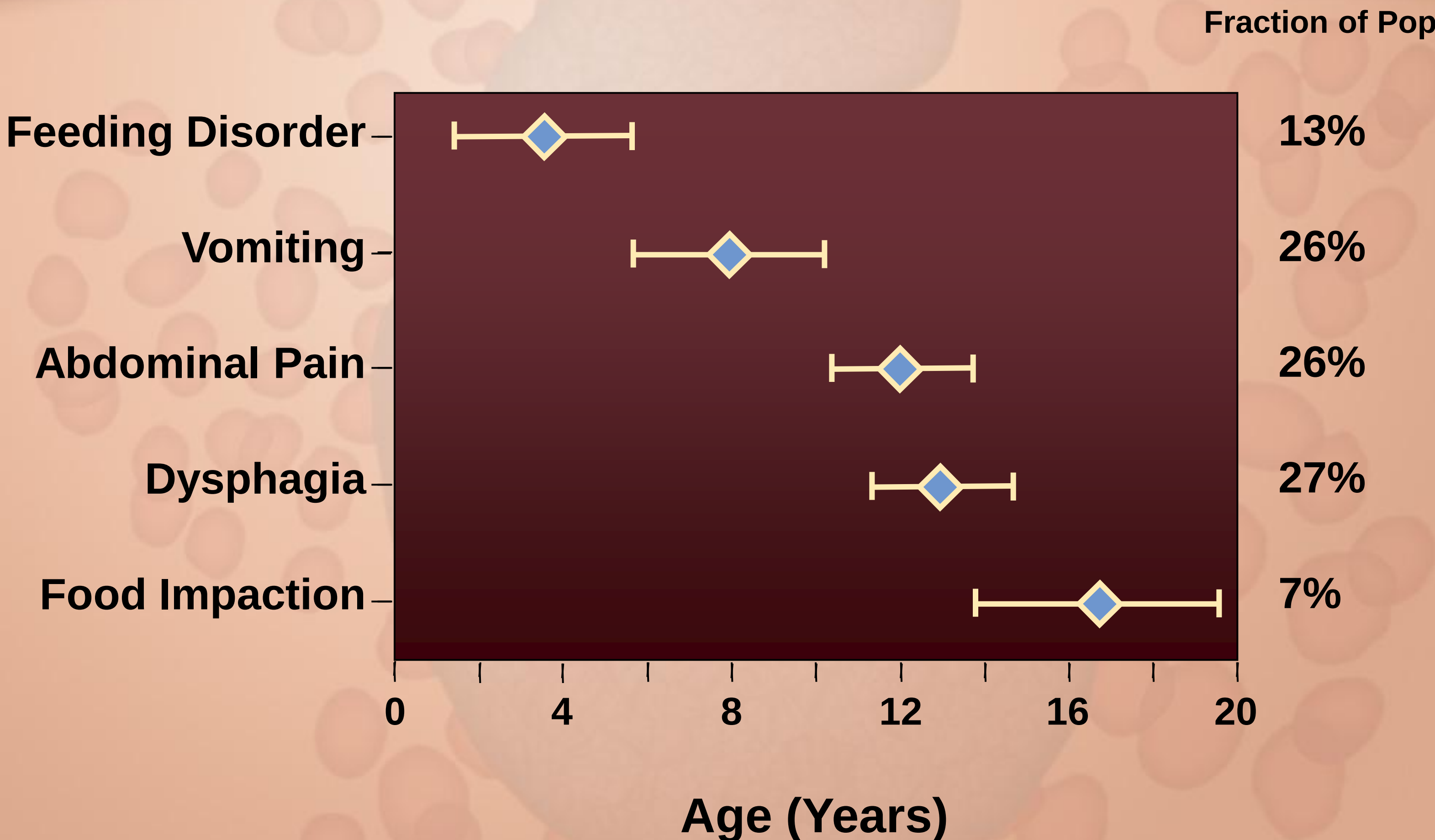
Pediatric Symptoms

- Symptoms similar to GERD
  - Heartburn, regurgitation
  - Vomiting
  - Epigastric/Chest pain
- Dysphagia, Food impaction
  - More common in older children and adolescents
  - Dysphagia > food impaction
- Failure to thrive
- Feeding issues

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Eosinophilic Esophagitis

Primary Presenting Complaint, by Age

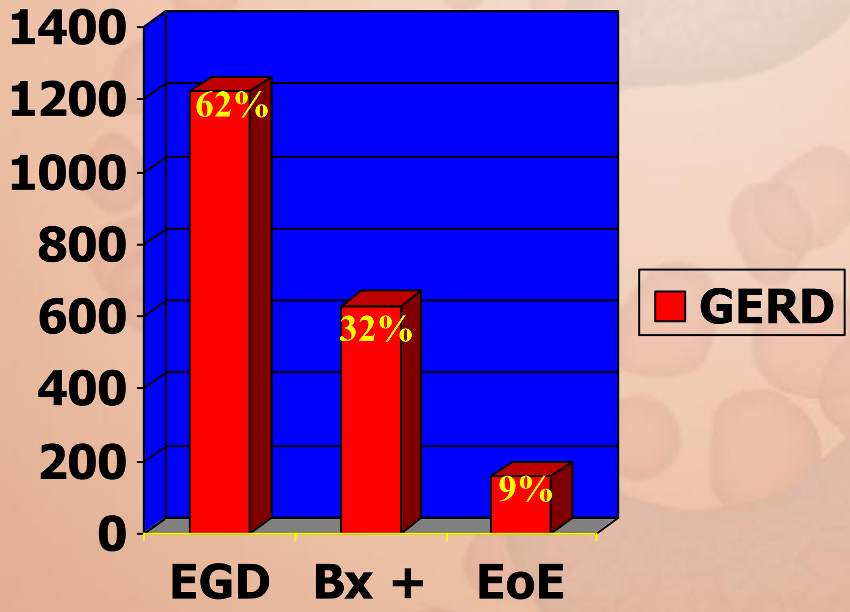


Noel RJ, Putnam PE, Rothenberg ME. Eosinophilic Esophagitis. NEJM 2004

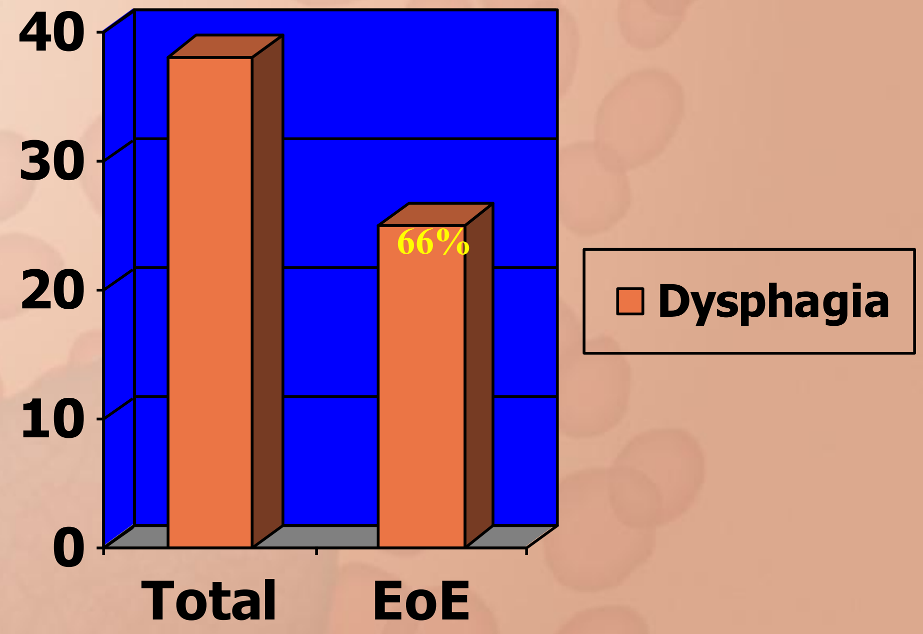
CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Pediatric Symptoms - CHOP

1964 pts – GER symptoms



38 pts - dysphagia



CHOP - 3 year period

Liacouras CA, et al, in press

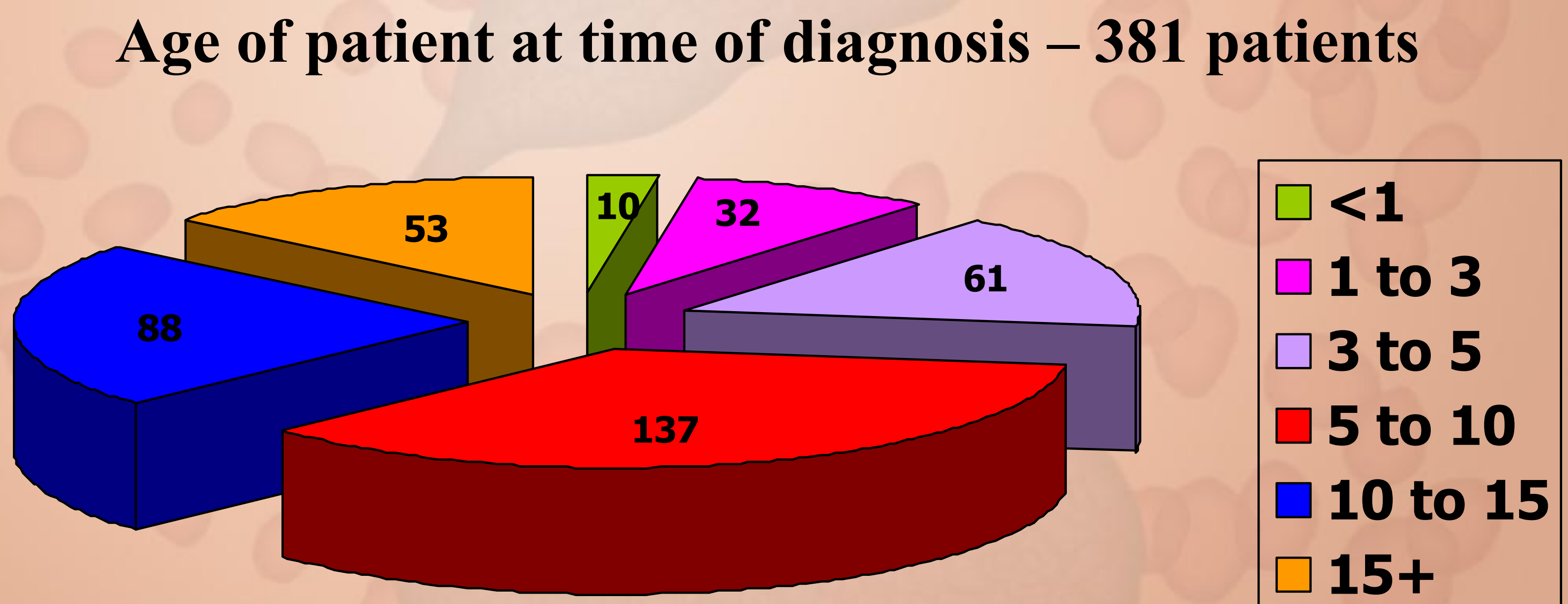
CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Adult Symptoms

- Dysphagia & Food Impaction
  - Studies conducted pre 2008
    - MacKenzie et al. 2008
    - Prasad et al 2007
- Chest pain, Heartburn & Reflux like symptoms
  - Reported more frequently in studies since 2008
    - Forouton et al. 2010
  - Similar to children - 5-10% of pts with chronic reflux
  - ? Early recognition of patients with chronic reflux symptoms may prevent dysphagia

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

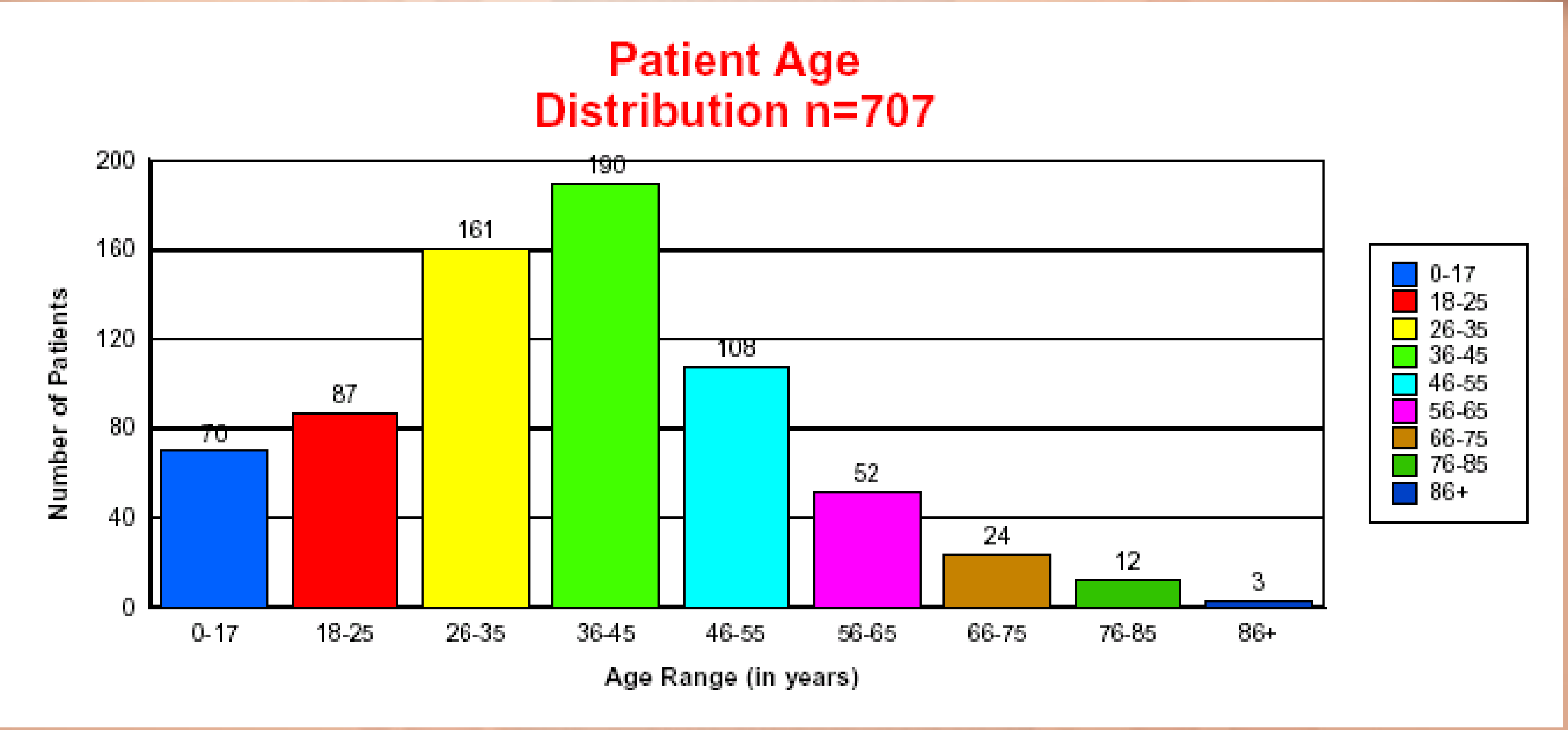
Eosinophilic Esophagitis
Age of patient @ diagnosis



Liacouras CA et al, 2005

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Adult EoE Presentation (Age)



CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Association of Atopy with EoE

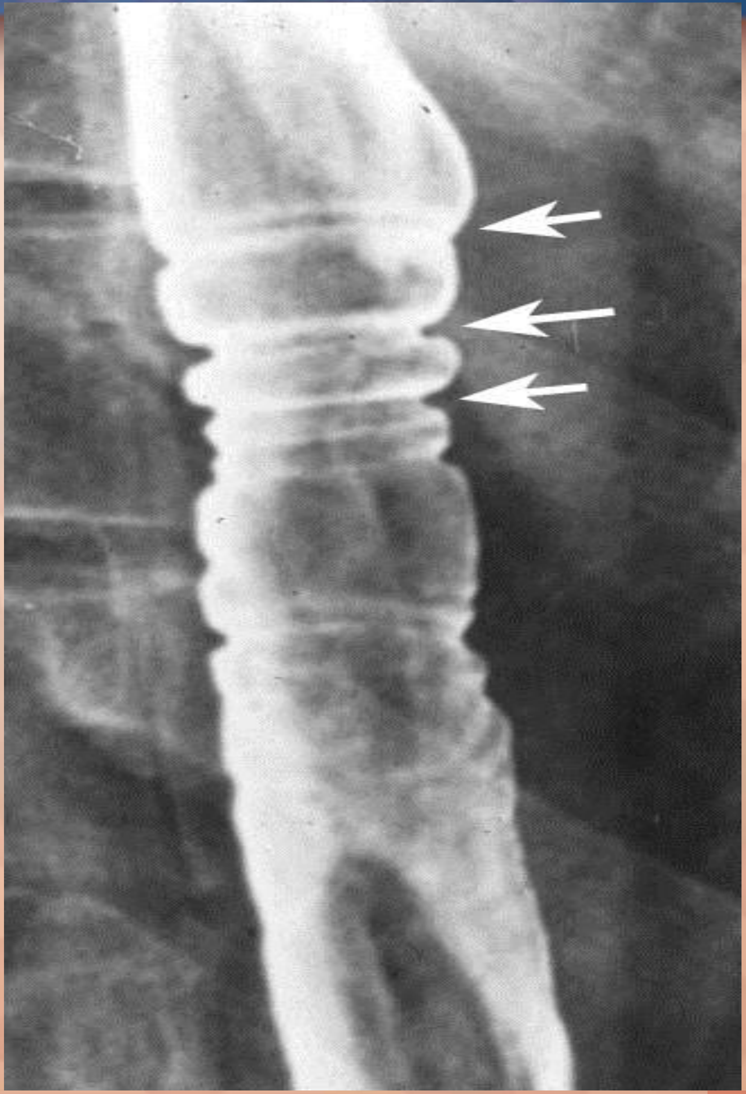
Ref	# of Pts	Age (Yrs)	Asthma	AR	AD	Food
General Population			10%	20-40%	5-20%	1-6%
Spergel	620	8m-20	50%	61%	21%	16%
Assad	89	3m-18 yr	39%	30%	19%	9%
Sugnanam	45	3m-16 yr	66%	93%	55%	24%
Guajardo	39	1m -31	38%	64%	26%	23%
Roy-Ghanata	23	18-57	26%	78%	4%	--

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Diagnostic Studies

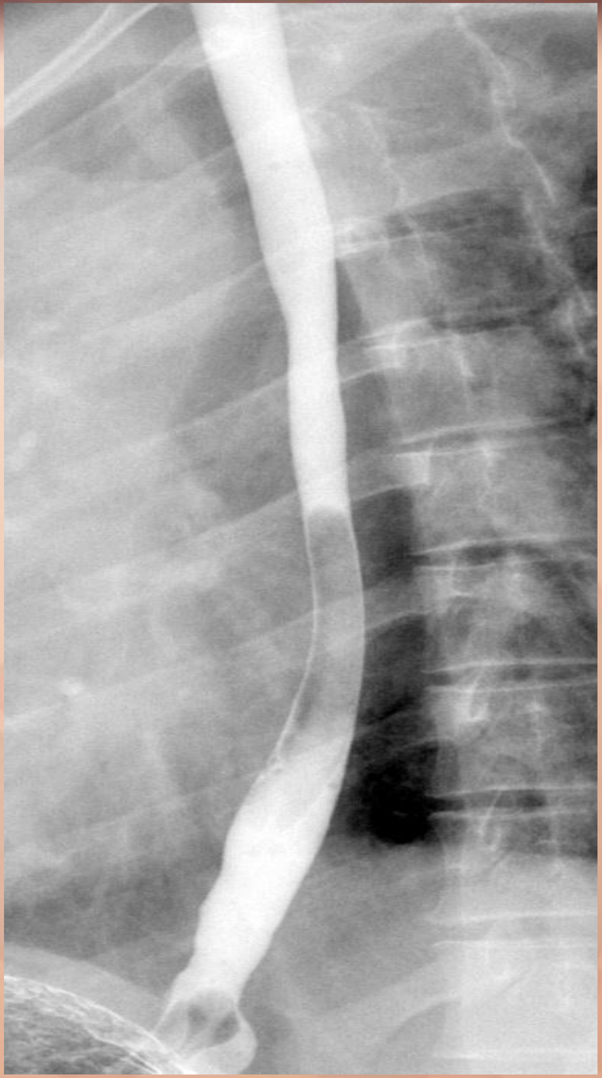
CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Esophageal Rings



Katzka DA

Small Caliber Esophagus



CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

EoE – Contrast Studies

- Not needed for every EoE patient
- Useful in EoE patients who
  - Have significant dysphagia
  - Food impaction
  - Severe chest pain
  - Patients with a history of strictures and dilation
- Information provides
  - Esophageal strictures (length and severity)
  - Esophageal diameter (small caliber esophagus)

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Endoscopic Findings & Complications

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Normal Esophagus

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

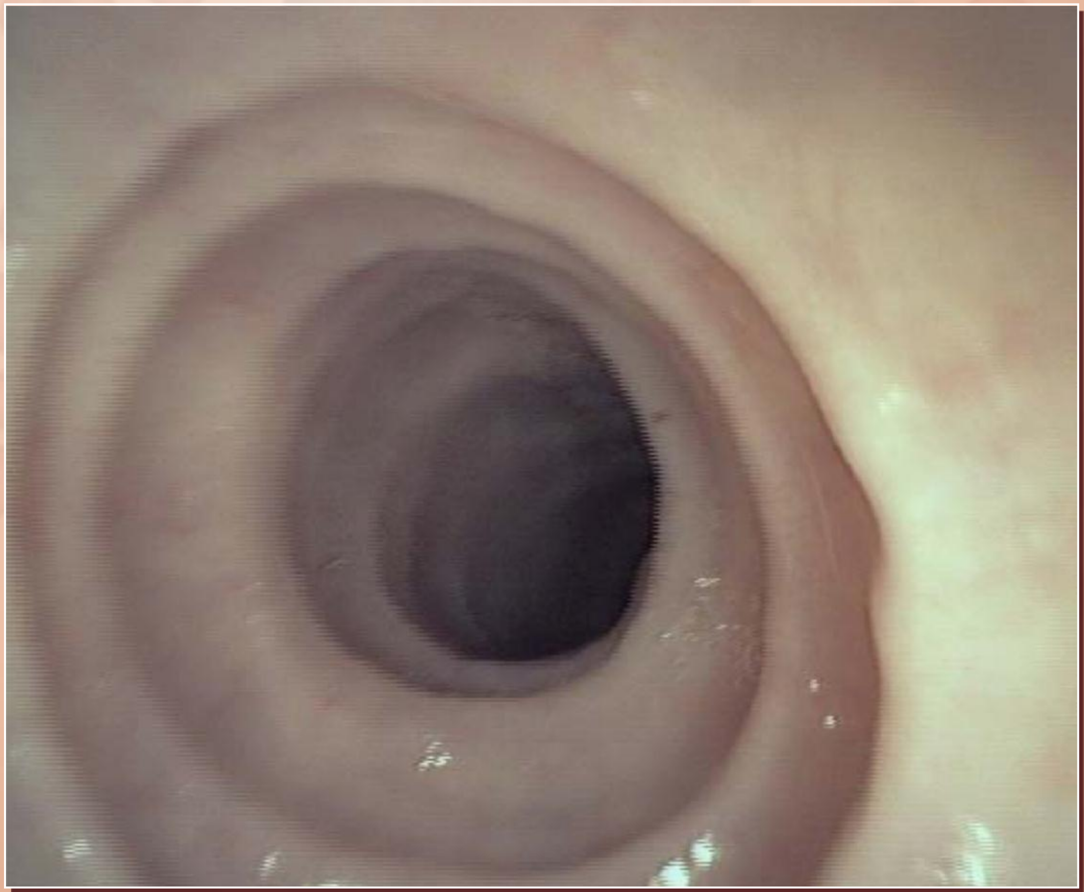
Esophageal Furrowing

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

White Plaques

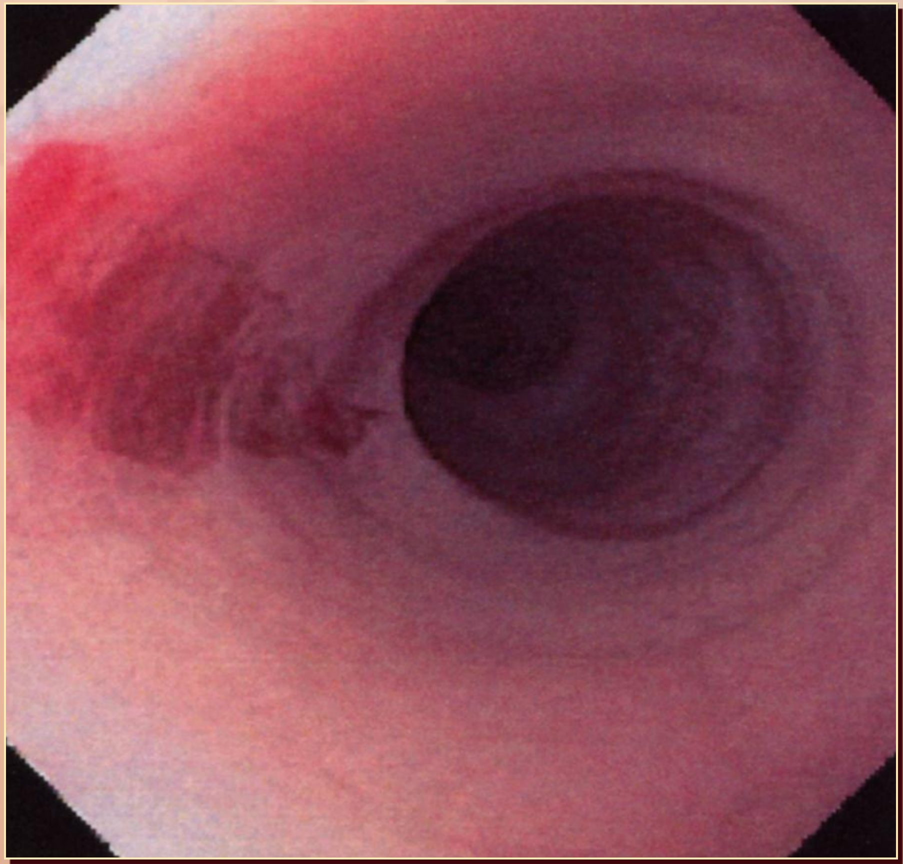
CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

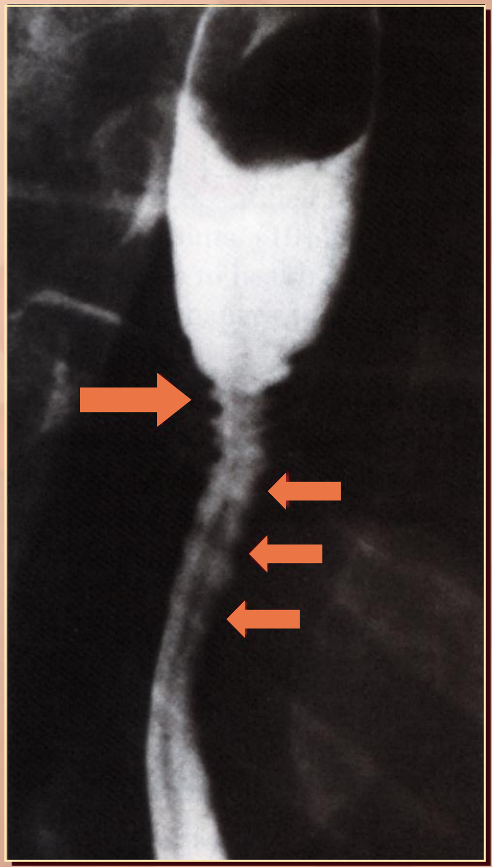
Esophageal Rings



CA Liacouras
Children’s Hospital of Philadelphia
University of Pennsylvania

Small Caliber Esophagus





CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

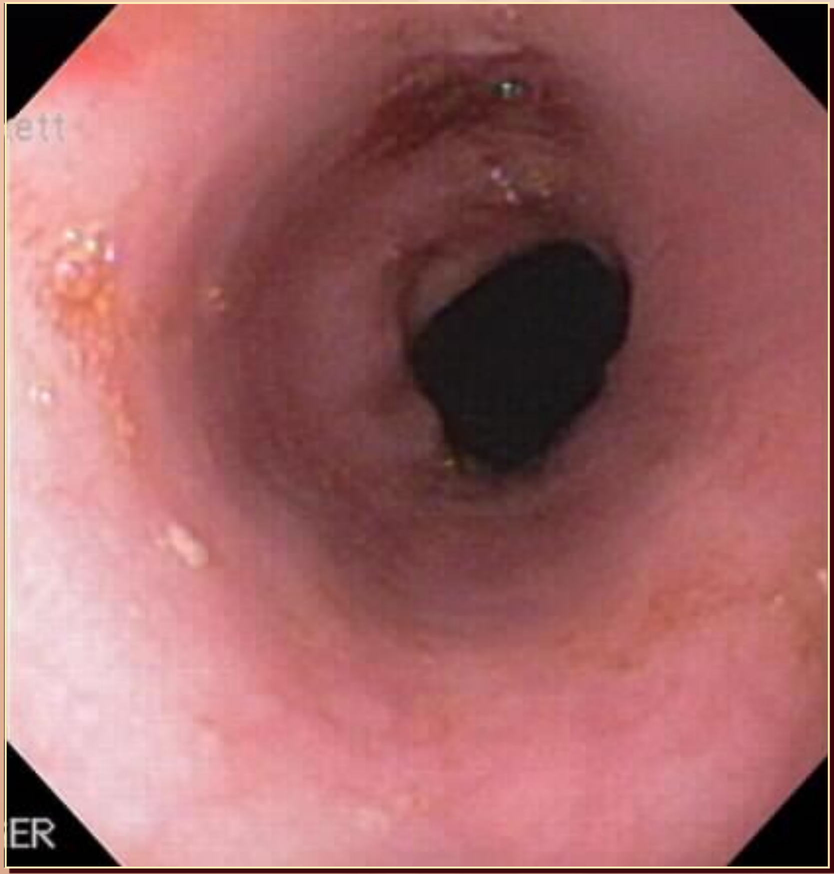
Pathognomonic?

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

EoE Complications – Sliding Hiatal Hernia

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

EoE – Sliding Hiatal Hernia



CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Visual Endoscopic Findings

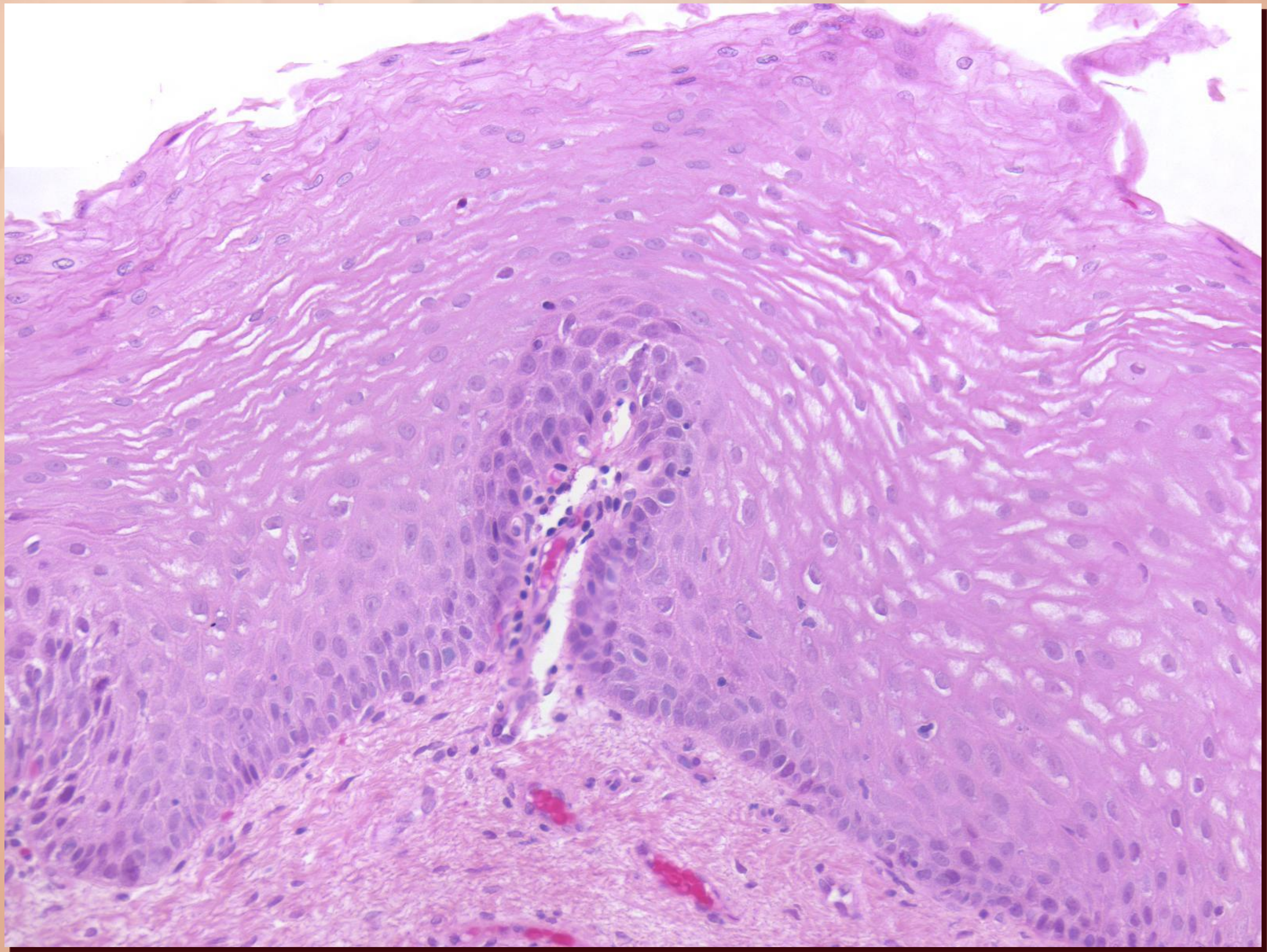
- Suggestive but not pathognomonic of EoE
- Up to 30% of visually normal endoscopies have been reported to have abnormal biopsies diagnosed with EoE
  - Extremely important during or after therapy when visual findings suggest resolution or ongoing disease but biopsies reveal the “opposite”
- Biopsies must be obtained

CA Liacouras
Children’s Hospital of Philadelphia
University of Pennsylvania

Histology of EoE

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

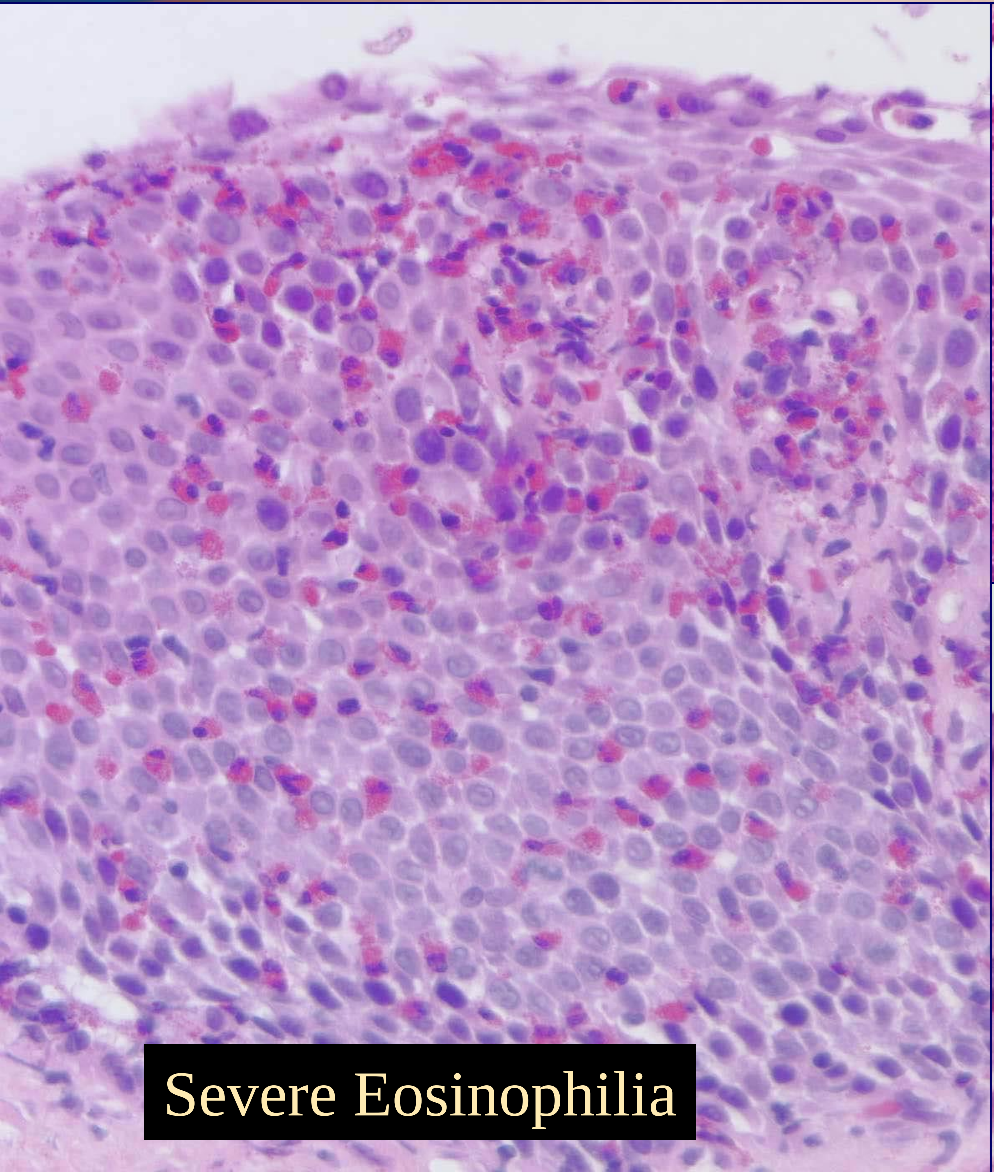
Normal Esophagus

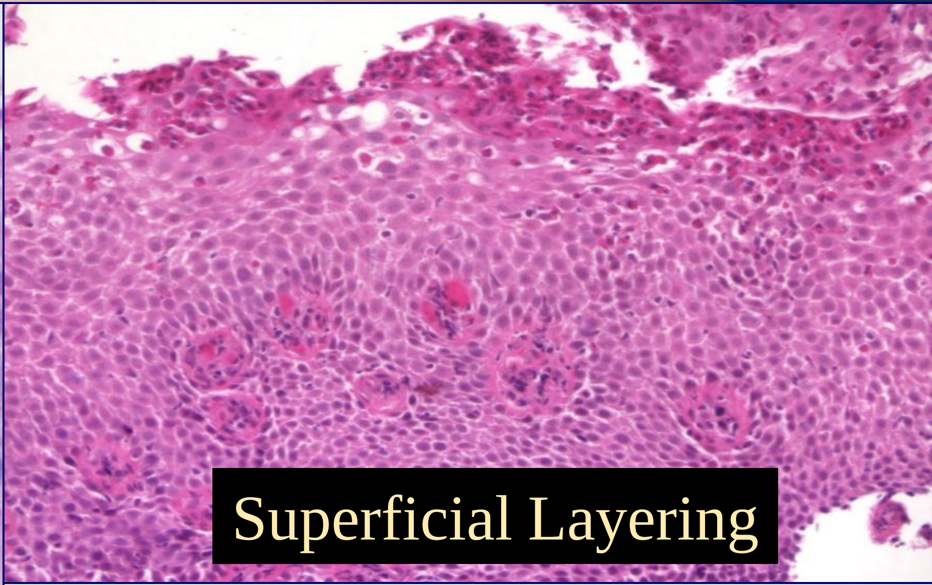


CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Eosinophilic Esophagitis

Histology





Other histologic findings

- Basal cell hyperplasia
- Rete peg elongation
- Subepithelial lamina propria fibrosis
- Extracellular eosinophil granules
- Increases in other cell types
  - Lymphocytes
  - Mast Cells

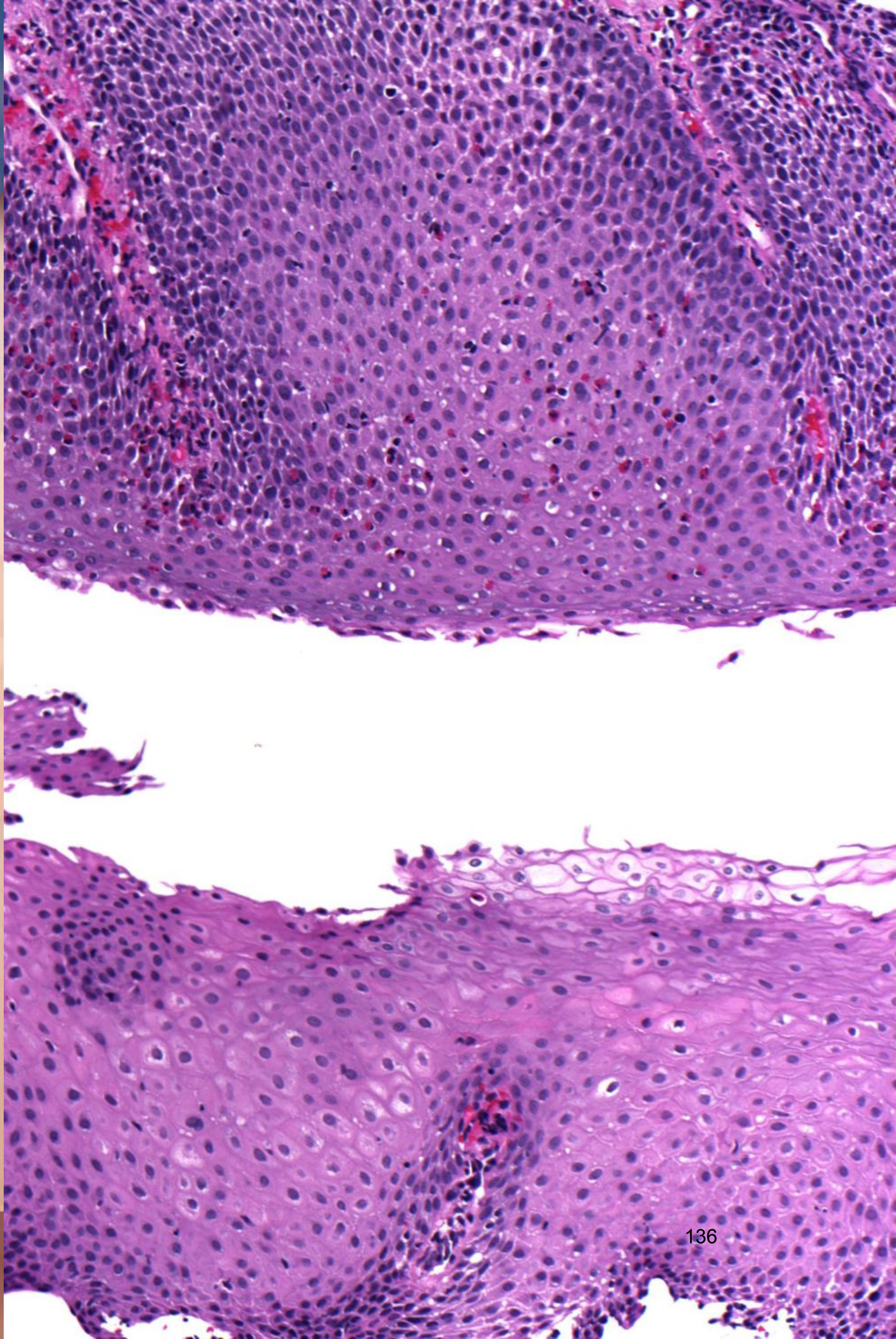
CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Eosinophilic Esophagitis

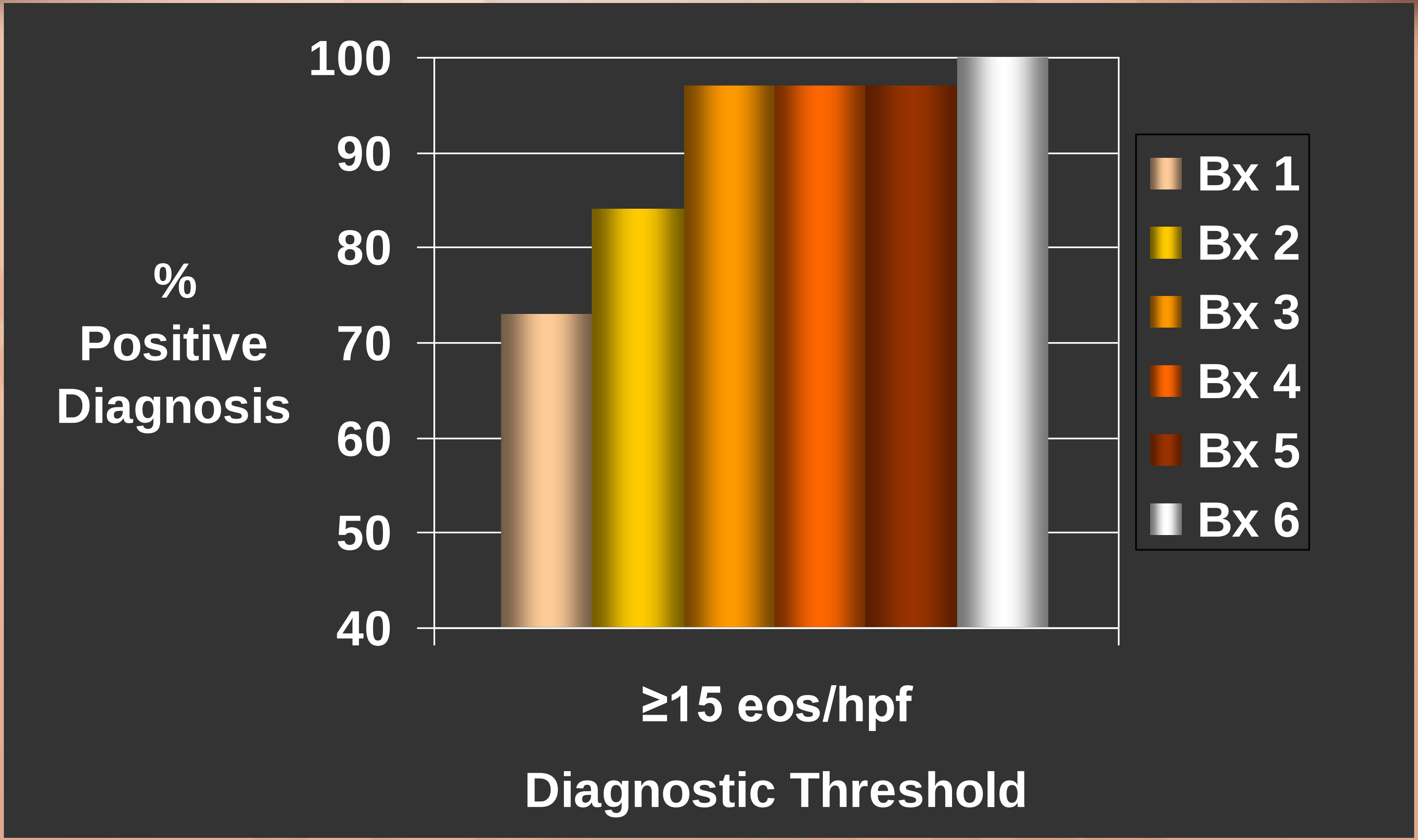
Eosinophilia is often patchy

Multiple biopsies are necessary

Number of eosinophils in most affected field



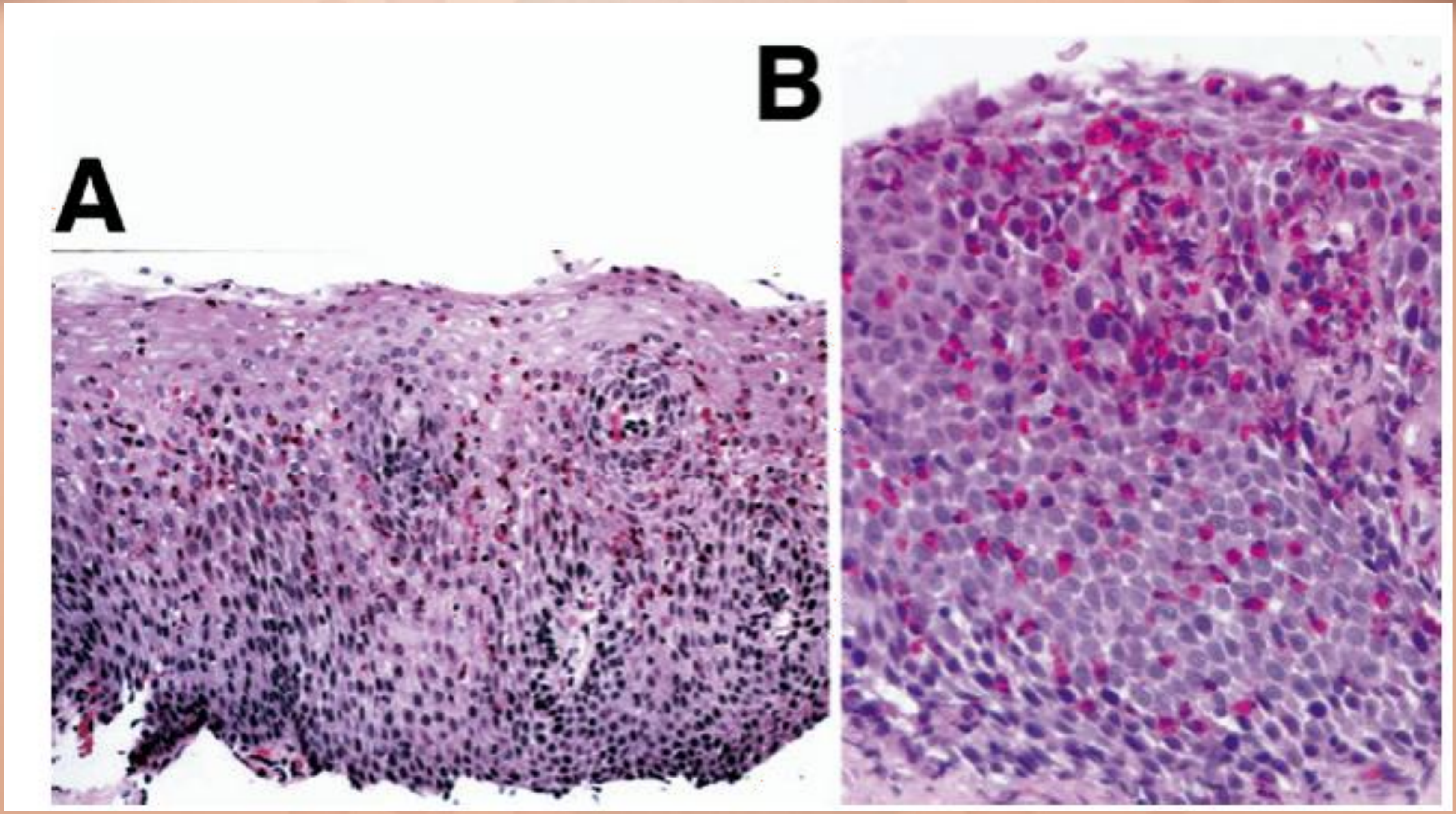
Number of Biopsies to Diagnose Pediatric EoE?



Shah, et al ;*Am J Gastroenterol*, In Press 2009.

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Distal vs Proximal Biopsies



CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Biopsies – EoE Guidelines

- Multiple mucosal biopsies of the distal (2-4) and proximal esophagus (2-4) must be obtained
- "15+ eosinophils per hpf" in the most densely involved hpf, in the single worst biopsy specimen
- Problems
  - Lack of standardization of size of "hpf"
  - Eosinophils may be partially digested
  - May not always correlate with clinical symptoms especially after beginning treatment
  - Is the number correct?

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Future Diagnostic Tests ?

