

Endoscopic Treatment: Barrett's Esophagus, HGD, CIS

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No Conflicts of Interest

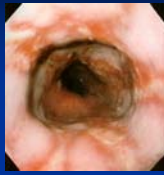
Barrett's Esophagus is Caused by Chronic GERD



Endoscopic Image of a Normal Esophagus



Barrett's Esophagus



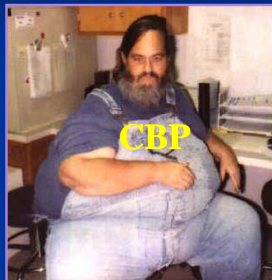
Chronic Injury



Increased Incidence of GERD



Coke



Chronic Biscuit Poisoning

Current Management of Barrett's Patients*

Intestinal Metaplasia → Surveillance (3 yrs)

Low grade dysplasia → Surveillance (6-12 mo)

High grade dysplasia → Surveillance (3 mo) vs. Esophagectomy

Adenocarcinoma → Esophagectomy vs. Palliative Care

* May Differ per Institution

HGD Treatment

Esophagectomy

Endoscopic surveillance

Endoscopic ablation

Endoscopic resection

AGS Guidelines

“esophagectomy is no longer the necessary treatment response to HGD”

Wang KK, and Sampliner RE. Updated Guidelines 2008 for the Diagnosis, Surveillance and Therapy of Barrett's Esophagus. Am J Gastroenterol. 2008;103:788-797.

Management of HGD

Endoscopic Surveillance

Barrett's "Ideal" Treatment

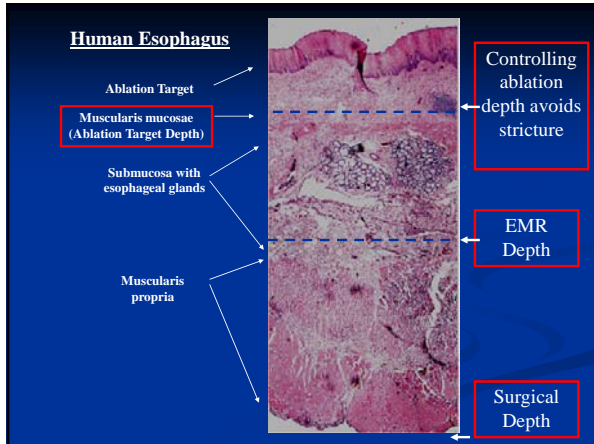
- Endoscopic approach
- Remove all intestinal metaplasia; circumferential
- Uniform, reproducible, treatment depth
- Target depth...muscularis mucosae
- No injury to submucosa or deeper structures
- Very low risk of complications
- No buried glands
- Quick and efficient; Re-treatment if required
- Prevent **Cancer** development

What We Know

- Consistent Thickness: Barrett's tissue is 500 μm in depth; range (390-590 μm)

Ackroyd R, et al., Ablation treatment for Barrett's esophagus: what depth of tissue destruction is needed? *J Clin Pathol* 1999;52:509-512.

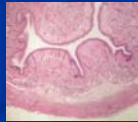
- Avoiding Damage to Muscularis Mucosae Prevents Strictures
- Consistent and complete removal of epithelium prevents buried glands

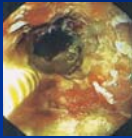


Techniques for Mucosal Ablation

- Thermal
 - Argon plasma coagulation
 - Lasers: Argon, Nd: YAG, KTP-YAG
 - Radiofrequency Ablation (HALO 360)
- Chemical
 - Photodynamic Therapy
- New Technology
 - CSA – CryoSpray Ablation

Ablation Technical Challenges

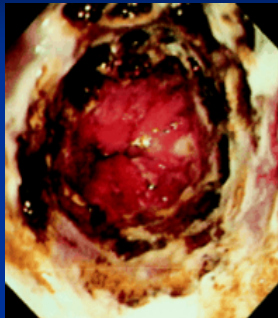
- Hand-held “Point and Shoot”
- Technically demanding
- Non-uniform ablation
- Uncontrolled power delivery
- Visual endpoint for completion
- Anatomy of distal esophagus not considered, its not round → 
- Repeat therapy is the rule



Endoscopic Ablative Therapy

Thermal

Argon Plasma Coagulation