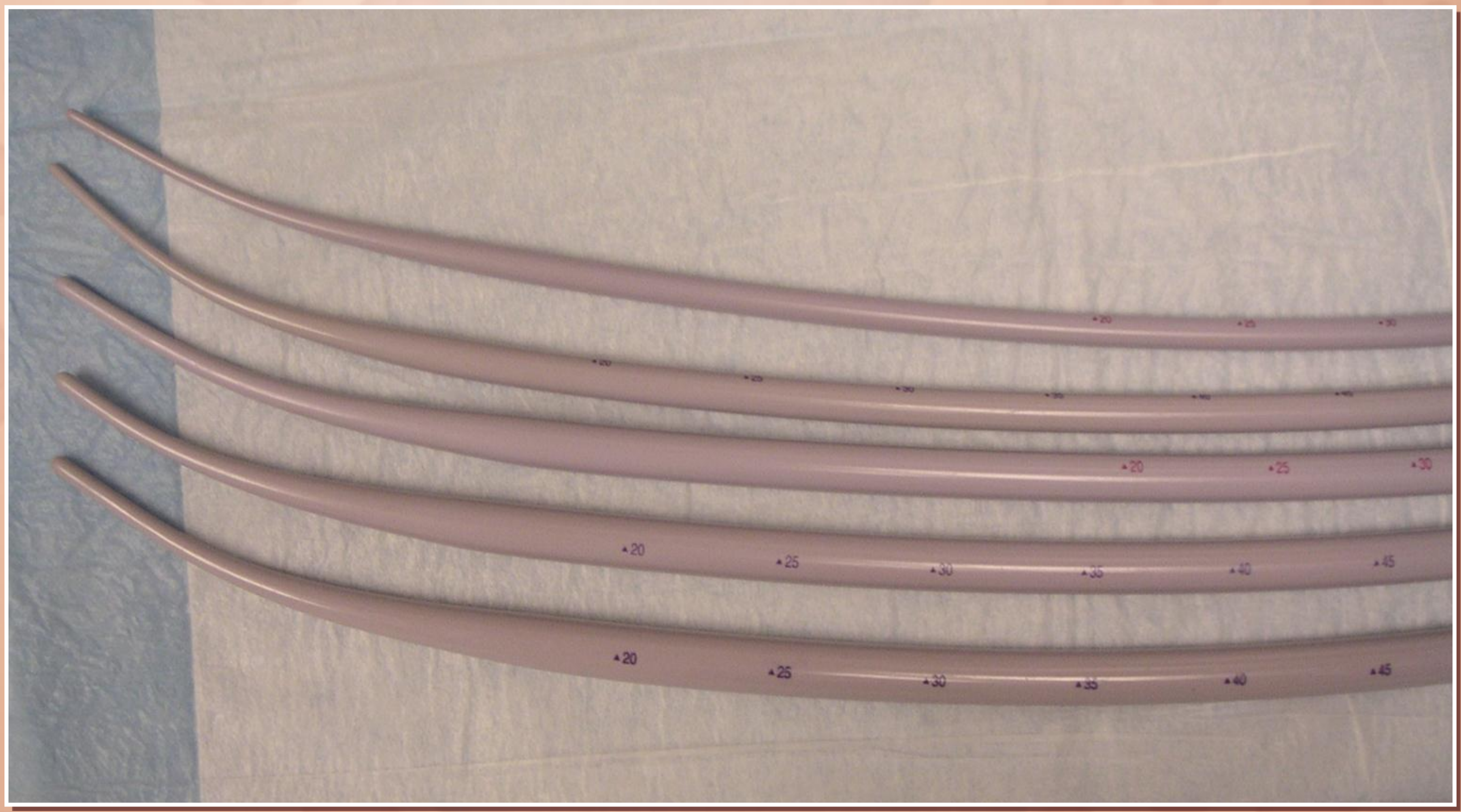
- Genetic markers – genotype
  - Serum
  - Esophageal Tissue
- Serum, Tissue or Stool Biomarkers
- Endoscopic Ultrasound

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Treatment
Esophageal Dilation

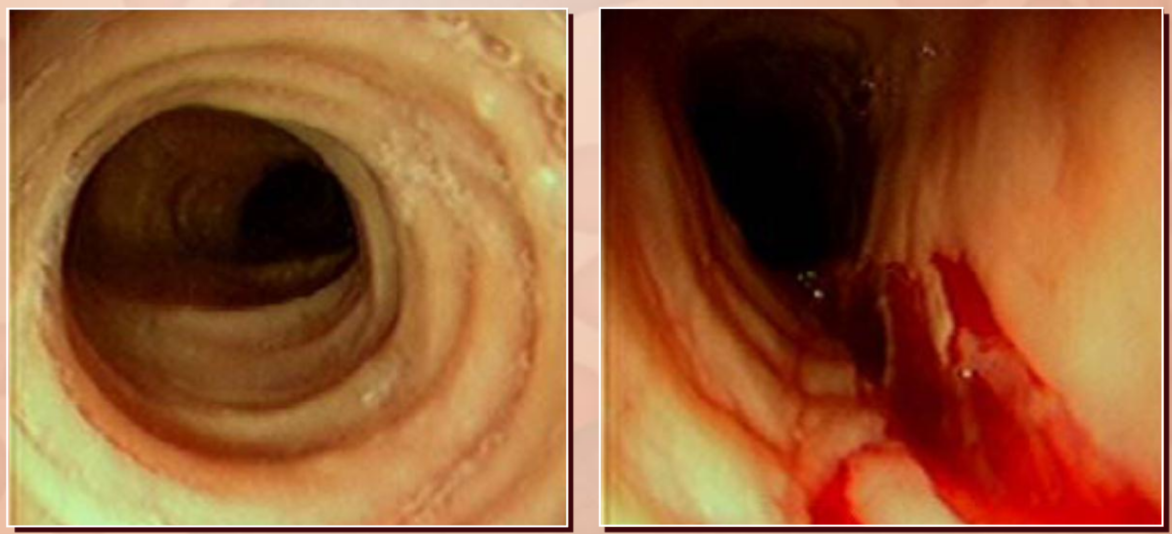
CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Savary Esophageal Dilators



CA Liacouras
Children’s Hospital of Philadelphia
University of Pennsylvania

Laceration After Dilation in EoE



Hirano C. Foreign Bodies in the Esophagus. In: Shields, LoCicero, Feins, Reed, eds. *General Thoracic Surgery 7th Ed*. Lippincott Williams & Wilkins Publ. Chapter 145.

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Esophageal Dilation in EoE Recommendations

- **Dilation does not address the underlying disease process**
- **Relapse is common after dilation although prolonged remission can occur**
- **Significant risk of long mucosal lacerations and pain**
- **Esophageal perforation risk is low but consequences can be substantial**
- **Pharmacologic and dietary therapy is effective at relieving symptoms and treating strictures**
- ***Whenever possible, pharmacologic or dietary therapy should be attempted prior to esophageal dilation***

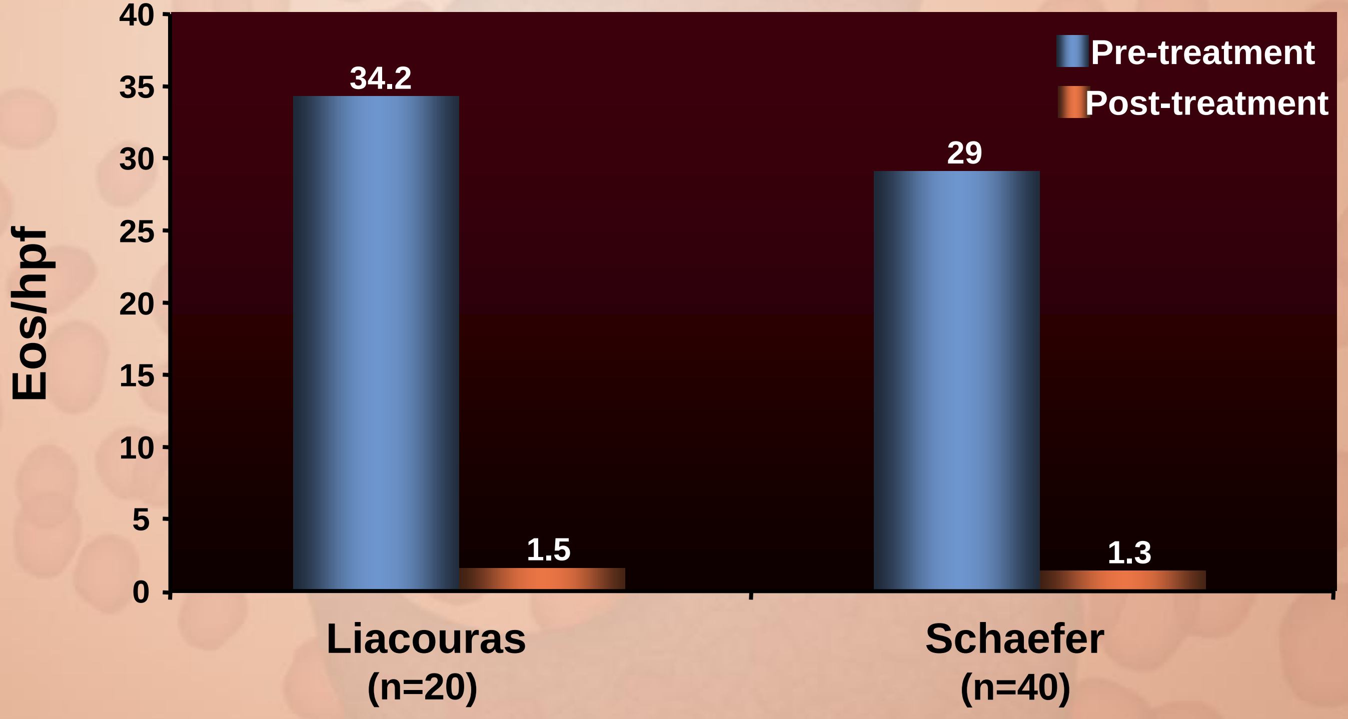
Furuta, Liacouras. AGA Institute Consensus Recommendations. *Gastroenterology* 2008;133(4):1342.

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Steroid Treatment in Pediatrics

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Oral Steroid Studies

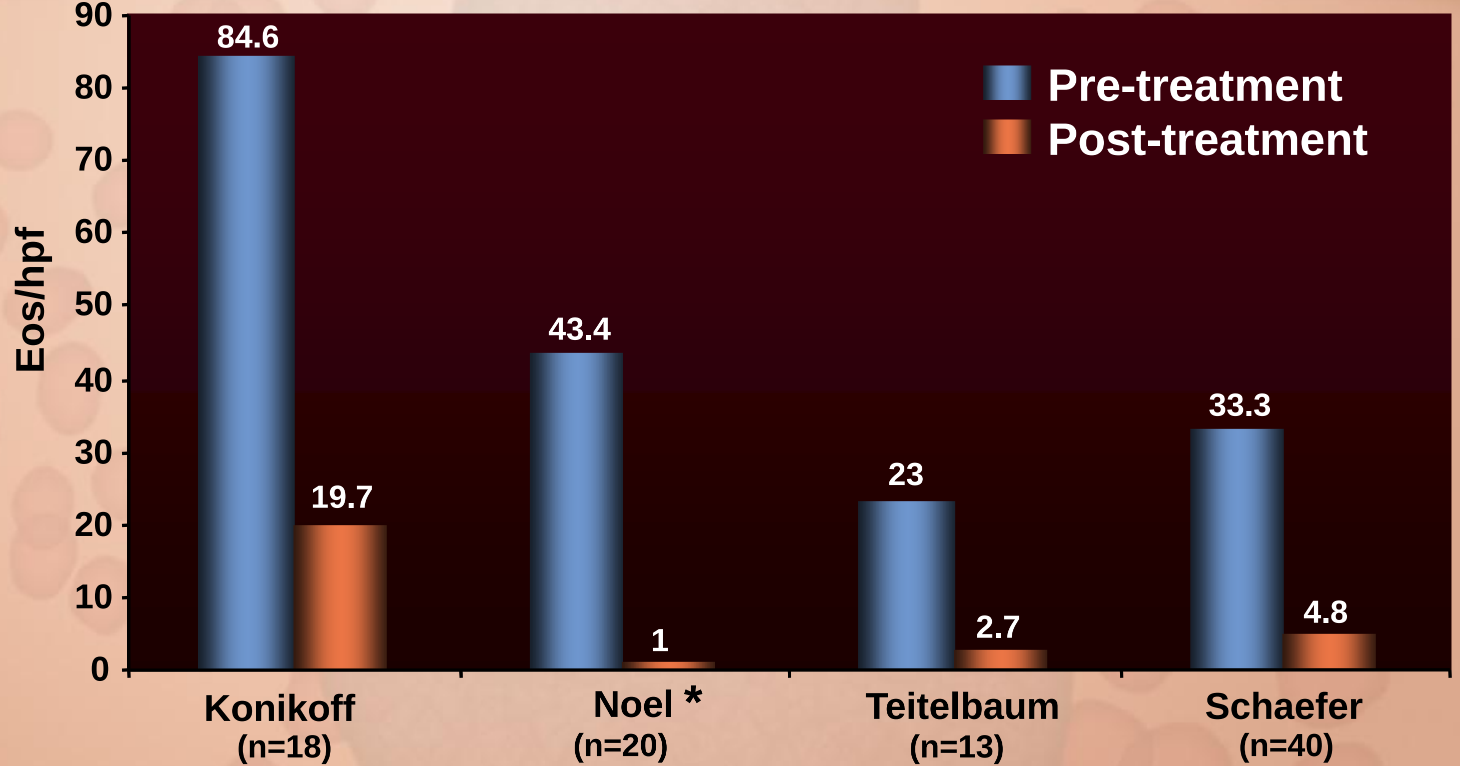


1 mg/kg BID; max 30 mg BID

Liacouras, et al; *J Pediatr Gastroenterol Nutr* 1998; 27:90.
Schaefer, et al; *Clin Gastroenterol Hepatol* 2008; 6:621.

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Topical Steroids



Design:	RCT	Retrosp	Prosp	RCT
Max Dose:	880 mcg/day	1320 mcg/day	880 mcg/day	1760 mcg/day

*Post treatment data on 16 patients.

Konikoff, et al; *Gastroenterology* 2006;131:1381. Noel, et al; *Clin Gastroenterol Hepatol* 2004; 2(7):523. Teilbauam, et al; *Gastroenterology* 2002; 125:1660. Schaefer, et al; *Clin Gastroenterol Hepatol* 2008; 6:621.

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Liquid Budesonide

- **20 children with EoE (baseline: 87 eos/hpf)**
- **Prescribed liquid budesonide (1-2 mg once daily) mixed with a sucralose (Splenda®) paste**
    - **16 responders (< 8 eos/hpf);**
    - **3 partial responders (8-23 eos/hpf);**
    - **1 non-responder (no change in eos) after 3-4 months of treatment**
    - **No significant adverse effects; esophageal candida in one**

Aceves, et al; *Am J Gastroenterol* 2007; 102:2271.

Recommendations for Corticosteroids

- Systemic and topical corticosteroids effectively resolve the acute clinicopathological features of EoE
- When discontinued, the disease generally recurs
- Systemic corticosteroids may be utilized in emergent cases such as dysphagia requiring hospitalization, dehydration due to swallowing difficulties and weight loss, etc.
  - Because of the potential for significant toxicity their long-term use is not recommended
- Topical corticosteroids are effective in inducing a remission of EoE when utilized in high doses (pediatrics & adults)
  - The incidence of long term side effects with this form of administration has not been formally studied, well tolerated (fungal infections)
- Topical corticosteroids are used for maintenance of EoE but have not been well studied

Furuta, Liacouras. AGA Institute Consensus Recommendations. *Gastroenterology* 2008; 133(4):1342

Dietary Treatment in Children

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

History of Diet and EoE

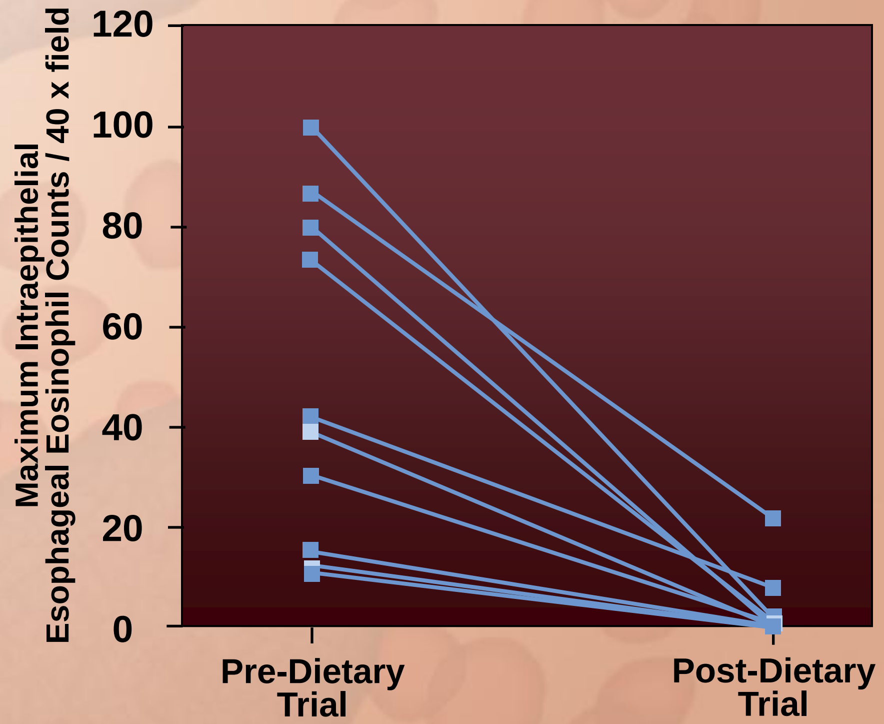
- In 1995: "*Eosinophilic esophagitis attributed to gastroesophageal reflux: improvement with an amino acid-based formula*"
  - 10 patients with refractory reflux symptoms
  - 6 had received anti-reflux surgery without resolution
  - All with markedly elevated esophageal eosinophils
- Patients given a trial of an "elemental diet"
  - Amino acid based formula
  - Minimized any risk of food allergy

Kelly , et al; *Gastroenterology* 1995; 109:1503.

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Diet and Eosinophilic Esophagitis

- **After elemental diet:**
  - **Symptom resolution in 8 patients, improvement in 2**
  - **Improvement occurred within 3 weeks**
  - **100% biopsies improved**
- **Symptoms returned after food was reintroduced**
- **Conclusions:**
  - **EoE is an antigen-driven disease**
  - **EoE improves with food elimination**



CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Dietary Management
Amino Acid–Based Formula

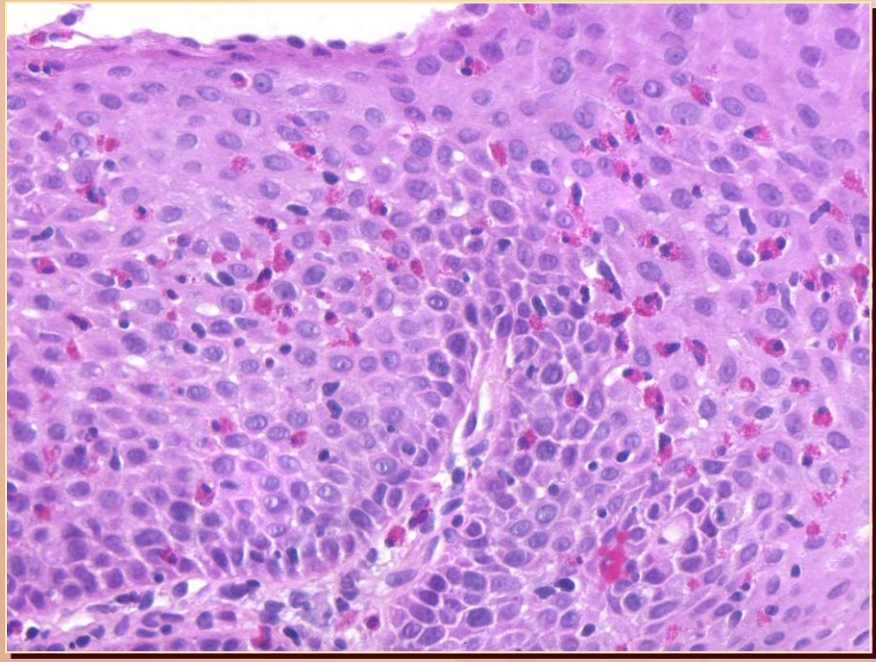
- 172 Patients (128 nasogastric tube, 32 oral, 4 failed, 8 noncompliant)
  - 160 patients completed therapy
- Patients evaluated 4-6 weeks after instituting diet

160 Patients	Pre-diet	Post-diet	*P* Value
Eosinophils per hpf	38.7 ± 10.3	1.1 ± 0.6	<.001
Dysphagia	30	1	<.01
GERD symptoms	134	3	<.01

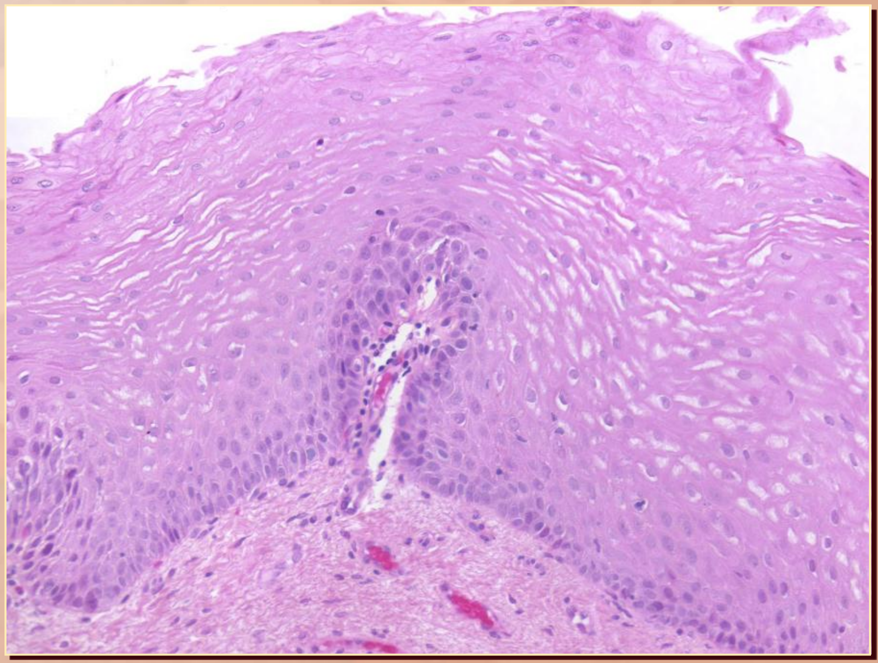
Liacouras, et al; *Clin Gastroenterol Hepatol* 2005; 3:1198.

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

EoE – Elemental Diet



Before



After

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

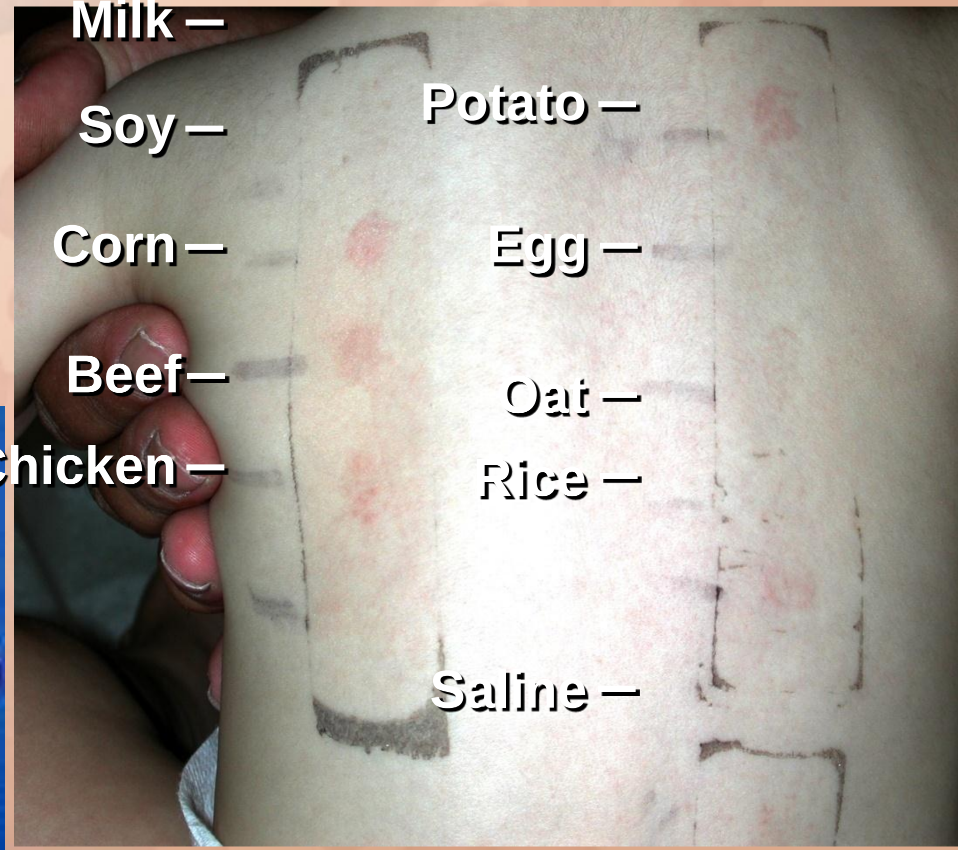
Empiric Elimination Diet

- Six food elimination diet (SFED)
- 60 EoE patients – retrospective review
  - 35 given diet without milk, soy, wheat, egg, peanut, nut and fish
  - 25 given amino acid formula
- Biopsies done at start compared with 6 weeks of diet therapy
- Improvement in restricted group 75% while amino acid group 90%

Kagalwalla, et al; *Clin Gastro Hepatol,* 2006; 117(2Suppl):S470.

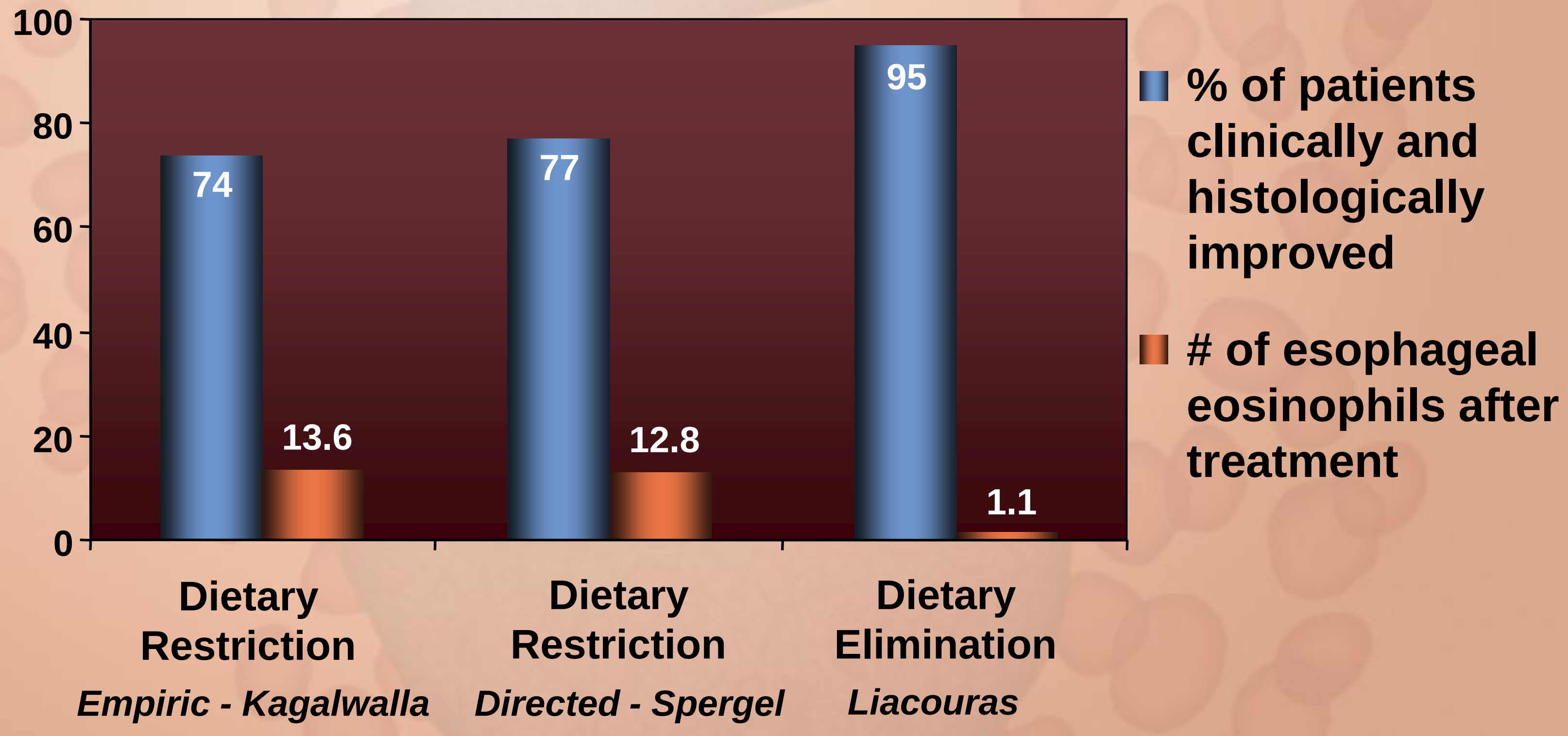
CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Direct Allergy testing for EoE



CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Which Diet to Use?



Kagalwalla, et al; *Clin Gastroenterol Hepatol* 2006; *117(2Suppl):S470*.
Liacouras, et al; *Clin Gastroenterol Hepatol* 2005; 3:1198.
Spergel, et al; *Ann Allergy Asthma Immunol* 2005; 95(4):336.

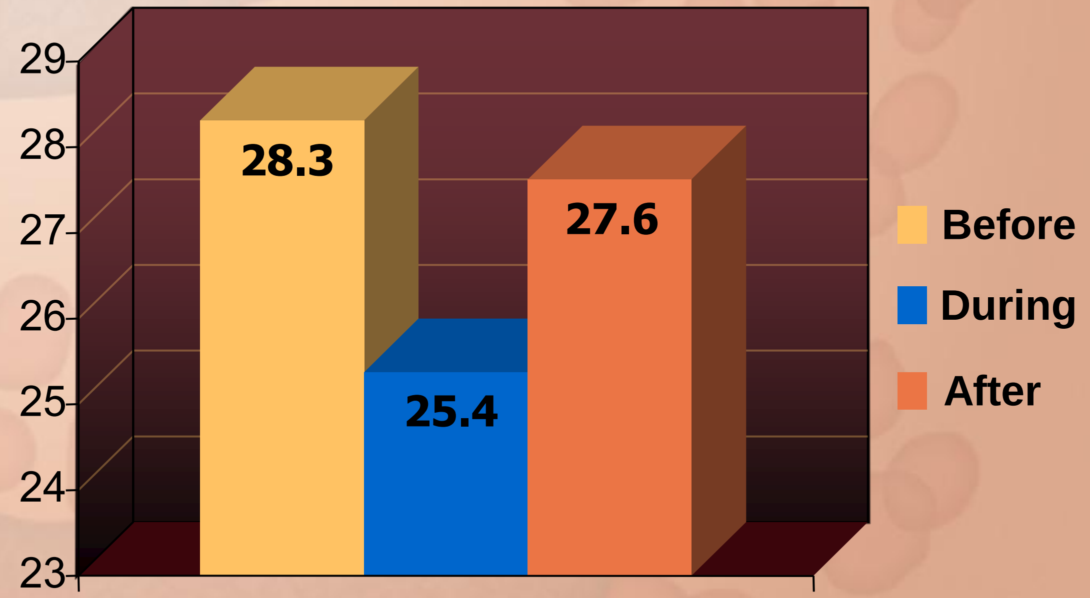
CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Other Treatments

CA Liacouras
Children’s Hospital of Philadelphia
University of Pennsylvania

Response of EoE to Cromolyn Sodium

- **14 patients**
- **GER symptoms**
  - **0/13 improved**
- **Dysphagia**
  - **0/1 improved**



Liacouras, et al; *Clin Gastroenterol Hepatol* 2005; 3:1198.

Children's Hospital of Philadelphia
University of Pennsylvania

Leukotriene Receptor Antagonists

- Montelukast (Singulair®)
  - Blocks the action of leukotriene D4 at $CysLT_1$
  - $CysLT_1$ found in eosinophils, among other places
- Trial of 8 EoE patients
  - 7 of 8 patients with dysphagia had resolution of symptoms
  - 5 patients remained in clinical remission for 14 months
  - Patients relapsed within 3 weeks of stopping the medication
  - No histologic changes occurred

Attwood et al; *Gut* 2003; 52(2):181.

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Biologic Treatment

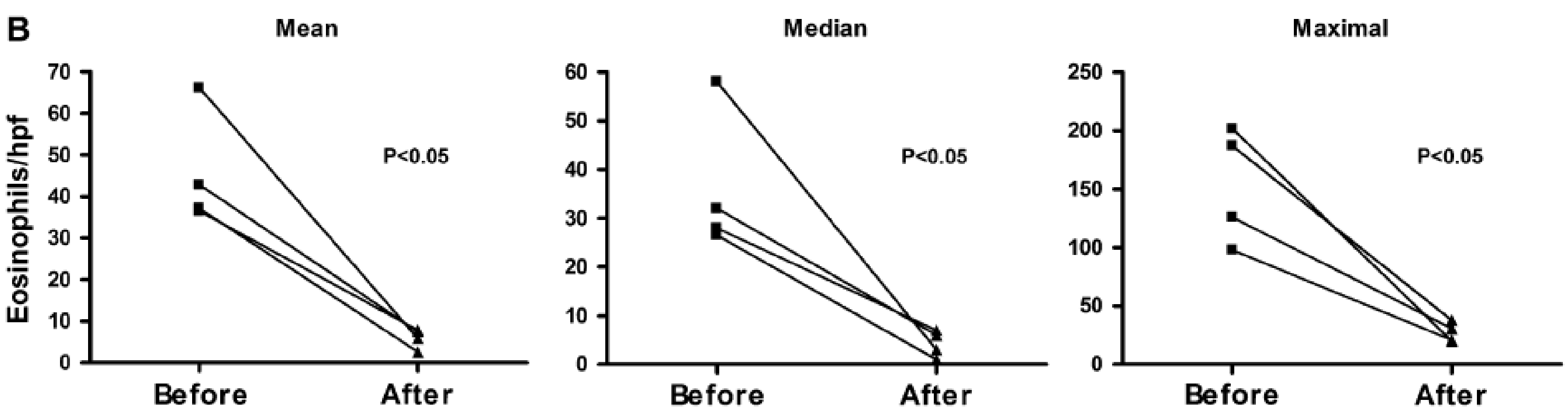
CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Interleukin 5 (IL-5)

- Cytokine that regulates eosinophil function
  - Proliferation and release from bone marrow
  - Maturation
  - Survival
  - Activation
- Several studies in patients with HES

Mishra, et al; *J Immunol* 2002; 168:2464.
Stein, et al; *J Allergy Clin Immunol* 2006; 118:1312.

Anti IL-5



Stein, et al.; JACI, 2007

TIGER

THE INTERNATIONAL GASTROINTESTINAL EOSINOPHIL RESEARCHERS

CA Liacouras
Children's Hospital of Philadelphia
University of Pennsylvania

Advocacy Groups

- American Partnership for Eosinophilic Disorders
  - www.apfed.org
- Campaign Urging Research for Eosinophilic Disorders
  - www.curedfoundation.org
- Food Allergy Network
  - www.foodallergy.org

Conclusions

- EoE is a clinico-pathologic disorder diagnosed by clinicians
- EoE can occur “at any age”
- Pediatric and Adult EoE are likely the same disease
- Incidence and prevalence have increased
- Important that you make the distinction between
  - Eosinophilic Esophagitis
  - Esophageal Eosinophila
  - “PPI-responsive” esophageal eosinophilia
- “Stay tuned”
  - Expect changes to occur within the guidelines as therapy, research and interest continues

CA Liacouras
Children’s Hospital of Philadelphia
University of Pennsylvania

Endoscopic Hemostasis

Section of Pediatric Gastroenterology, Hepatology & Nutrition

Texas Children's Hospital®

BCM
Baylor College of Medicine

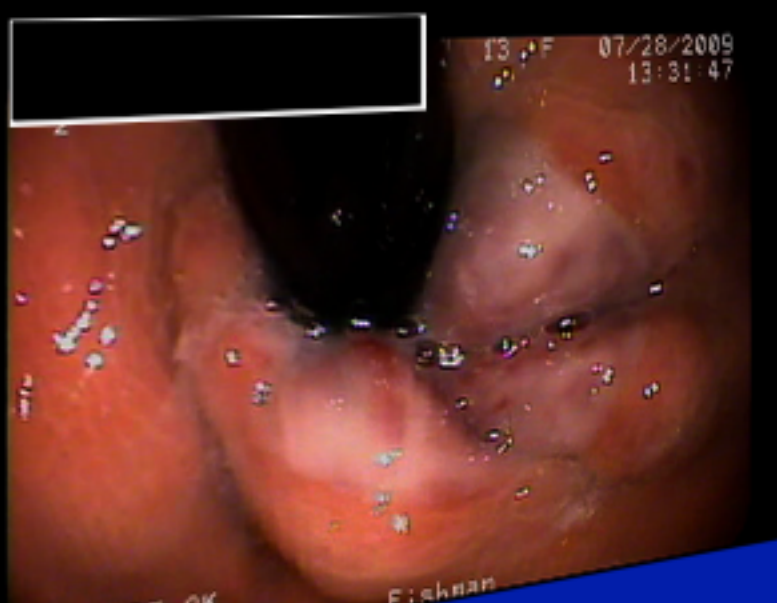
Douglas S. Fishman

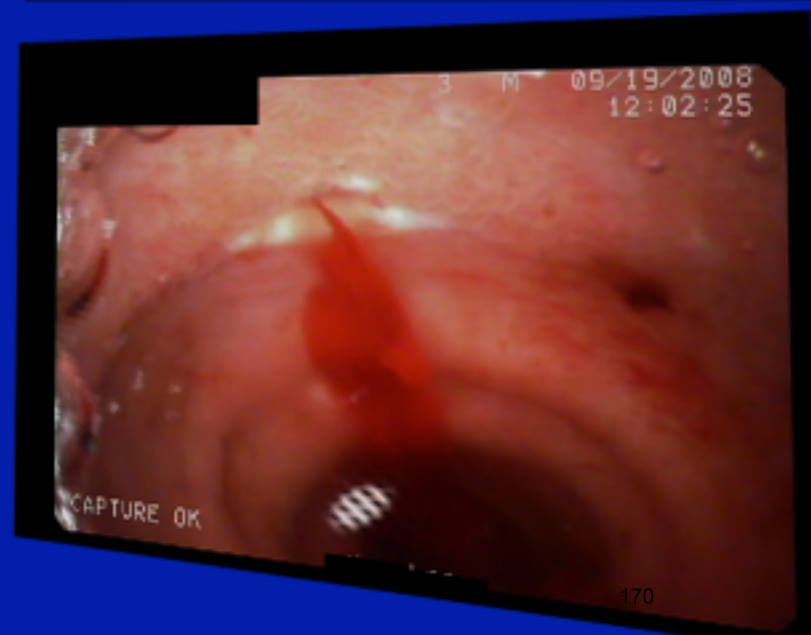
Director, GI Endoscopy

Interim Co-Director TCH Liver Center

Assistant Professor of Pediatrics


8 M 08/27/2009
12:27:29
CAPTURE OK

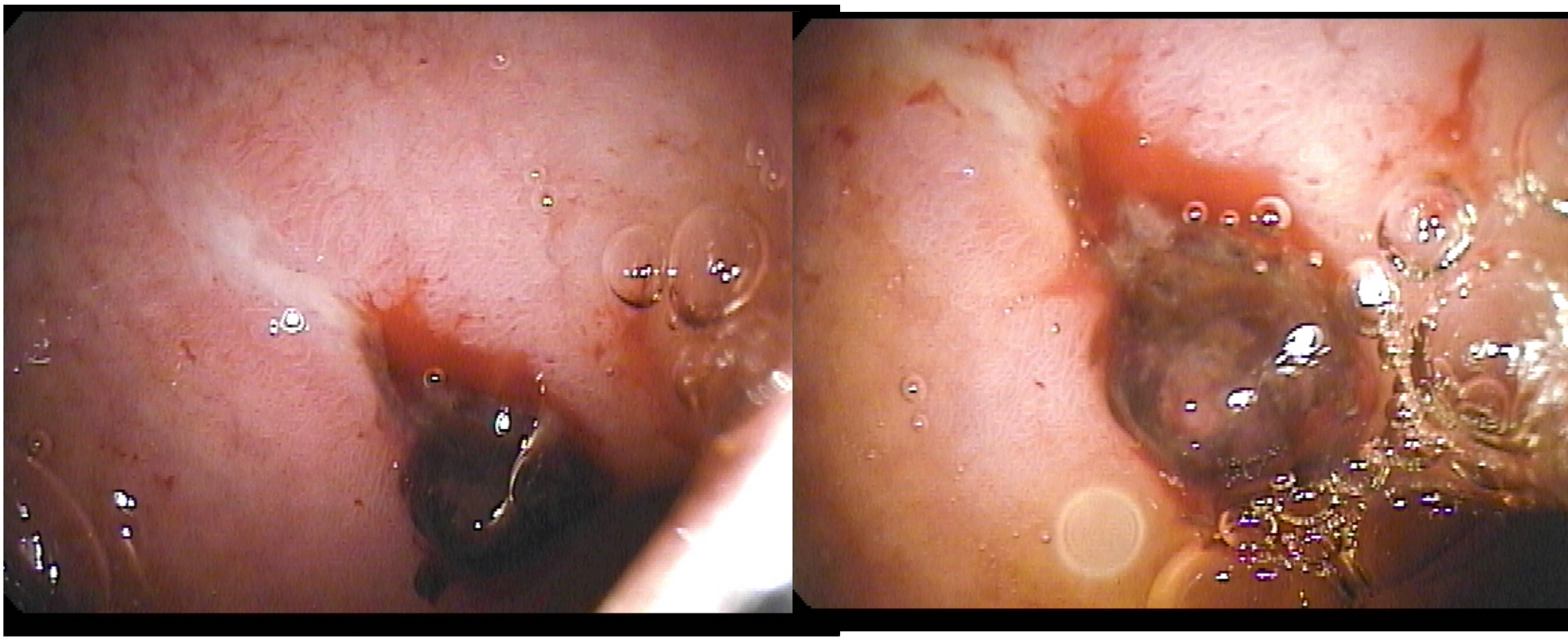

[redacted]
13 F 07/28/2009
13:31:47
Fishman


3 M 09/19/2008
12:02:25
CAPTURE OK

CASE

- 12 y/o male with a massive obstructing neck tumor
- Received several days of high dose corticosteroids
- Hgb 7-8, stable with decreased need for transfusion over 72 hrs
- Planned EGD with fiberoptic intubation

DUODENAL BULB



Goals

- Discuss the role of endoscopy in the management of non-variceal and variceal UGI bleeding
- Review the role of combined therapeutic modalities and demonstrate practical uses of endoscopic techniques
- Define potential limitations and complications of therapeutic endoscopy

The techniques

- Injection therapy
- Thermal coagulation
  - Multi-polar electrocautery (MPEC)
  - Argon Plasma
- Clip application
- Variceal band ligation

Patient Assessment

- High risk stable vs. unstable
  - Shock, hypovolemia, or marked anemia
  - Co-morbidity (Cardiac, BMT)
  - When?
- Hemodynamics, measures of hemostasis
  - Blood products available
- Where to do your endoscopy? (**OR, ICU,** ED,GI Unit)-
  - general anesthesia and protected airway

Equipment

- Endoscopy Technicians
- Nursing
  - Endoscopy Unit
  - Operating Room
- Pediatric Endoscopists
  - Fellows
  - Attendings
  - Endoscopy “Back-up”
- Surgical Staff
- Adult GI Endoscopists

Equipment

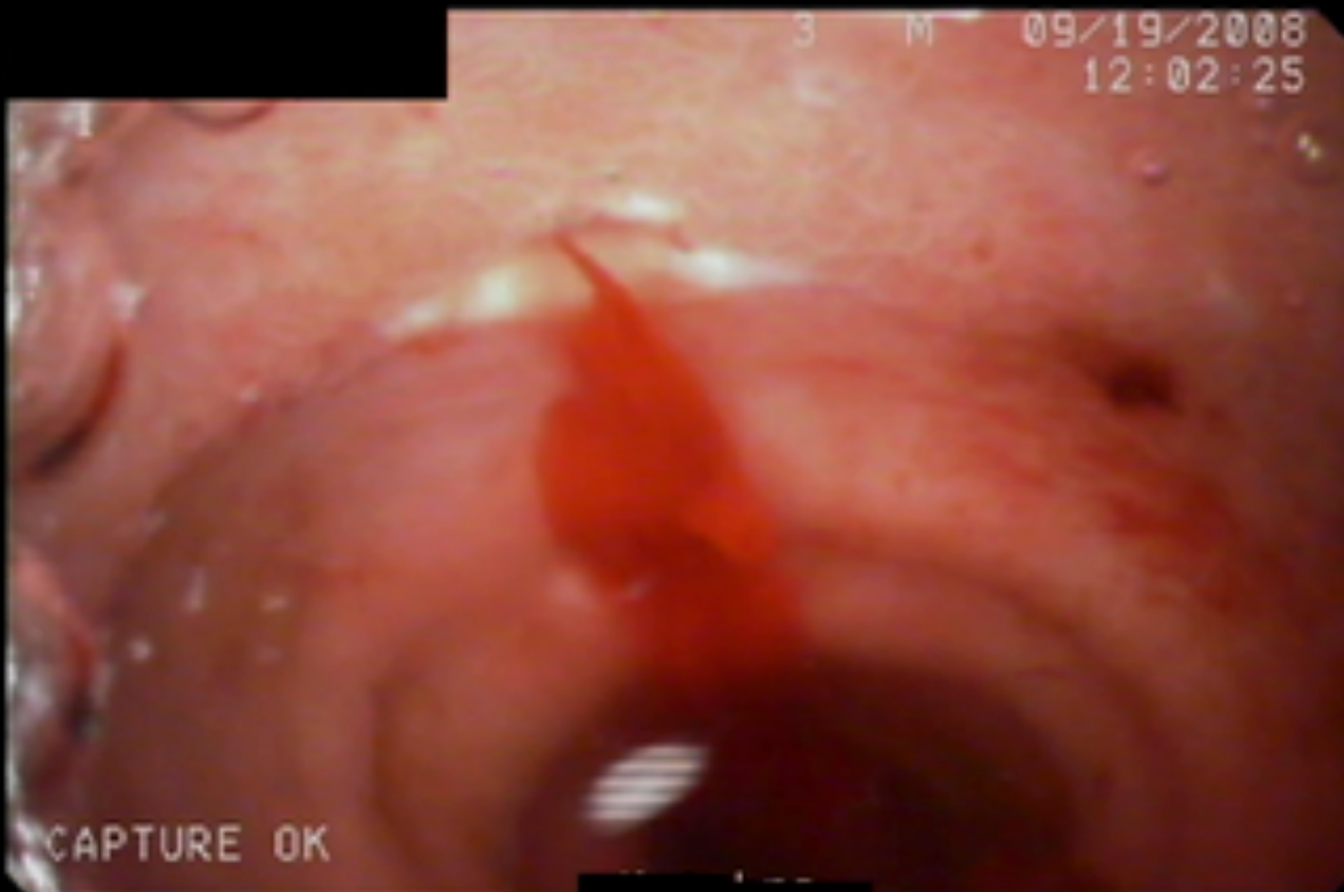
- Bleeding kit (“tackle-box”)
  - Band ligation kit, multiple hemostatic clips
  - Flexible and stiff sclerotheapy needles
  - Injectables (epi, sodium morrhuate)
- Irrigation and Suction
- Endoscopes
  - Scope diameter
  - Channel size (2.4, 2.8, 3.2+)
  - Duodenoscopes
  - Enteroscopes

Endoscopic Criteria

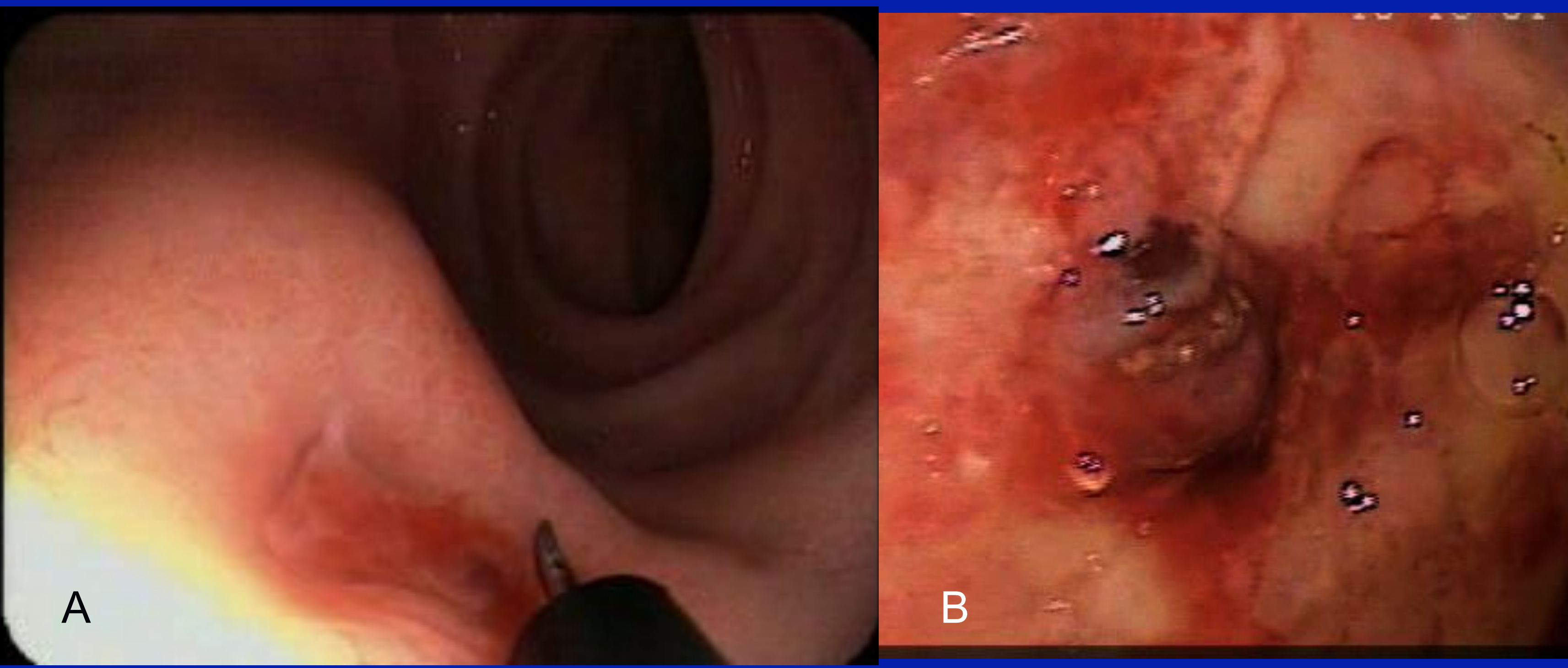
- **Acute hemorrhage**
  - **Forrest I a (Spurting hemorrhage)**
  - **Forrest I b (Oozing hemorrhage)**
- **Signs of recent hemorrhage**
  - **Forrest II a (Visible vessel)**
  - **Forrest II b (Adherent clot)**
  - **Forrest II c (Hematin on ulcer base)**
- **No signs of recent hemorrhage**
  - **Forrest III**

Forrest et al. Lancet 1974; 11: 394-7
Lau et al. GIE 1997; 46: 33-6.

Forrest 1a-”spurters”

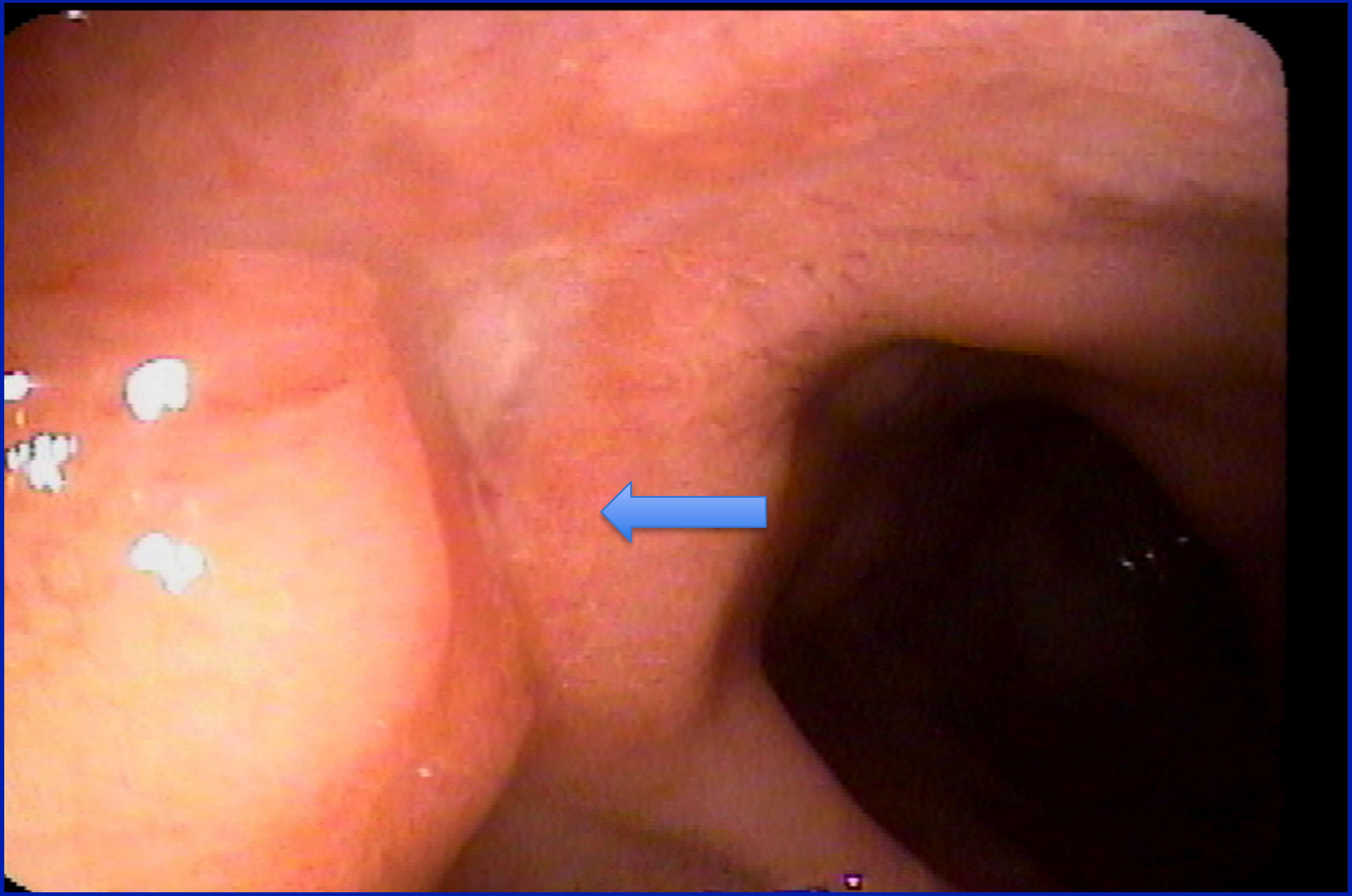


Visible Vessel or Adherent Clot ?



Visible Vessel or Adherent Clot ?

Forrest IIc vs. Forrest III



Forrest III

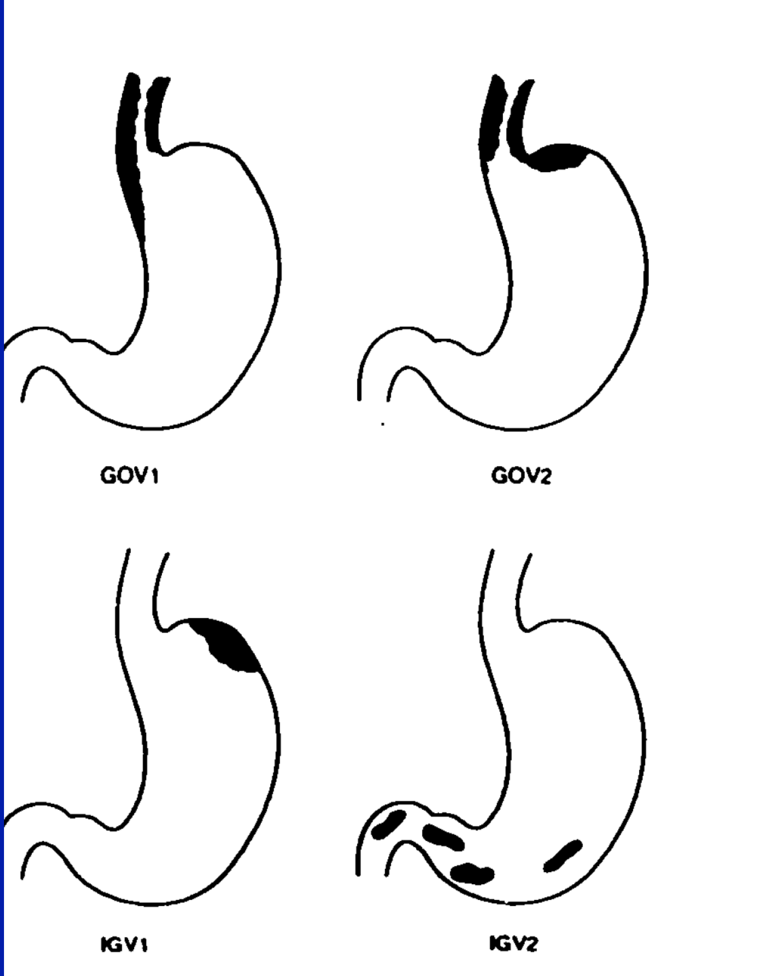
Variceal Grading

- Esophageal Varices
  - I, II, III, IV
  - Small, medium, large
  - % obstruction of lumen
  - Vessel on Vessel
- Additional signs:
  - cherry red spots (petechiae of 1-2 mm on the variceal surface)
  - red wale marks (fine capillaries on the variceal surface, resembling whipping marks)

- Gastroesophageal and Gastric Varices

Sarin Classification of Gastric Varices

Sarin et al. Hepatology. 1992



Endoscopy Consenus Statement

- An high-risk endoscopic stigmata (active bleeding or a visible vessel in an ulcer bed) is an indication for immediate endoscopic hemostatic therapy
- Monotherapy, with injection or thermal coagulation, is an effective hemostatic technique for high-risk stigmata; however, the combination is superior to either treatment alone.

Barkun et al. Annals of Internal Medicine 2003

Endoscopy Consensus Statement

- Low-risk endoscopic stigmata (a clean-based ulcer or a nonprotuberant pigmented dot in an ulcer bed) is not an indication for endoscopic hemostatic therapy
- A clot in an ulcer bed warrants targeted irrigation in an attempt at dislodgment, with appropriate treatment of the underlying lesion

Barkun et al. Annals of Internal Medicine 2003

Benefits of Endoscopic Therapy

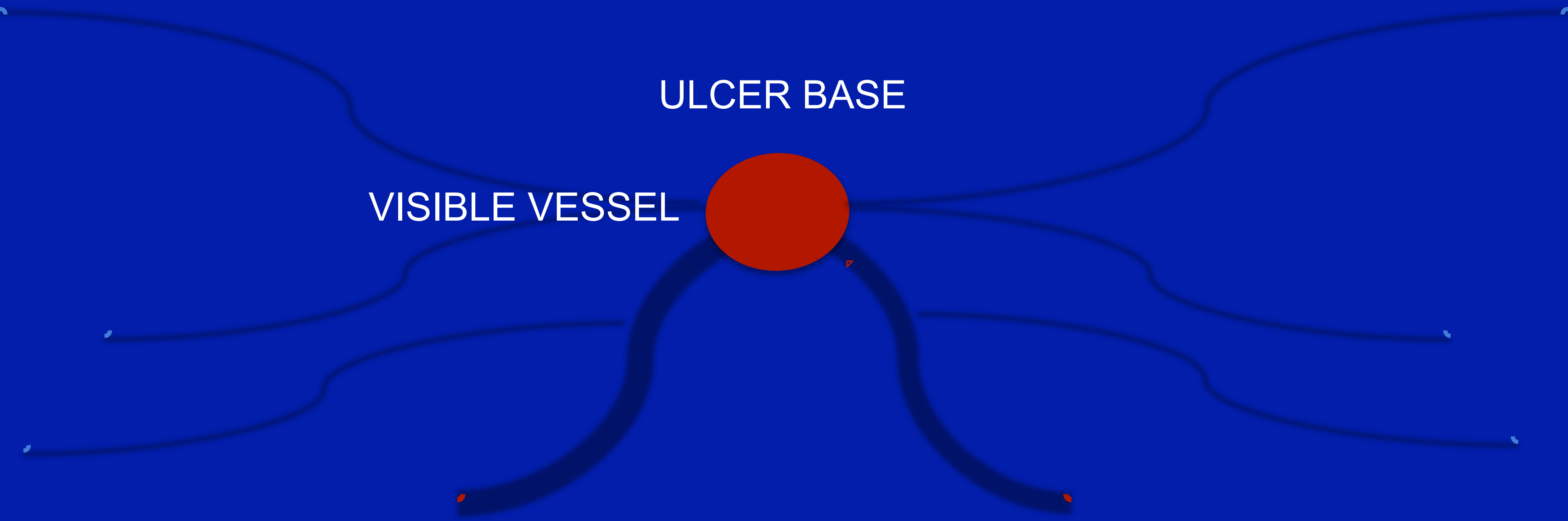
- Endoscopic therapy better than no therapy for risk of rebleeding and need for surgery :
  - ACTIVE BLEEDING
  - Non-bleeding visible vessels
- Epinephrine compared to other monotherapies:
  - epinephrine alone was less effective and discouraged its use as a solitary agent
  - rebleeding or need for surgery

Laine and McQuaid, Clin Gastroenterol Hepatol 2009; 7: 33-49

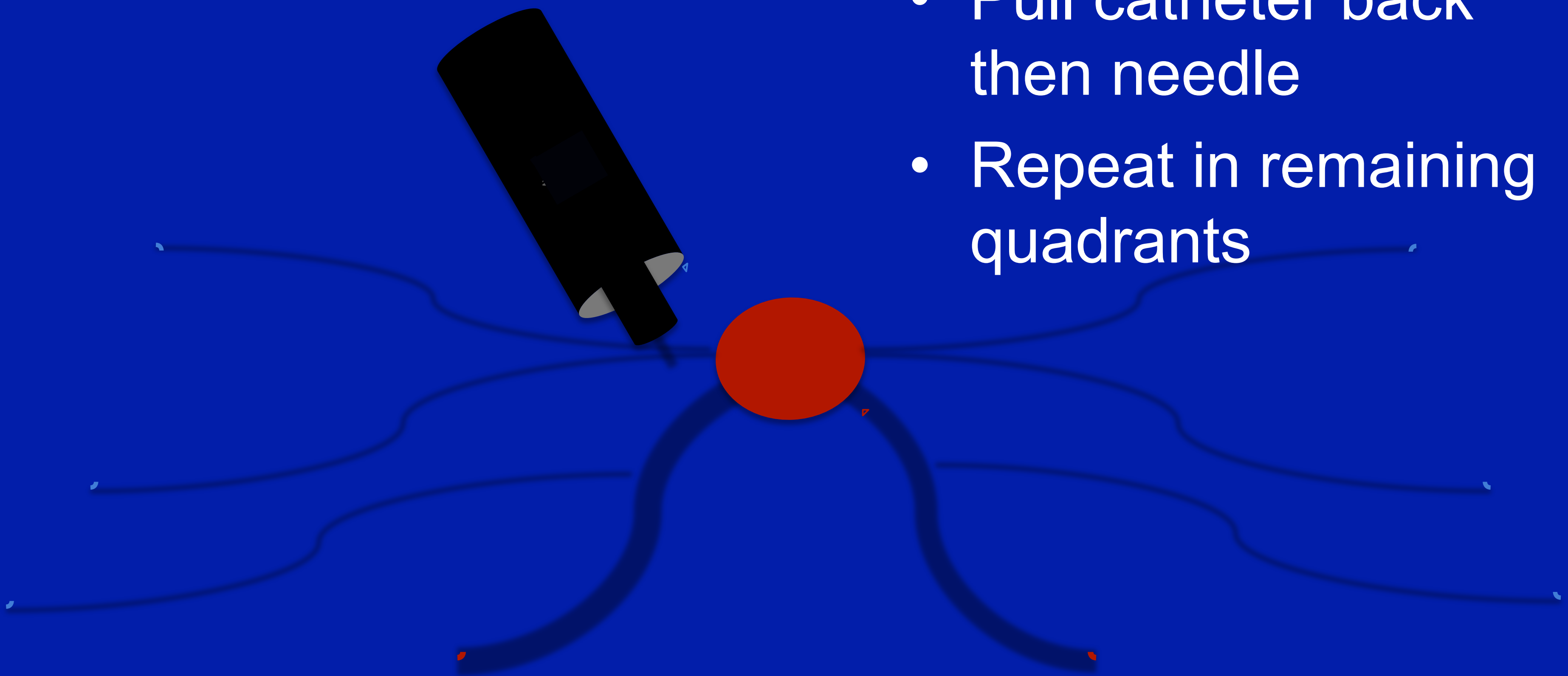
Injection Therapies

- Epinephrine (vasoactive)
  - (1:10,000) 9 mL NS with 1 mL 1:1000)
  - Best in combination with thermal or mechanical coagulation
- Sclerosants (lead to thrombosis)
  - Sodium morrhuate (2.5-5%)
  - Sodium tetradecyl sulfate
  - Absolute alcohol
- Polymers
  - Cyanoacrylate
    - » N-butyl-2 (Histocryl and Lipiodol) or 2-octyl (Dermabond)
  - Fibrin glue (fibrinogen and thrombin)

INJECTION



- Prime needle outside
- Identify lesion (wash)
- Insert catheter
- Leave space between lesion and scope to extend needle



- Inject 0.5 mL until bleb formed
- Pull catheter back then needle
- Repeat in remaining quadrants

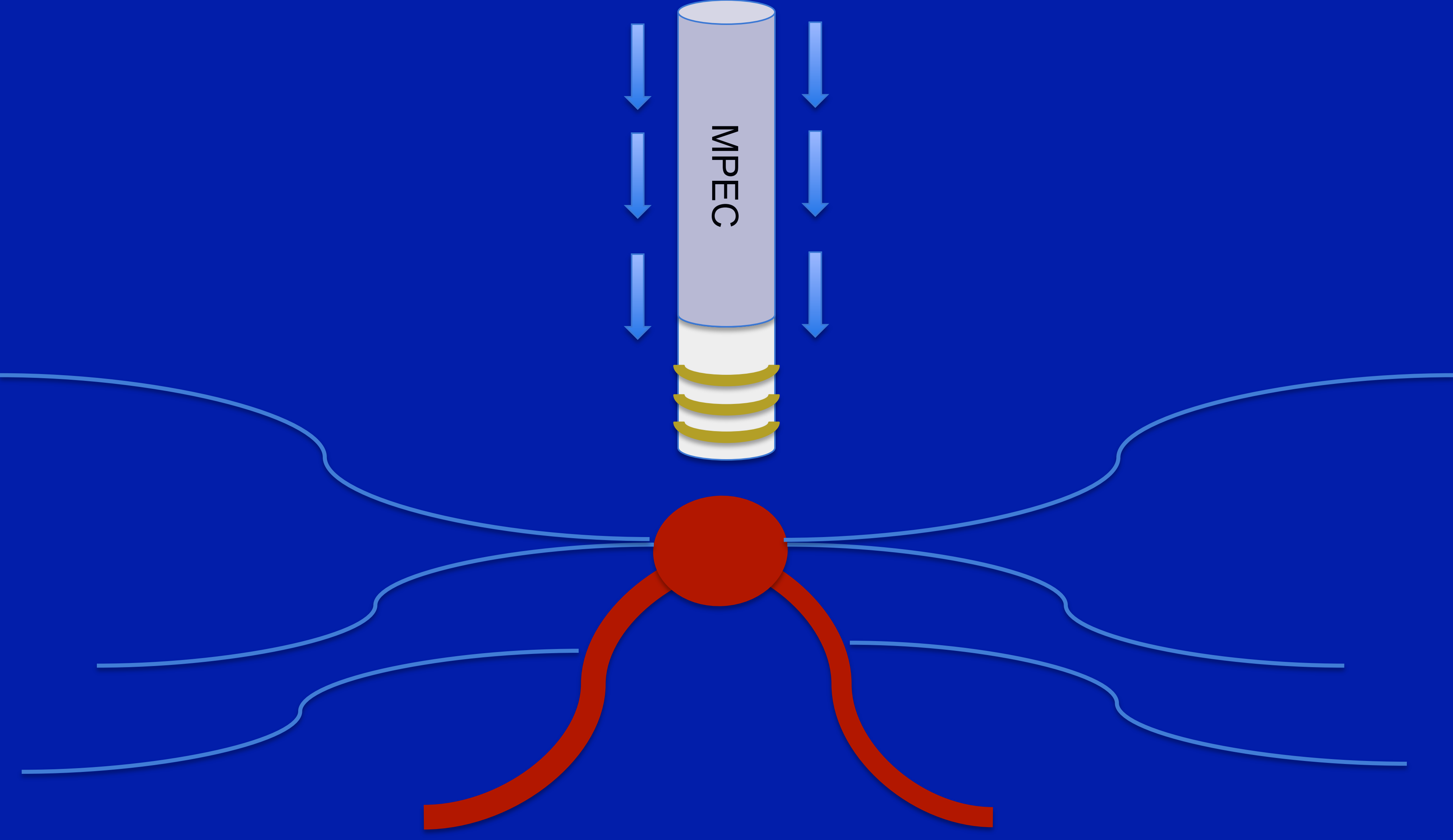

Duodenal ulcer
1:10,000 epinephrine

The techniques

- Injection therapy
- Thermal coagulation
  - MPEC
  - Argon Plasma
- Clip application
- Variceal band ligation

Thermal and Biothermal

- Thermal coagulation
  - Heater Probe
  - Bi-polar Coagulation
  - Multi-polar Coagulation (MPEC)
- Bio-thermal coagulation
  - Argon Plasma Coagulation (APC)


MPEC

Multi-polar Electrocautery (MPEC)

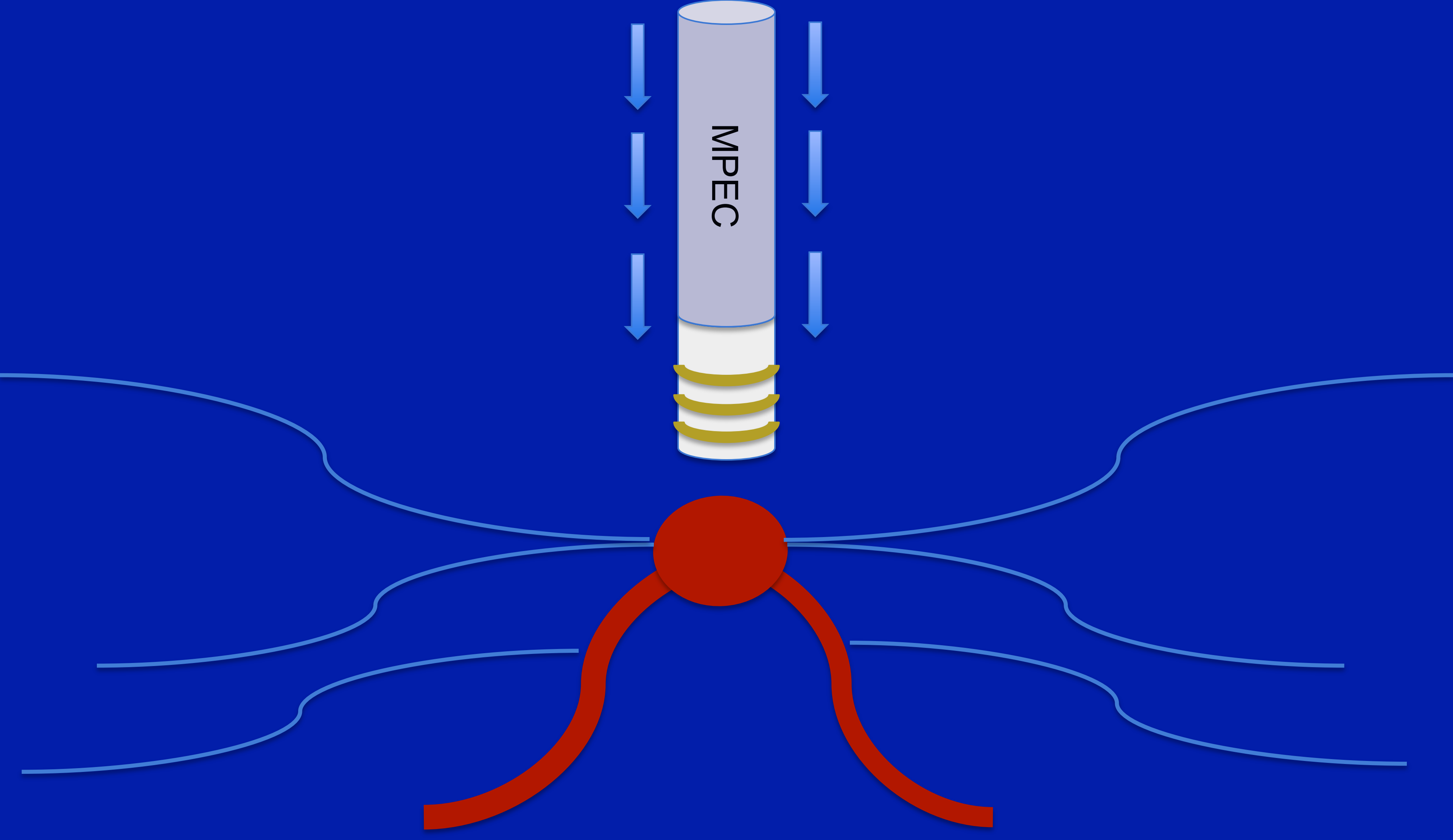
- Generates heat indirectly by passage of current through tissue
- Allows for coaptation
- Leads to coagulation and vessel contraction

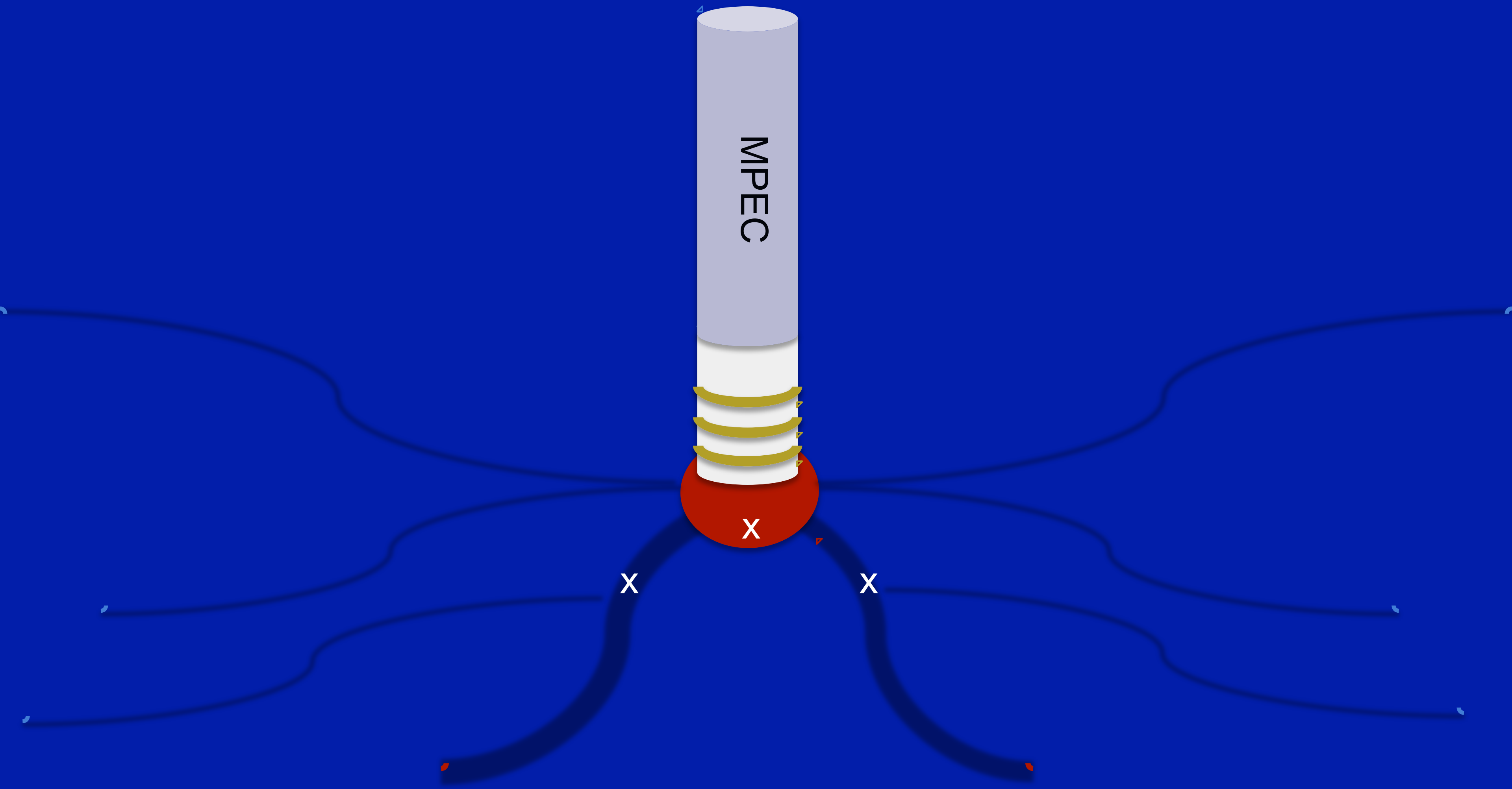
When to use multipolar or heater probe

- Duodenal ulcer
- Gastric ulcer
- Mallory-Weiss Tear
- Dieulafoy lesions
- Vascular malformations (GAVE, radiation-induced)

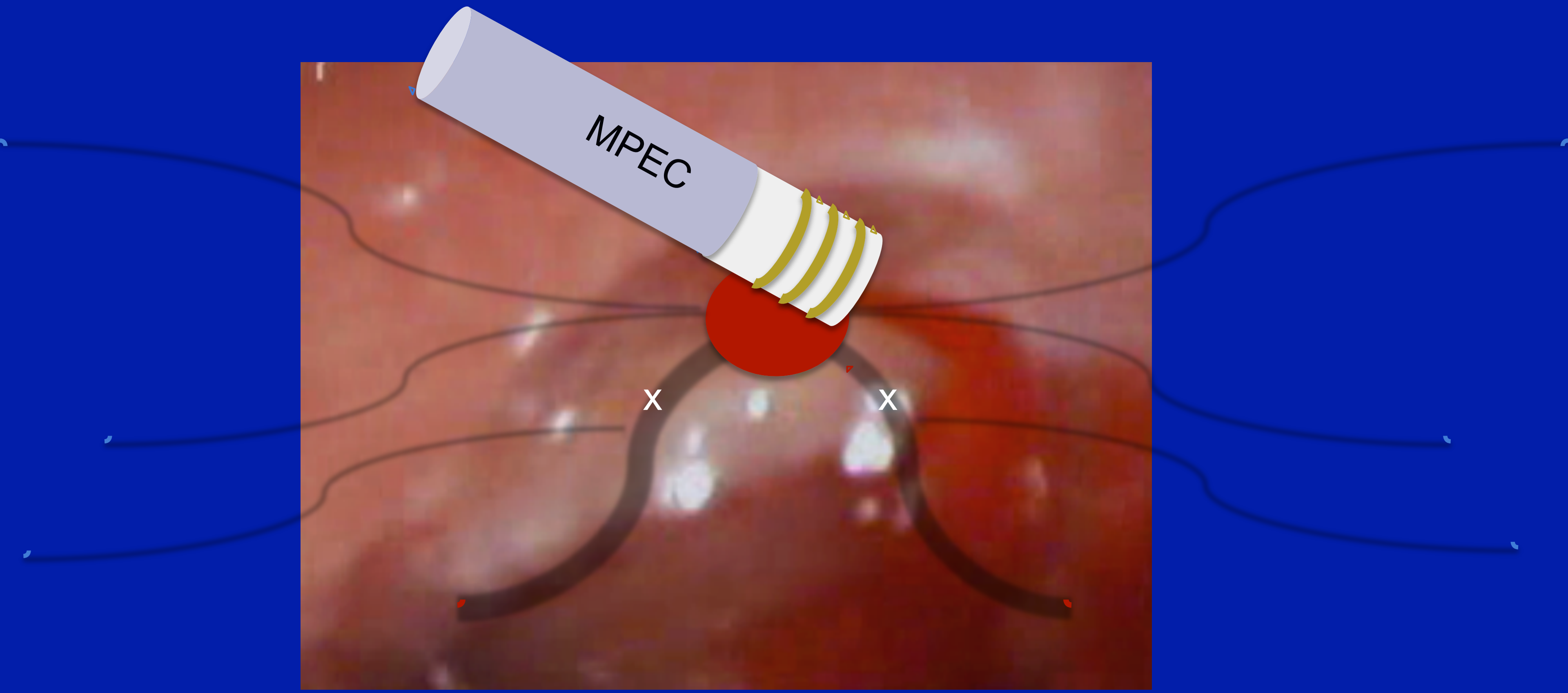
Multi-polar Electrocautery (MPEC)

- Use 7 or 10 French catheter
- No grounding necessary but requires electrosurgical unit
- Set power to 15 to 20W (less for colon)
- Apply pressure first to tamponade
- Depress foot pedal 2-4 seconds (repeat as needed)
- Pull probe back gently and irrigate


MPEC


MPEC
X
X
X

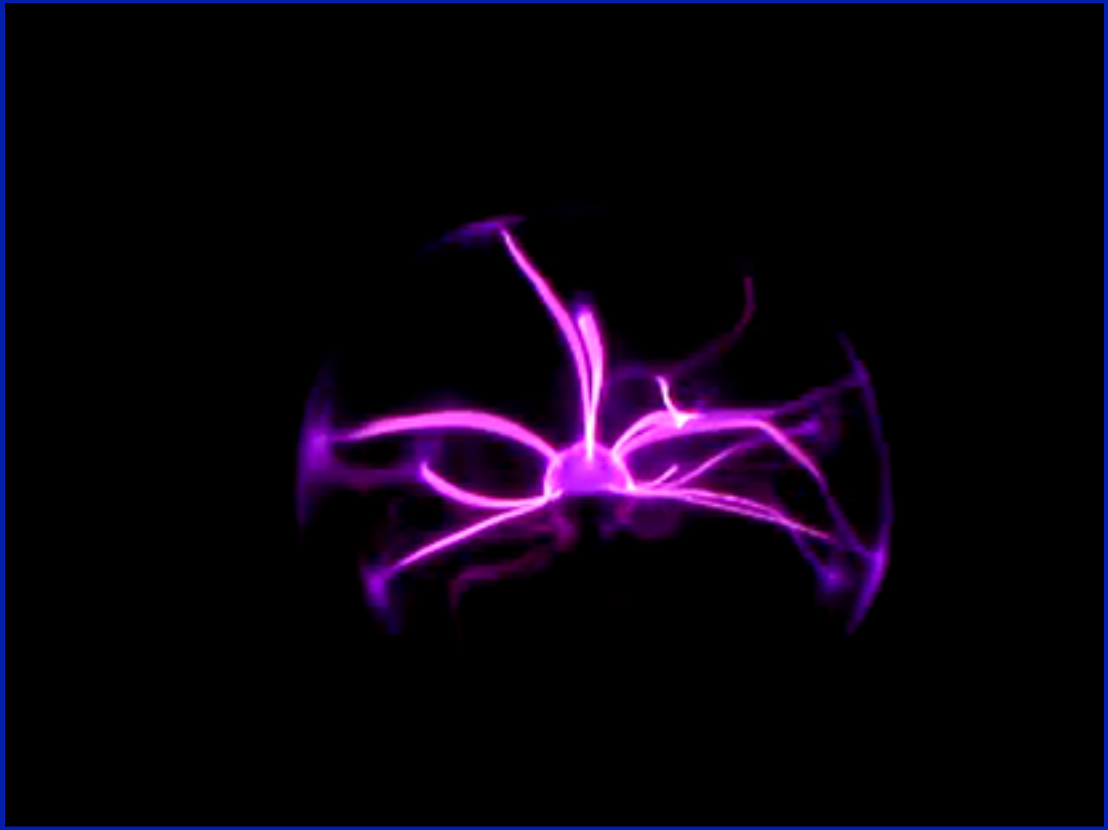
Multi-polar Electrocautery (MPEC)



MPEC Tips

- Due to various angulations, may need to bring catheter out prematurely (e.g antrum for duodenal ulcer)
- Catheters with combined sclerotherapy needle may be difficult in retroflexion
- Larger vessels require larger probe
- Less optimal for coagulopathy

Argon Plasma Coagulation



www.youtube.com

Argon Plasma Coagulation

- Non-contact thermal hemostasis
- The tungsten electrode in the probe ionizes argon gas
- Argon beam seeks nearest tissue
- Limited depth of coagulation (2-3 mm) with contact at surface
- Catheter can accommodate 2.4 mm channel

APC Uses

- Vascular ectasias (GAVE and DAVE)
- Mallory-Weiss tears
- Duodenal and Gastric Ulcers
- Radiation induced injury
- Destruction of sessile polyps (duodenal adenomas in FAP)

APC Tips

- Decompress frequently
- Use 7F or 10F catheter
- Set at 40W (15-20 in colon)
- Set flow 0.5-1L/min
- Use pulse setting and paint the area of interest
- Keep the black strip of catheter in view to avoid damage to endoscope


BCM
ARGON PLASMA
0 F 06/07/2008
16:34:24
CAPTURE OK

Mechanical

- Endoclips
  - Single Clip (Resolution, QuikClip2, TriClip)
  - Multi Clip (InScope)
- Endoscopic “Loops”
- Elastic band ligation
  - Esophageal Varices
  - Dieulafoy lesions
  - Polypectomy
  - EMR (Endoscopic mucosal resection)

The techniques

- Injection therapy
- Thermal coagulation
  - MPEC
  - Argon Plasma
- Clip application
- Variceal band ligation

Hemostatic Clips

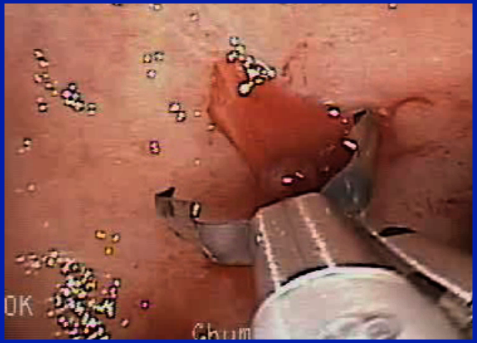
- Mucosal/sub-mucosal defects < 3 cm
- Arteries < 2-3 mm
- Polyps < 1.5 cm in diameter
- Need endoscopes with working channels equal to or greater than 2.8mm.
- Active bleeding or lesions with coagulopathy

When to use clips for hemostasis

- Duodenal and Gastric ulcer
- Mallory-Weiss Tear
- Early anastomotic bleeding
- Post-polypectomy
- Prophylaxis (pre-polypectomy, EMR)
- Post-variceal banding

Hemostatic Clip Options

- Boston Scientific (Resolution Clip)
- Olympus (Quick Clip2)
- Wilson Cook (Tri-Clip)



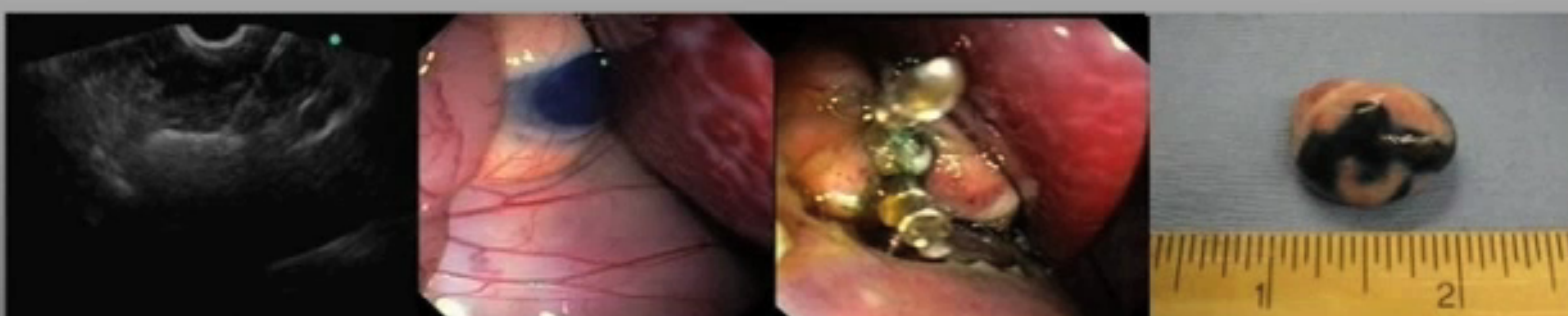

Endoscopic Clipping Techniques
Used With Permission ASGE

Beth Israel Deaconess Medical Center

A TEACHING HOSPITAL OF HARVARD MEDICAL SCHOOL

Courtesy of Kai Matthes, MD

Closure of gastrotomy with over-the-scope clips



Clip Tips

- Practice with assistant prior to “live” use
- May need to bring out in antrum and assess opening, closing and angles
- To close: Snap, Crackle, and then may need two hands to create… POP
- To release, assistant should open their hand, endoscopist should keep catheter steady and even pull back slightly
- Have both lengths available (155 and 235 cm)

More Clip Tips

- Be familiar with clips
- Have multiple available, can tamponade feeding vessels
- Work close
- Inject with epinephrine if oozing
- Head-on or tangential, don't pinch the vessel
- Rotate clip
- Push into mucosa and gently suction
- Close

Hemostatic Clip Tips: Troubleshooting

- Deployment of clip too far from endoscope
- Knock off clips already deployed
- Premature closure of clip
- Insufficient number of clips available
- Failure to release clip…open the hand
- Attempt to clip erosive surface, best to have some intact mucosa to clip

Case

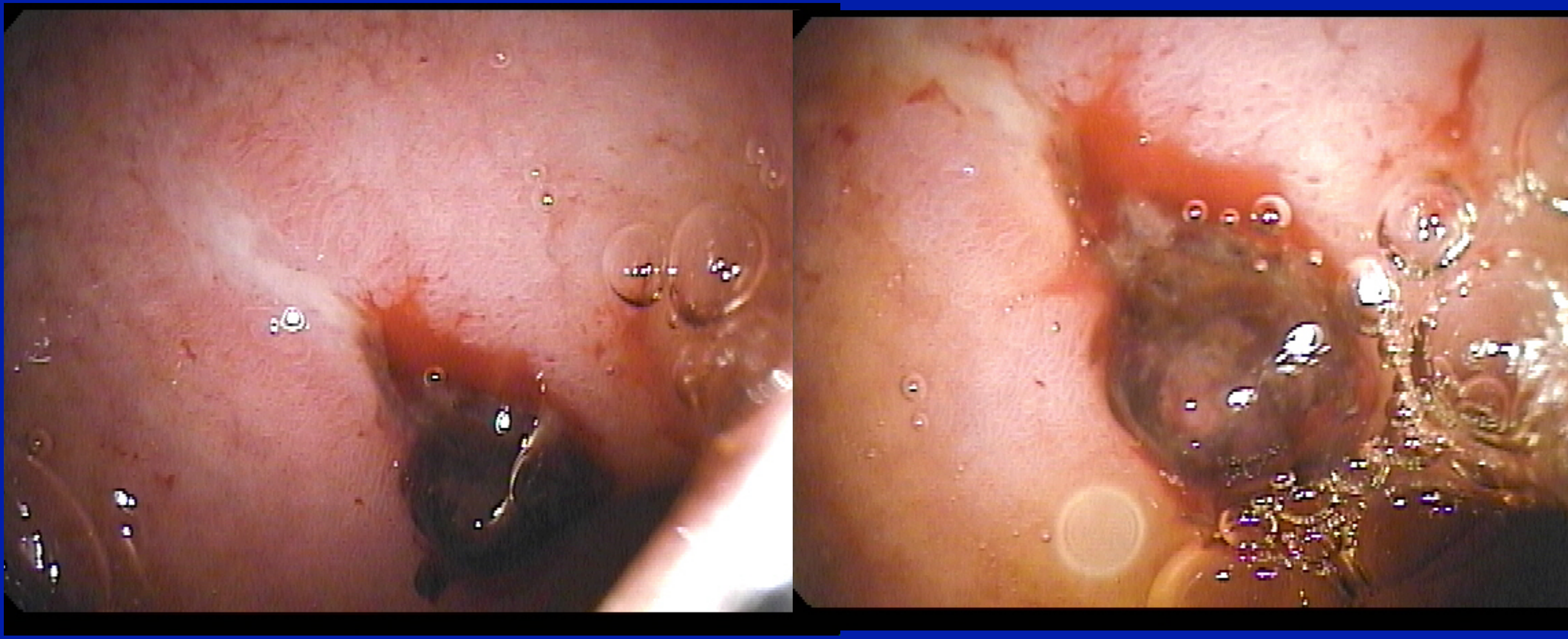
- 12 y/o male with facial anomalies receiving gastrostomy feedings
- presented with hematemesis and melena
- EGD done via the gastrostomy tract as a port of entry for the upper endoscope
  - gastric body ulcer with a visible vessel was seen, likely secondary to mechanical stress from his gastrostomy button.


11/16/2007
00:13:47
Jensen
Facility
EG-1540
PENTAX

Back to our Case

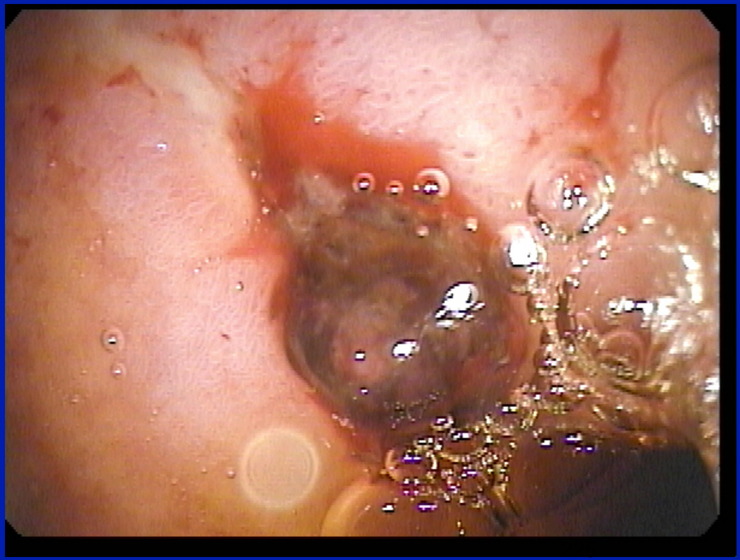
- 12 y/o male with a massive obstructing neck tumor
- Received several days of high dose corticosteroids
- Hgb 7-8, stable with decreased need for transfusion over 72 hrs
- Planned EGD with fiberoptic intubation

DUODENAL BULB



DISCUSSION

What should you do with a CLOT?



What to do with adherent clots

- 56 patients at seven centers found to have fresh adherent clots with no active bleeding
- The clot was irrigated with 200 cc of forcibly injected water.
- Randomized into treatment with injection and heater probe or medical management
  - Those randomized to endoscopic therapy had the base of the adherent clot injected with 1/10,000 epi in four quadrants with at least 1 cc in each quadrant.

Bleau et al. GIE; **2002;56:1-6.)**

To remove or not?

- The clot was removed and heater probe (30 J) a minimum of 3 coaptive pulses.
- Rebleeding rates were 34.3% (12/35) in the medical treatment arm vs 4.8% (1/21) in endoscopic group. **($p<0.02$).**
- Endoscopic treatment with injection of the base of the clot, removal, and heater probe coagulation significantly reduces rebleeding rates.

Bleau et al. GIE; **2002;56:1-6.**
Kahi et al. Gastro 2005;129:855–862

Endoscopic Therapy vs. No Endoscopy for Treatment of Clots

- Meta-analysis
- No signficant benefit in further bleeding, surgery or mortality
- 2/5 favored endoscopy, 1/5 had n=5 patients
- NNT = 2
- Did not include rebleeding

Laine and McQuaid, Clin Gastroenterol Hepatol 2009; 7: 33-49

How to remove the clot

- Vigorous irrigation will expose high-risk vessels and remove clot
- Snare removal (like polyp)
- Probe with biopsy forceps
- Manipulate with endoscope
- Suction
- Surgical availability?

The techniques

- Injection therapy
- Thermal coagulation
  - MPEC
  - Argon Plasma
- Clip application
- Variceal band ligation

Variceal Band Ligation (VBL)

- Arrest bleeding and obliterate/eradicate the varix
- VBL is a the use of a rubber band when placed over a varix, leads to thrombosis


00:01:33
27 Aug 08
Texas Children's Hospital
BCM
Baylor College of Medicine
Biliary Atresia–Grade 2

Variceal Band Ligation

Wilson Cook
4,6, 10 Shooter®

Boston Scientific
Super 7®

ConMed
Auto-Band Ligator®



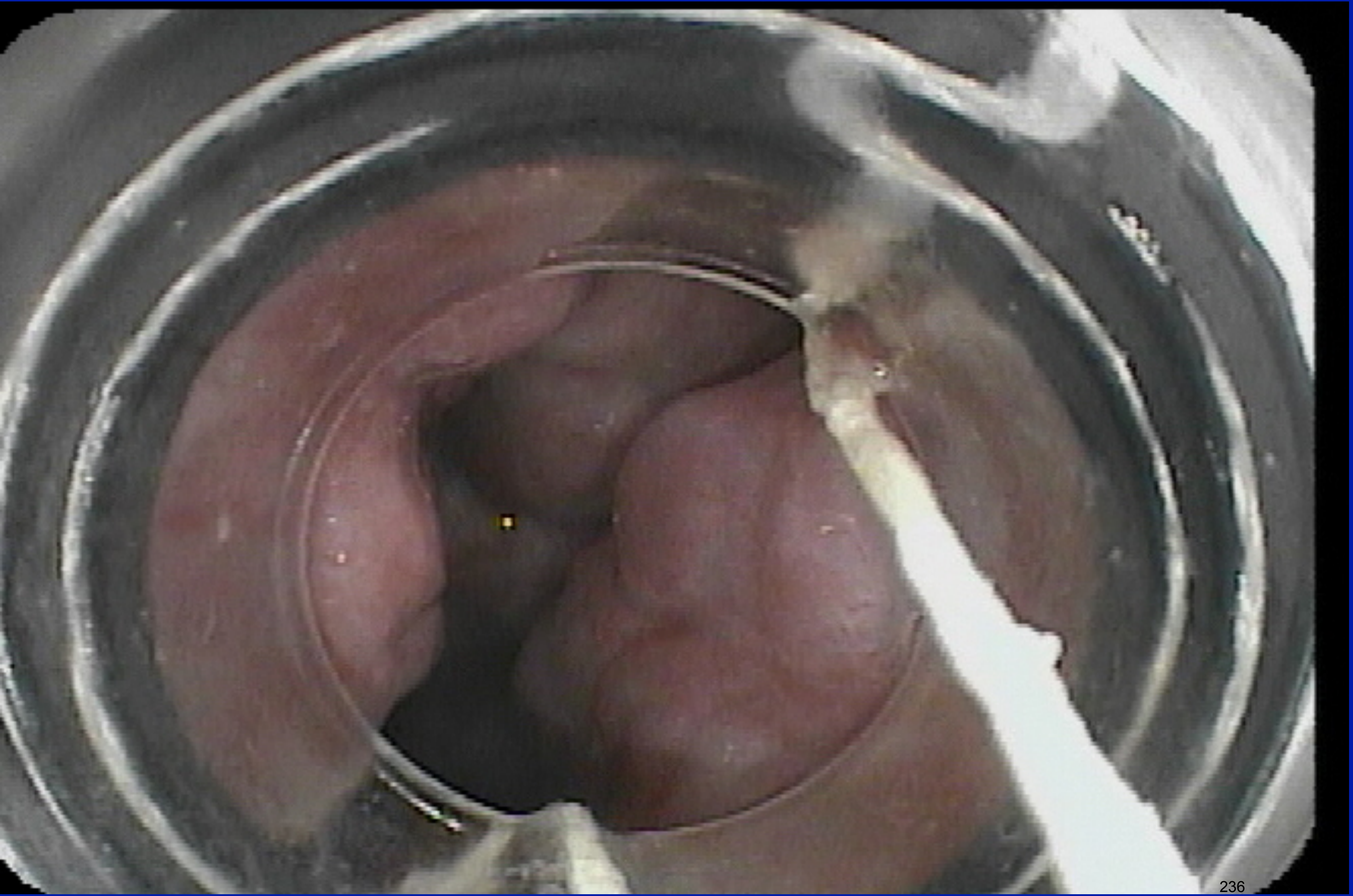
VBL use in children

- In adults, compared to sclerotherapy
  - Decreased mortality (45% vs 28%)
  - Decreased complications (22% vs 2%)
  - Less recurrent hemorrhage and fewer sessions (NS)
- Majority of studies include patients with both intrahepatic and extrahepatic disease
- >90% variceal eradication in most series

Stiegmann GV et al. NEJM 1992; 326: 1527-1532
McKiernan P et al. JPGN 2002; 34: 207-211
Celinska-Cedro et al. J Pediat Surg; 38: 1008-11

VBL technique

- Identify varix of concern (map out remainder)
- Remove scope and attach ligation device
- Start low in the distal esophagus with high risk lesions first



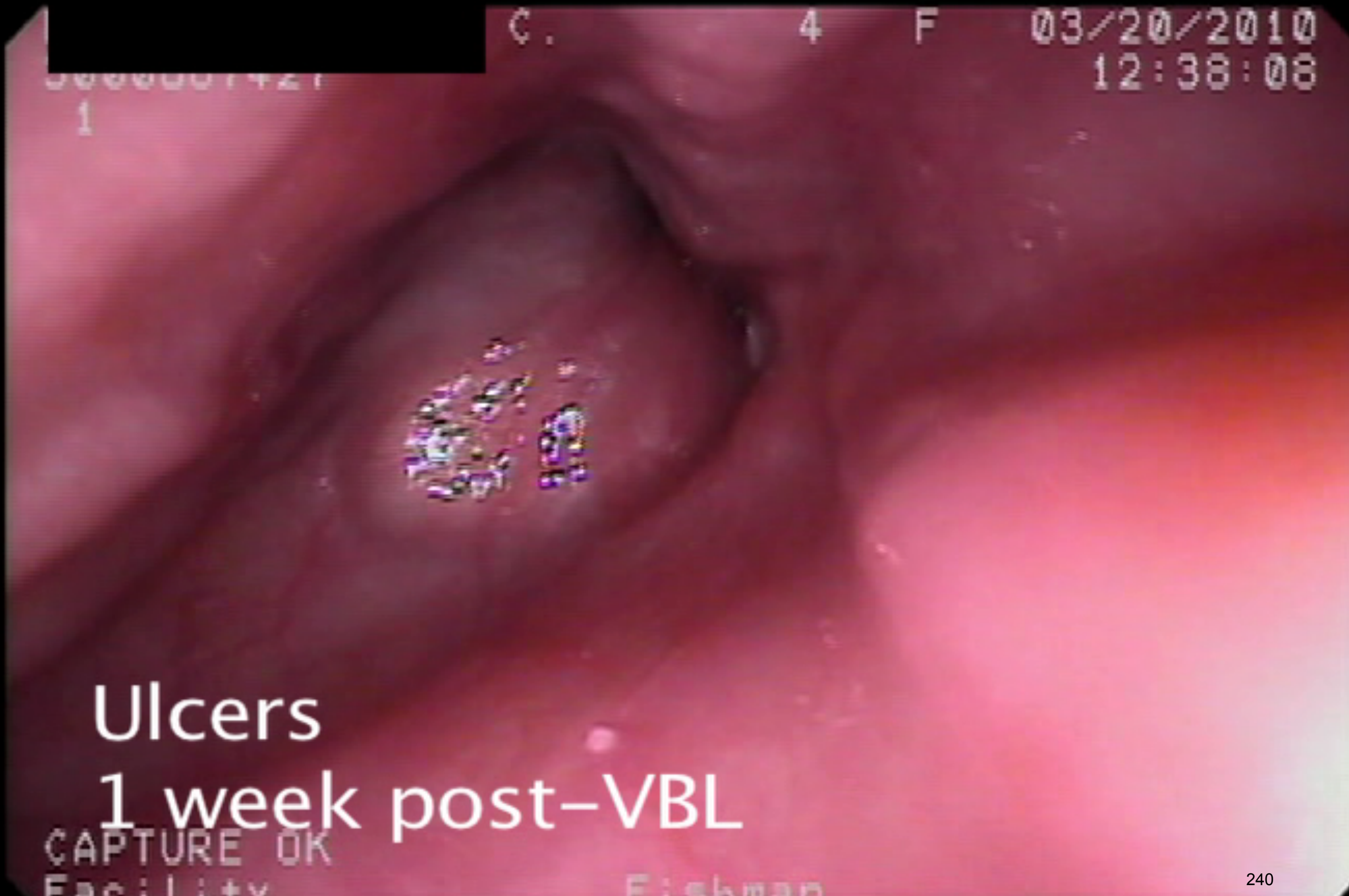
VBL technique

- Angle scope so that varix can roll into banding cap. All edges of the cap should surround the varix (circumferential).

VBL technique

- Apply suction-when varix engorges ¾ of cap obstructing endoscopic view-get ready
- Turn the banding device when there is a full “red out”

VBL technique


[redacted]
C.
4
F
03/20/2010
12:38:08
1
Ulcers
1 week post–VBL
CAPTURE OK

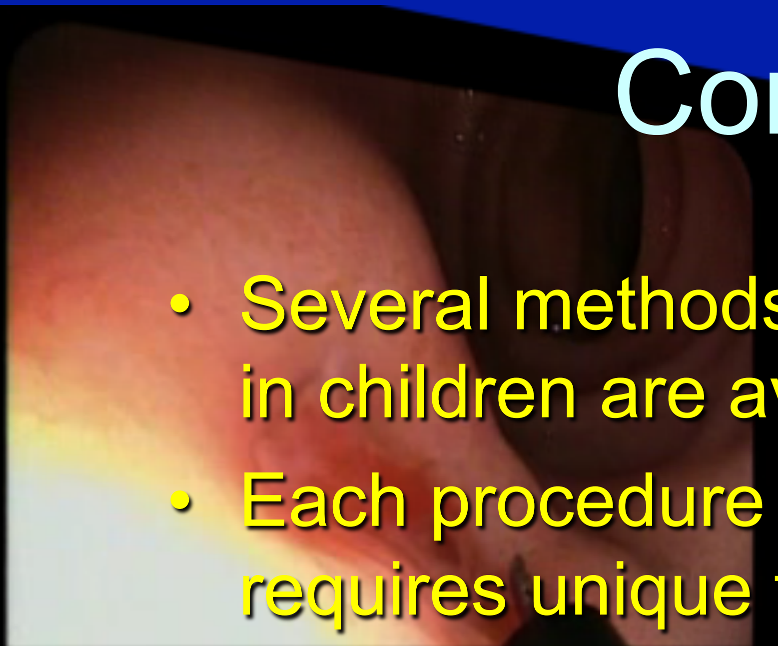
VBL Tips

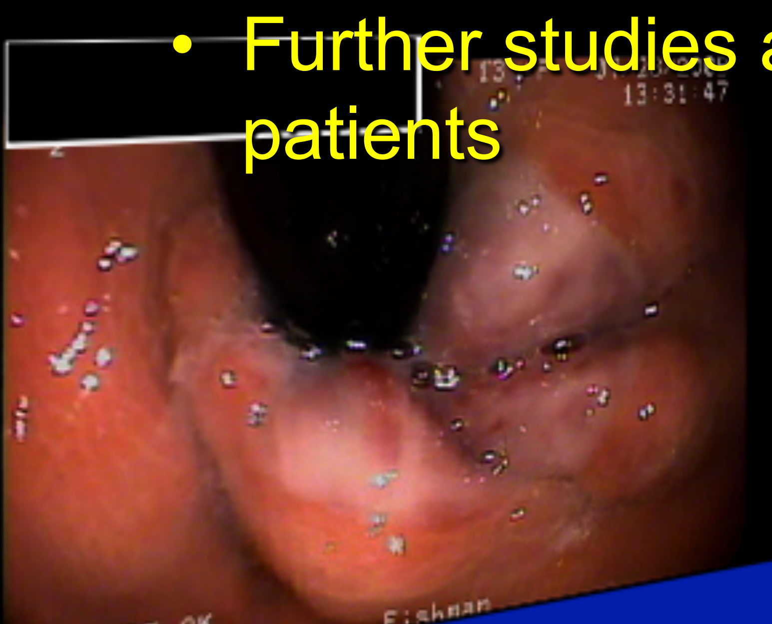
- Re-intubation with ligation device can be difficult
- Major limitation is patient size (10 kg?)
- Minimize touching bands with endoscope after placement
- Have sclerotherapy equipment available

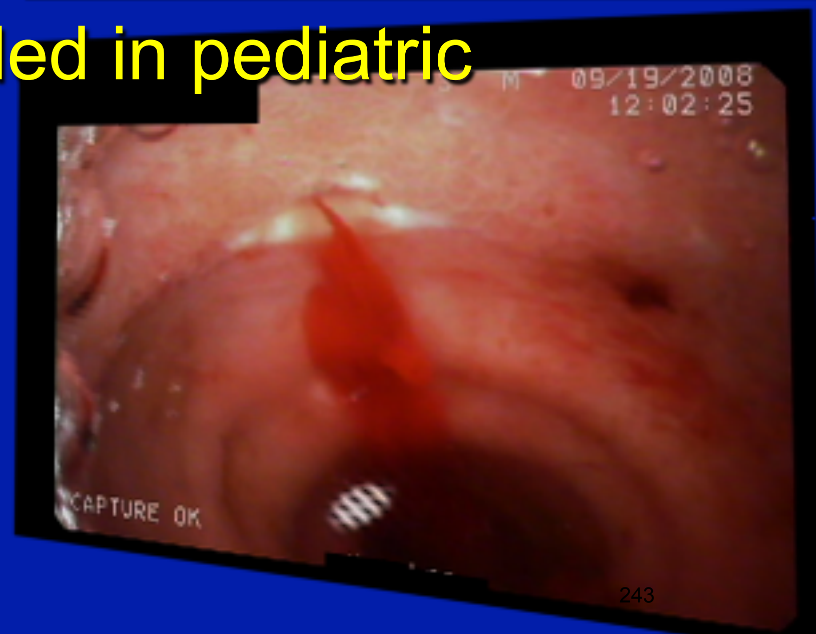
Complications of VBL

- Bleeding (early and late)
- Infection
  - SBE prophylaxis not recommended
  - Antibiotics for acute bleeding only
- Perforation (rare)
- Stricture (rare)

Conclusions





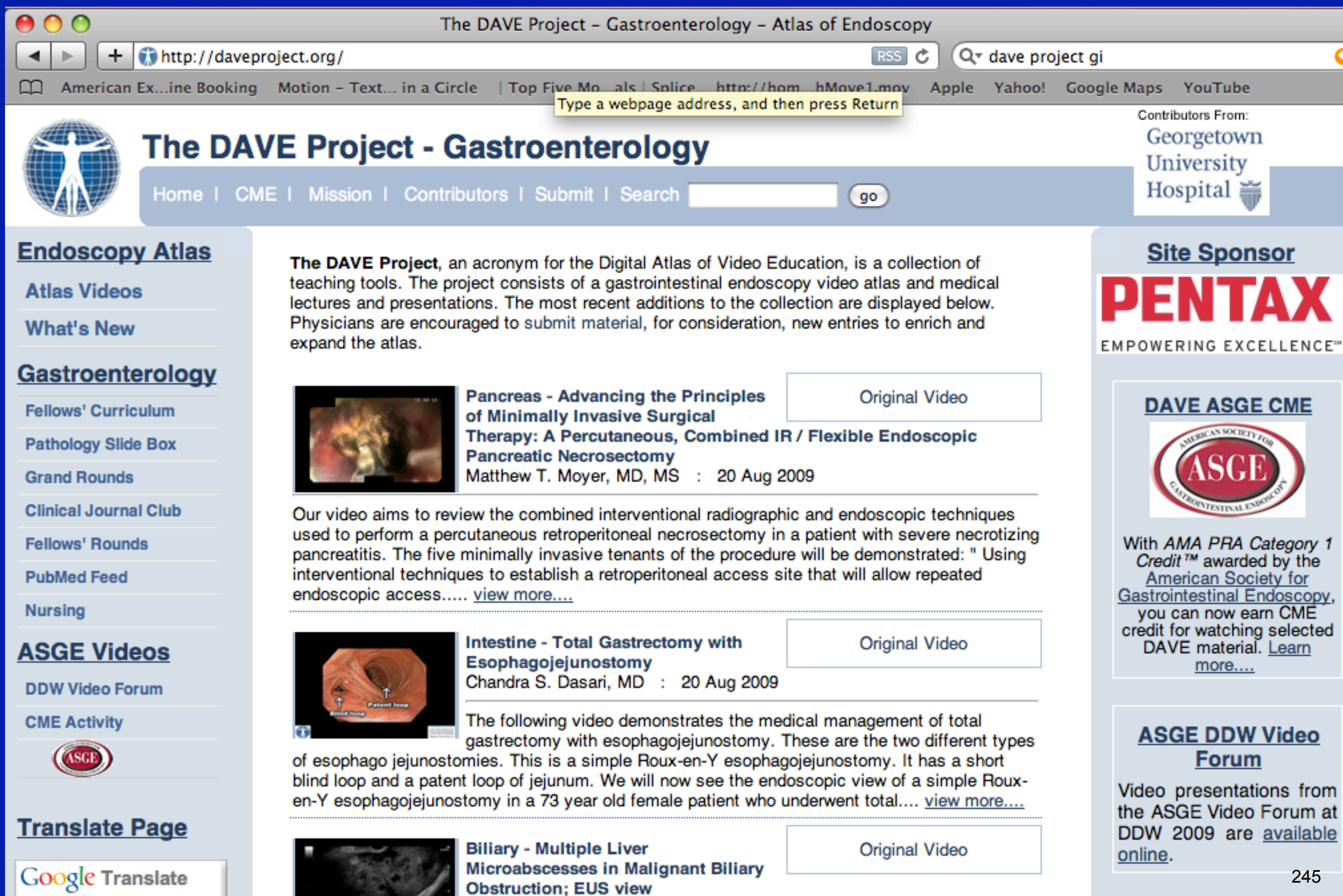


- Several methods for treatment of gi bleeding in children are available
- Each procedure is patient specific and requires unique tools
- Further studies are needed in pediatric patients

Training

- Text/Journals
  - Handbook of Gastroenterologic Procedures (Drossman)
  - JPGN, AJG, Gastrointestinal Endoscopy (GIE) and Endoscopy
- Video
  - DAVE project
  - ASGE Training Library
- Computer Simulation (bleeding modules)
- “Hands-On” Training
  - NASPGHAN/ASGE courses
  - ASGE Center (Chicago, IL)
- Adult GI Collaboration (observation, preceptorship)

http://daveproject.org



Special Thanks

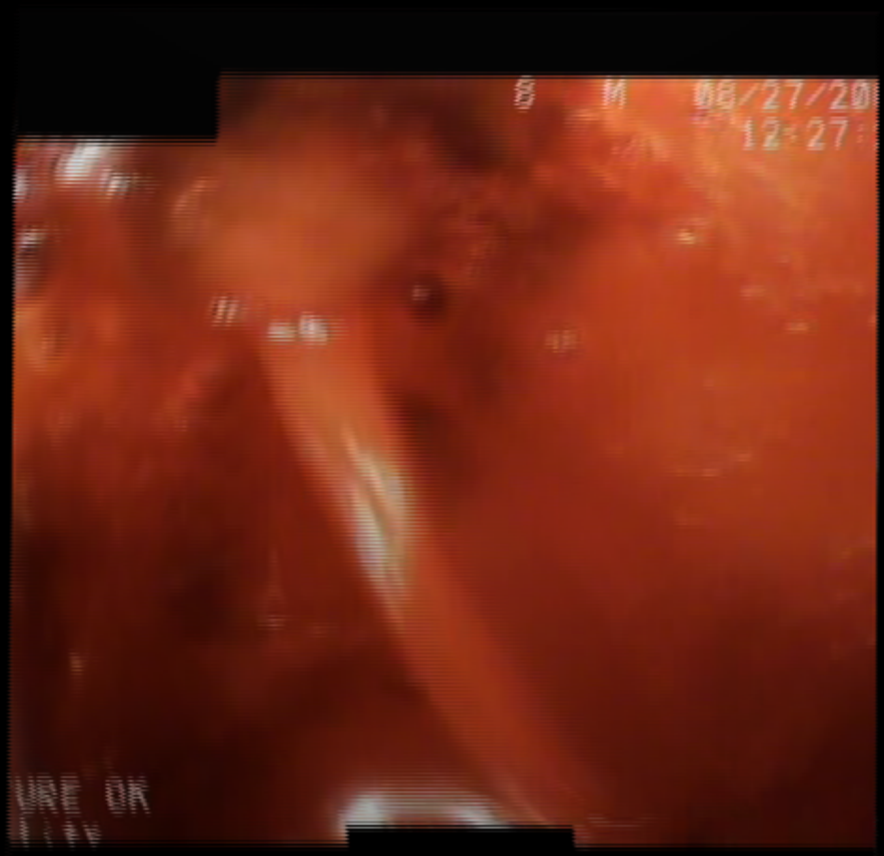
Texas Children's Hospital:

GI Procedure Suite Staff and

Therapeutic Endoscopy Team:

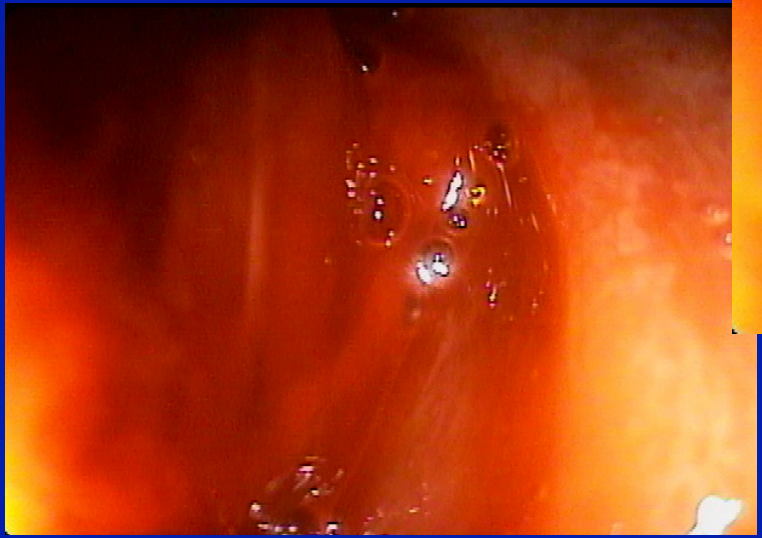
- **Bryan Vartabedian**
- **Anthony Olive**
- **Bruno Chumpitazi**
- **Kalpesh Thakkar**
- **Mark Gilger**
- **Isaac Raijman**

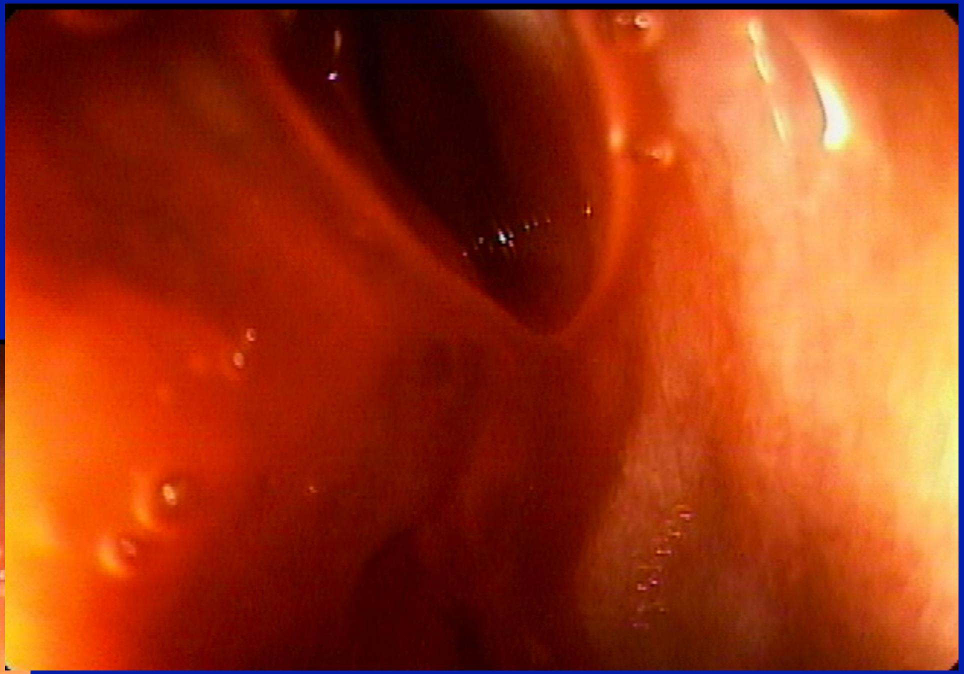
Thank you!!



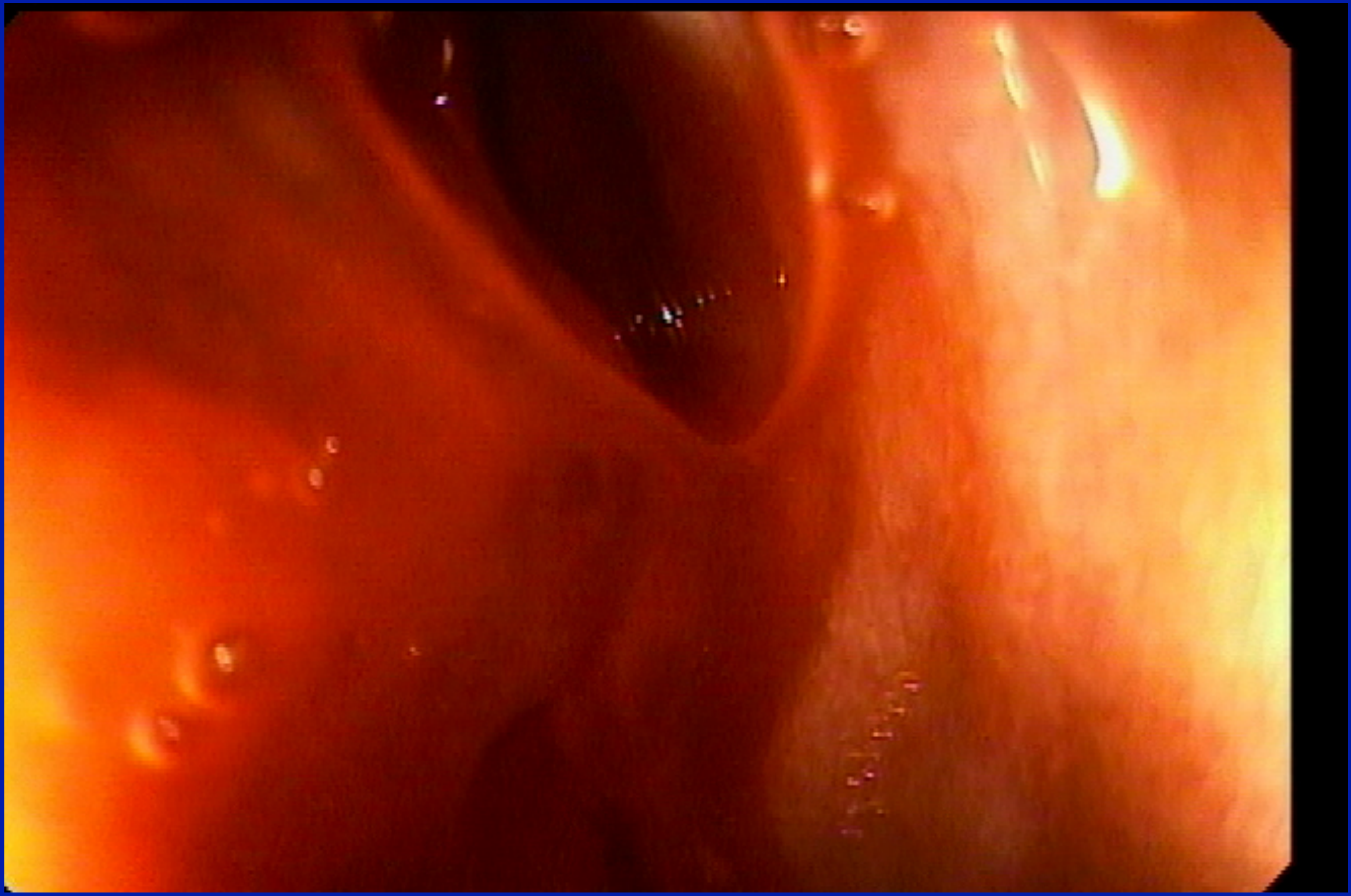
dsfishma@bcm.edu

Duodenum





Duodenum



Guidelines

- Adult
  - Correct fluid loss/coagulopathy
  - +/- NG placement; 15% with no blood have high risk lesions
  - Endoscopy within 24hrs
    - Less than 8hrs has not been shown to reduce morbidity/ mortality
      - » NEJM 2008, ASGE guideline 2004
- Pediatrics
  - None

Incidence

- Rare
- Only studied in PICU setting
- 6%-25%

- Pediatrics 1998, Chaibou, et al.
- 881 Patients in Sainte-Justine Hospital, Motreal, Canada
- Clinically significant bleeds: 16 (1.6%)
  - Hgb drop > 2gm/dL, blood tx, hypotension > 2SD, multi-organ failure
- Upper GI bleed 103 (10.2%)
- No EGD's performed
- No deaths associated with UGIB

Causes

- Gastritis
- Esophagitis
- Mallory-Weiss tear
- Coagulopathy

- Gastroduodenal ulcer
- Vascular anomaly
- Varices
- GVHD

Management

- IV PPI / Octreotide
- Consider endoscopy with protected airway
- Method based on experience of endoscopist

- Imaging serves limited role
  - Consider angiography if massive bleed with suspected vascular anomaly
  - KUB to eval for perforation
- Surgical backup

Rationale for Expectant Management

- Inadequate visualization
- Potential for spontaneous resolution
- Allowing for medical therapy to take effect
- Co-morbidities
- Age/size of patient dictates size of scope
  - No water flush or suction port on smaller scopes

Considerations for Endoscopy

- Hgb < 8 or 3gm/dl drop
- Continued hemodynamic instability following fluid/PRBC
- Use of pressors
- Available backup
  - GI Tech, GI Endo Nurses, Surgeons
  - Endoscopy team
- Goal of endoscopy is intervention

Other Considerations

- Etiology
  - GVHD
  - Neurosurgery pt
  - HgbSS
- Use of concomitant medication
  - Steroids
  - Anticoagulants
  - NSAIDS

Summary

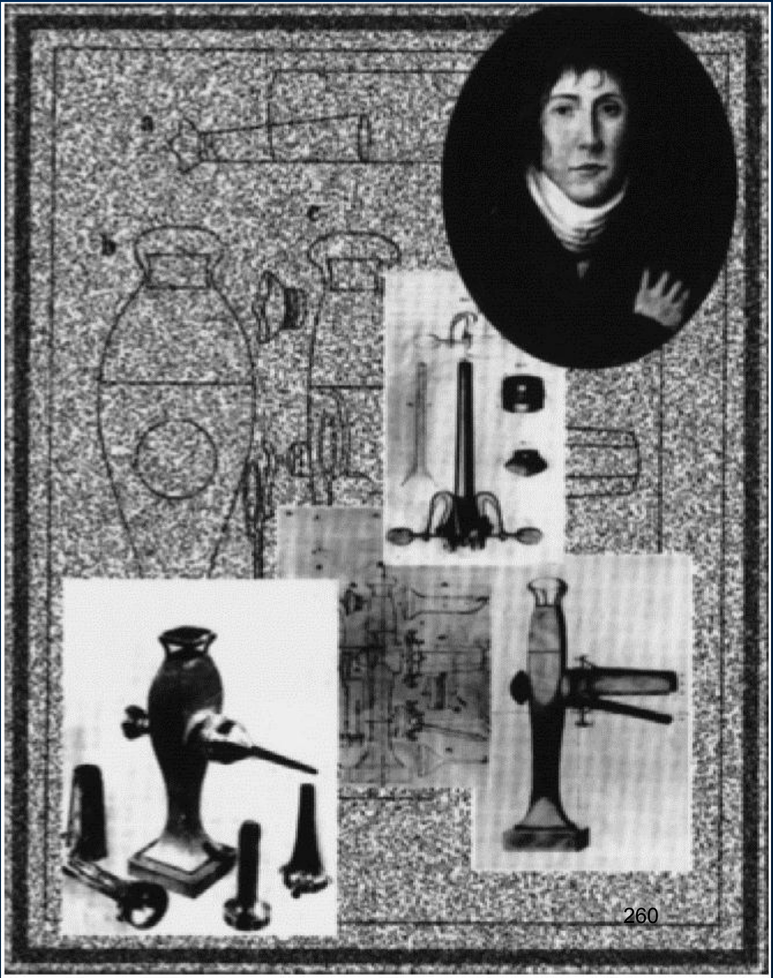
- No guidelines in pediatrics due likely to large variations in patient presentation and physician practice
- Mortality extremely rare
- Allow time for effect of medical management
- Practical realities may dictate management

From Sward Swallowers To Buckyballs

Petar Mamula, M.D.
The Children's Hospital of Philadelphia

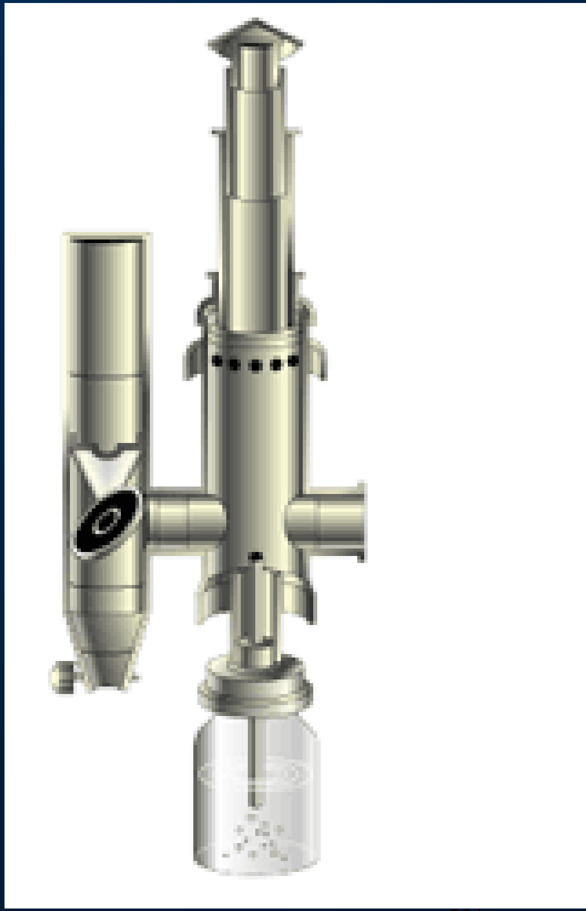
History of Endoscopy

- Greek origin- "*to view within*"
- Prototype discovered in the ruins of Pompeii
- Phillip Bozzini created "*Lichtleiter*" in 1805



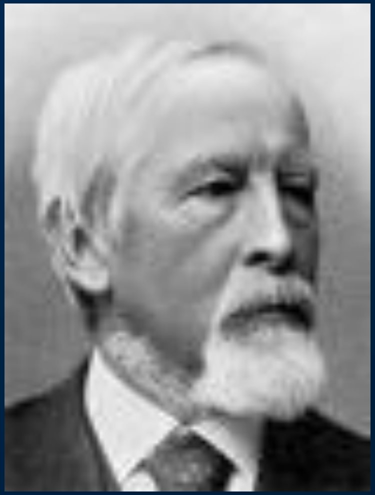
History of Endoscopy

- Antoine Jean Desormeaux in 1853 created an instrument to examine the bladder and for the first time used the term “endoscope”



History of Endoscopy

- Adolf Kussmaul- the first GI endoscopist, intubated professional sward swallower in 1868.



History of Endoscopy

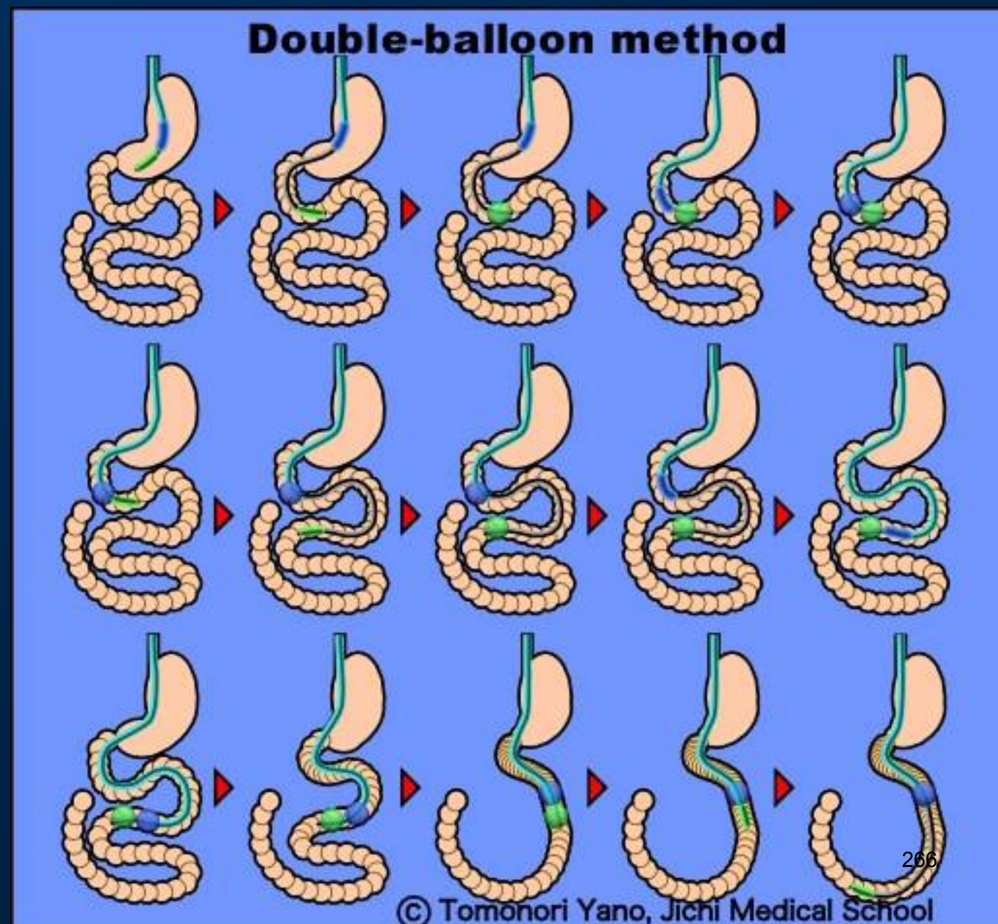
- Early 1900s lighted fully rigid telescopes developed
- 1930s first semi-flexible endoscope developed by Rudolph Schindler

History of Endoscopy

- Basil Hirschowitz in 1957 introduced first fiber-optic endoscope at the University of Michigan

Enteroscopy Single Balloon Enteroscope System® (Olympus Inc., Center Valley, PA)

Enteroscopy EN-450T5 and EN-450P5/20 (Fujinon Inc., Wayne, NJ)

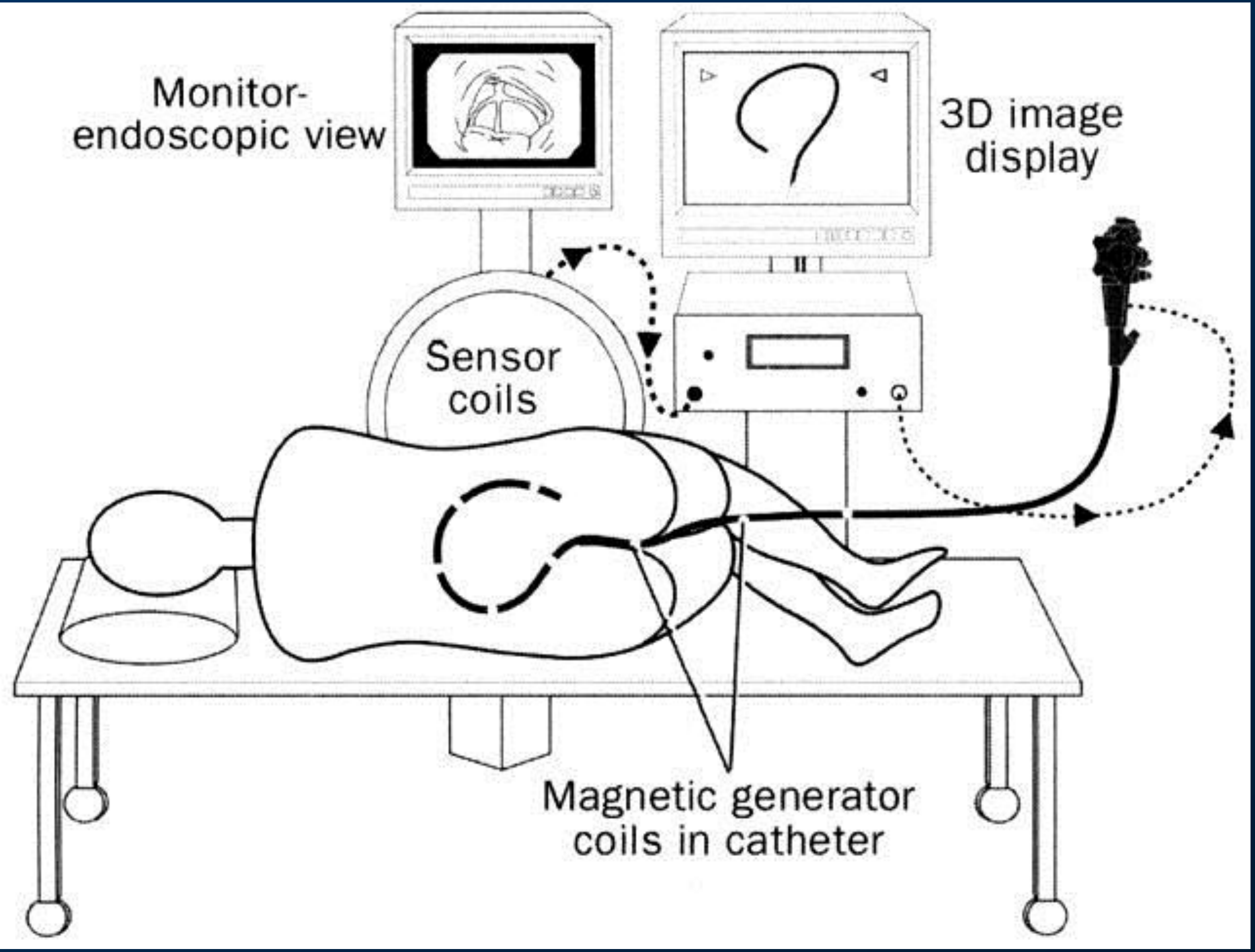


Colonoscopy

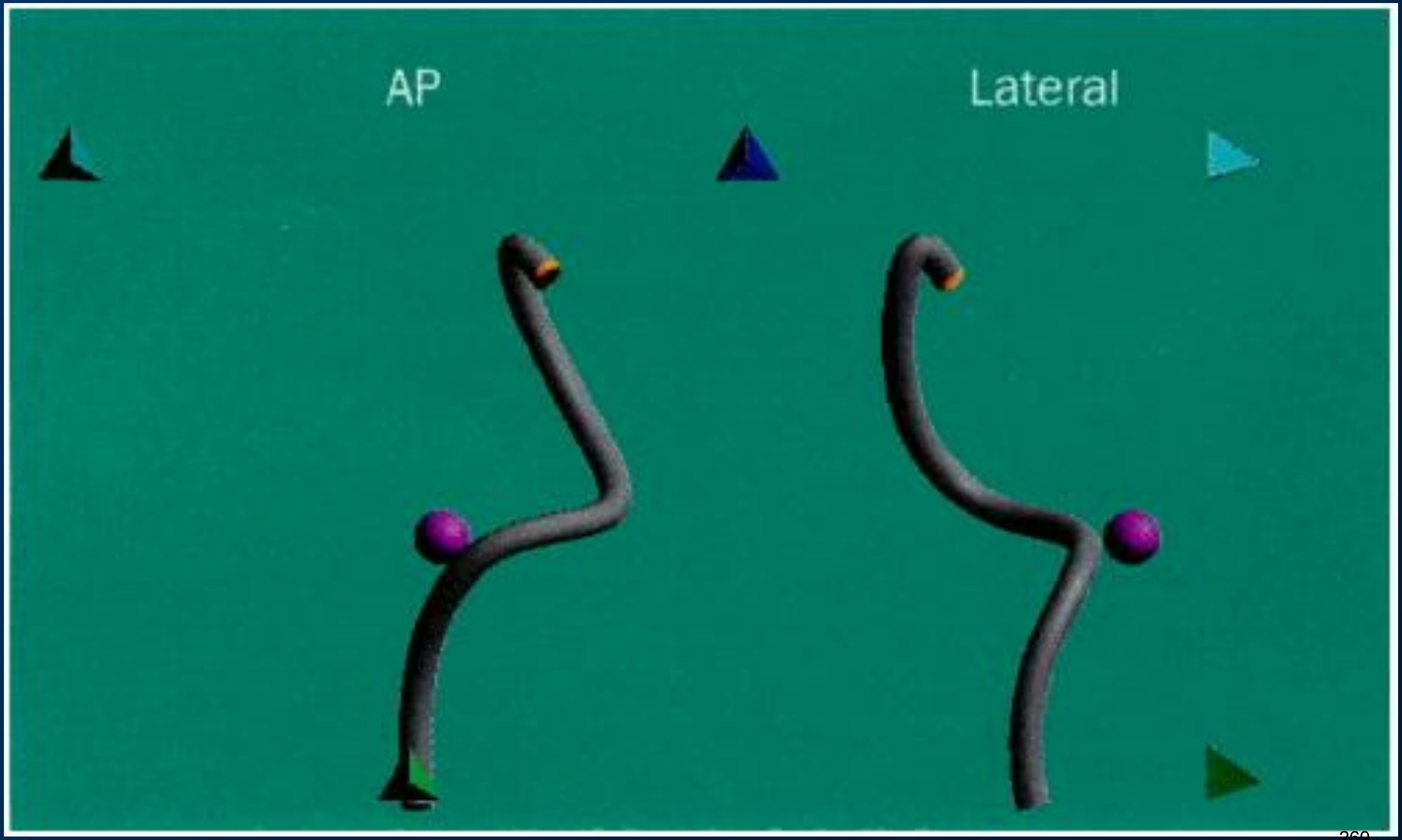
Methods and devices to improve visualization and technique

- Water- and oil-lubrication
- CO_2 insufflation
- Variable stiffness and wide angle lens instruments
- Enteroscopes and pediatric colonoscopes
- Transparent cap
- Magnetic positioning device

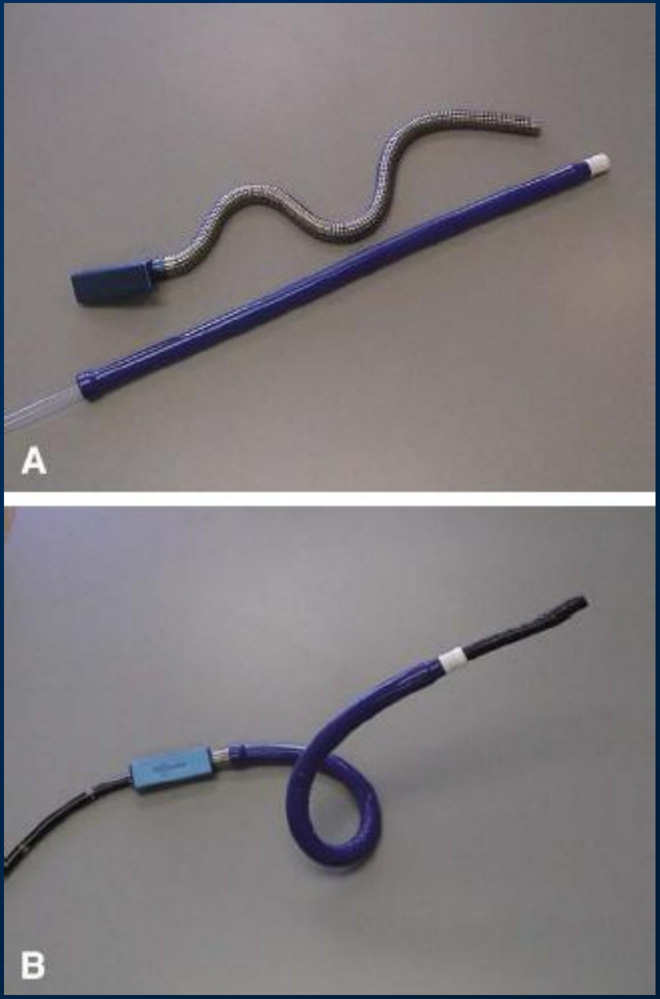
ScopeGuide® (Olympus Corporation, Tokyo, Japan)



ScopeGuide®

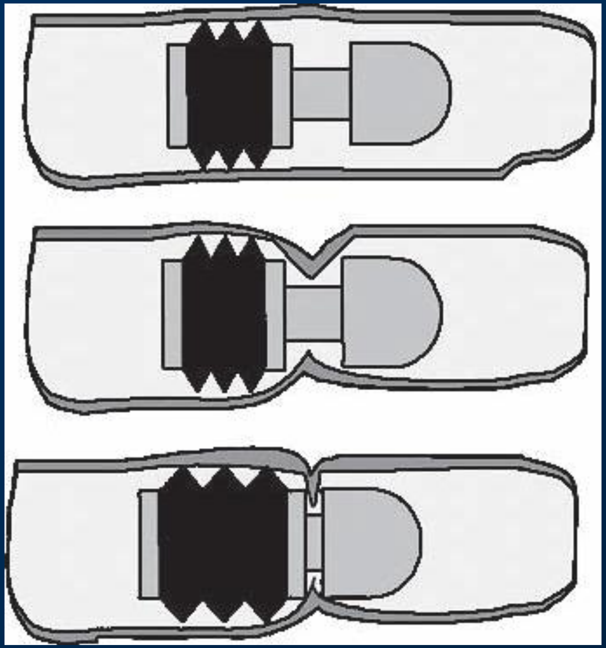


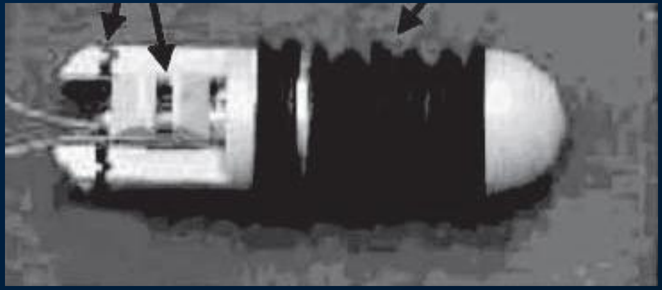
ShapeLock® (USGI Medical, San Clemente, California)



Colonoscopy- Locomotion

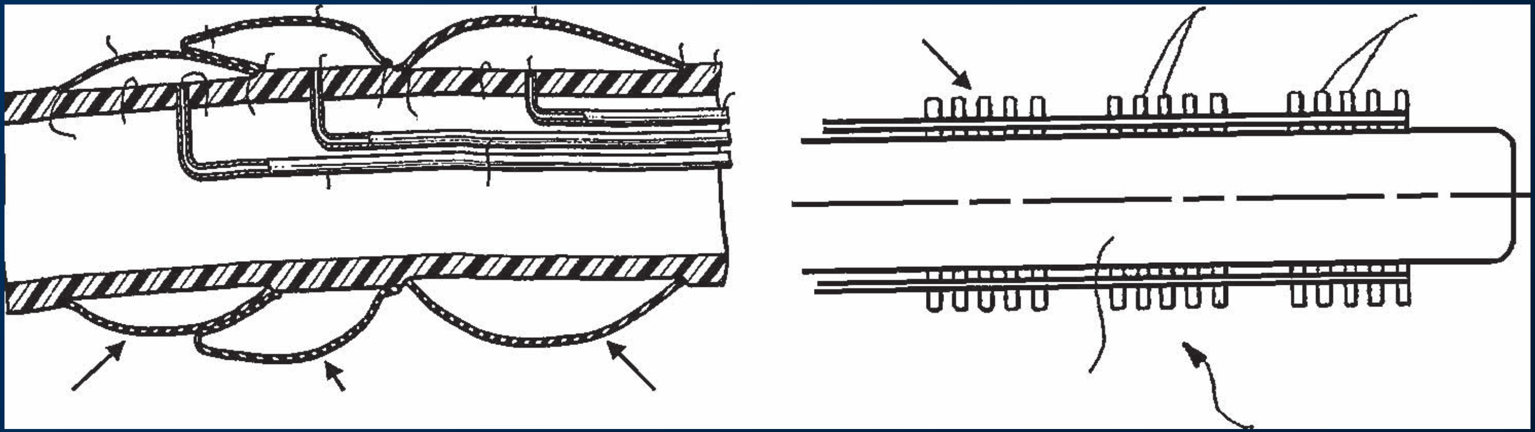
- Earthworm/inchworm (two clampers at its ends and one extensor at its midsection)





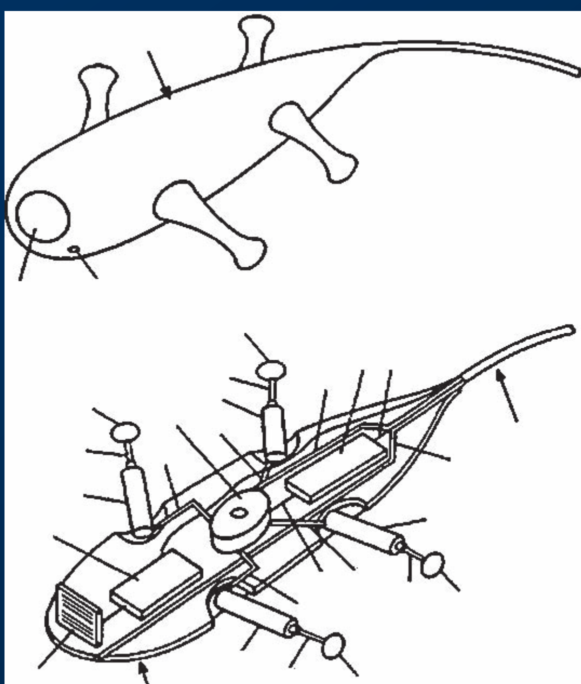
Colonoscopy- Locomotion

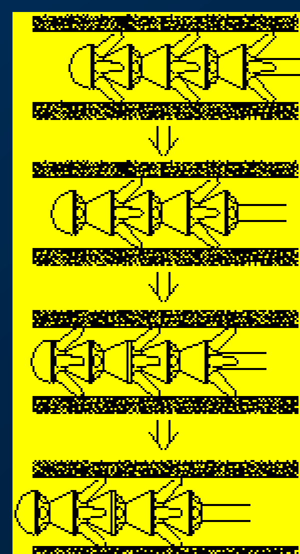
- Milipede (many legs that move in waves)



Colonoscopy- Locomotion

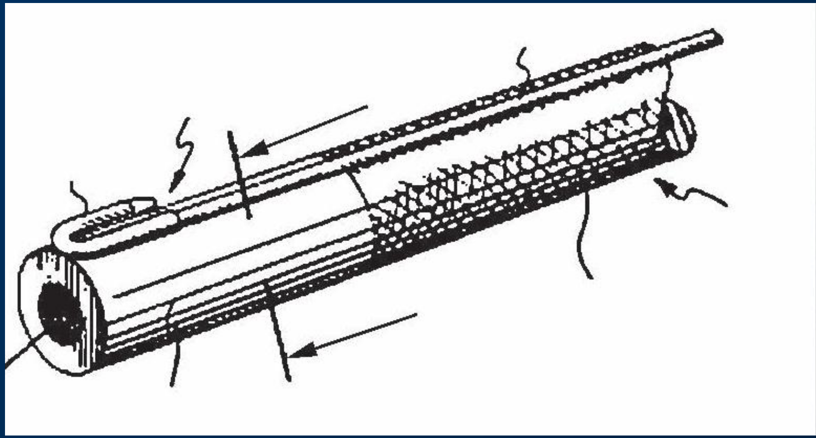
- Lizards and ants (toe scales that stick to surfaces)





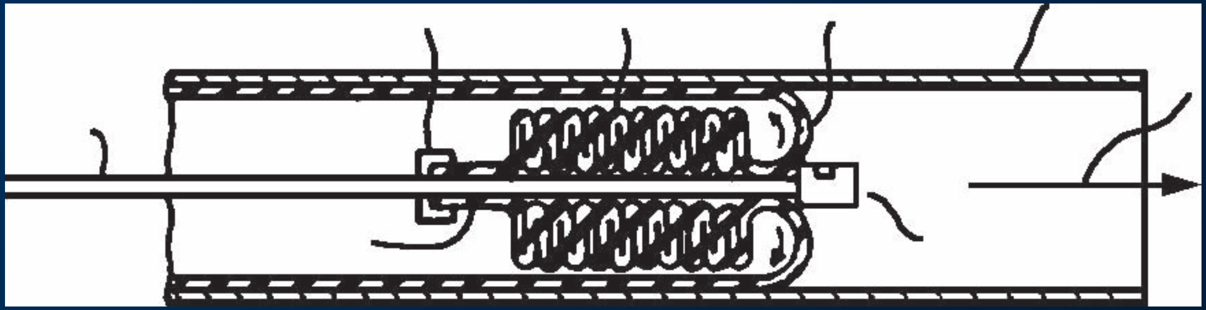
Colonoscopy- Locomotion

- Octopus (water jet)

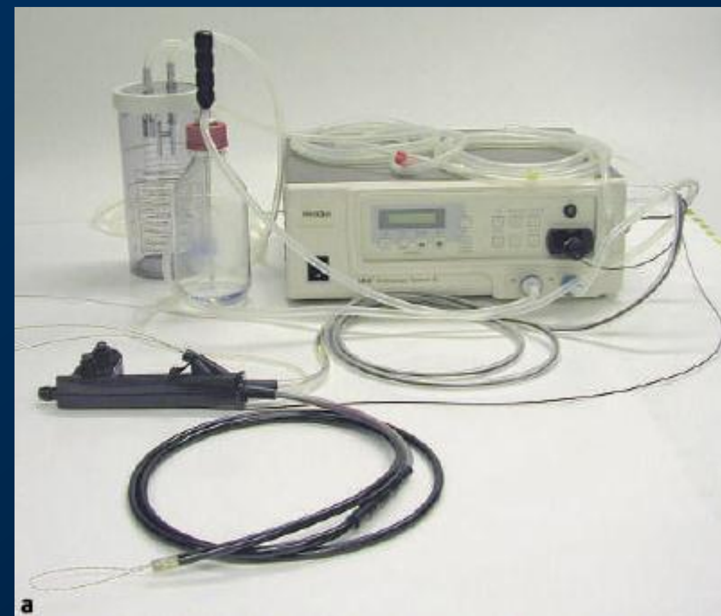


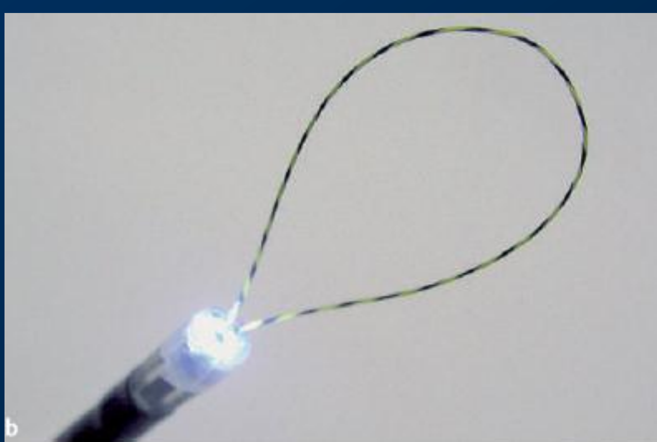
Colonoscopy- Locomotion

- Telescopic technique, Impact (magnets), and Natural Peristalsis



CathCam® (Ethicon Endo-Surgery, Cincinnati, OH)



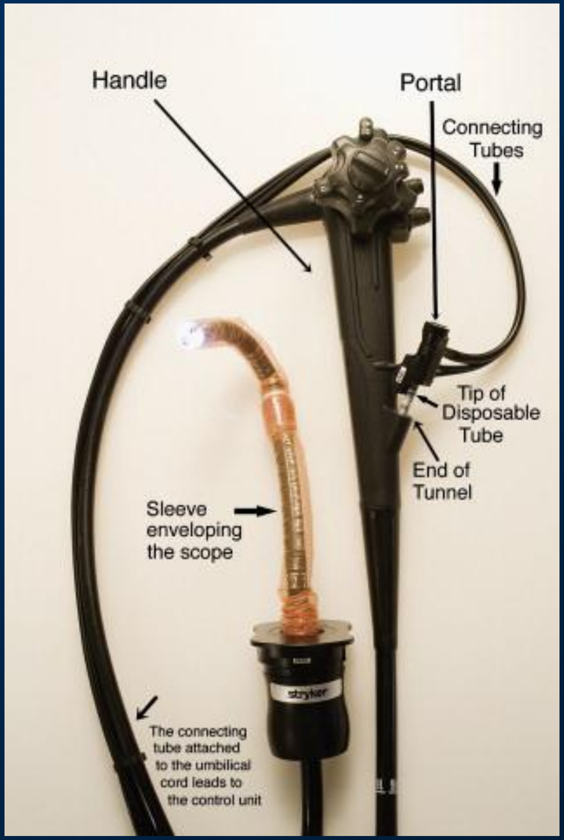


Sightline ColonoSight Colonoscope®

(Stryker GI, Dallas, TX, Haifa, Israel)

- Disposable component that isolates the reusable colonoscope from the colonic contents
- IntraPull technology (Stryker): an air-pressure-powered engine, which helps propel the colonoscope proximally in the colon
- An integrated light emitting diode (LED) light source at the tip of the colonoscope

ColonoSight®



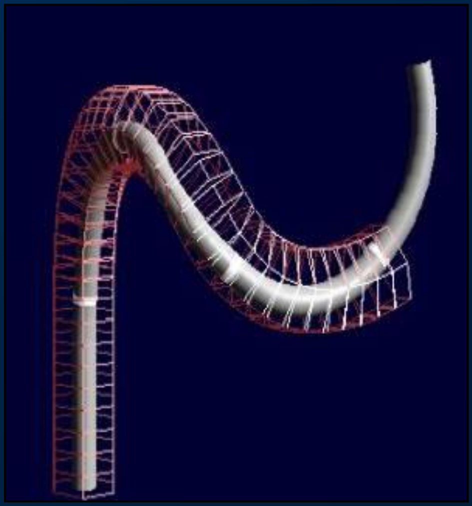
NeoGuide Endoscopy System®
(NeoGuide Systems Inc., Los Gatos, CA)

NeoGuide Endoscopy System®

External Position Sensor
Disposable device
Constantly measures tip depth

Tip Position Sensor
Constantly measures tip position

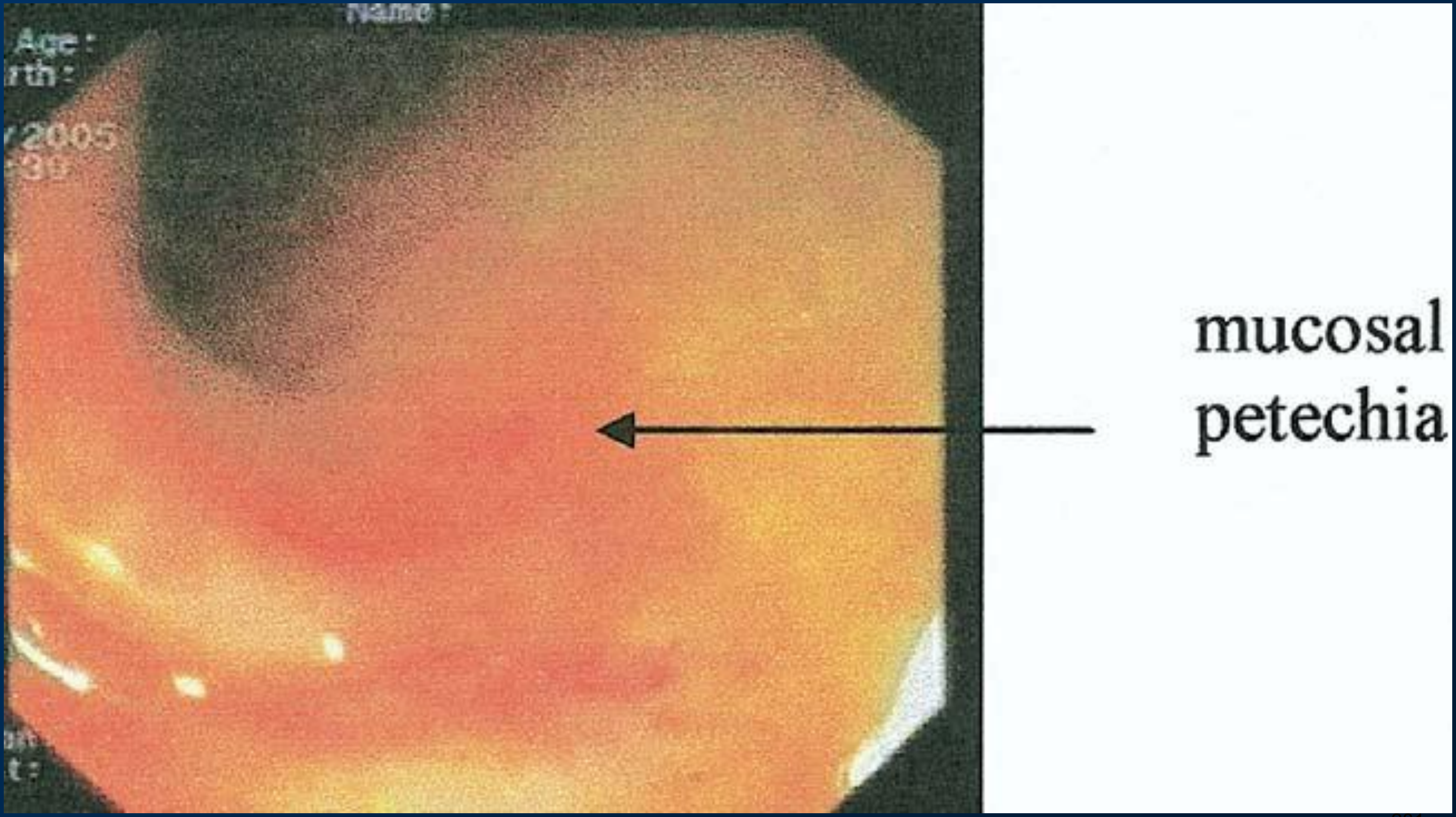
3D Map
Generated as scope advances



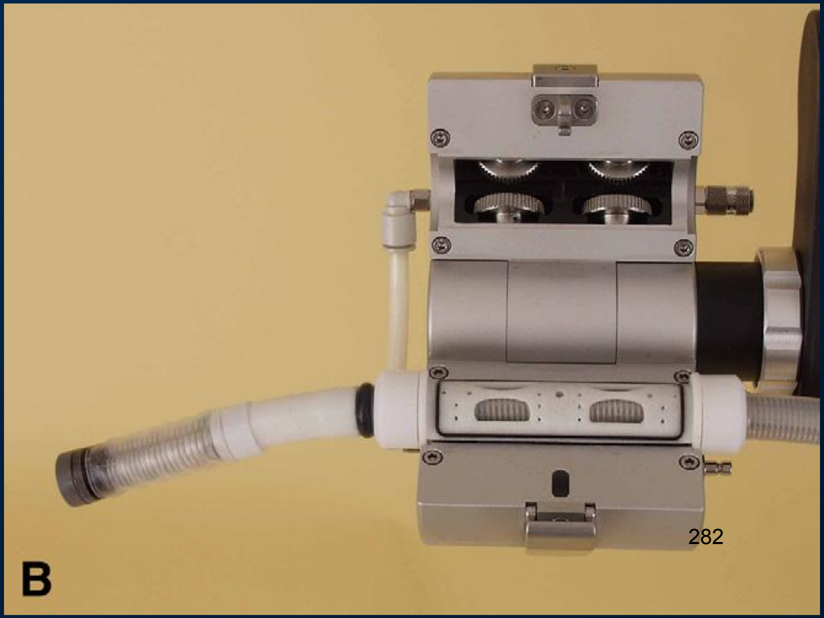
Console
Uses map to control segments
Motors drive segments

Colonoscope
Multiple articulating segments controlled by system

The Aer-O-Scope®

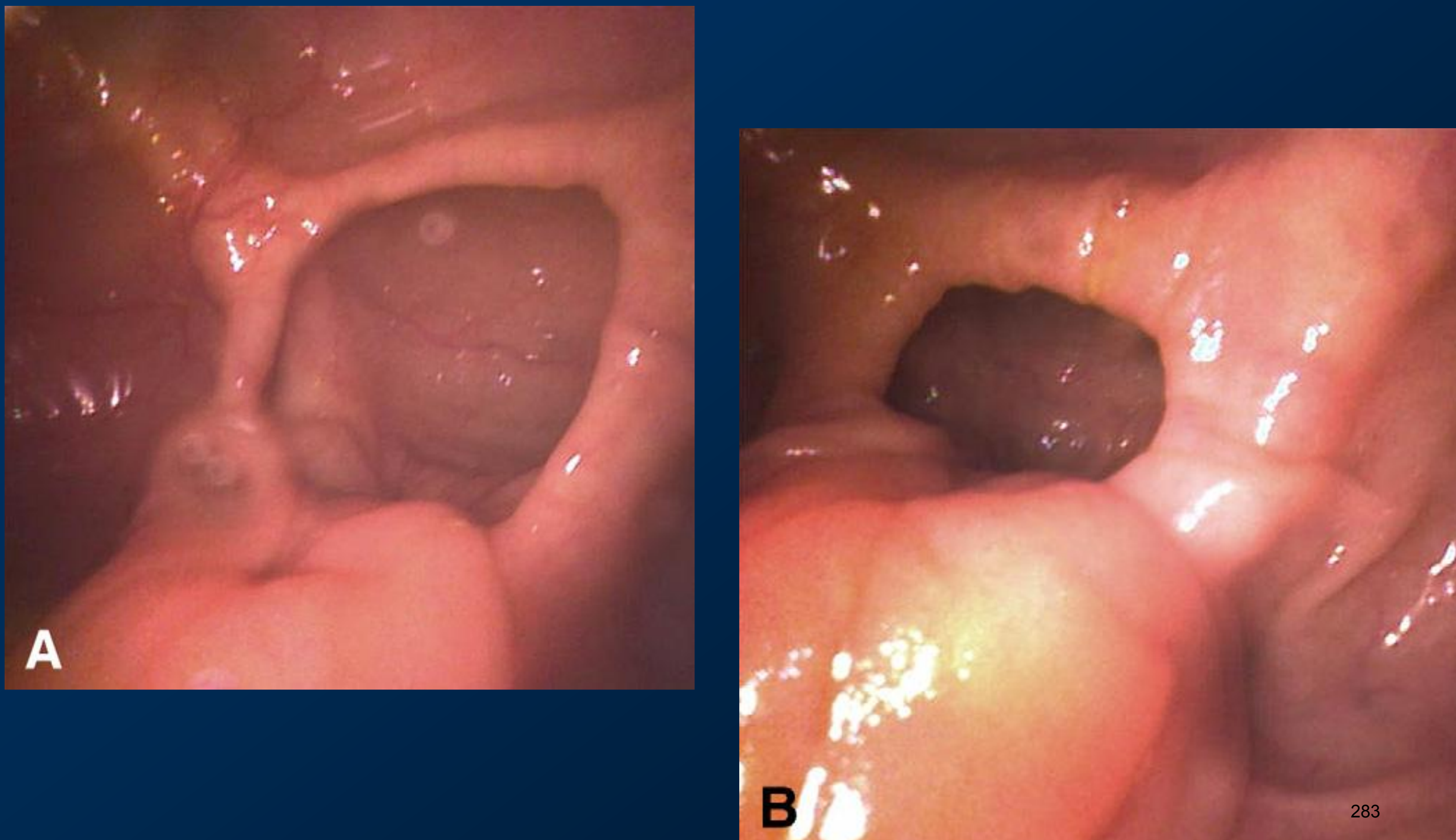


Invendo® (Invendo Medical, Kissing, Germany)



282

Invendo®



Wireless Devices

- Wireless pH testing (Bravo pH capsule, radio-telemetry based, 25 x 6 x 5.5 mm, pH sampled every 6 seconds, recorded every 12 seconds for 48 hours)

- Wireless pH/Impedance testing (battery-less system using inductive links between 2 coils, one worn externally and one implanted in the esophagus)

Wireless Devices

- Wireless whole gut pressure and pH monitoring (Smart Pill system, SmartPill Corporation, MotiliGI, Buffalo, NY, 26.8 x 11.7 mm, RF-technology, measures pH, temperature, and pressure, FDA approved for gastroparesis)

Capsule Endoscopy

- PillCam, PillCam ESO and PillCam Colon (Given Imaging Ltd., Israel)
- EndoCapsule (Olympus, Center Valley, PA)
- MiroCam (Intromedic, Seoul, Korea)
- OmOm capsule (Jinshan Science and Technology, Chongquing, China)
- Sayaka (RF System Labs, Nagano, Japan)

Capsule Endoscopy

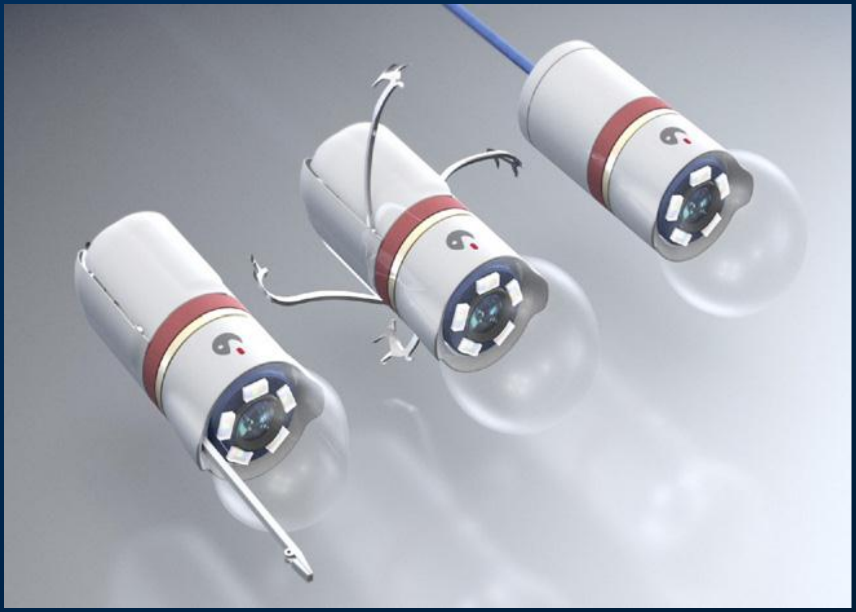
• Prototype Rotational Micro Biopsy capsule Device

Capsule Endoscopy

- Locomotion- electrostimulation, hydrojets, shape memory alloy coils, MEMS-based modular actuators
- Compact Photonic Explorer (CPE)- external manipulation, imaging, data transmission, collection, 5 mm, laser tissue removal, tissue welding

Capsule Endoscopy

- Versatile Endoscopic capsule for gastrointestinal TumOr Recognition and therapy (VECTOR)- minirobot

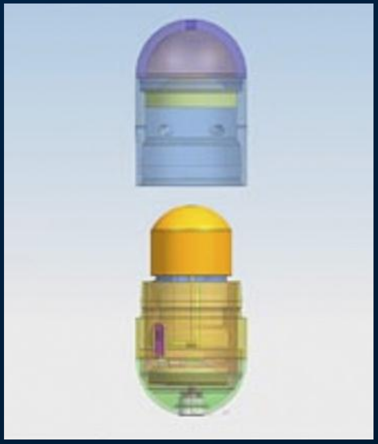


Capsule Endoscopy

- High-frequency capsule (Battelle-Institute V, Frankfurt am Maine, Germany, RF trigger to melt a thread releasing a needle that pierces balloon delivering therapeutic agent, fluoro-guided)
- Gastrotarget telemetric capsule (Gastrotarget, Tonawanda, NY) and telemetric capsule (INSERM U61, Strasbourg Cedex, France)

Capsule Endoscopy

- IntelliSite Capsule (Innovative Devices, Raleigh, NC) and Enterion capsule (Pheaton Research, Nottingham, UK)
- iPill (Phillips Research, Eindhoven, Netherlands, 11 x 26 mm with microprocessor, battery, pH and temperature sensor, fluid pump, drug reservoir)

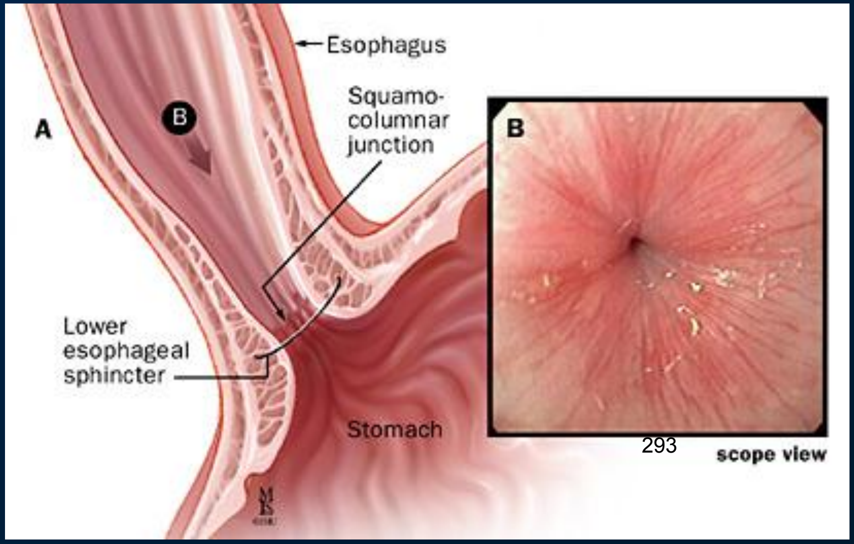


Capsule Endoscopy

• Bion (Advanced Bionics Corporation, Valencia, CA, remotely programmable microstimulator, 3.3 x 27 mm, raising LES pressure)

GERD Endoscopic Therapy

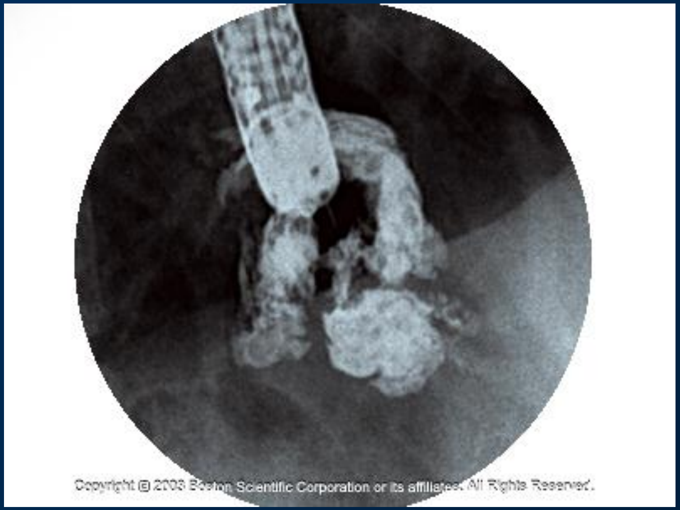
- Implantable and Injections
- Radiofrequency Ablation
- Tissue Apposition

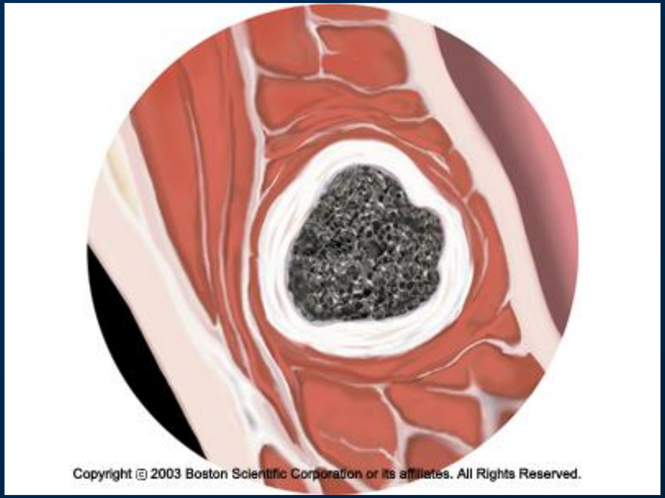


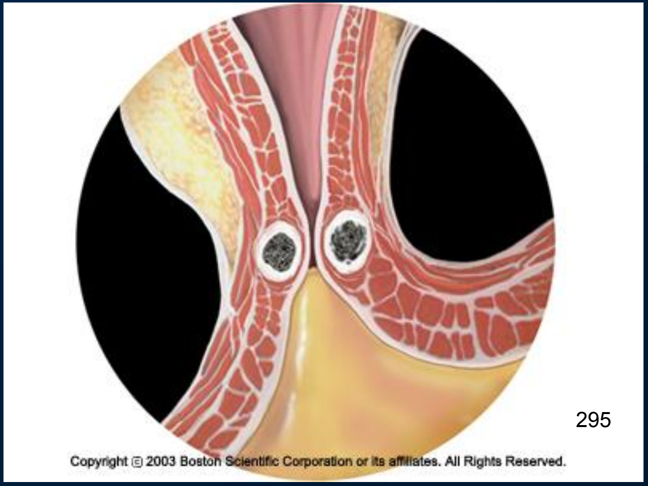
Implantable Bulking Agents

- Collagen
- Plexiglass (polymethylmethacrylate) microspheres (Artes Medical Inc., San Diego, CA)
- Polytetrafluoroetylene (Polytef, Mentor O & O Inc., Hingham, MA)
- Ethinyl-vinyl-alcohol polymer (Enteryx)
- Hydrogel prosthesis (Gatekeeper)
- Pyrolitic carbon-coated graphite beads (Durasphere)

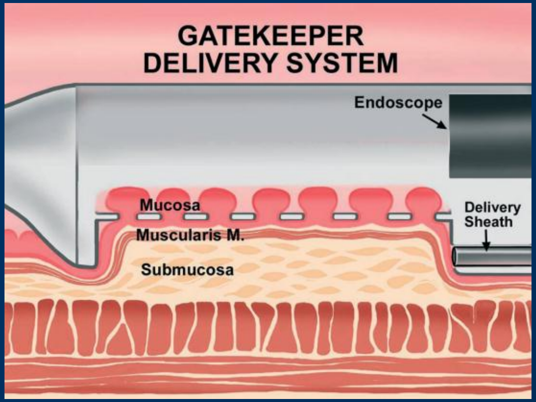
Enteryx® (Boston Scientific Corp., Natick, MA)

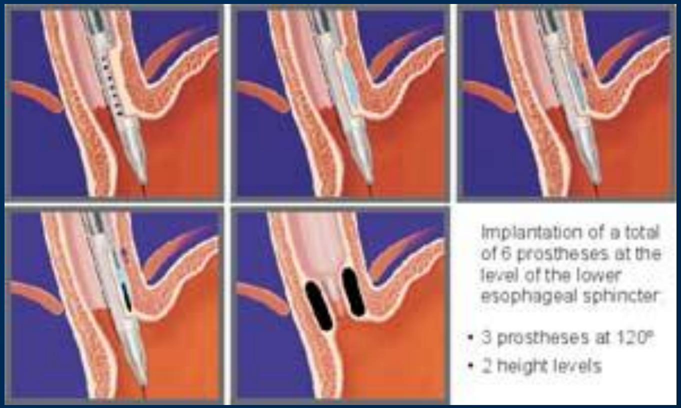


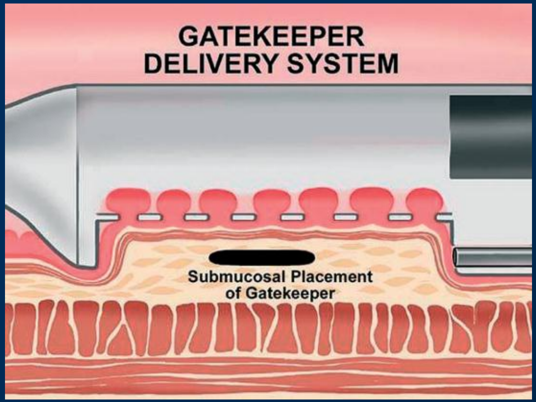


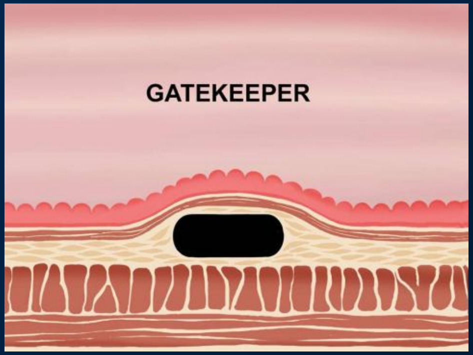


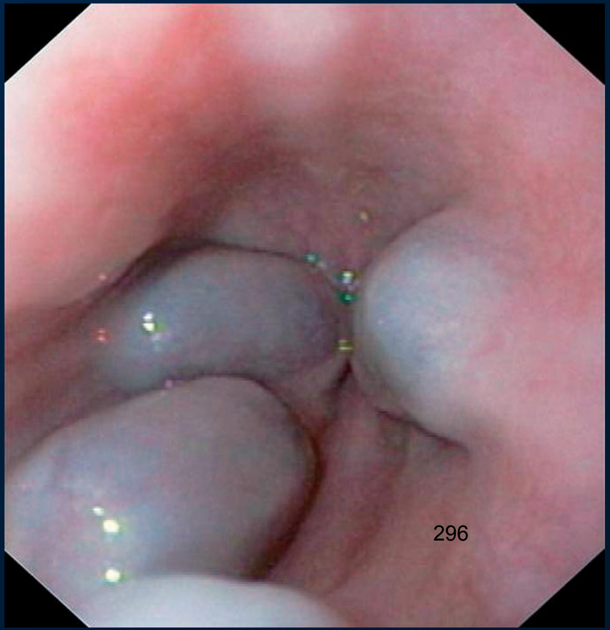
GateKeeper® (Medtronic Inc., Minneapolis, MN)





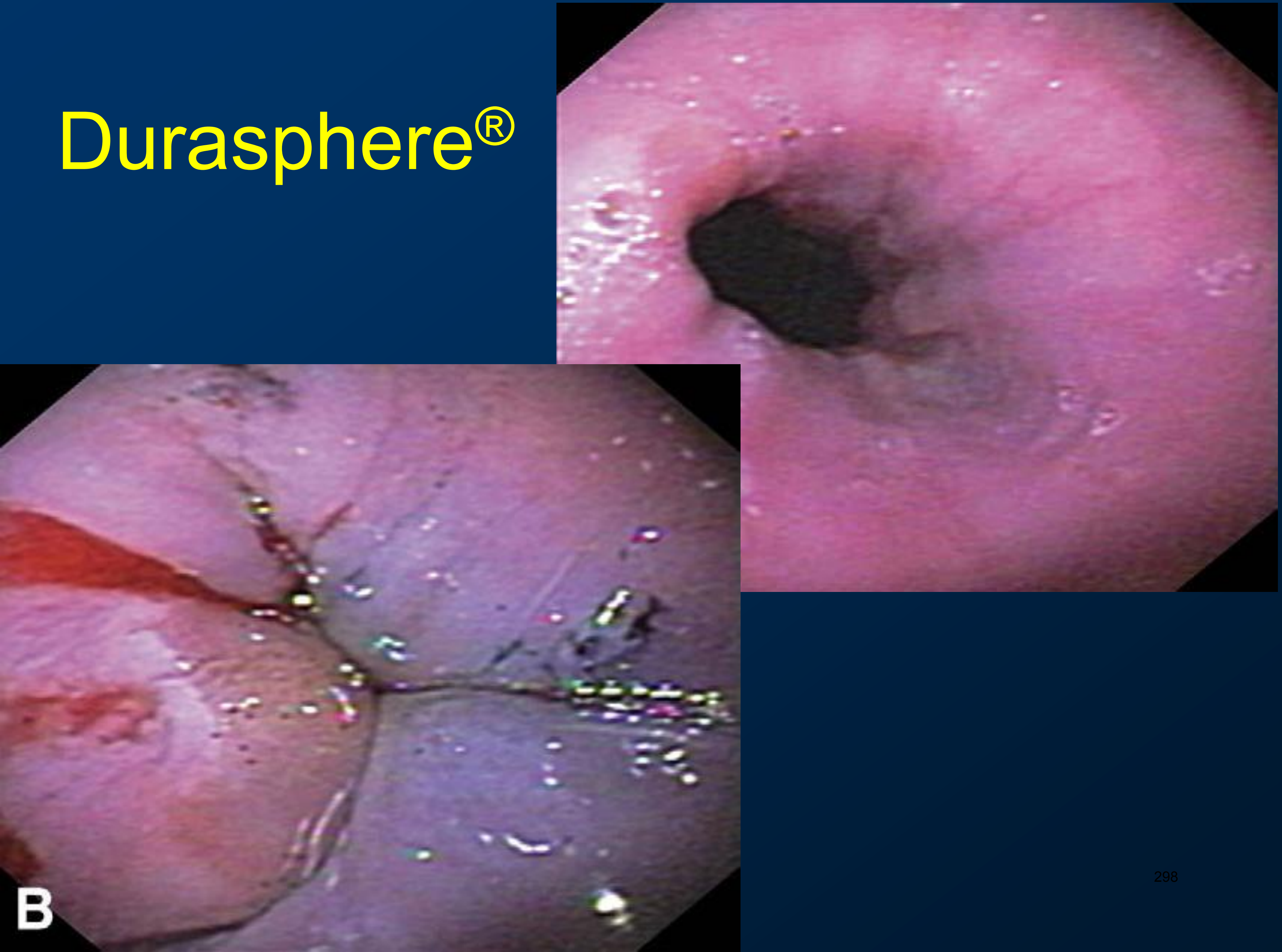




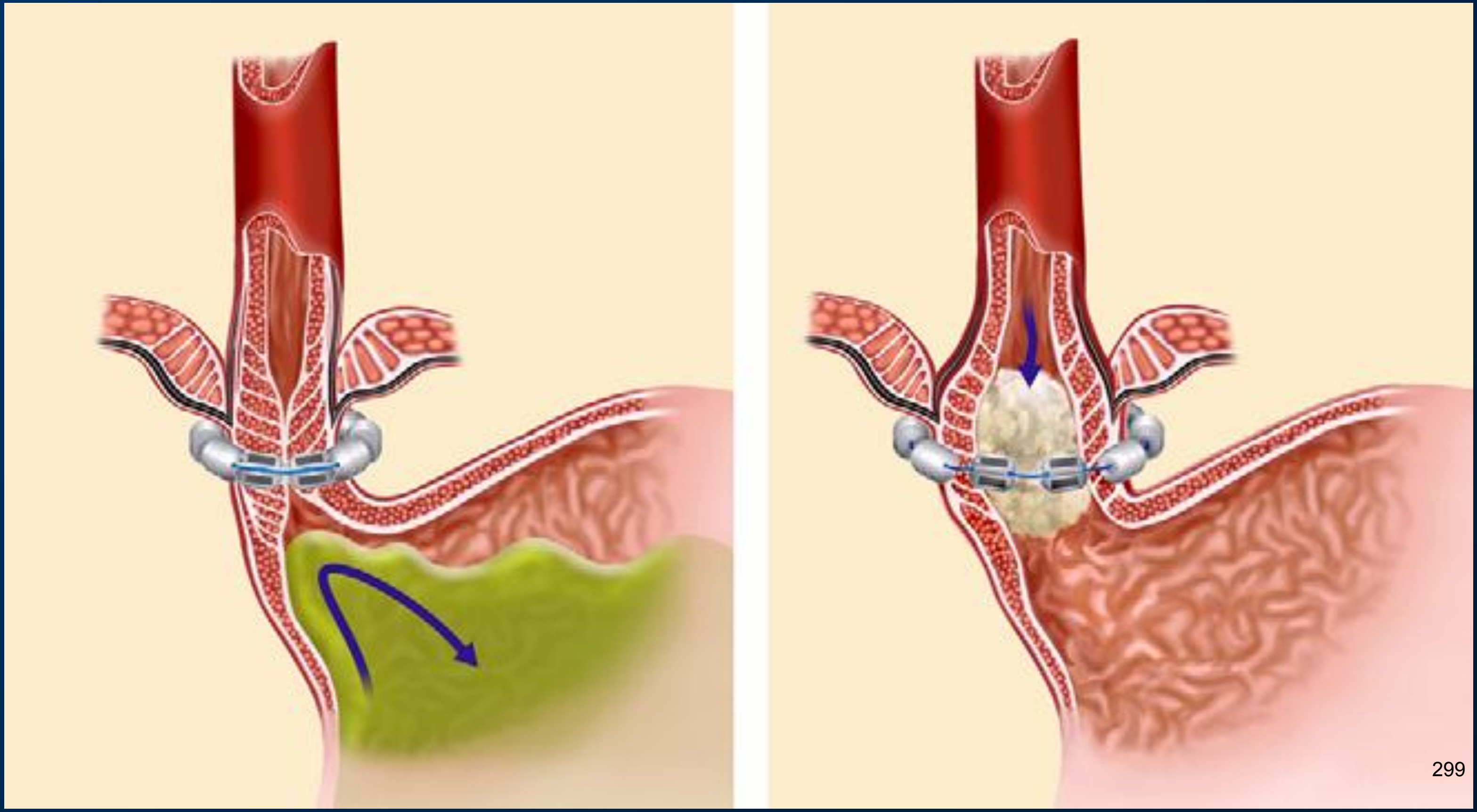


Durasphere® *EXP* (Carbon Medical Technologies, St. Paul, MN)

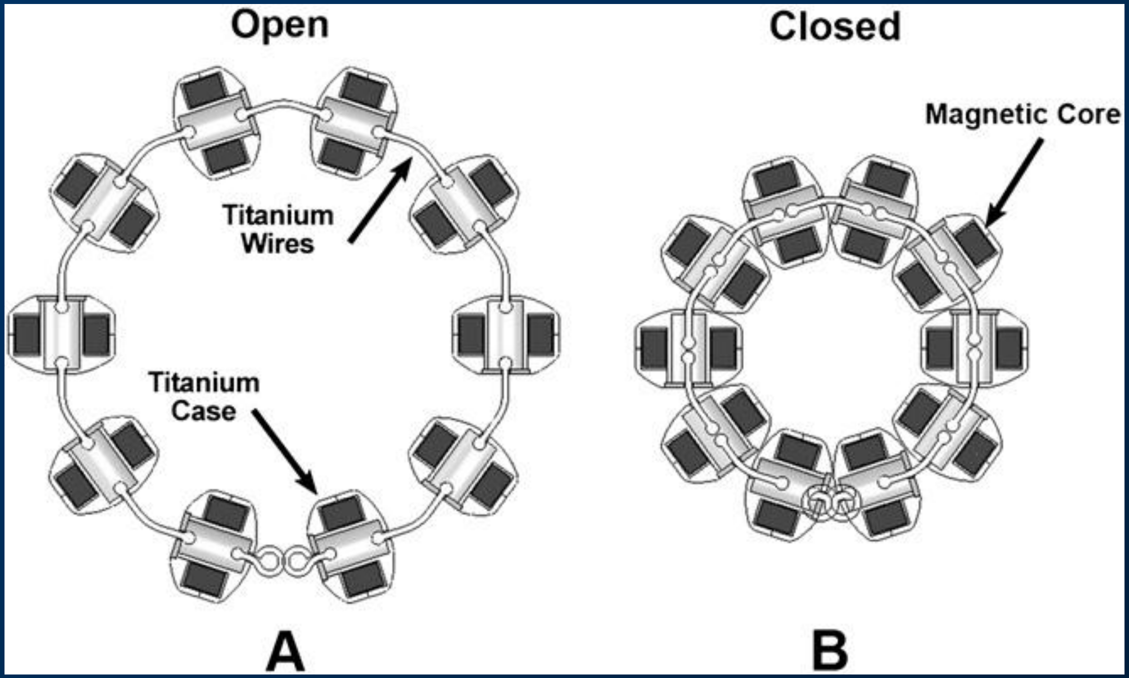
Durasphere®

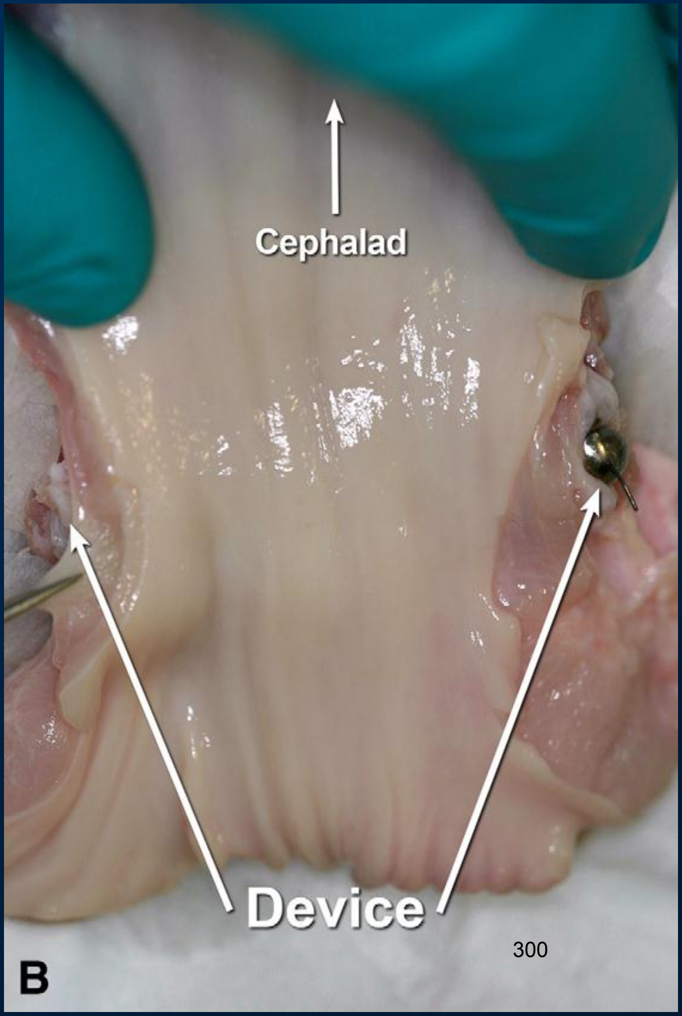


Magnetic sphincter augmentation device (Torax Medical, Maple Grove, MN)



Magnetic sphincter augmentation device





GERD Endoscopic Therapy

- Implantable and Injections
- Radiofrequency Ablation
- Tissue Apposition

Radiofrequency Ablation Therapy

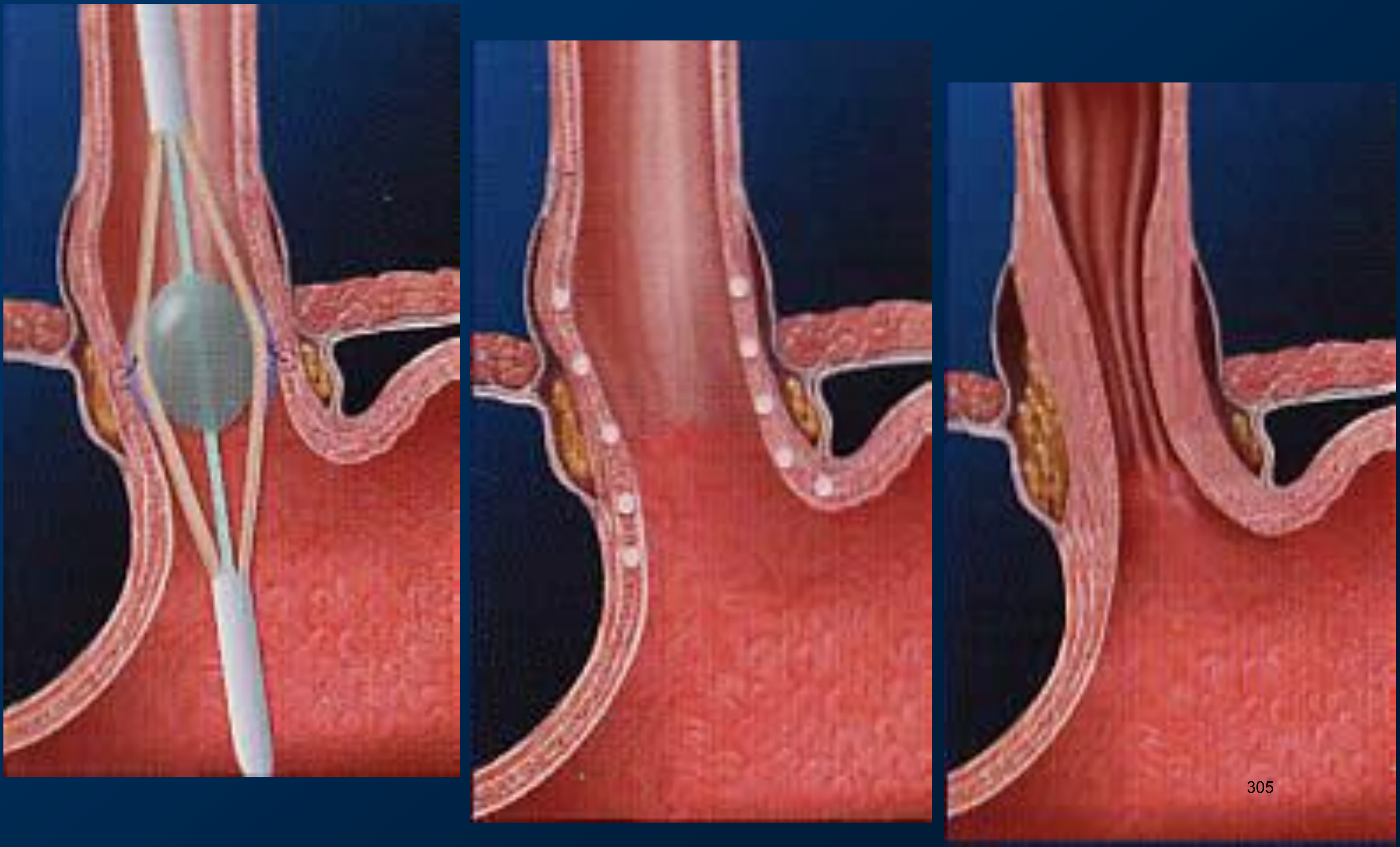
- Radiofrequency (RF) energy (400kHz to 1 MHz) has been used since 1921 for general surgical cutting, coagulation, and neural ablation
- In monopolar RF energy delivery, current flows between the active and return (ground) electrodes, thereby heating tissue through inductive and frictional heating of water molecules
- Temperature-controlled RF energy currently used to treat benign prostatic hypertrophy, liver tumors, aberrant myocardial conduction pathways, snoring and sleep apnea, and lax joint capsules

Radiofrequency Ablation Therapy

- A thermocouple (electrical thermometer) resides in the active electrode to provide temperature feedback (target temperature is preselected 85°C)
- Collagen contraction occurs when temperatures reach 65°C, resulting in tissue shrinkage
- With prolonged heating, the acute phase of wound healing ensues with influx of macrophages, neutrophils, and myofibroblasts
- The wound volume is reduced over time as fibroblasts contract and collagen is deposited

Stretta® (Curon Medical, Sunnyvale, CA)

Stretta®



Radiofrequency Ablation Therapy

(J Ped Surg 39:282-286, 2004.)

- n=6 (5 post Nissen fundoplication)
- Retrospective, outpatient
- Age 18 ± 3.4 years
- Mean time 80 ± 15 minutes
- 12-14 month f/u
- One gastric distention requiring in-patient observation (spontaneously resolved)

Radiofrequency Ablation Therapy

(J Ped Surg 39:282-286, 2004.)

- Improved GERD scores in 5 evaluated patients at 6-month f/u ($p<0.05$)
- 4/5 asymptomatic at 6-month f/u
- 1 required Nissen redo
- 1 required repeat Stretta
- 3 stopped anti-secretory medications

Radiofrequency Ablation Therapy

(Liu et al. J Ped Surg 40, 2005.)

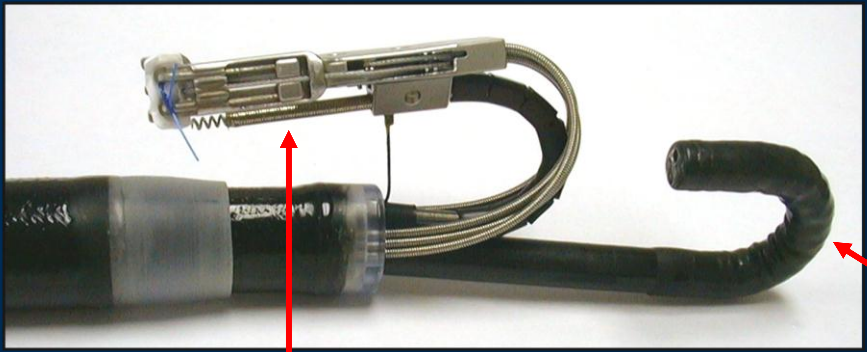
- n=8, 3 with PEG
- 6 improved (3 off medication)
- 1 required Nissen fundoplication
- 1 short duration response
- 1 aspiration pneumonia

GERD Endoscopic Therapy

- Implantable and Injections
- Radiofrequency Ablation
- Tissue Apposition

Prototype

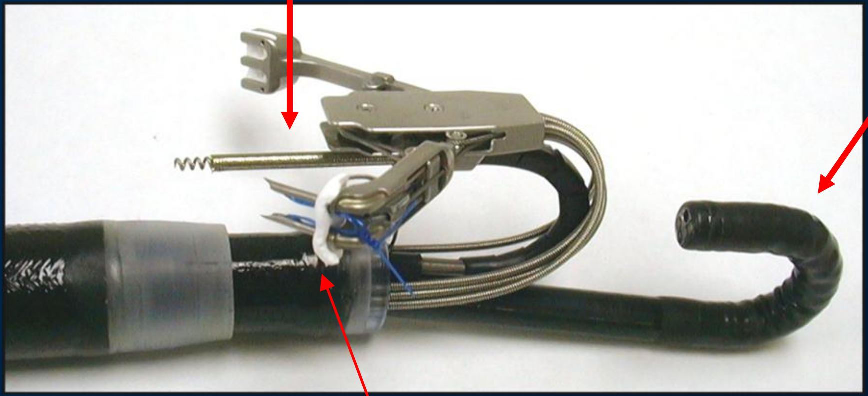
Retroflexed arms closed



Tissue retractor

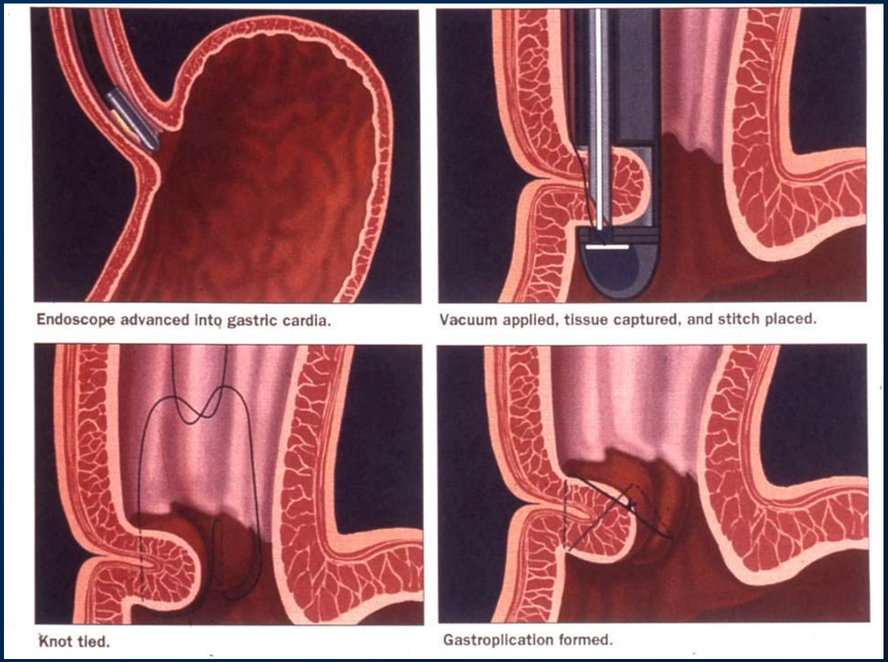
Gastroscope

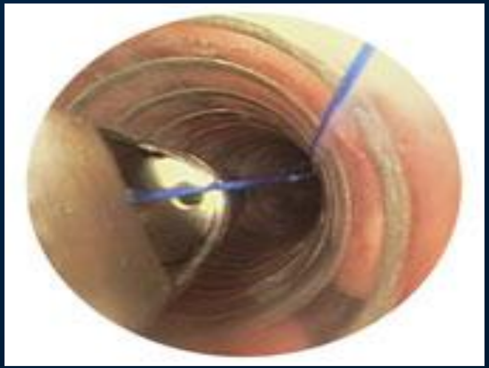
Retroflexed arms open



Pledget/pre-tied suture

EndoCinch® (C.R. Bard Inc., Billerica, MA)





EndoCinch®

(Thomson et al., JPGN 39:Suppl. 1, S55, 2004)

- 17 (5 male) children - age 12.4 yrs (6.1-15.9) with GERD dependent on PPIs for >12 months or refractory to PPIs
- Follow up median 15 months
- Symptom scoring, upper GI endoscopy, oesophageal manometry, gastric scintiscan, 24 hour oesophageal pH, and QOLRAD at 0, 6 and 52 weeks
- Median duration of the procedure for 3 plications- 65 minutes

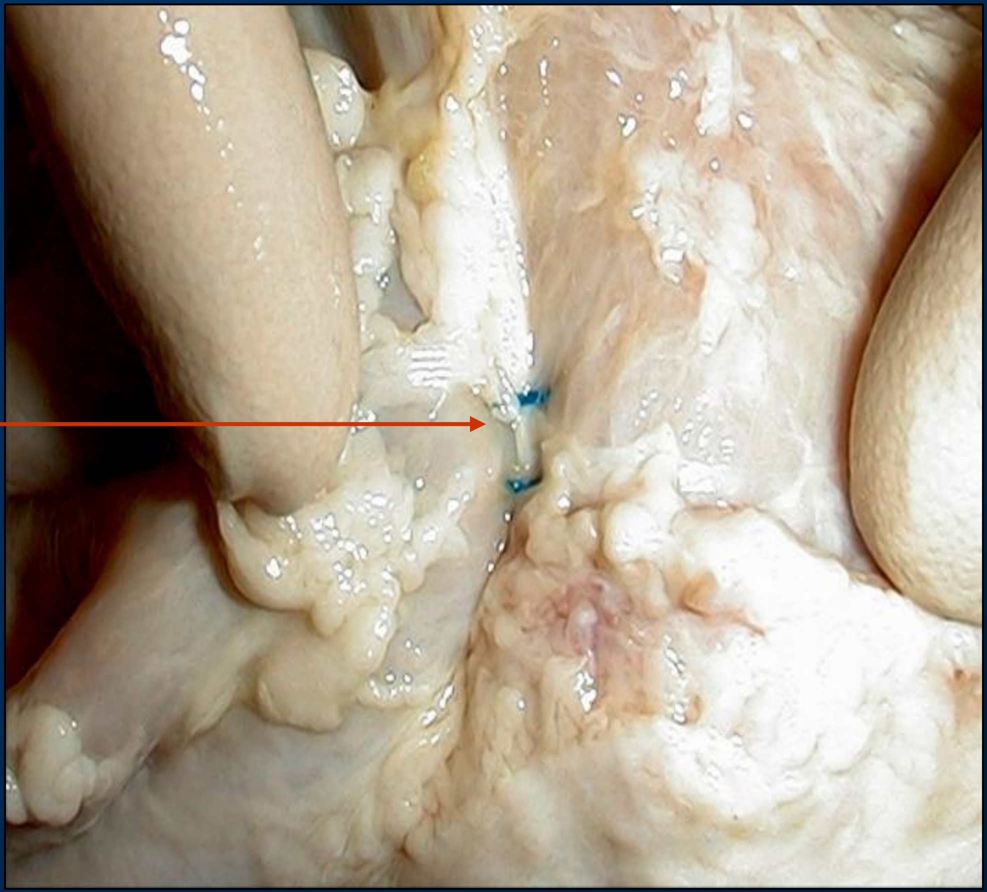
EndoCinch®

(Thomson et al., JPGN 39:Suppl. 1, S55, 2004)

- Improvement in heartburn (p=0.001), regurgitation (p=0.002,) and nausea score (p=0.013) sustained at 12 months
- QOLRAD showed sustained improvement
- All pH parameters improved significantly
- 14/17 did not require any further PPI use at any stage
- One patient had localized gastric bleeding requiring transfusion

NDO Plicator®

Suture through full-thickness



Full-thickness plication with serosa-to-serosa union

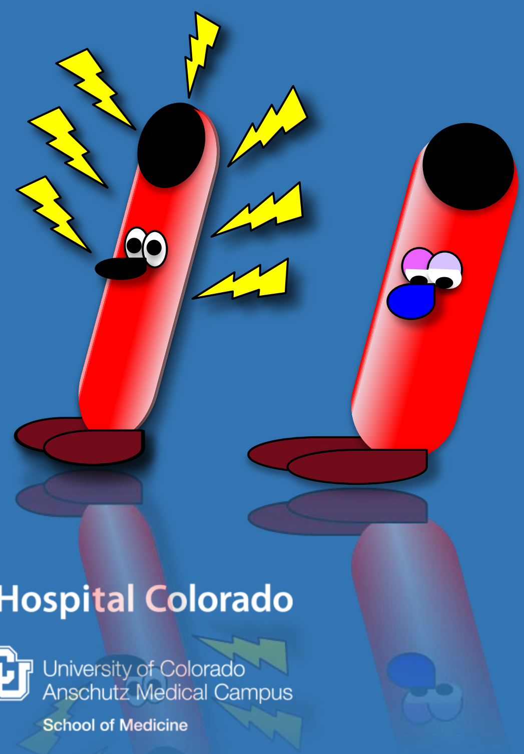
References

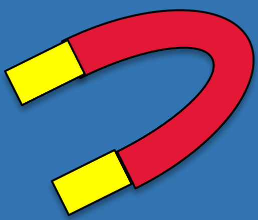
- Reavis, K., et. al., Advanced Endoscopic Technologies, Surg. Endosc (2008) 22:1533-1546
- Boris, V., et. al., The Aer-O-Scope: Proof of Concept of a Pneumatic, Sill-Independent, Self-Propelling, Self-Navigating Colonoscope, Gastroenterology 2006; 130:672-677
- AGA Institute Technical Review on the Use of Endoscopic Therapy for Gastroesophageal Reflux Disease, Gastroenterology 2006; 131: 1315-1316
- Fritscher-Ravens A., et. al., Pilot Study of CathCam Colonoscopy, Endoscopy 2006; 38:209-213
- Moshe Shike, et. al., Sightline ColonoSight system for a disposable, power-assisted, non-fiber-optic colonoscopy (with video), Gastrointestinal Endoscopy Volume 68, No. 4, 2008
- Simon Bar-Meir, et. al., Diagnostic Colonoscopy: The End is Coming, Gastroenterology 2006; 131: 992-994
- Ganz, Robert A., et. al., A new injectable agent for the treatment of GERD: results of the Durasphere pilot trial , Gastrointestinal Endoscopy, Volume 69, No. 2: 2009
- Sgouros, Spiros N., et. al., Endoscopic Therapy for Gastroesophageal Reflux Disease: A Systematic Review, Digestion 2006; 74:1-14
- Pace, F., et. al., Review article: endoscopic antireflux procedures-an unfulfilled promise? Aliment PharmacolTher 27, 375-384 2008
- Ryou, Marvin, et. al., Endoscopic Therapy for GERD: Does It Have a Future? Current Gastroenteroloy Reports 2008, 10:215-221

References

- Rothstein, R. I., et. al., Endoscopic Therapy of Gastroesophageal Reflux Disease, Outcomes of the Randomized-controlled Trials Done to Date, J Clin Gastroenterol, Volume 42, No. 5, 2008
- Iqbal, A., et. al., Endoscopic therapies of gastroesophageal reflux disease, World J Gastroenterol 2006; 12(17): 2641-2655
- Rosch, T., et. al., A motor-driven single-use colonoscope controlled with a hand-held device: a feasibility study in volunteers, Gastrointestinal Endoscopy Volume 67, No. 7: 2008
- Kassim, I., et. al., Locomotion Techniques for Robotic Colonoscopy, IEEE Engineering in Medicine and Biology Magazine, May/June 2006
- Ganz, R. A., et. al., Use of a magnetic sphincter for the treatment of GERD : a feasibility study, Gastrointestinal Endoscopy, Volume 67, No. 2: 2008
- Eickhoff, A., et. al., Computer-Assisted Colonoscopy (The NeoGuide Endoscopy System): Results of the First Human Clinical Trial ("PACE Study"), American J Gastroenterol 2007; 102:261-266
- Rosch, T., et. al., The New Scopes-Broadening the Colonoscopy Marketplace, Digestion 2007; 76:42-50
- Sharma, V. K., The Future is Wireless: Advances in Wireless Diagnostic and Therapeutic Technologies in Gastroenterology, Gastroenterology 2009; 137:434-465
- Hsu, Lun-Chen, et. al., An Implantable, Batteryless and Wireless Capsule with Integrated Impedance and pH Sensors for Detecting the Reflux of Acidic and Non-Acidic Materials, Gastroenterology 2009; 136 (Suppl 1):W1080

Deadly Ingestions in Children: Button Batteries and Magnets





Robert E. Kramer, MD
Medical Director, Endoscopy
Associate Professor of Pediatrics
Digestive Health Institute
Children's Hospital Colorado/
University of Colorado

Children's Hospital Colorado

Affiliated with

University of Colorado
Anschutz Medical Campus
School of Medicine

Disclosure Statement

No significant financial interests or disclosures related to this presentation

Objectives

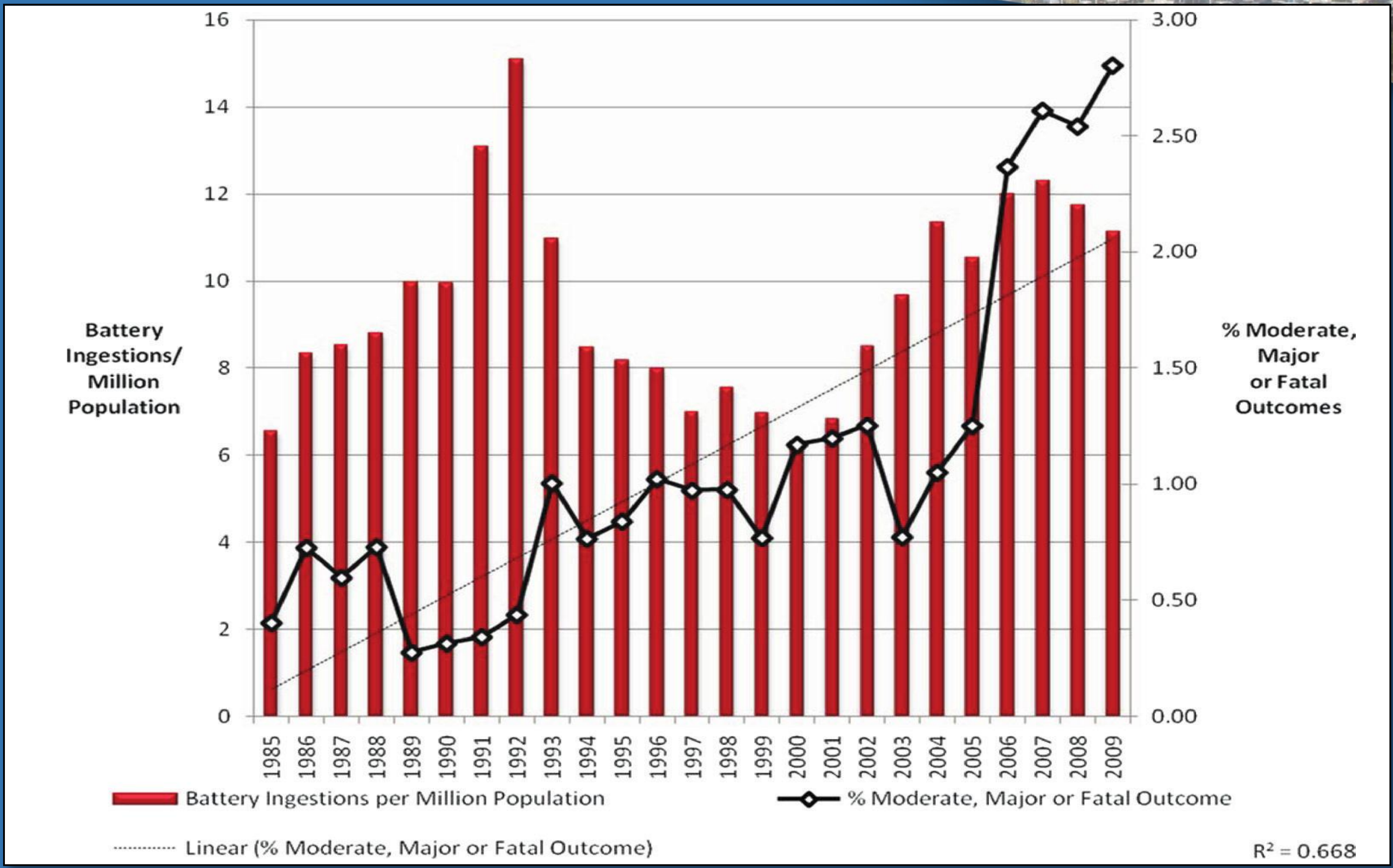
- Button Battery Ingestions (BBI)
  - Review the evolution of button battery ingestion in the US over the past 20+ years
  - Discuss the pathogenesis of BB-related injury in children
  - Identify risk factors for injury and recommendations for management
- Magnet Ingestions
  - Recognize the increased morbidity and mortality from magnet ingestions since the advent of neodymium magnets as toys
  - Review the spectrum of severity of these ingestions
  - Discuss a proposed algorithm for management of magnet ingestions in children

The Charged Esophagus: Background

- Initial report published by National Capital Poison Center in 1992[1]
  - 2320 BBI's, 62 cylindrical batteries
  - Major effect (2 strictures) noted in 0.1%, no deaths
  - As a result of this experience, endoscopic management of BBI's decreased from 13.1% of cases (1983) to 2.1% (1990)
- Follow up publication in 2010 showed a new disturbing trend[2]
  - 8648 ingestions between 1990 and 2008
  - Major effect in 73 cases, 13 deaths

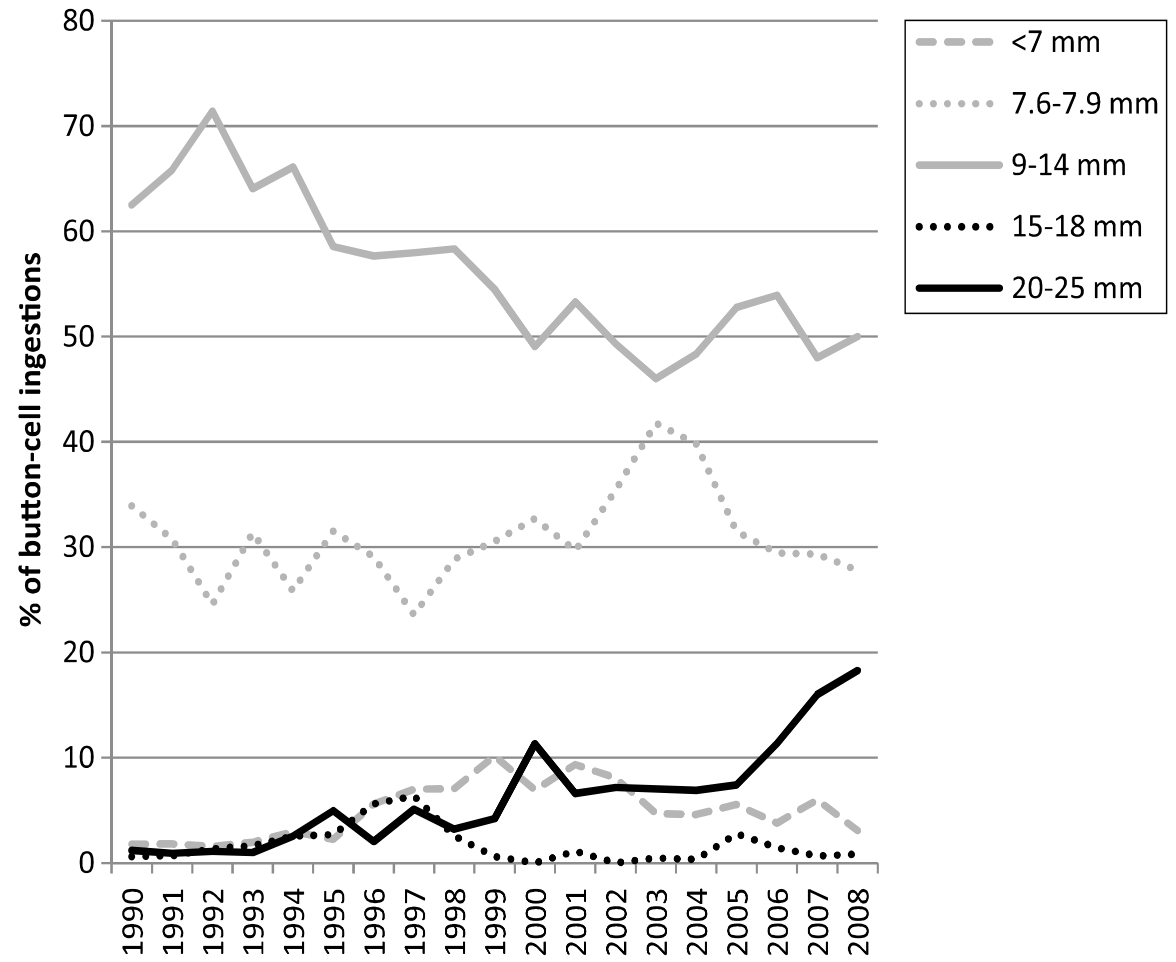
1. Litovitz T, Schmitz BF, Pediatrics 1992;89;747-757
2. Litovitz T, et al. Pediatrics 2010;125;1168-1177

2010 Report



Litovitz T, et al. Pediatrics 2010;125;1168-1177

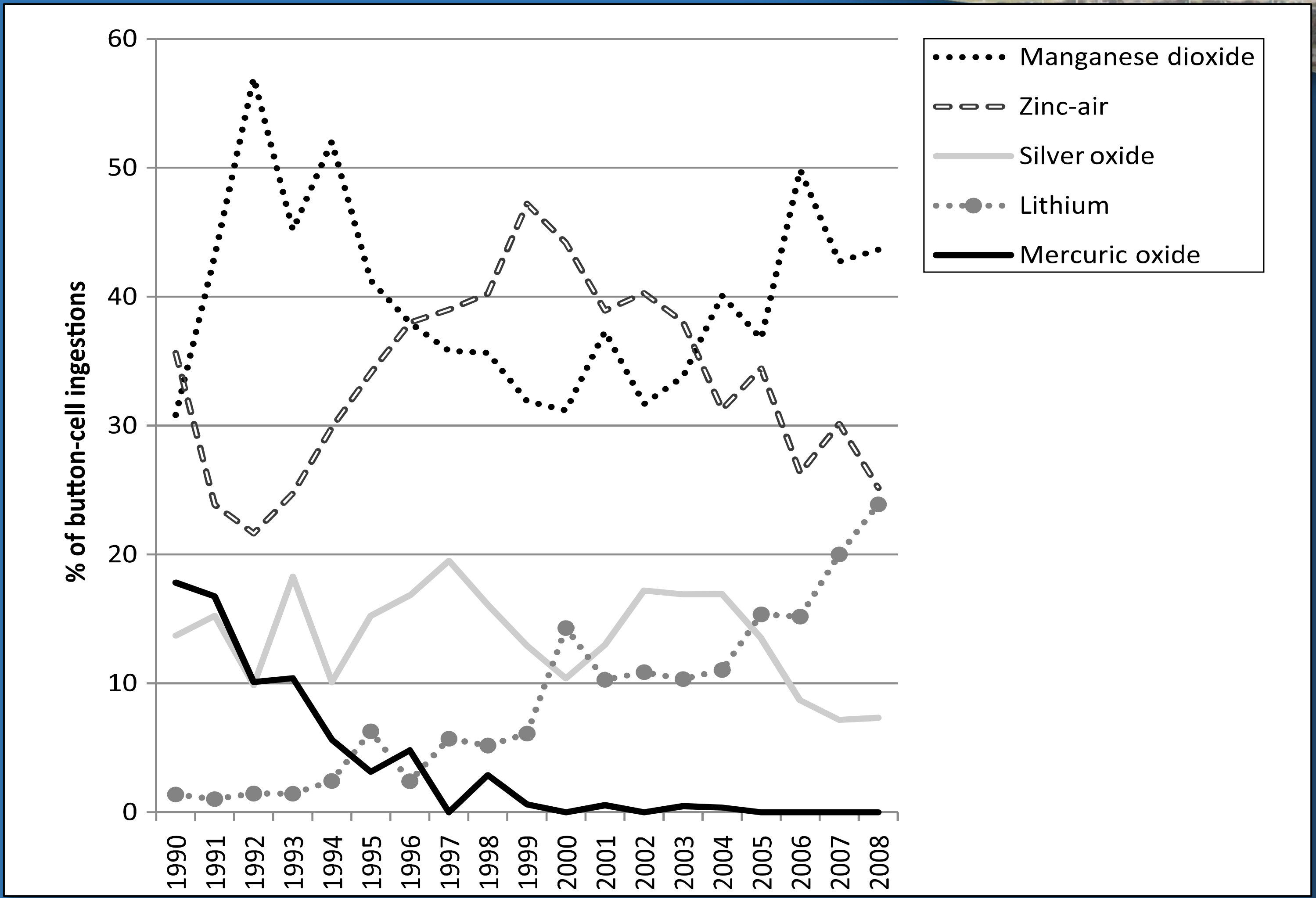
Temporal Changes in diameter of button cells



Litovitz T, et al. Pediatrics 2010;125;1168-1177

Temporal change in chemical system of ingested BB's

Children's Hospital Colorado



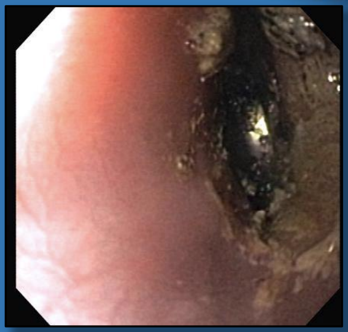
Litovitz T, et al. Pediatrics 2010;125;1168-1177

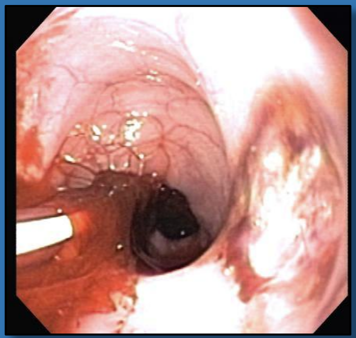
Why, why, why?

- Lithium cells preferred because they are lighter, have long shelf-life, are more stable at cool temps
- Have TWICE THE VOLTAGE of non-lithium cells (3.5 vs 1.7 V)
  - Have higher capacitance, generate more current
  - Most common offenders CR2032, CR2035
- Combination of size and voltage seems to be important
  - Small lithium cells (< 20 mm) have similar outcomes as other small cells
- Mechanism if injury is primarily generation of external current that hydrolyzes tissue fluids to produce hydroxide at negative pole of battery
  - Supported by greater risk of injury (3.2x) with new vs spent cells
  - Anatomic position of negative pole may predict subsequent injury
  - Injury continues for days to weeks following cell removal
  - “leakage” of fluid does not seem to be a significant factor

Pathogenesis of injury

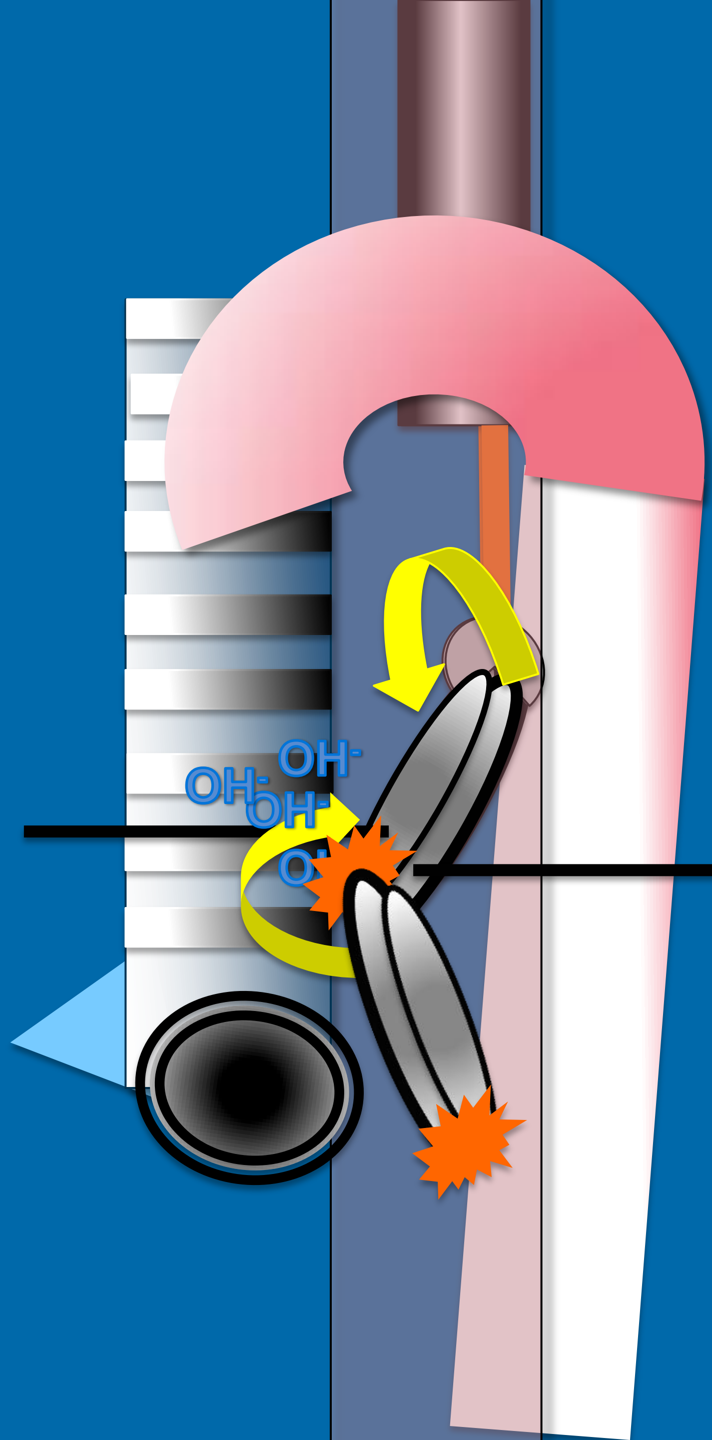
- May cause significant injury within 2 hours of ingestion
- Animal models have shown necrosis from the lamina propria to inner muscular layer within 15 min
  - Within 30 min outer muscular layer partially necrosed
  - Within 1 hour necrosis extending to trachea[1]
- Further study suggests in dog model suggests that repeated bolus of fresh water reduced the consumed electricity of the cells and delayed corrosive changes in esophagus in the first 30 minutes[2]
  - No studies in humans

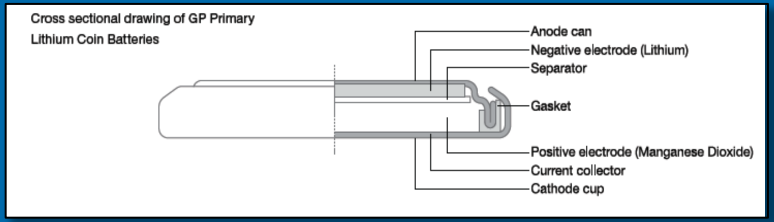


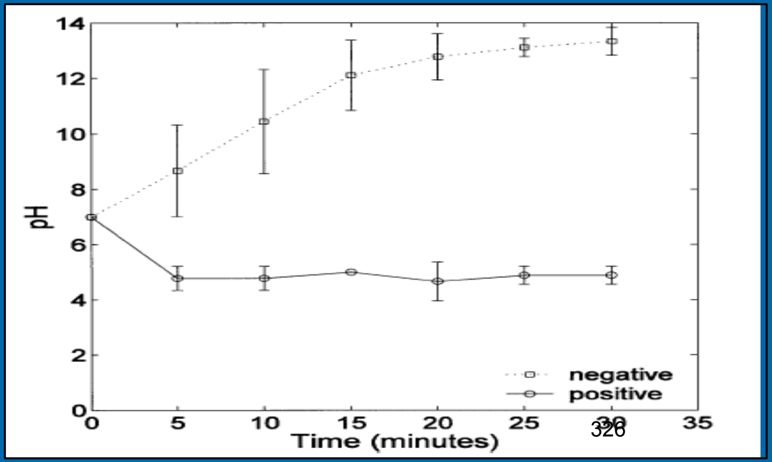


1. Tanaka J, et al, Vet Hum Toxicol 1998;40(4):193-6.
2. Tanaka J, et al, Vet Hum Toxicol 1999;41(5):279-82.

pH Inc



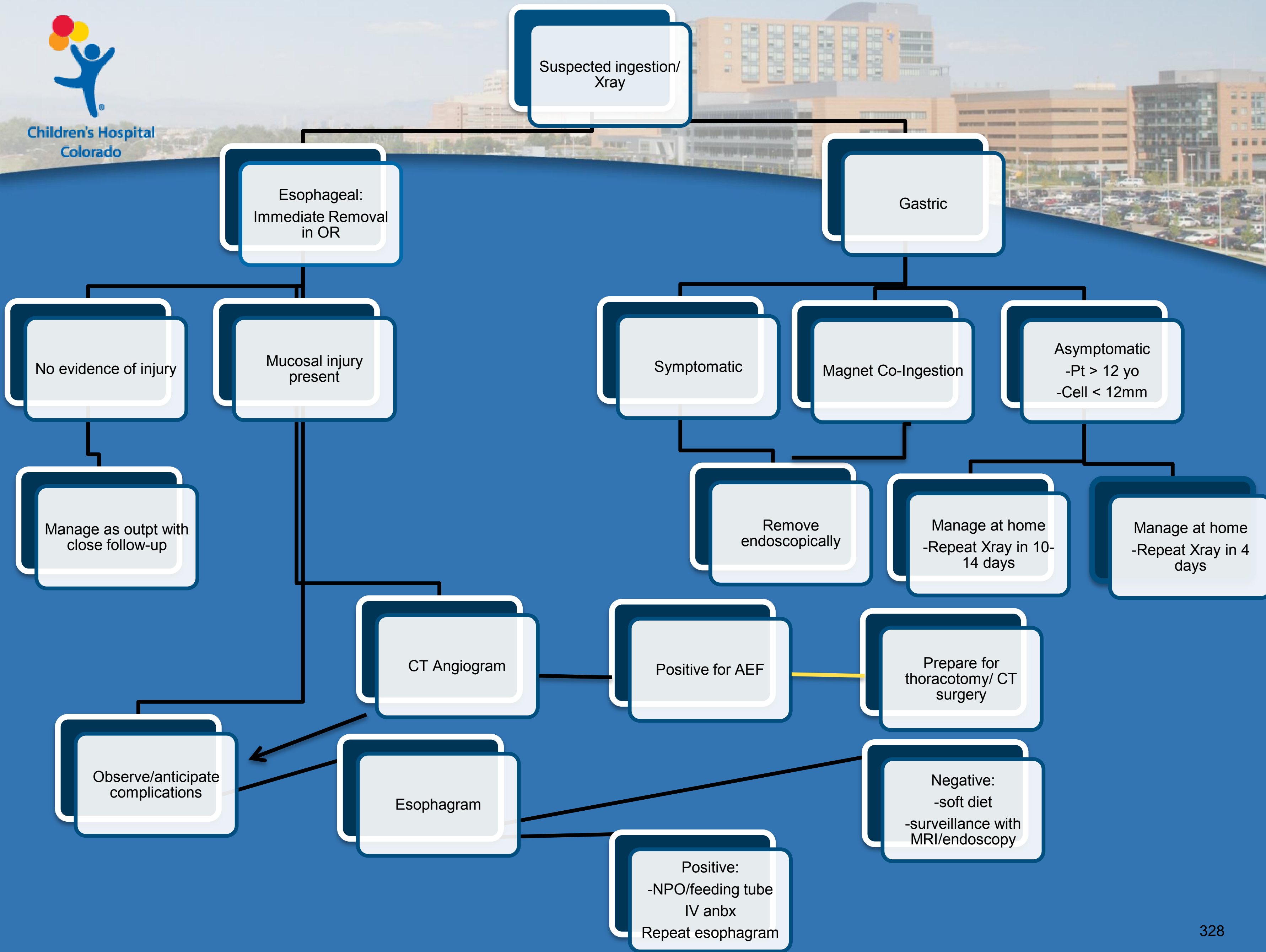




Geddes LA et al. *J Clin Monit* 2004.

Risk Factors For Serious Injury

- Types of injury reported: TE fistula (47.9%), esophageal perforation (23.3%), esophageal strictures (38.4%), vocal cord paralysis from RL nerve injury (9.6%), mediastinitis, cardiac arrest, , pneumothorax, and aortoenteric fistula (7 of 13 fatalities)
- Large cells size (>= 20 mm, 93.9%, most important predictor, OR 24.6)
  - Lithium tightly correlated with size (99.3% of ingestions >= 20 mm)
- Age less than 4 years of age (OR 3.2)
- Ingestion of > 1 battery (OR 2.1)
- New cells 3.2x more likely for those >= 20 mm
- 3 N's: Negative, Narrow, Necrosis



*Adapted from Litovitz, et al Pediatrics 2010;125;1168-1177

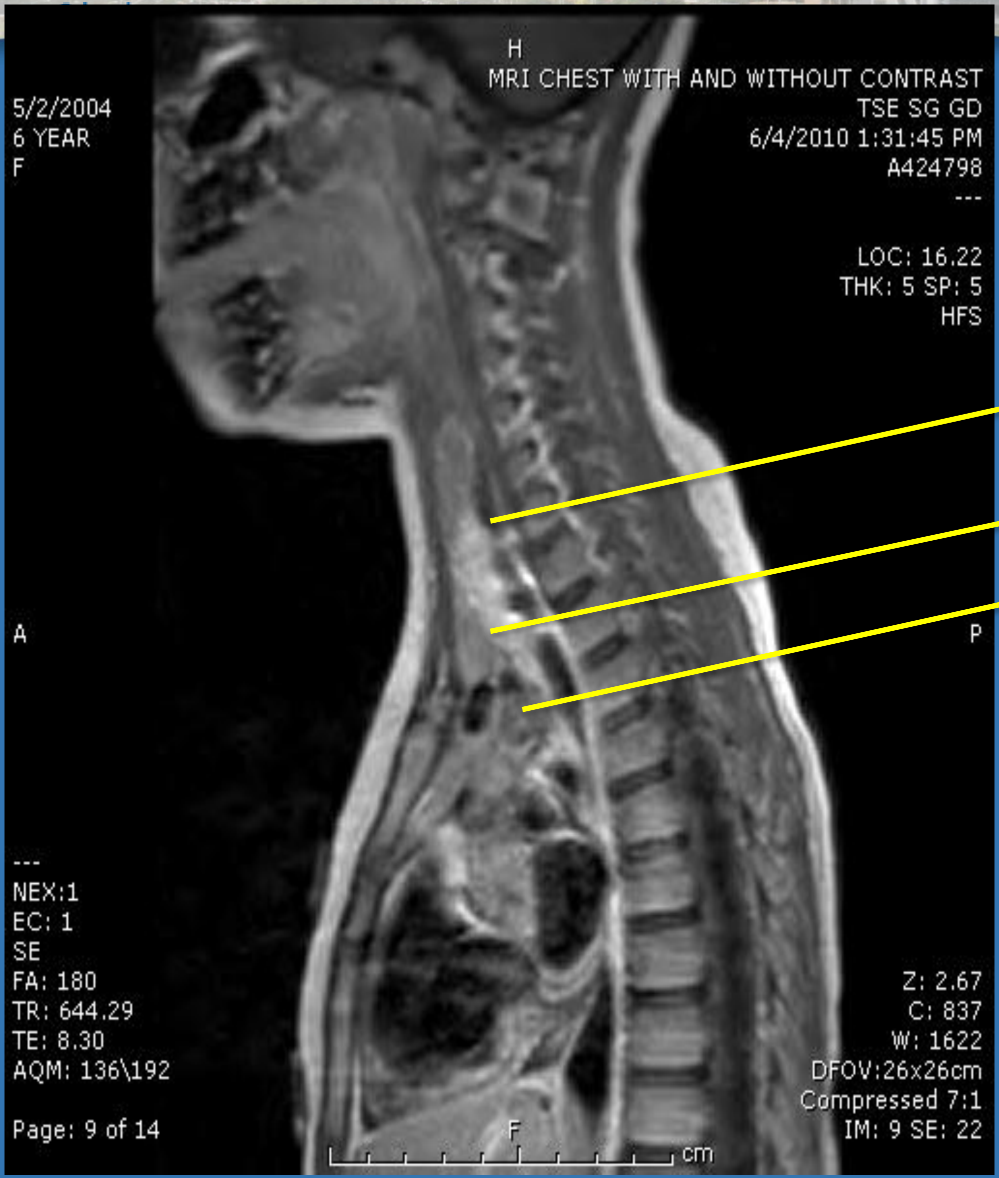
Management Caveats

- Pay attention for evidence of sentinel bleed
  - Fatal AEF's have occurred as long as 19 days *after* BB removal
- Blakemore Tube: Have at bedside, train on use
  - Need to have manometer pump to inflate to proper pressure
  - Keep on hand in all critical areas (ED, PICU, GI Procedures)
- Have Surgeons (CV and General) on hand early
- Conservative surveillance: repeated endoscopy, esophagrams, MRI

CT Angiography

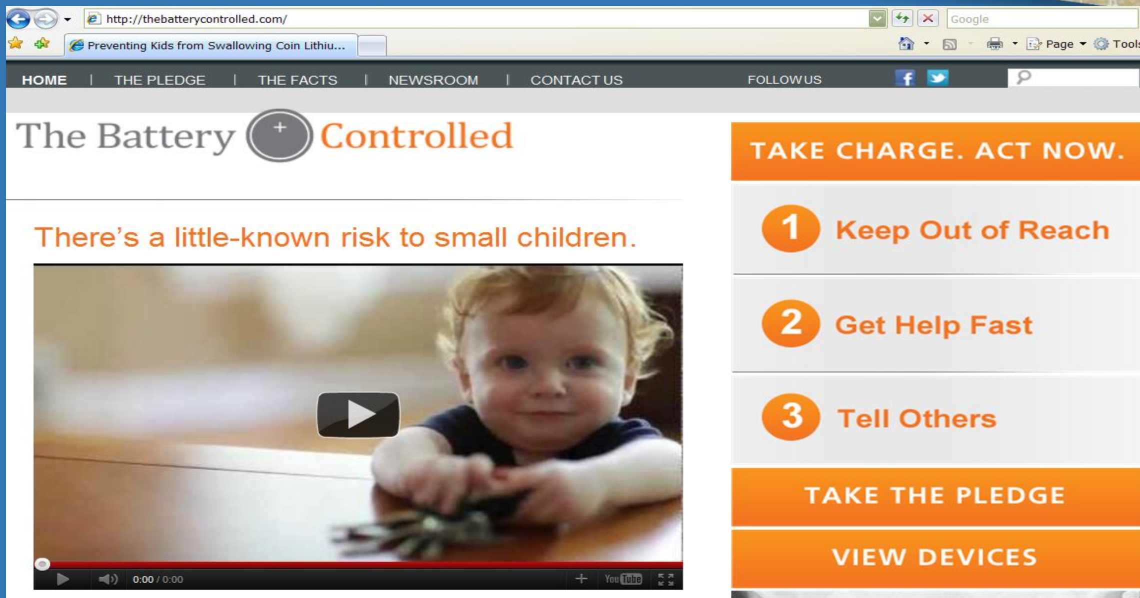
- Diagnostic yield of 30-60%
- Has been used successfully in adults for aortoenteric fistulae
- May be useful in care algorithm for determining need to go to OR in case of sentinel bleed

MRI Surveillance



Children's Hospital Colorado

Resources



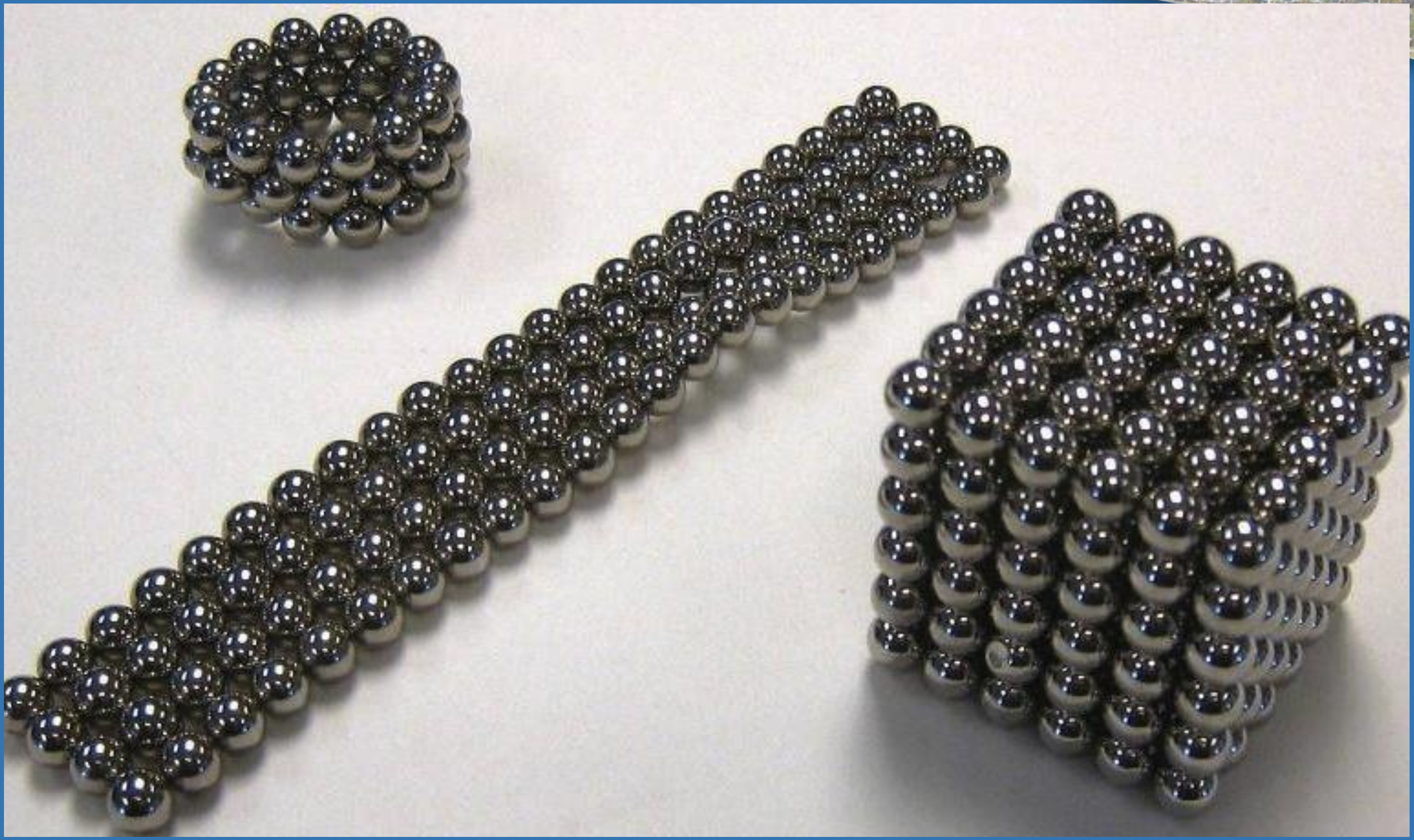
TheBatteryControlled.com

Facebook.com/TheBatteryControlled

@BatteryControl

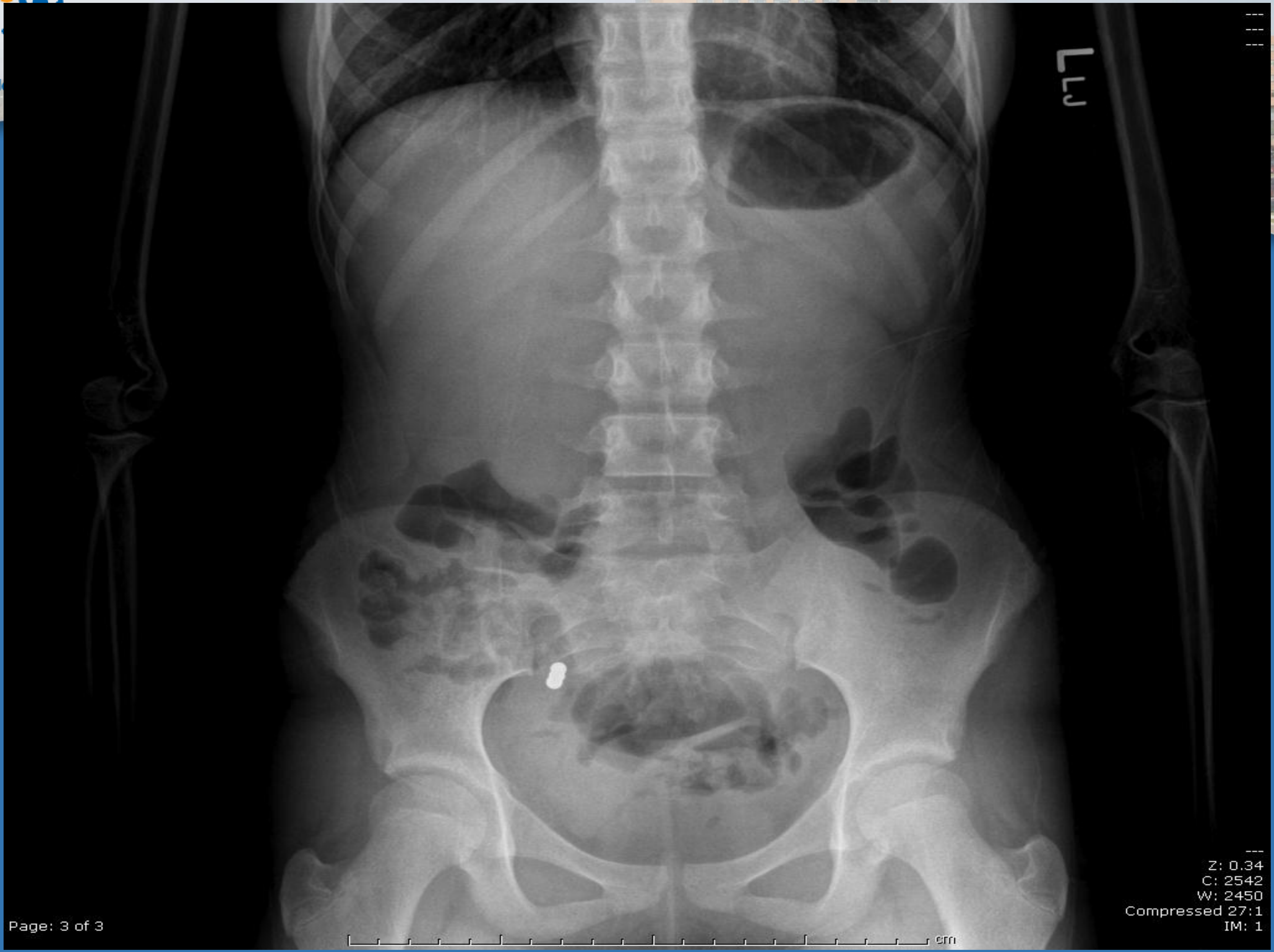
National Battery Ingestion Hotline: 202-625-3333

Magnet Ingestions In Children



Magnet Ingestions: Background

- Neodymium magnets (aka rare earth magnets) 5-10x more powerful than traditional magnets
- 2002 first reported series of injury in 24 children from neodymium magnets (GI, airway)
- 2003-2006: 20 cases of magnet ingestion injury reported in CDC M&M Weekly Report
  - 75% bowel perforation
- 2006: US Consumer Product Safety Commission raises age recommendation from 3 to 6 years of age
- 2007: Death in a 20 month old, 18 surgical removals
- 2008: More than 200 documented cases
  - Patent rights for neodymium magnets had expired, resulting in large number of manufacturers (ie Buckyballs, Neocube)
- 2009: CPSC issues ban on sales to children < 14 yrs


L
Z: 0.34
C: 2542
W: 2450
Compressed 27:1
IM: 1
Page: 3 of 3
cm

Case 1

- Patient sent home on Miralax cleanout regimen, with instructions to have a repeat film the following AM.
- Repeat film performed but no clear follow-up with MOC
- MOC calls GI office 3 days later for recommendations.
  - Repeat film had shown a small amount of movement, but still positioned together in RLQ.
- On call GI physician orders repeat film, which shows no change in position from second film and position suspected to be within small bowel.

- WHAT WOULD YOU DO NOW?

Case 1


LOC: 31.50
THK: 2
FFS
R
L
RD: 320
Tilt: 0
mA: 184
KVp: 120
Acq no: 2
Page: 83 of 91
P
cm
Z: 1
C: 40
W: 350
DFOV:32x32cm
Compressed 11:1
IM: 83 SE: 4

Case 1

- Patient allowed to go home with instructions for another Miralax cleanout and follow-up film in the AM.
- Repeat film the next day (#4), now 7 days out from original ingestion, shows no interval movement from CT scan results the day prior.
- Pt remains asymptomatic.

- AND NOW?

- Pt scheduled for colonoscopy the next day, with continued Miralax cleanout. Upon arrival for colonoscopy a spot film was performed which showed the magnets had cleared.

Case 1: Discussion Points

- Overall a good outcome, but certainly with risk for significant morbidity and mortality due to lack of oversight.
  - Specifically in regards to lack of “ownership” of patient discharged from ED.
- Some reassurance from the fact that the magnets were swallowed together and in all imaging appeared to remain connected.
- Difficulty in confidently identifying anatomic position (ie small bowel vs colon) with plain films and even with CT scan.

Case 2: Symptomatic

- 4 yo male, presented to PCP c 1 day of crampy abdominal pain, lethargy, and decreased appetite, but no fever.
- KUB showed small round FB's in abdomen and sent to ED
  - In ED admitted he had swallowed magnets (which he had received for his birthday) 4 days prior.
  - Repeat KUB showed 4 adjacent radiopaque objects in RLQ, possibly in TI, and some AFL's, c/w partial SBO.
  - Seen by surgery who felt abdomen to be benign and recommended discharge with follow-up by PCP with repeat films.
- Next day pt with abdominal pain and bilious emesis so returned to ED.
  - CBC showed a slightly elevated WBC of 13.6, with 85% segs.
  - Repeat film showed unchanged position of magnets but improved gas pattern and no free air.
  - Surgery again evaluated and felt abdomen was benign and discharged home on Miralax and enemas.

Case 2

- Returned to ED two days later with increasing pain and low fever.
  - Repeat film with no movement of magnets and increased bowel dilatation and concern for partial bowel obstruction, but no free air.
  - WBC 17.5 with some left shift but no peritoneal signs on exam.
  - CT scan with IV contrast performed, showing 4 radiopaque FB's anterior to the cecum within a distal loop of small bowel, but no free air or fluid in the peritoneum.
  - Given lack of progression and increasing symptoms decision made to bring him to the OR.
- In OR he was found to have 3 walled-off ileal perforations and one in the cecum, c magnets lodged in each site, but drawn together to create a single site of fistulization.

Case 2

- The cecal perforation was overseen and an ileal resection (8.9 cm) was performed to repair the other sites, with primary anastomosis. Pt was placed on anbx and had an uneventful recovery, discharged home on POD #6.
- DISCUSSION POINTS
  - Repeated return to ED for GI symptoms in context of magnet ingestion and lack of movement on films should have prompted more concern and quicker decision to move toward removal.
  - Earlier recognition of bowel injury may have allowed for endoscopic removal and prevented the need for bowel resection.
  - Lack of free air or peritoneal signs can easily be misleading in these cases. Waiting for fever, elevated WBC or other signs may inappropriately delay treatment and result in increased morbidity and mortality.
  - Importance of getting GI involvement early in these cases to help guide management

Rare Earth Magnet Ingestion Algorithm

Initial Presentation

- Obtain History
  - Known magnet ingestion
  - Unexplained GI symptoms with rare earth magnets in the child's environment
- Obtain an abdominal x-ray. If magnets are present on flat plate of abdomen, obtain lateral x-ray of abdomen
- Determine single versus multiple magnet ingestion

Single Magnet

Within the stomach, or esophagus

- **Option 1**: Consult pediatric gastroenterologist if available.
  - Consider removal especially if patient is at increase risk for further ingestion.
- **Option2**: Follow with serial x-rays as outpatient and educate parents:
  - Remove any magnetic objects nearby
  - Avoid clothes with metallic buttons and belts with buckles
  - Ensure no other metal objects or magnets are in the child environment for accidental ingestion

Beyond the stomach

- Consult pediatric gastroenterologist if available. Consider removal if accessible.
- Follow with serial x-rays as outpatient
- Educate parents :
  - Remove any magnetic objects nearby
  - Avoid clothes with metallic buttons and belts with buckles
  - Ensure no other metal objects or magnets are in the child environment for accidental ingestion
- Confirm passage with serial x-rays
- In case of delayed progression, may use PEG 3350 solution or other laxative prep solution to aid in passage

Multiple Magnets (or single magnet and a metallic foreign body)

All within the stomach or esophagus

- If pediatric gastroenterologist if available notify for removal, especially if ingestion is less than 12 hours
- If no Pediatric Gastroenterologist is available, transfer to center where pediatric endoscopy is available
- If ingestion is greater than 12 hours prior to the time of procedure, then consult pediatric surgery prior to endoscopic removal

Successful removal

- Discharge home with appropriate follow-up and education

Unsuccessful removal

- Refer to pediatric surgery for removal

Beyond the stomach

- Consult pediatric gastroenterologist and pediatric surgery if available
- If pediatric gastroenterologist and pediatric surgeon are not available, send to referral center
- Management depends whether symptomatic or asymptomatic

Symptomatic

Refer to Pediatric surgery for removal

Asymptomatic

- If no signs of obstruction or perforation on x-ray, may remove by enteroscopy or colonoscopy if such service is available
- Consult pediatric surgery prior to endoscopic removal
- May follow serial x-rays for progression if no signs of bowel obstruction, partial bowel obstruction or perforation on x-ray. **Note: symptoms maybe subtle**

Successful removal

- Discharge home after hospital observation to ensure tolerance of feeds with appropriate follow-up and education

No Endoscopic Removal

- Refer to Pediatric surgery
- May do serial x-rays in emergency room to check for progression by checking films 4 to 6 hours apart

No progression of magnets on serial x-rays

- Admit to hospital for further monitoring and serial x-rays or surgical removal
  - May use PEG 3350 solution or other laxative prep solution to aid in passage and to help prepare for colonoscopy or other procedure.
- Continue serial x-ray every 8 to 12 hours. If no movement in 24 hours or if patient becomes symptomatic then proceed with surgical removal or endoscopic removal with surgical back-up

Progression of magnets on serial x-rays

- Educated parents on precautions and discharge with close follow-up
  - Remove any magnetic objects nearby
  - Avoid clothes with metallic buttons and belts with buckles
  - Ensure no other metal objects or magnets are in the child environment
- Confirm passage with serial x-rays
- If at any time magnets do not progress or patient becomes symptomatic, admit to hospital for removal of magnets

Children's Hospital Colorado

Conclusions

- Neodymium magnet ingestions represent a clear and present danger due to entrapment of the bowel with subsequent perforation
- There should be a low threshold for endoscopic removal of multiple magnets when they are “reachable” by conventional endoscopy, even in asymptomatic patients
- When they are not retrievable by endoscopy, they should be surgically removed as quickly as possible if there are GI or systemic symptoms (even subtle ones)
- If pt is asymptomatic and surgery is not deemed appropriate, there must be close follow-up (possibly inpatient) with serial films, with reconsideration for surgery if evidence of stalled passage

Acknowledgements

- Button Battery Ingestion
  - David Brumbaugh, MD
  - Toby Litovitz, MD
  - John Bealer, MD
  - Fritz Karrer, MD
  - Steve Colson, MD
  - John Sandoval, MD
- Magnet Ingestion
  - Mark Gilger, MD
  - Adam Noel, MD

Quality Sedation for Pediatric GI Endoscopy: Assessing, Monitoring and using Crisis Resource Management (CRM)

Jenifer R. Lightdale, MD, MPH
Children's Hospital Boston

Children's Hospital Boston

Objectives

- Describe current guidelines and practice standards
- Discuss recent advances
  - Endoscopic sedation strategies
  - Patient monitoring
  - Crisis Resource Management
- Apply practice strategies to minimize risks

Introduction

- Gastrointestinal endoscopy is a very safe procedure
- Routinely performed
- Inherently risky
- Serious adverse events rare
- Staff must be prepared for low frequency, high risk events

Background

- Increased awareness about medical errors
  - Affect all healthcare workers

- Root causes for healthcare errors
  - Fatigue
  - Stress
  - Busy work environments
  - Poor communication

Background

- IOM goal: to reduce medical errors by 50% within 5 years
- Emphasis on improvement of teamwork skills
  - one of the most effective ways to increase patient safety
- Particularly relevant to pediatric endoscopy
  - Risks and benefits of sedation

Goals (Advantages) of Sedation

- Patient
  - Safety, comfort, cooperation, immobility and amnesia
  - Contributes to satisfaction and willingness to repeat
- MD
  - Successful completion of procedures
  - Maximize efficiency
  - Cost-effectiveness

Disadvantages of Sedation

- Medication risks and side effects
- Increased recovery time
- Costs
  - Use of conscious sedation adds >$100 to procedural costs (med costs + recovery times)*
  - May require presence of 2 nurses**

*Hedenbro, 1991

**Kesteloot, 1996

Sedation for Pediatric Endoscopy

- No single agent/regimen ideal
- Complications related to sedation are biggest risk of pediatric endoscopy*

* Thakkar, 2007

Commonly Used Sedatives for Pediatric Gastrointestinal Procedures (<50kg).

Drug	Route	Maximum dose (mg/kg)	Time to onset (min)	Duration of action (min)
Benzodiazepines				
Diazepam	IV	0.1-0.3	1-3	15-30
	Rectal	0.2-0.3	2-10	15-30
Midazolam	Oral	0.5-0.75 (Max dose 20mg)	15-30	60-90
	IV	0.05-0.15	2-3	45-60
	Rectal	0.5-0.75	10-30	60-90
Opioids				
Meperidine	IV	1-2	<5	2-4
	IM	1-2	10-15	2-3
Fentanyl	IV	0.001-0.005 (1-5 µgm/kg in 0.5-1.0 µgm/kg increments)	2-3	30-60
Ketamine	IV	1-2	1	15-60
	IM	2-7	3-5	15-150

Two Main Types of Sedation

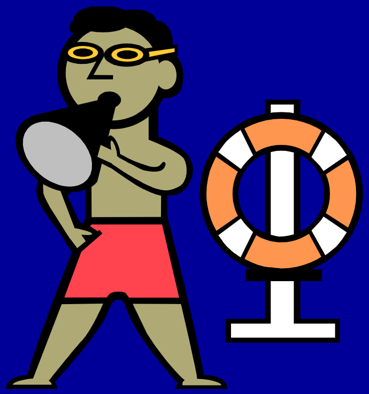
- IV sedation (Endoscopist-administered)
- General Anesthesia (Anesthesiologist)

- To choose, pediatric GI's must consider:
  - Patient age
  - Medical history
  - Clinical status
  - Anxiety level

* Lightdale, 2007

Pediatric Sedation and the Joint Commission

- Q: What must we consider when sedating our patients?



A: The sedation plan and the patient's status.*

* JCAHO, 2001

A Good Sedation Plan

Documents both *before* the procedure:

1. Type of sedation
   - Drug(s)

2. Level of sedation to be targeted
   - Patient
   - Procedure

Levels of Sedation and Quality Sedation Decision-Making

- Optimal levels of sedation may be different for different procedures
  - (e.g. EGD vs. colonoscopy vs. ERCP)

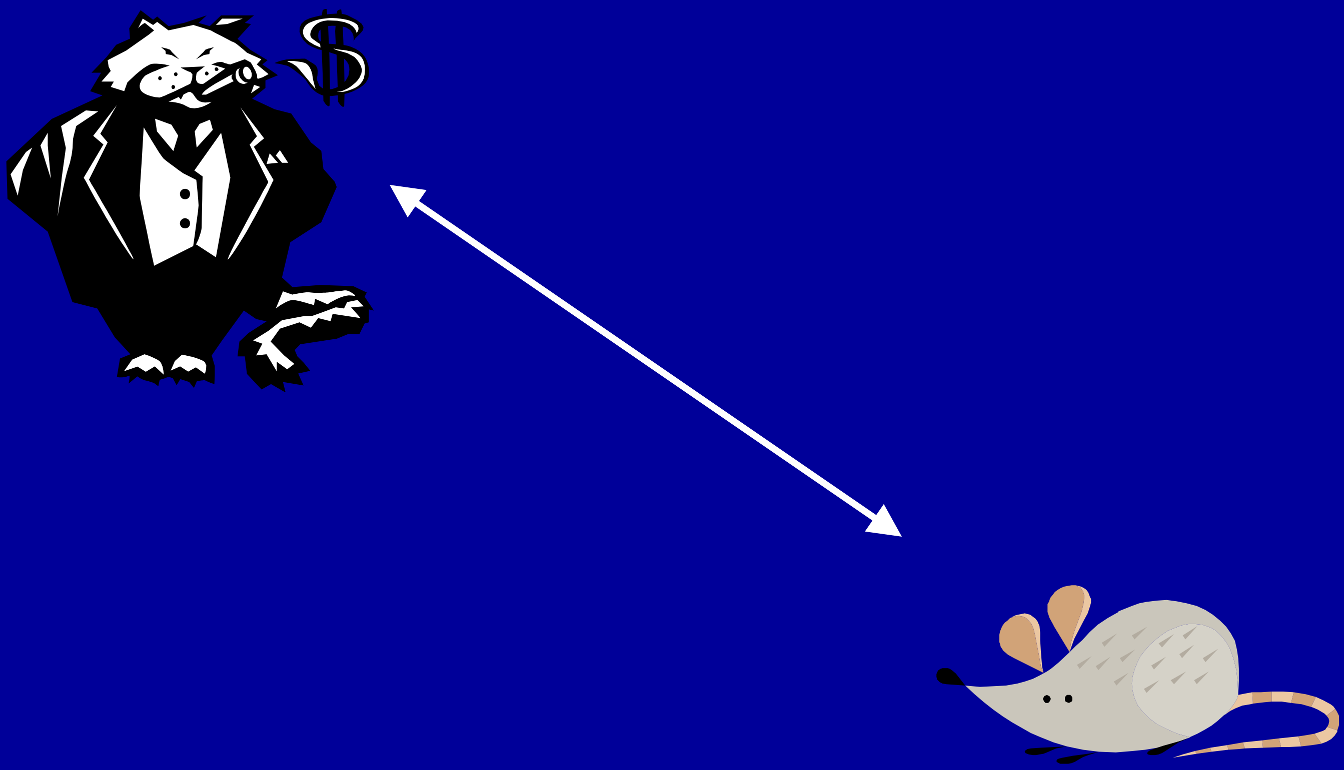
- ** Level of sedation is not necessarily equal to degree of immobility

Levels of Sedation as a Continuum

Sedation levels	Commonly used terms
Awake, alert ↕ Light sedation	"Conscious Sedation" *
Awake, alert ↕ Light sedation ↕ Deep sedation	*"Moderate" or* "Procedural sedation"**
General anesthesia	"General anesthesia"***

* Endoscopist may administer sedation alone
** May require presence of anesthesiologist
*** Always requires presence of anesthesiologist

Documenting Patient Status



Apply the ASA Classification System

American Society of Anesthesiologists (ASA) suggestion for non-anesthesiologist classification of patients' physical status:

ASA Class	Physical Status
1	Normal healthy patient
2	Patient with mild systemic disease
3	Patient with severe systemic disease
4	Patient with severe systemic disease that is a constant threat to life
5	Moribund patient not expected to survive without emergent procedure

- Classes 1,2 - Conscious Sedation (CS)
- Class 3 - careful evaluation/decision
- Classes 4,5 - General Anesthesia (GA)

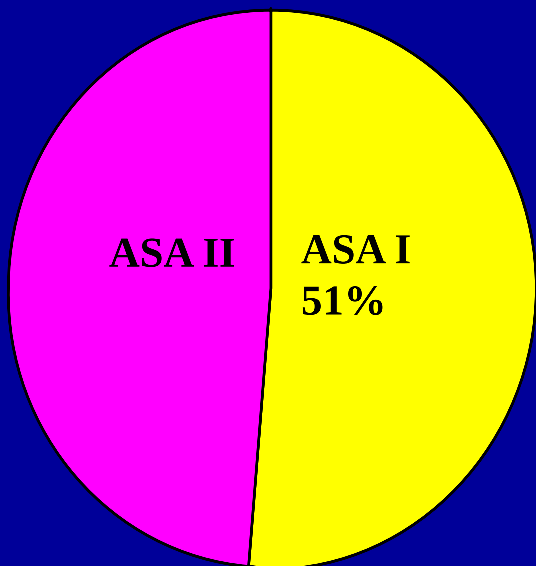
Caveats of ASA Classification

- Crude patient categories that don't capture complex clinical scenarios
- GIs may disagree with RNs and with anesthesiologists

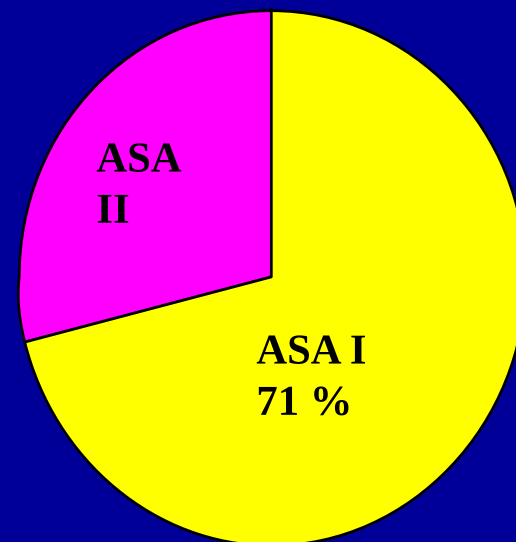
* Thakkar, 2007

Anesthesiologists may label more patients as ASA II*

Anesthesiologist



Endoscopist



- Consider GER in their decision making
- GER NOT a systemic disease

* Lightdale, 2005.

Is there a current *standard* choice for sedation for pediatric endoscopy?

- 2005 survey of NASPGHAN attendees*
  - Wide practice variation
  - Sedation decisions affected by
    1. Procedural volume
    2. Access to anesthesia support
    3. Institutional policies
    4. Presence of Trainees

* Lightdale, 2007

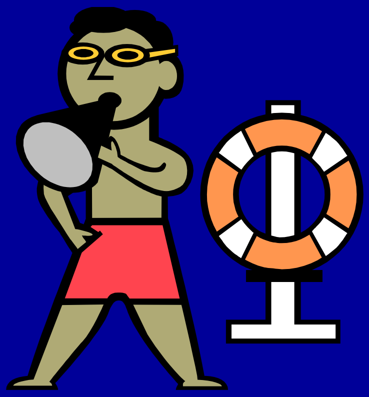
2005 Survey Respondents

- 1/3rd reported >75% of cases with endoscopist-administered IV sedation
- 1/3rd >75% GA in main OR
- 1/3rd >75% anesthesiologist-administered propofol in dedicated Endoscopy Suite

- 10% reported <u>all</u> cases with anesthesiologist-assistance
- 23% <u>all</u> cases endoscopist-administered sedation

Pediatric Sedation and Patient Safety

- Q: Does patient age matter?



- A: Patient age should be considered
  - **58% of pediatric GIs say it doesn't…*

* Lightdale, 2007

Propofol in the Endoscopy Unit

- Increasing experience and use among pediatric endoscopists
  - 60% of pediatric GIs report at least occasional use*
- Involves less agitation than endoscopist-administered M/F (0.4% vs. 6.4%, $p<.001$)*
- Excluding agitation, same rate of adverse events (1.6% vs. 1.8%, $p=.20$)

* Lightdale, 2005; Lightdale, 2007.

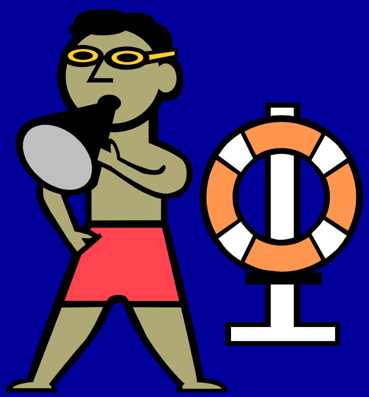
Propofol in the Endoscopy Unit: Caveat Emptor!!

- Anesthesiologist-administered propofol sedation in pediatric endoscopy unit vs. GA in OR settings may have higher adverse events rates
  - (5.8% vs. 0.8%, p<.001)*
  - May reflect *dis*comfort of pediatric anesthesiologists working in different environments
  - Targeting lighter sedation levels
- No data exists for AE rates during pediatric endoscopy with anesthesiologists accustomed to working with adults

* Lightdale, 2005.

Pediatric Sedation and Patient Safety

- Q: How can sedation be safer?



- A: Patient monitoring
  - Useful for both endoscopists and anesthesiologists
  - Use to improve detection before adverse events
  - Recent technological advances

Current Guidelines for Patient Monitoring:

- ASGE, ASA and JCAHO
- MD + RN or otherwise trained assistant responsible for patient monitoring
- Supplemental O2
  - via NC @ 2L/min
  - Reduces hypoxemia
  - Advantages of low cost, high benefits
  - Disadvantage of masking CO2 retention

Patient Monitoring:

- Pulse oximetry
  - Current standard of care
  - Vs. “old standard” Cyanosis
    - Noticeable when O2 sats <70%
    - May be difficult to see in darkened room
  - Lack of pulse oximetry monitoring well associated with increased complication rates

Patient Monitoring:

- Pulse oximetry disadvantages
  - Technical issues/movement artifacts
    - May actually increase vigilence of staff
  - Does not reflect ventilation, just oxygenation
  - Does not indicate hemodynamic instability or shock

Capnography

- "New wave" for monitoring ventilation
  - Electronic measure of exhaled $ETCO_2$
  - Generates real-time waveforms of respiration in non-intubated patients
  - Provides early detection of respiratory compromise (an "early warning system")*
  - Allows intervention to minimize hypoxemia
  - Should be considered for moderate or deep sedation

*Vargo, 2002

Microstream Capnography

Microstream ETCO2 canula

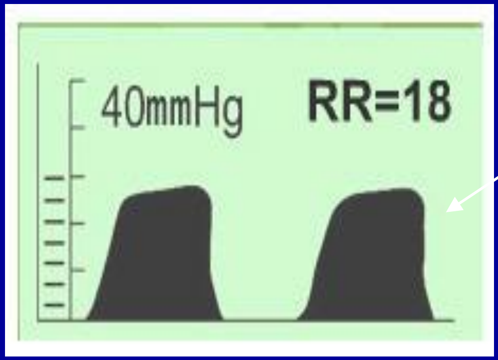
What info does capnography provide?

ETCO2 display

- Numerical value for ETCO2

- Distinct waveform (tracing)
  for each respiratory cycle

Capnometer



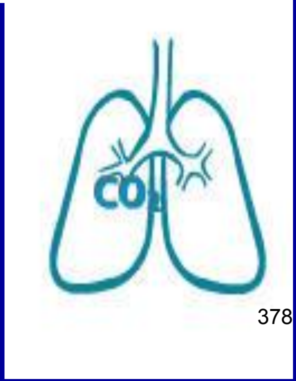
Capnograph

Oxygenation and Ventilation

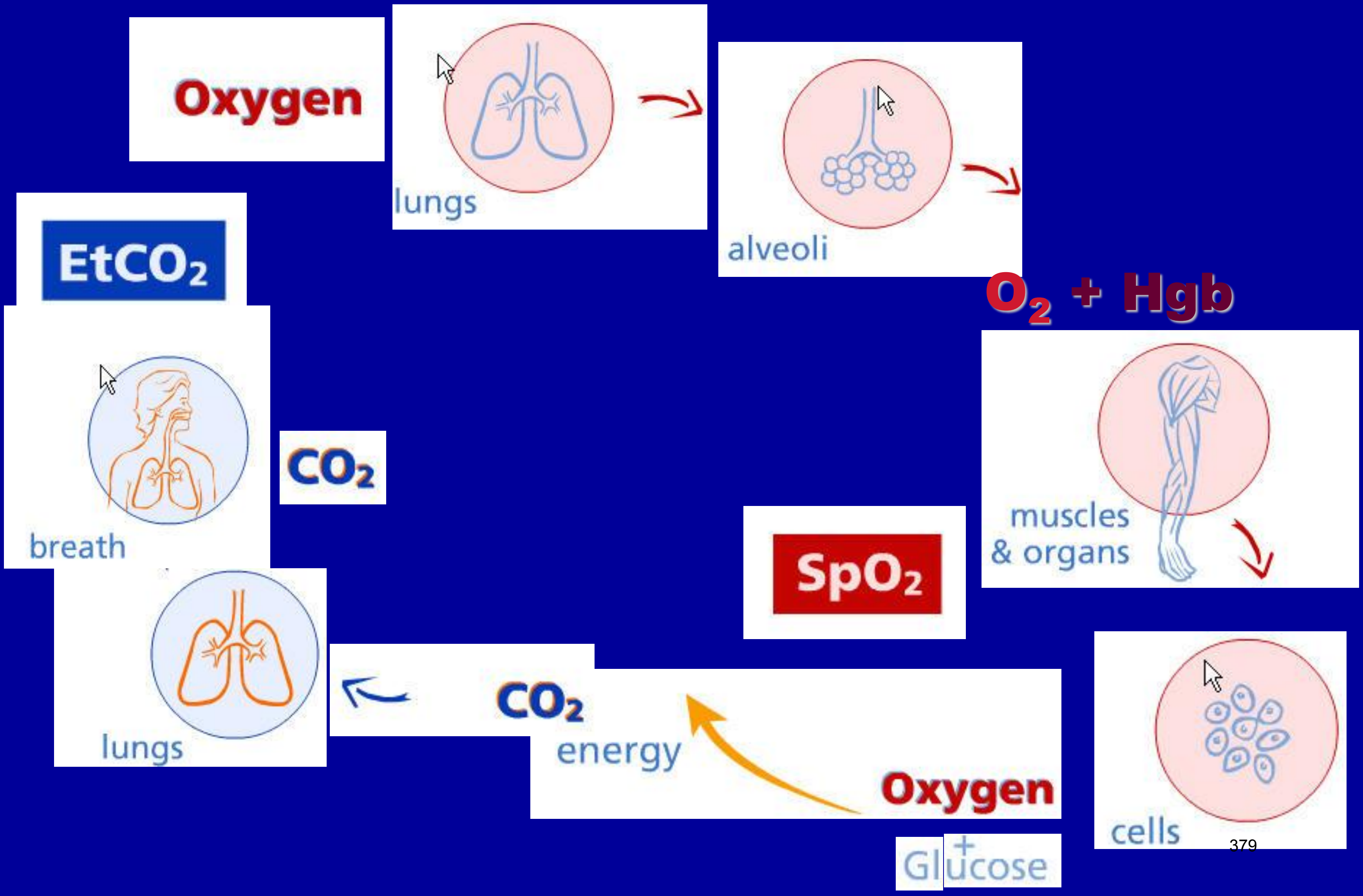
- Respiratory Cycle = two-phase
  - related, *but separate* physiologic processes

- Oxygenation

- Ventilation



Physiology of Oxygenation and Ventilation



Oxygenation vs. Ventilation

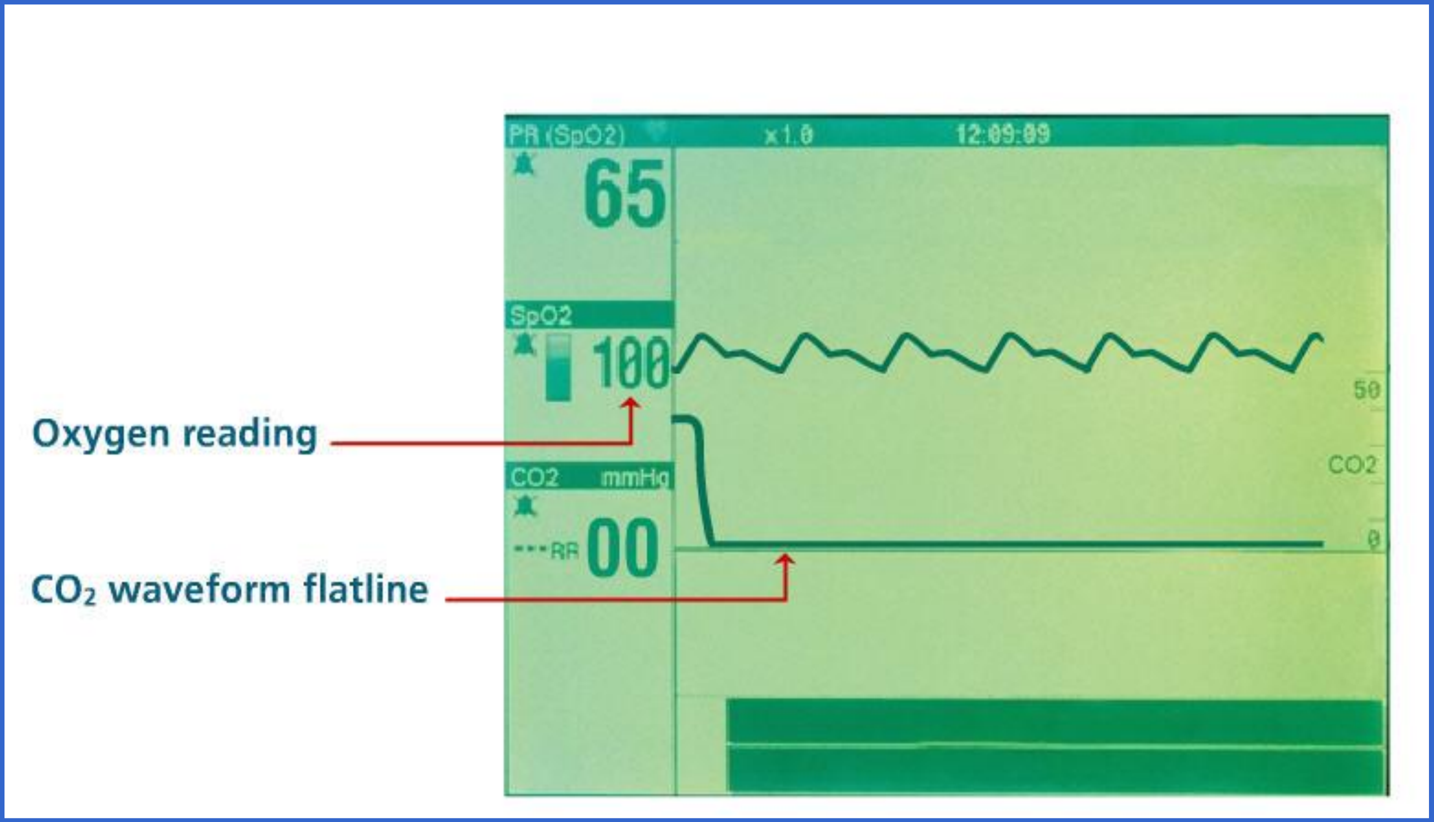
Oxygenation

- Measured by pulse oximetry
  - O_2 attached to hemoglobin
- Influenced by supplemental O2
- May remain normal even after patient stops breathing

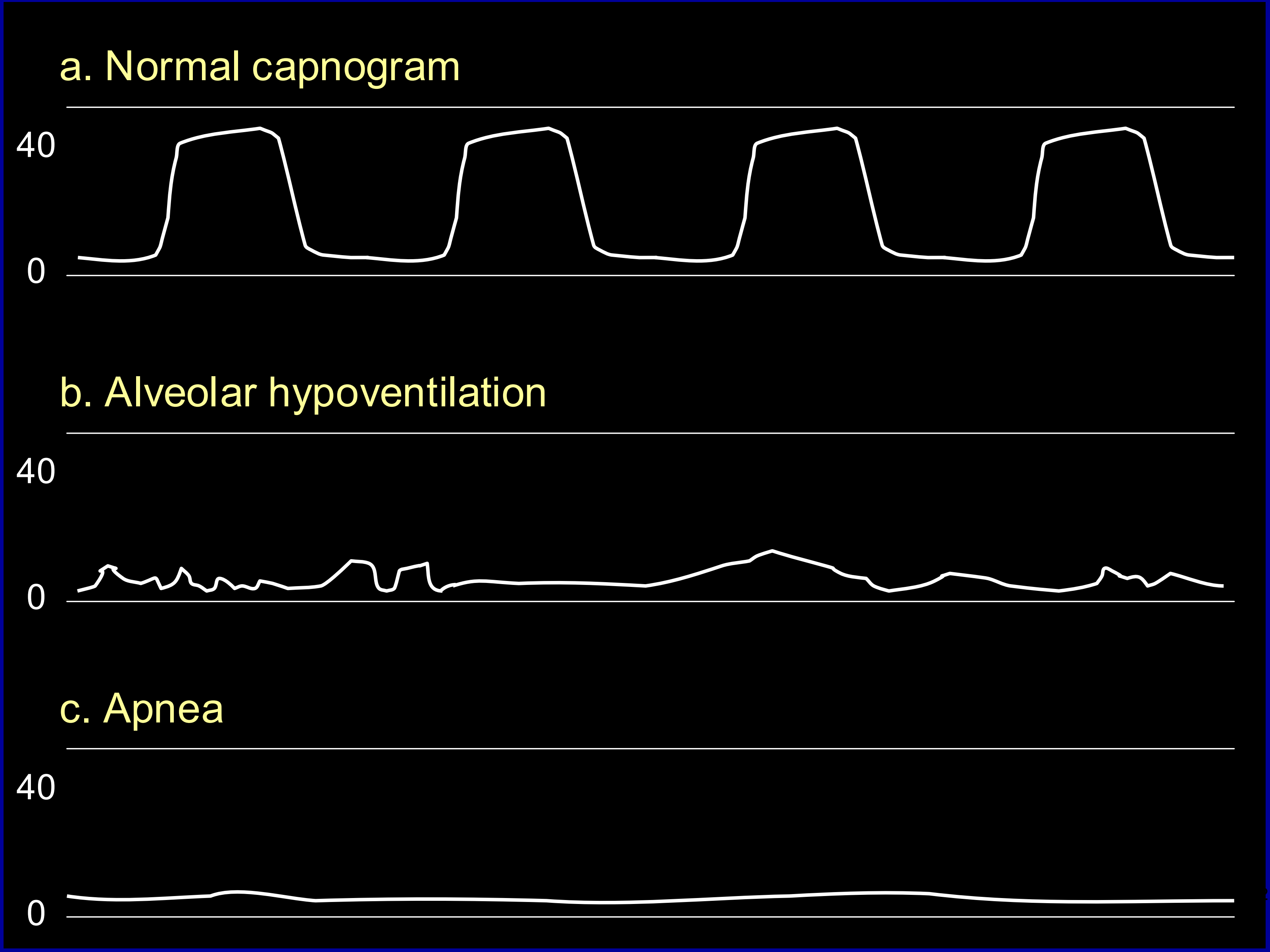
Ventilation

- Measured by capnography
  - Expired and inspired levels of $ETCO_2$
- Not affected by O2 delivery
- Does not appear normal if patient is not breathing

Oxygenation and Ventilation



Capnograms


a. Normal capnogram
40
0
b. Alveolar hypoventilation
40
0
c. Apnea
40
0

Randomized Controlled Trial*

184 patients assessed for eligibility

20 excluded
(16 declined)

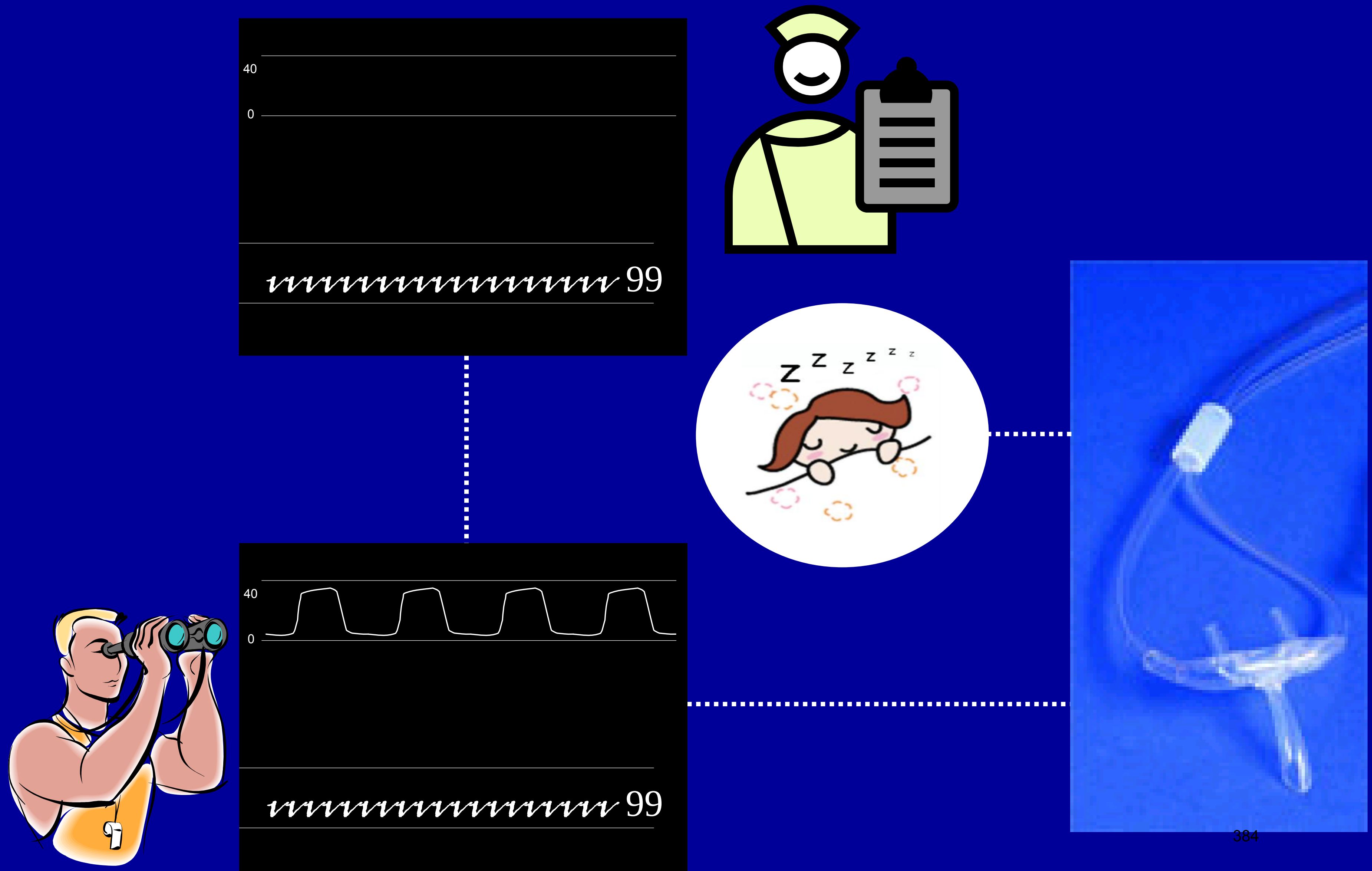
163 randomized and analyzed

83 intervention arm
(>15 secs alveolar hypoventilation)

80 control arm
(>60 secs alveolar hypoventilation)

* Lightdale, 2006.

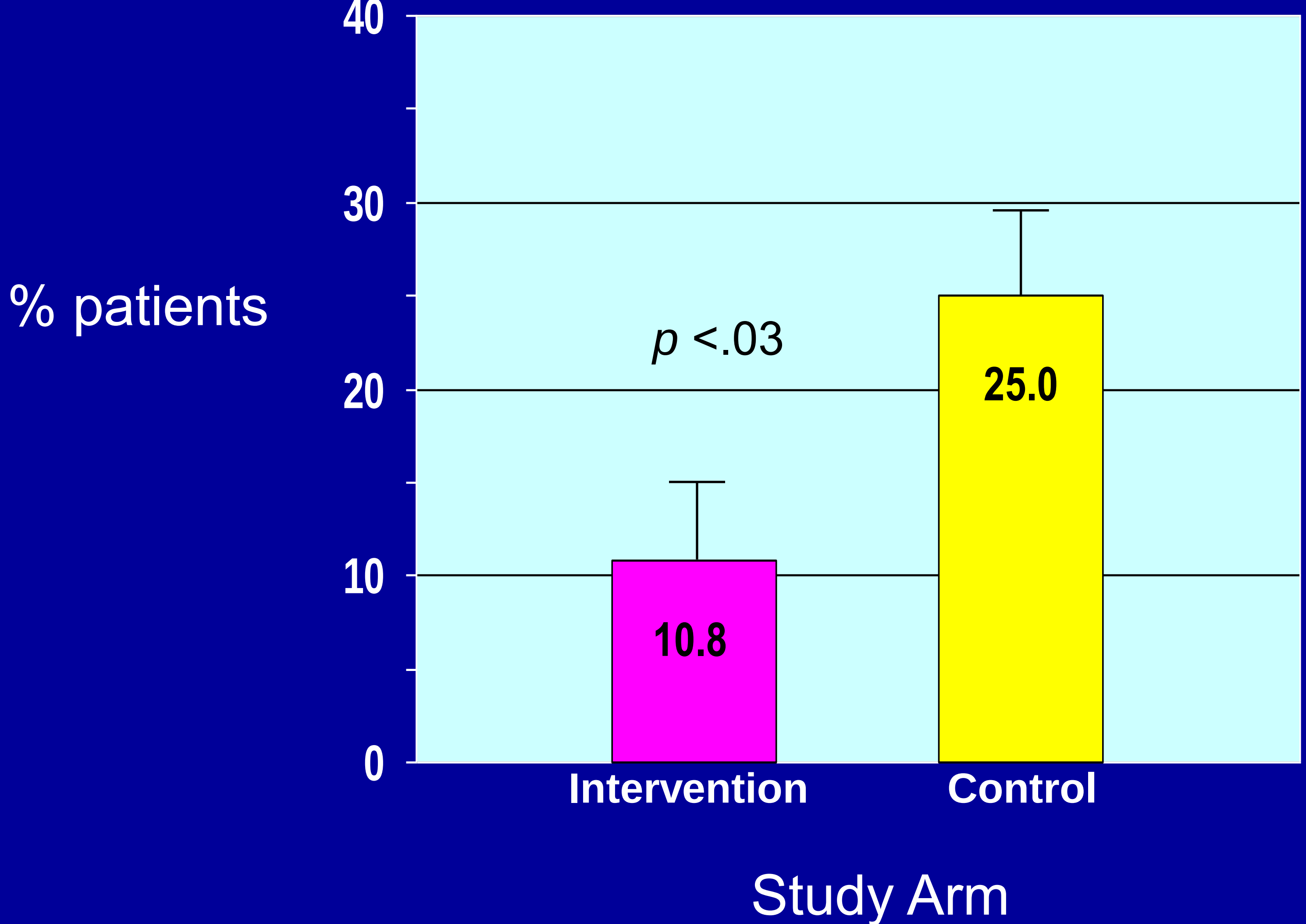
Methods



Capnography detects aberrations in ventilation not detected by RNs

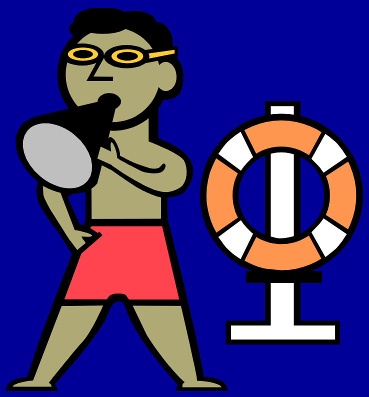
- Endoscopy RNs documented:
  - Poor ventilation 2.7%
  - Apnea 0
- Capnography indicated:
  - Alveolar hypoventilation 56%
  - Apnea 24%

Intervention Directed Capnography Lessens Arterial O_2 Desaturation



Pediatric Sedation and Patient Safety

- Q: What practice strategies can be applied to minimize risks ?



- A: Follow quality standards:
  - Put sedation plan in place
  - Ascertain ASA Status
  - Emphasize patient monitoring
  - Make wise sedation choices

Wise Sedation Choice

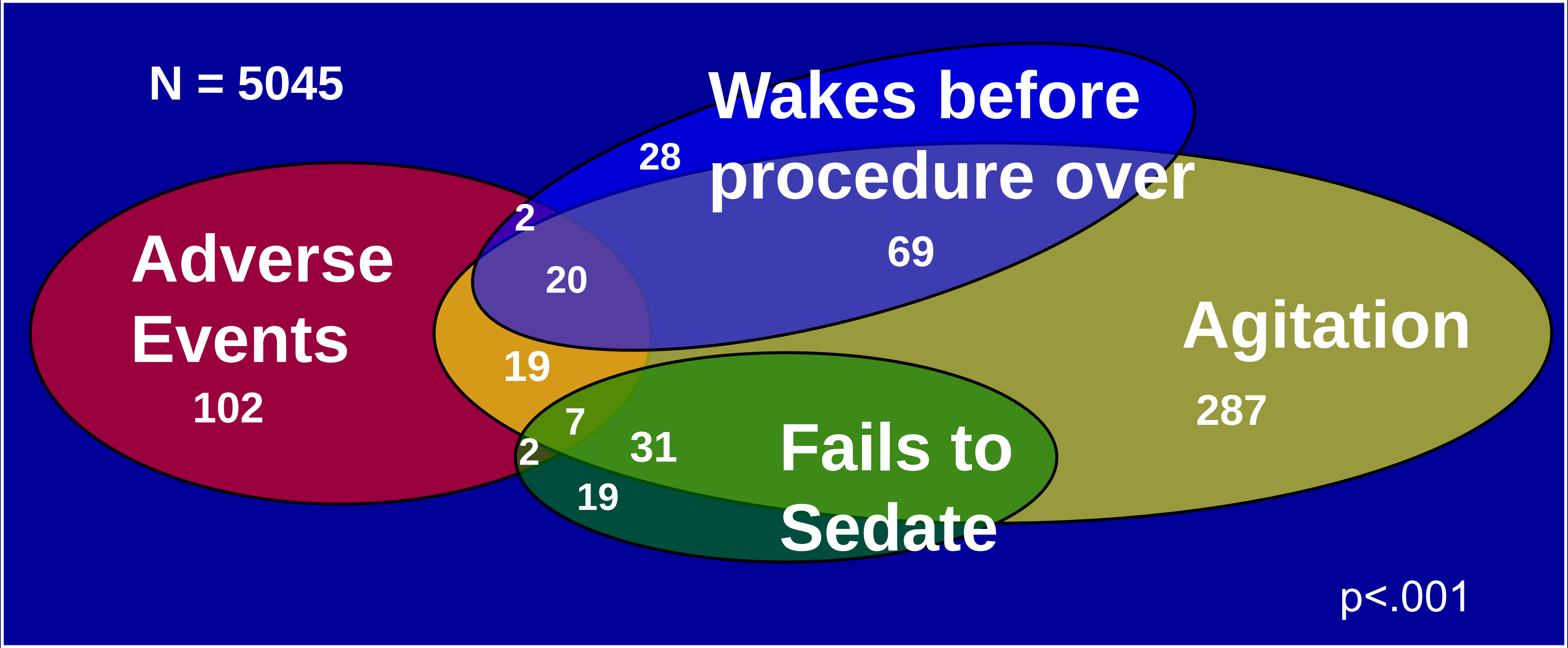
- Choice of medications must be tailored to
  - Procedure
  - Patient
- Risk-benefit approach
  - Less sedation possible incurs lowest risk
  - Inadequate sedation incurs risks as well

Agitation as risk of sedation

- Approximately 5%-25% of patients will exhibit agitation* during sedation
  - Crying, moving, requiring restraint
- Agitation more common
  - School-aged children
  - When sedation plan calls for moderate, not deep sedation

* Squires, 1995; Malviya, 1997; Thakkar, 2007; Lightdale 2007.

Agitation associated with other adverse events



- Increased staff stress
- Error-prone procedure environment

390

* Lightdale, 2009

What is a crisis?

- A time of difficulty
- Situation with potential for great da
- Non-routine circumstance
- Increase in workload
  - Pace
  - Complexity

Consequences of a Crisis

- Load shedding
  - Tasks neglected
  - Loss of situational awareness
- Confusion
- Lack of Coordination
- Increased potential for errors
  - Fixation
  - Omission

Crisis Resource Management

- 5 major elements critical to success:

*** Role Clarity**

- Event Manager
- Assign Roles

*** Communication**

- Close the Loop
- Transmit Frequent Plans

*** Personnel Support**

- Call for Help Early

*** Resources**

- Understand the Hospital System

*** Global Assessment**

- Avoid Fixation
- Keeping the “50,000 Foot View”

Simulation Based Training

- Important means of teaching CRM
- Recreates real-life crisis scenarios while monitoring the effects of human performance
  - Provides opportunities to apply principles of patient care in near real-life circumstances
- Can be used to cultivate a number of skills
  - Team performance
- All without compromising patient safety


Forward

Conclusions

- Quality Sedation involves
  - Clear and appropriate sedation plan
  - Assessing ASA Status
- Possible to employ new sedation strategies
  - None without risks
- Patient monitoring may improve detection before adverse events
- Wise sedation choices are imperative

Furthermore…

Early detection using new technologies

+

Early intervention using effective Crisis Resource Management

+

Teamwork practice using optimal tools (i.e. CRM and capnography) through simulation

=

! Improved patient safety

Thank you

Clips

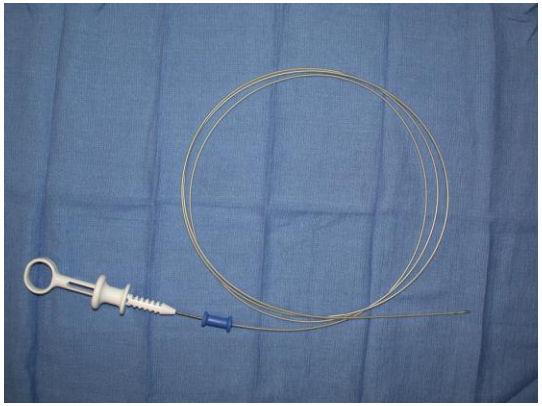
Brad Barth, MD, MPH
University of Texas Southwestern
Children's Medical Center Dallas
June 29, 2012

Clips

- Objectives
  - Improve familiarity with the different types of clips available
  - Understand how clips can be helpful in the management of pediatric patients
  - Leave Oak Brook confident that clips can be successfully utilized in your pediatric GI practice

Clips

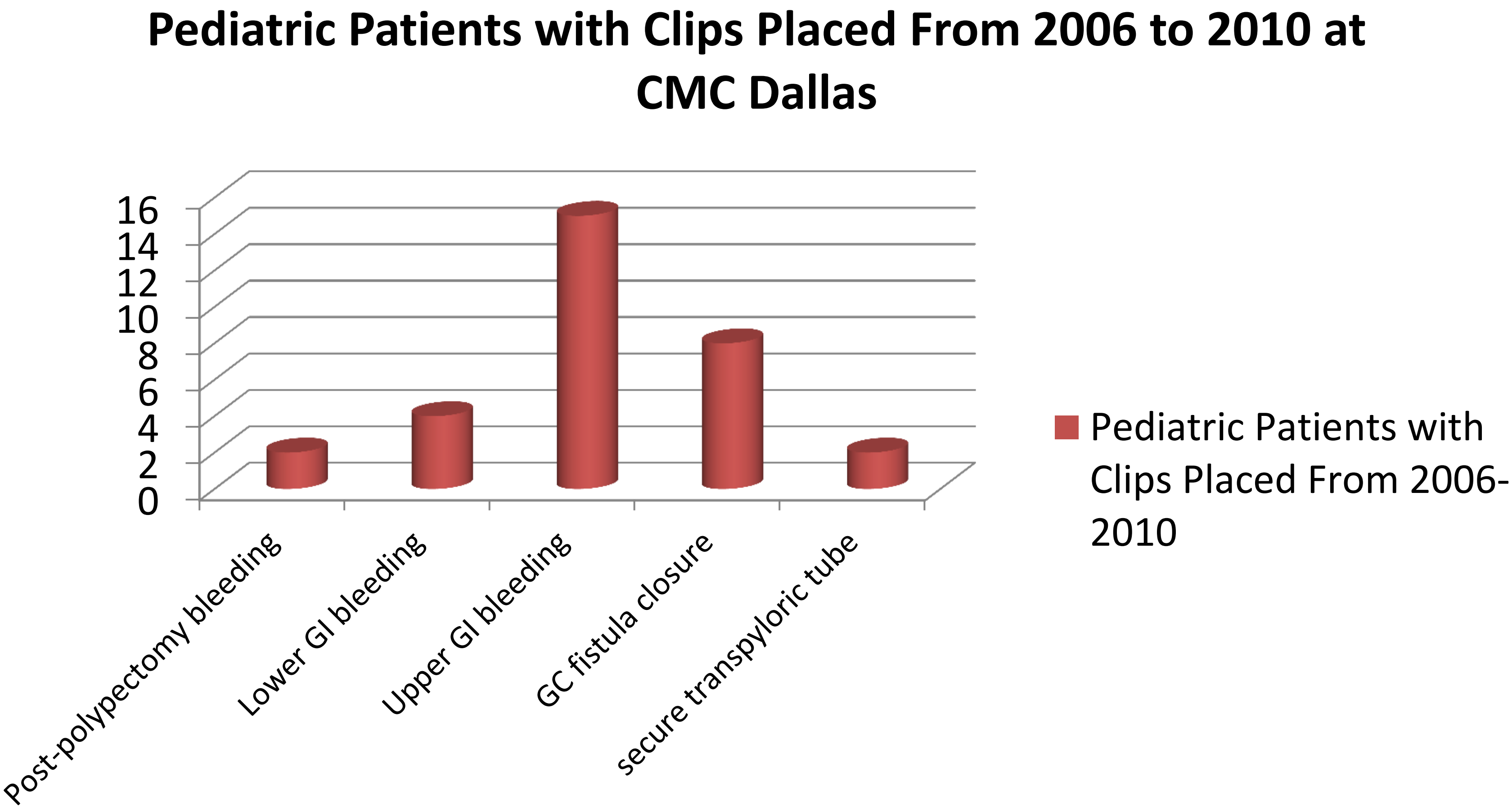
- What are they?
  - Instruments designed to accomplish approximation of tissues during GI endoscopy (ASGE TSER, GIE 2006)
  - Metallic (stainless steel)
  - Minimum 2.8 mm working channel



Clips

- Indications
  - Hemostasis
  - Closure of perforation or MW tear
  - Closure of gastrocutaneous fistula (n=3)
    - Teitelbaum et al, GIE, 2005
  - Prevention or treatment of post-polypectomy bleeding
  - Marking for surgical or IR therapy
  - Anchoring of feeding tubes to mucosa

Clips



Pediatric Patients with Clips Placed From 2006 to 2010 at CMC Dallas
16
14
12
10
8
6
4
2
0
Post-polypectomy bleeding
Lower GI bleeding
Upper GI bleeding
GC fistula closure
secure transpyloric tube
Pediatric Patients with Clips Placed From 2006-2010

Clips

- Do clips work?
  - Yes
- How well do clips work?
  - Operator dependant
- Are clips better than other hemostatic techniques?

Clips

- Are clips better than other hemostatic techniques?
- ***Comparison of the hemostatic efficacy for epinephrine injection alone and injection combined with hemoclip therapy in treating high-risk bleeding ulcers***

  Lo et al, GIE, 2006 Kaohsiung, Taiwan

	Initial Hemostasis	***Rebleed***	***Surgery***
• **Injection alone n= 53**	92 %	21 %	5 %
• **Clip + injection n=52**	98 %	3.8%	0 %
• P value	p=*0.18*	*p= .008*	*p=.02*

Clips

- Are clips better than other hemostatic techniques?
- ***Endoclips versus heater probe in preventing early recurrent bleeding from peptic ulcer: a prospective and randomized trial***

  Cipolletta et al, GIE 2001 *Naples, Italy*

	Failure	Rebleed	Death
• Heater probe n=57	8	21%	3 %
• Clips n=56	6 (size)	1.8% (p=<.002)	3 %

- On follow up all clips dislodged spontaneously by 8 weeks in all but 1 patient (7 months)

Clips

- Is *dual therapy* better than *mono-therapy*?

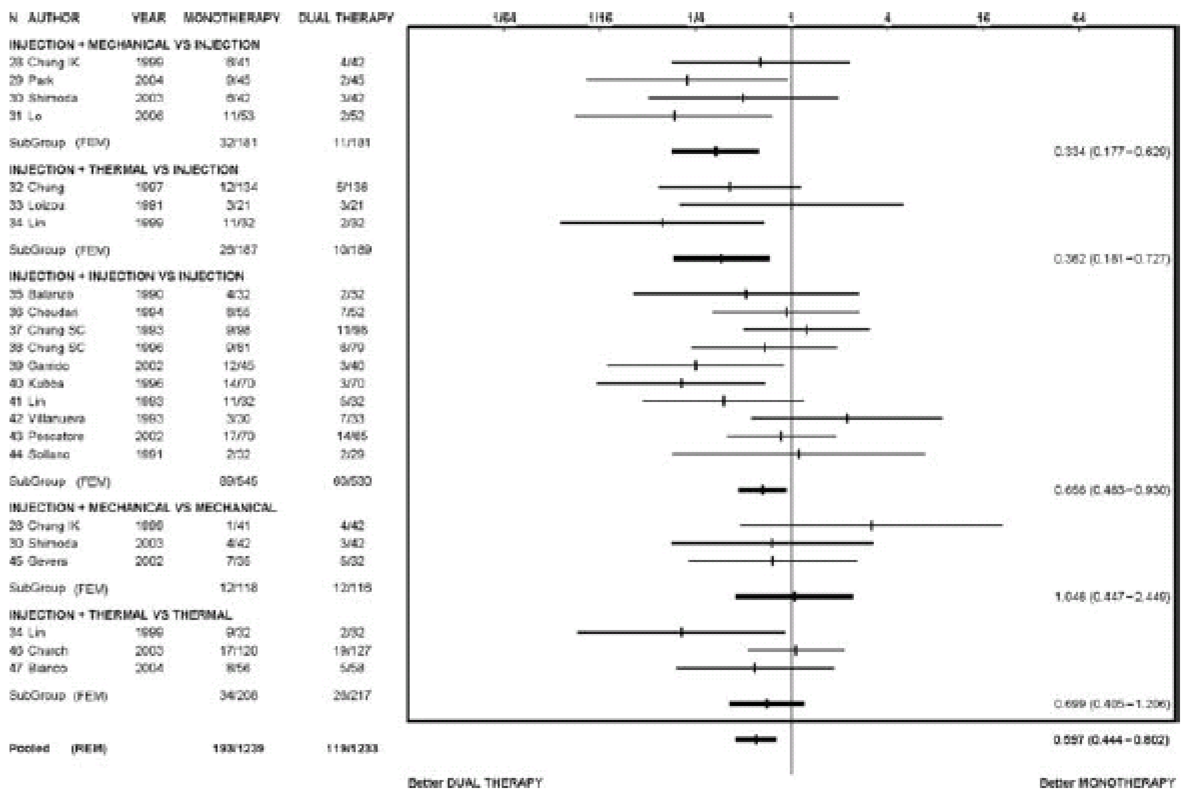


Figure 3. Meta-analysis: Efficacy of dual *versus* single endoscopic treatment. Outcome: Recurrent bleeding.

Marmo et al, Am J Gastro 2007;102:279-289

Clips

- Is *dual therapy* better than *mono-therapy*?

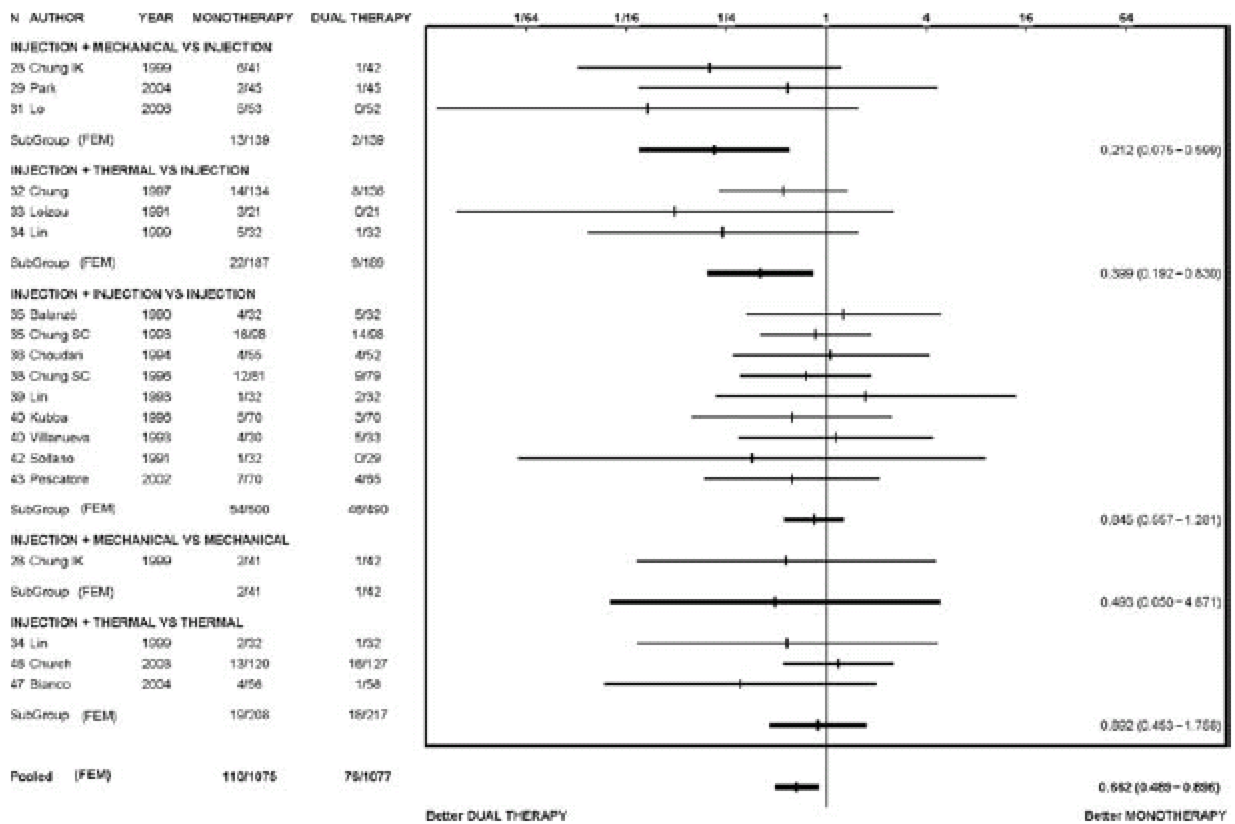


Figure 4. Meta-analysis: Efficacy of dual *versus* single endoscopic treatment. Outcome: Need for surgery.

Marmo et al, Am J Gastro 2007;102:279-289

Clips

- Is *dual therapy* better than *mono-therapy*?

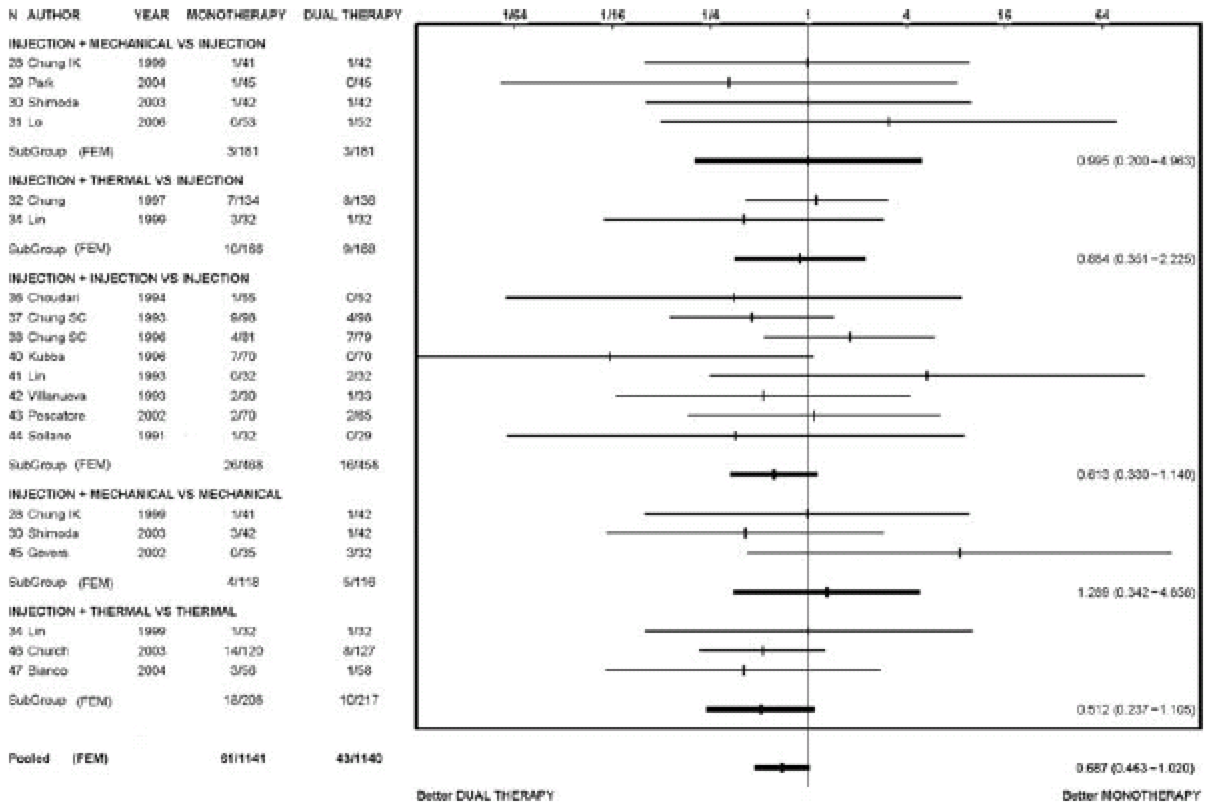


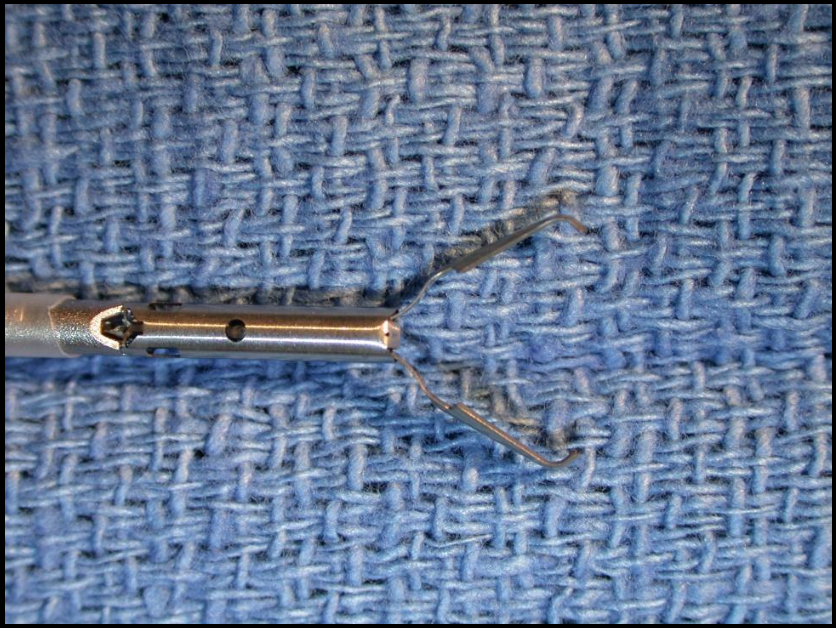
Figure 5. Meta-analysis: Efficacy of dual *versus* single endoscopic treatment. Outcome: Death.

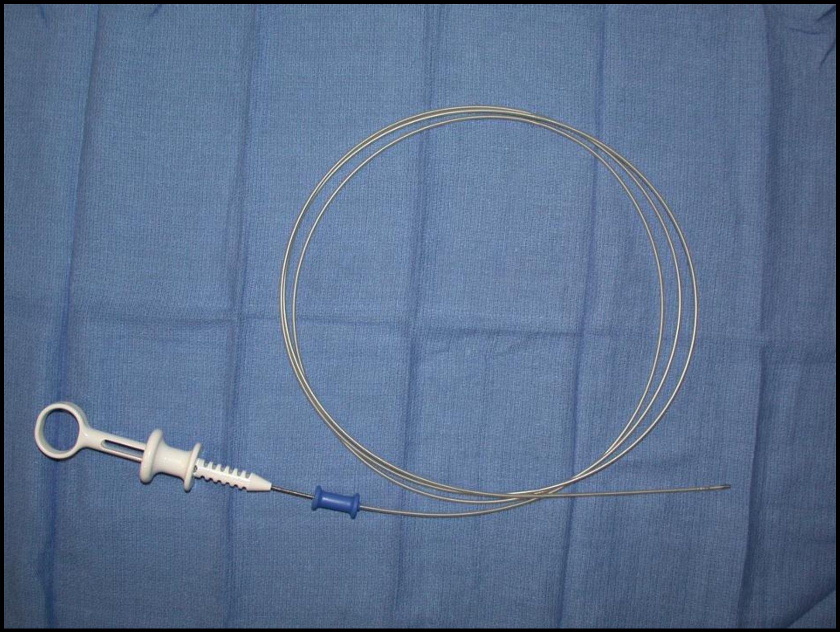
Marmo et al, Am J Gastro 2007;102:279-289

Clips

- Reusable clipping device (Olympus)
  - Tip of metal cable has a hook to which clip is attached
  - Can be rotated
  - Open from 6 to 12 mm
  - After deployment can be reloaded
  - 10 dollars per clip
  - Anecdotally, difficult to load and clean

www.bostonscientific.com
Resolution Clip

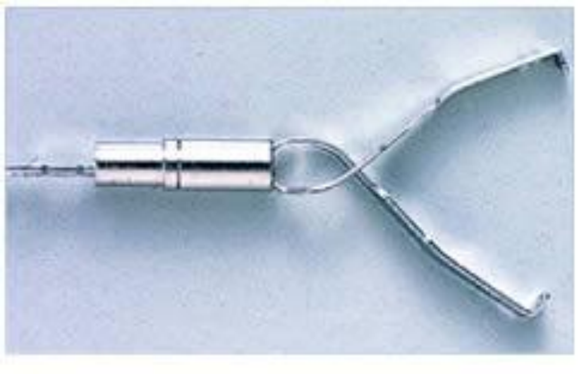




Eleven mm opening width
Difficult to rotate*
<u>Able to close up to 5 times prior to deployment enabling precise targeting</u>
One hundred fifty dollars per clip
Median retention time 4 weeks (Shin et al, GIE, 2007)

www.olympusamerica.com

Quick Clip 2



Nine or 11 mm opening width
Easily rotatable for better orientation
Care should be taken to avoid premature deployment
Seventy-five dollars per clip
Median retention time 2 weeks (Shin et al, GIE 2007)

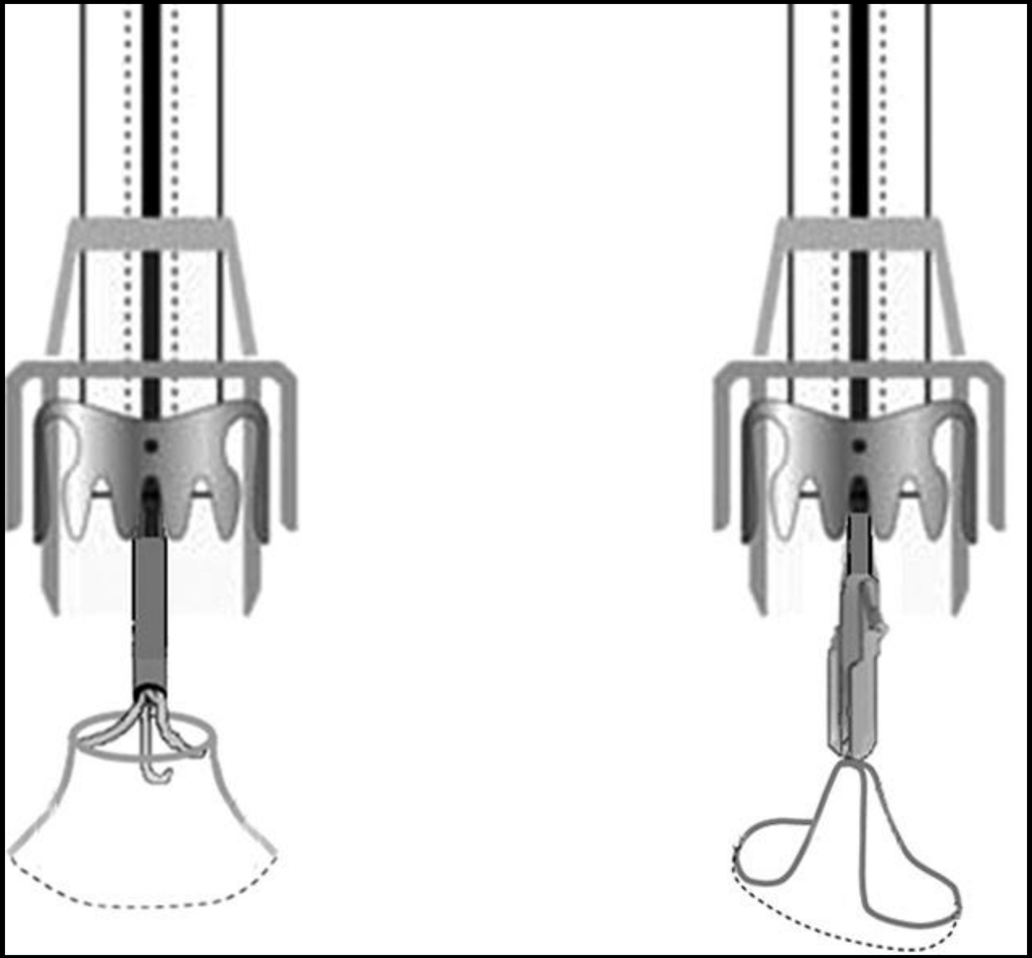
www.cookmedical.com
Tri Clip

Twelve mm opening width
Circumferential tissue approximation
Three prong design necessitates “en face” positioning
Narrow wire prongs are very malleable
One hundred twenty five dollars per clip
Median retention time < 1 week (Shin et al, GIE, 2007)

www.cookmedical.com
"Instinct"

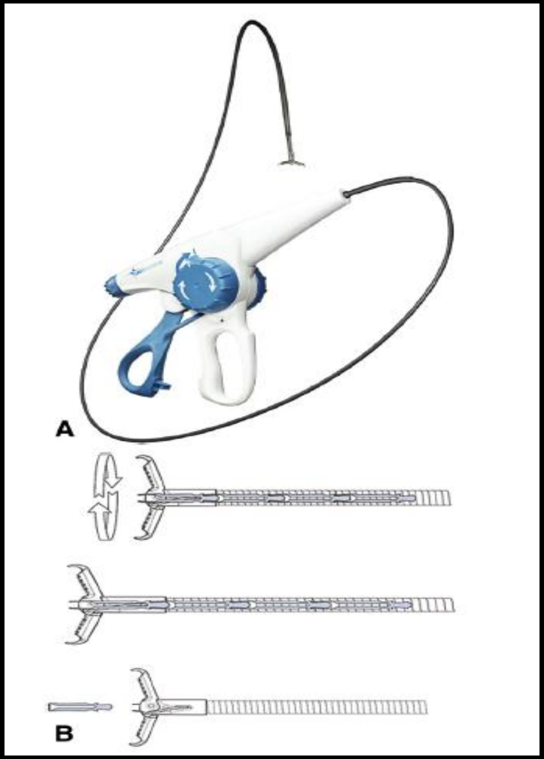
Limited release currently
16 mm opening width
1:1 rotation, either direction
Able to close up to 5 times prior to deployment enabling precise targeting
MR compatible up to 3 TESLA

Over the Scope Clips



Iacopini et al., World J Gastro, 2010

InScope multi-clip Device



Fourteen mm opening width
Four titanium clips per device (MRI compatible)
Rotatable
Can check location prior to deployment
Requires 3.2 mm channel
????available

Gottumukkala et al, GIE, 2006

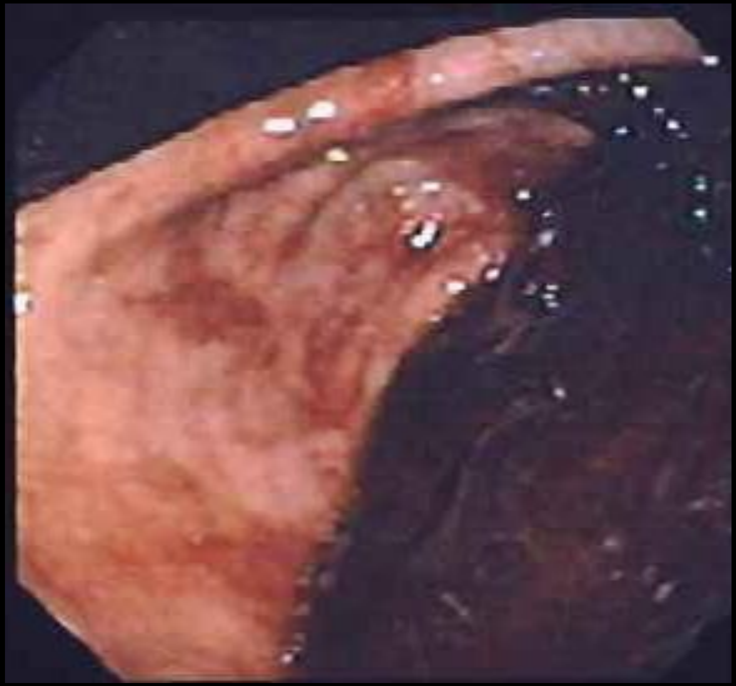
Clips

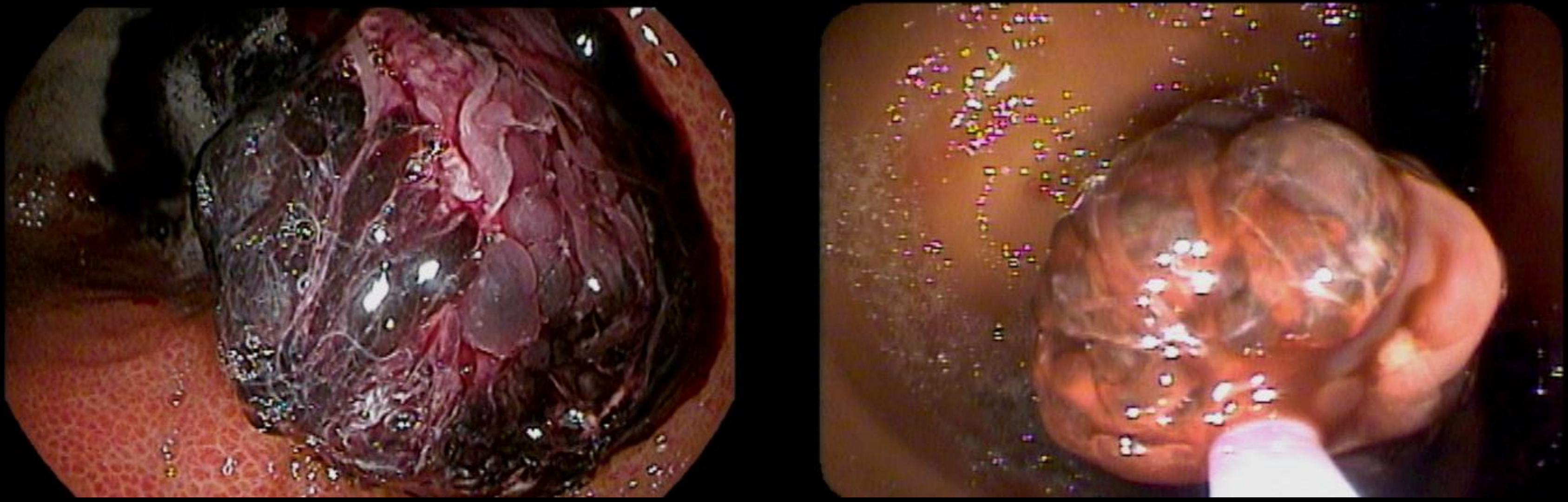
High Risk Lesions	Risk of Rebleeding without therapy
– Actively bleeding/spurting	90%
– Oozing clot	30%
– Non-bleeding visible vessel	50%
• Red, blue or white plug	
Low Risk Lesions	
– Clean ulcer base	3-5%
– Clot without oozing	10-20%

Kay, 2009
AND
Interventional and Therapeutic GI Endoscopy, 2010, Monkemuller ed, pg 40

Clips

- Tips for application
  - Practice targeting
  - CLEAR THE FIELD





Clips

- Tips for application
  - Practice targeting
  - CLEAR THE FIELD
  - +/- injection of epinephrine
  - Perpendicular or tangential approach, with pressure on either side of lesion
  - Work close to the lesion
  - Advance the scope rather than the catheter
  - Clip most difficult site FIRST

Complications

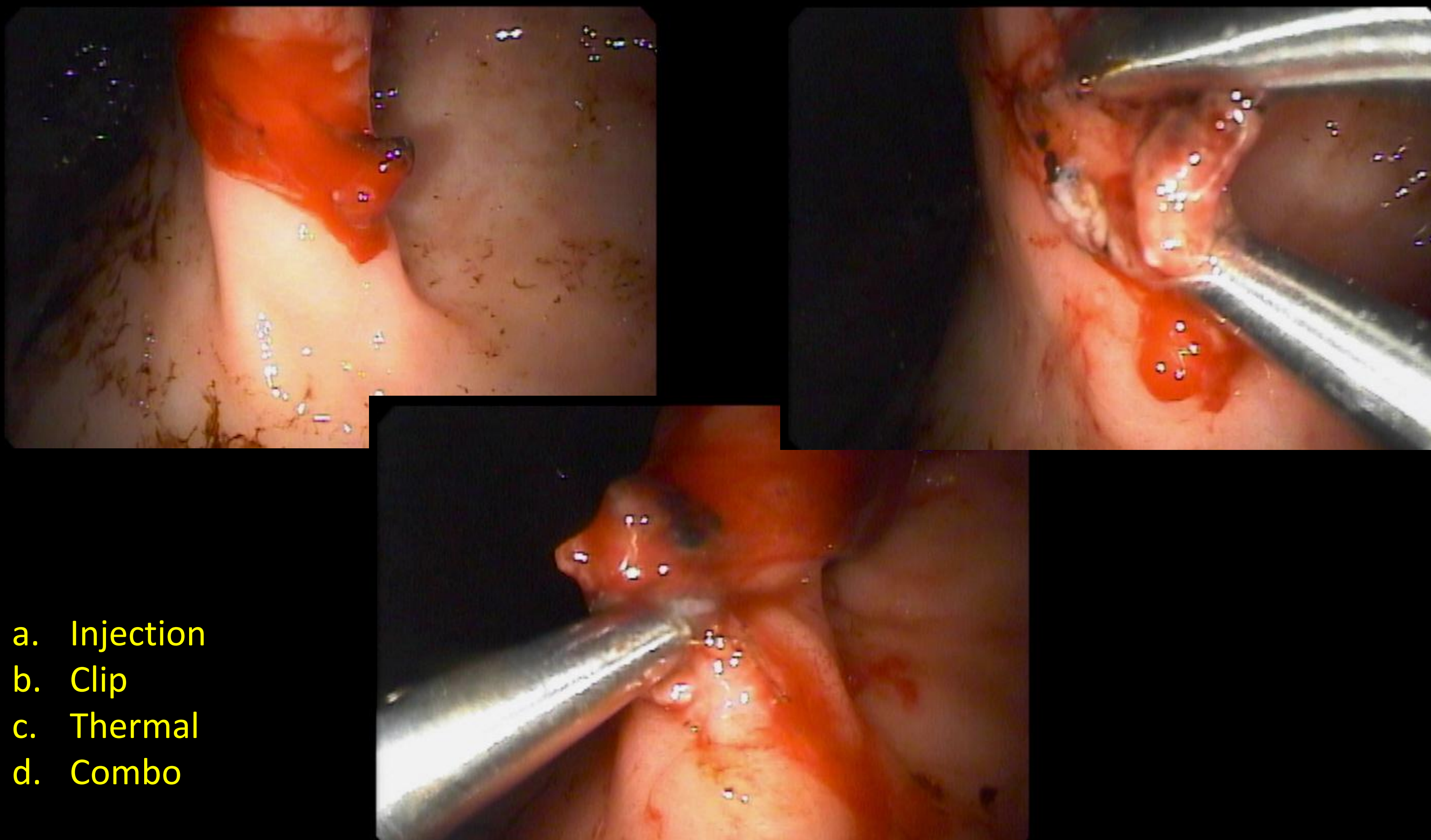
- Safe devices
- Increased bleeding due to trauma
- Perforation (rare)
- ?MRI compatible (but could be safe)

Clips and MRI

- Rupinder et al. GIE 2009
  - Resolution clip, Quick Clip 2, Tri-clip all put on pig stomach and into MRI machine
  - All had some degree of deflection
  - Only Tri-clip detached

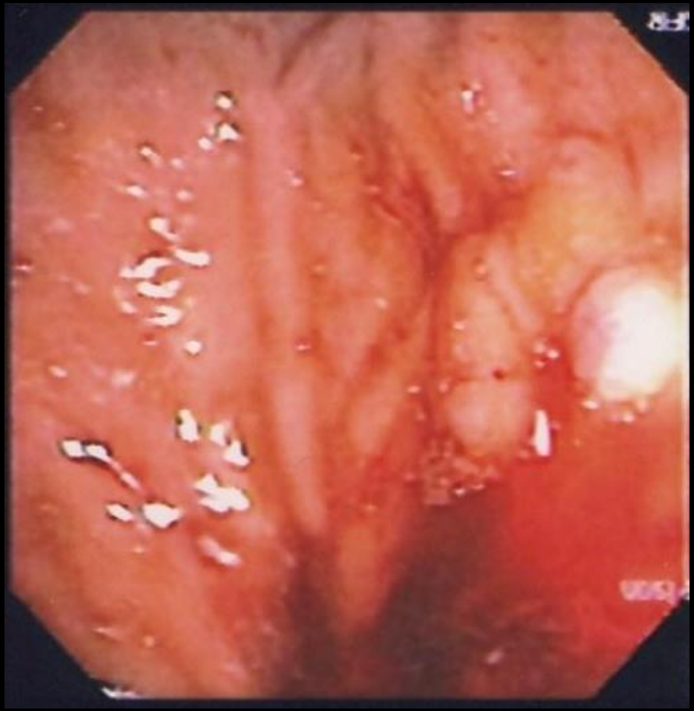
Take Home Points

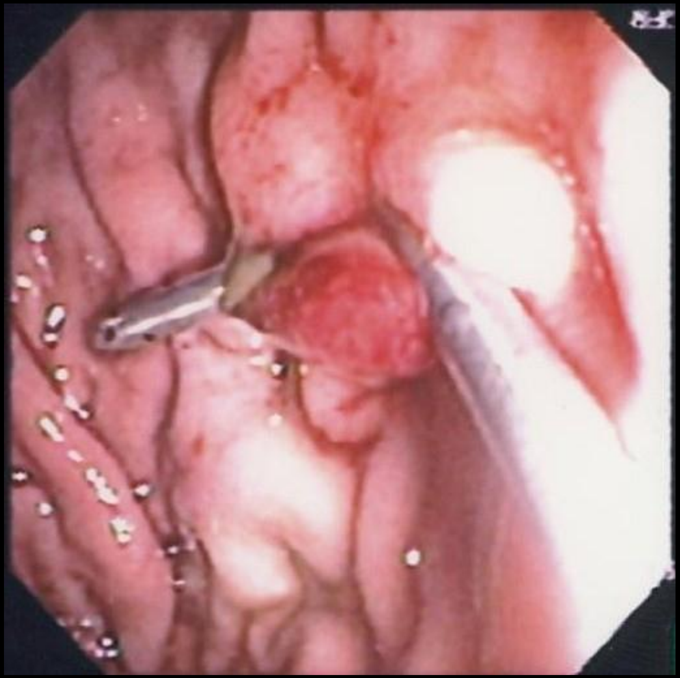
- Clips are safe, effective and reasonably easy to apply, and can be used to solve a number of endoscopically encountered problems
- All available clips require at least a 2.8 mm working channel, but can be used in any child able to tolerate this size endoscope
- Endoscopic management of gastrointestinal bleeding can be accomplished by pediatric gastroenterologists (with a little hands-on training)
- Bradley.barth@utsouthwestern.edu



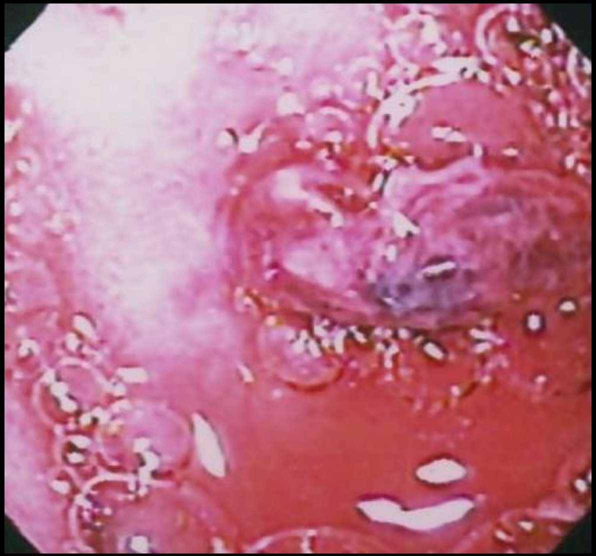
a. Injection
b. Clip
c. Thermal
d. Combo

a. Injection
b. Clip
c. Thermal
d. Combo

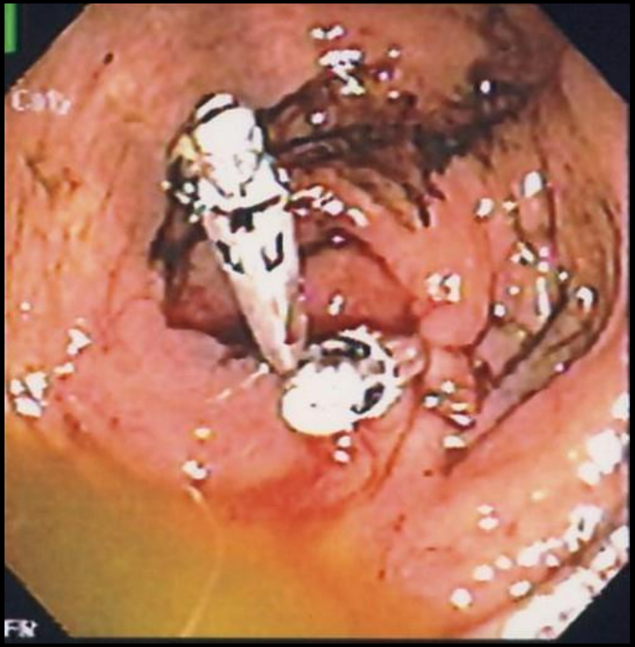




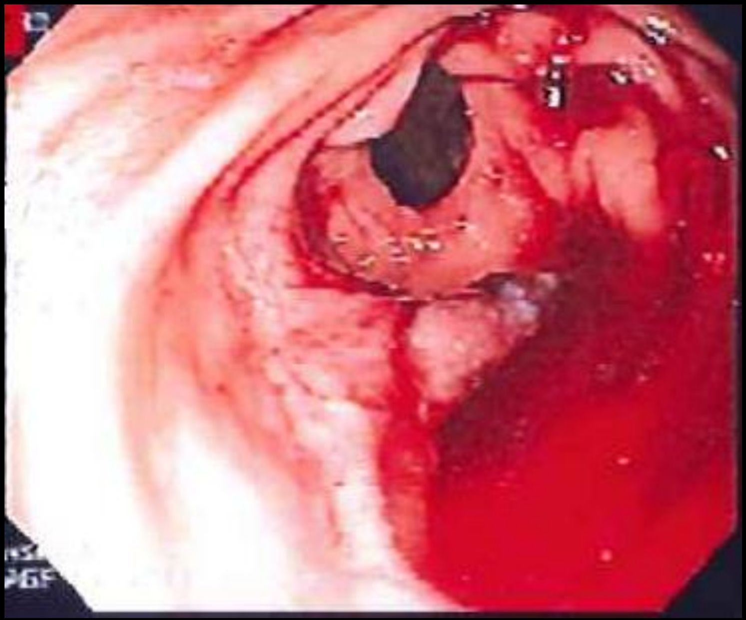
a. Injection
b. Clip
c. Thermal
d. Combo

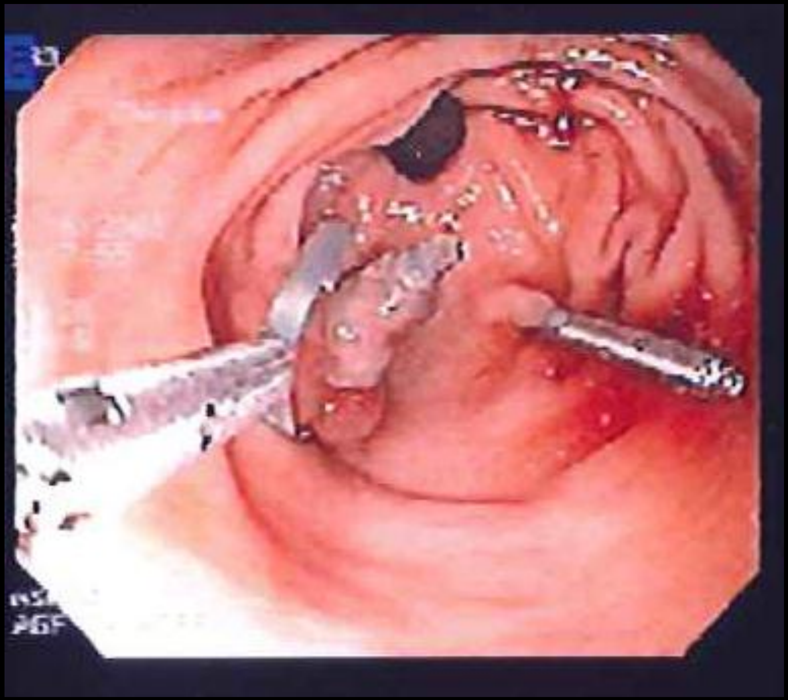


a. Injection
b. Clip
c. Thermal
d. Combo

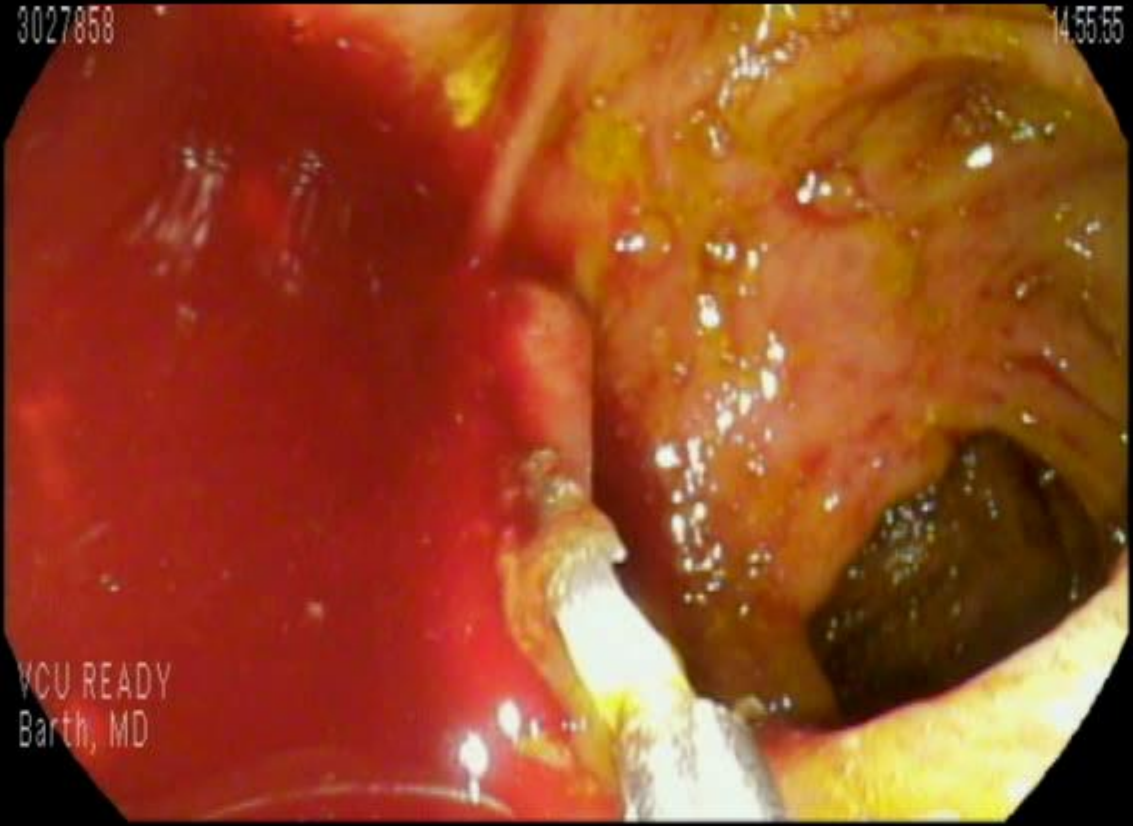


a. Injection
b. Clip
c. Thermal
d. Combo



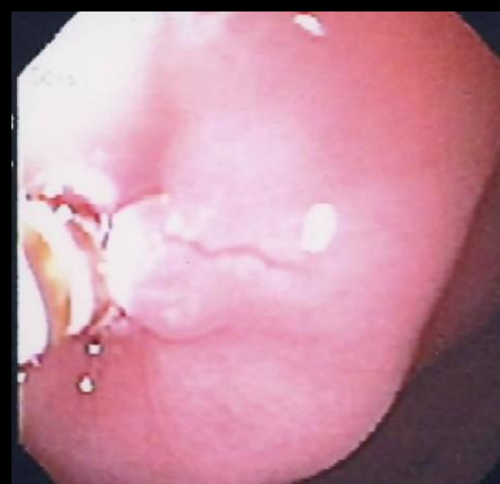


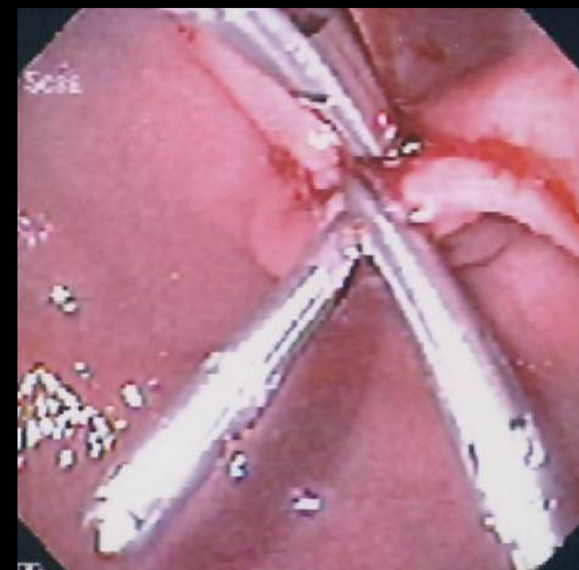
a. Injection
b. Clip
c. Thermal
d. Combo

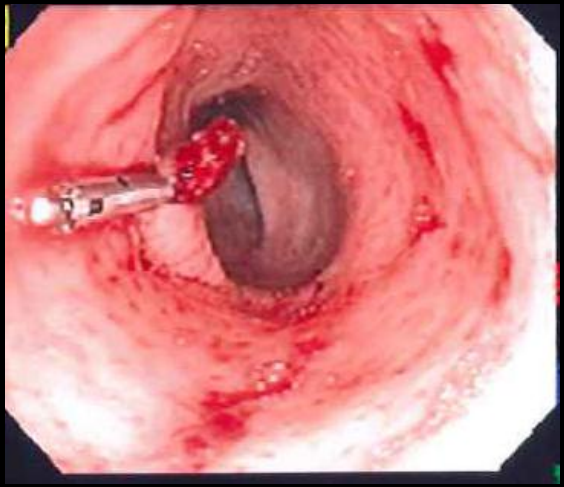

3027858
14:55:55
VCU READY
Barth, MD


3027858
15:02:28
VCU READY
Barth, MD

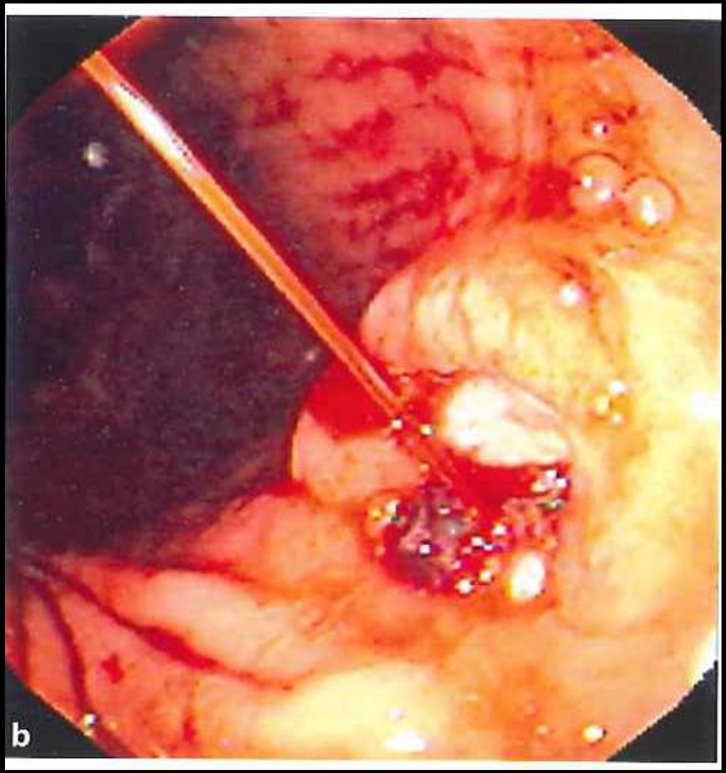
Endoscopic Closure of GC Fistula





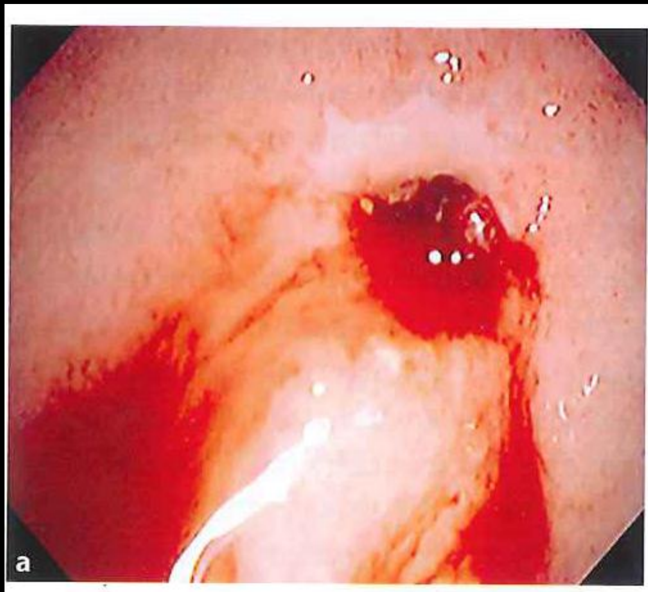


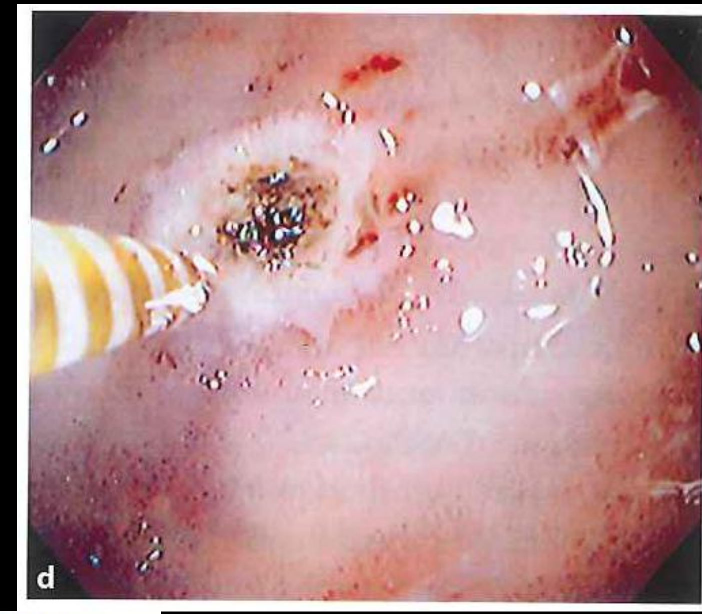
a. Injection
b. Clip
c. Thermal
d. Combo

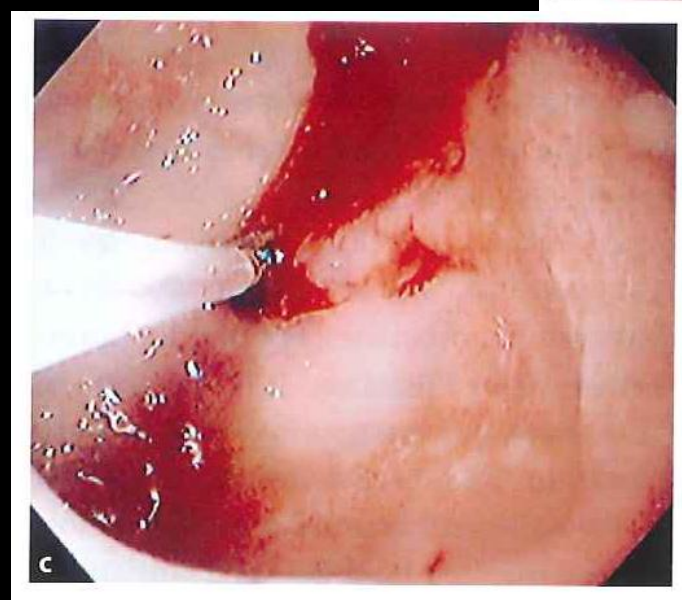


a. Injection
b. Clip
c. Thermal
d. Combo

Interventional and Therapeutic GI Endoscopy, 2010, Monkemuller

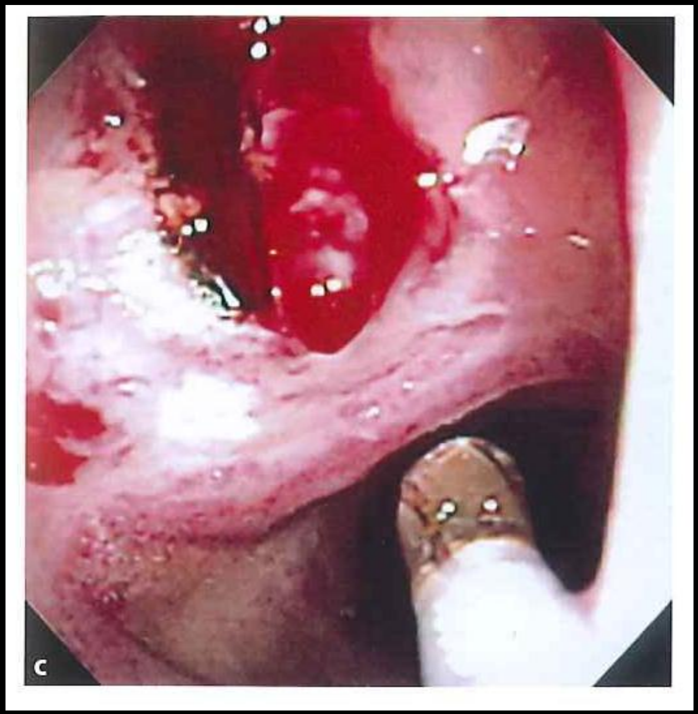


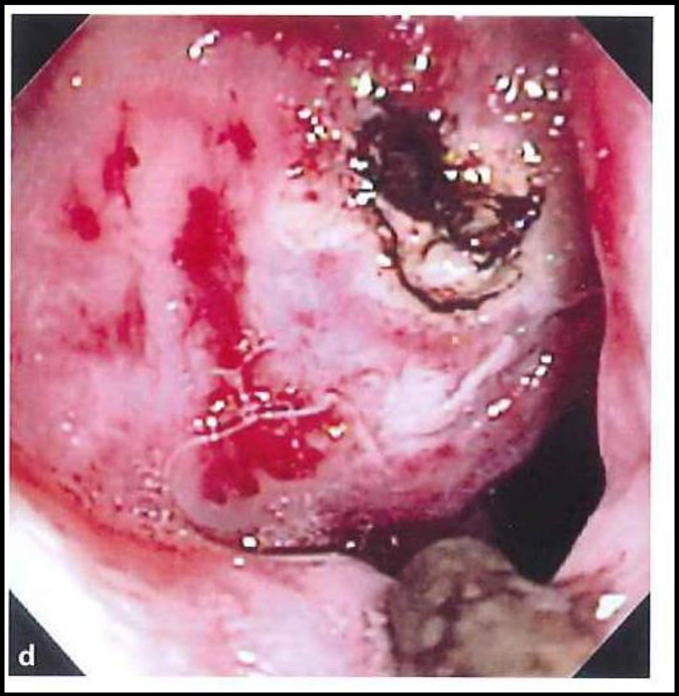




a. Injection
b. Clip
c. Thermal
d. Combo

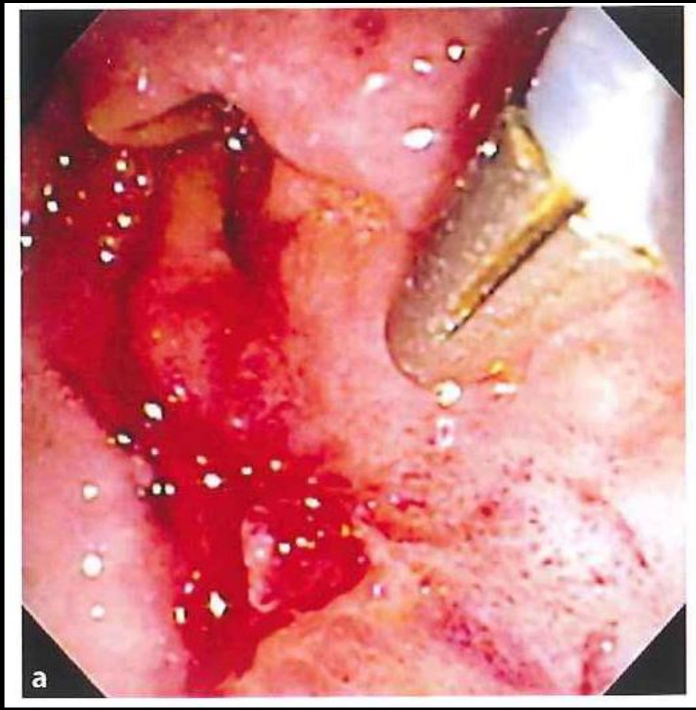
Interventional and Therapeutic GI Endoscopy, 2010, Monkemuller

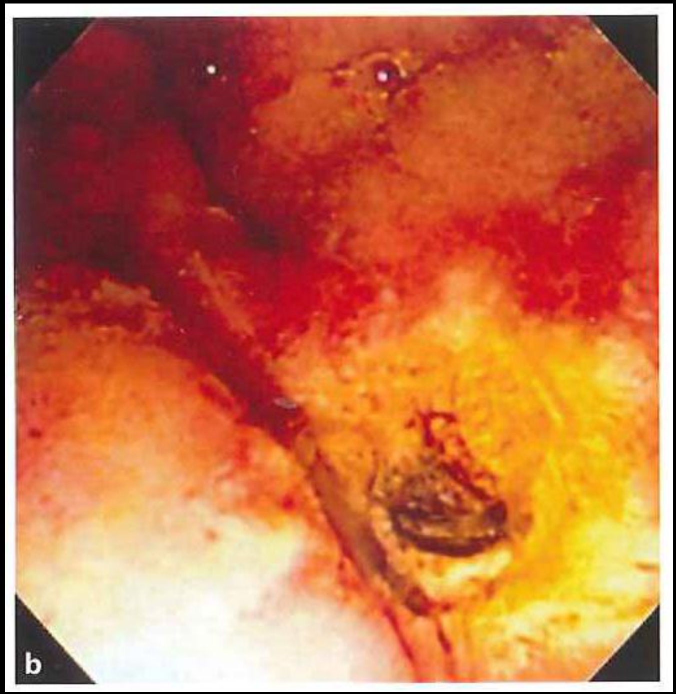




a. Injection
b. Clip
c. Thermal
d. Combo

Interventional and Therapeutic GI Endoscopy, 2010, Monkemuller



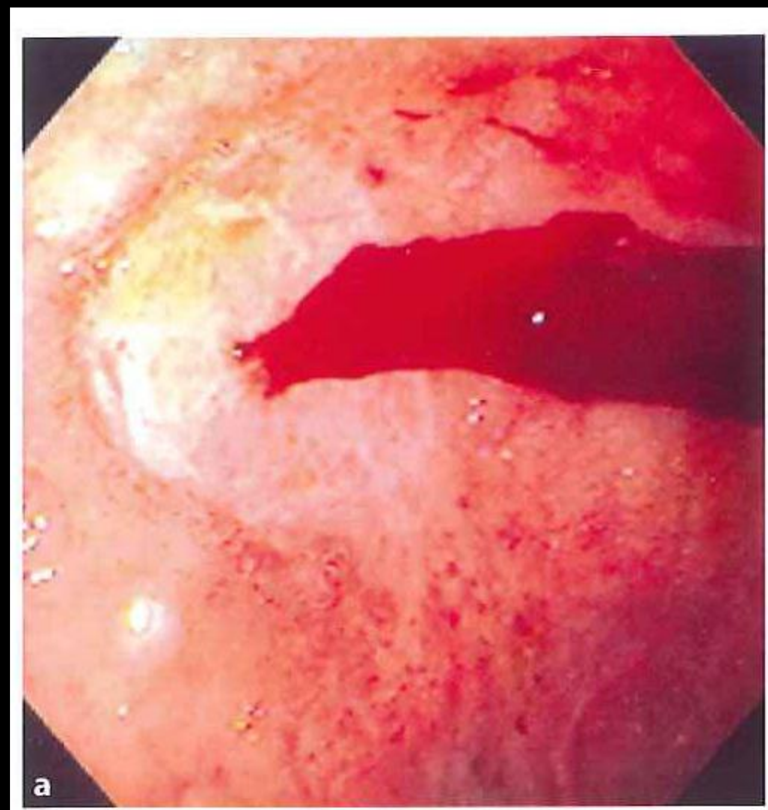


a. Injection
b. Clip
c. Thermal
d. Combo

Interventional and Therapeutic GI Endoscopy, 2010, Monkemuller

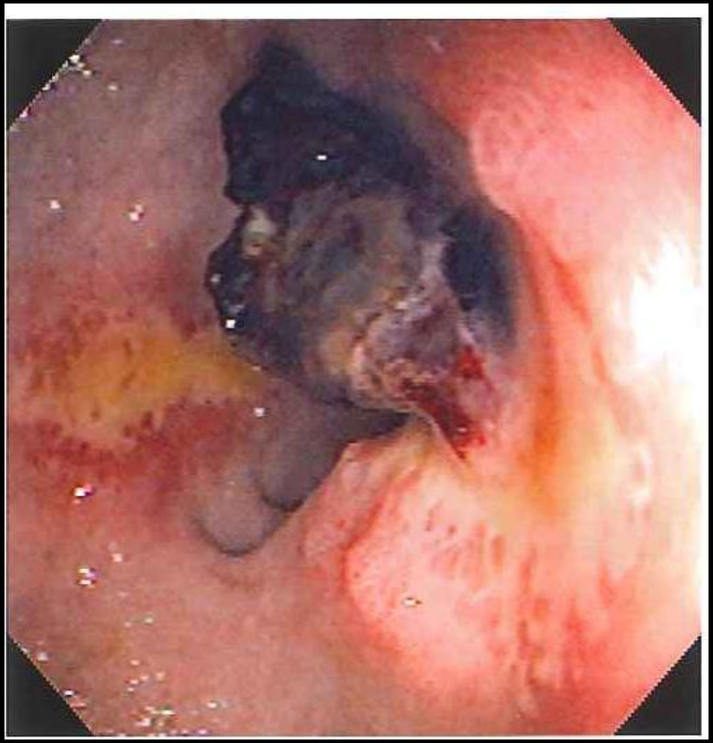
a. Injection
b. Clip
c. Thermal
d. Combo

Interventional and Therapeutic GI Endoscopy, 2010, Monkemuller



a. Injection
b. Clip
c. Thermal
d. Combo

Interventional and Therapeutic GI Endoscopy, 2010, Monkemuller



a. Injection
b. Clip
c. Thermal
d. Combo

Interventional and Therapeutic GI Endoscopy, 2010, Monkemuller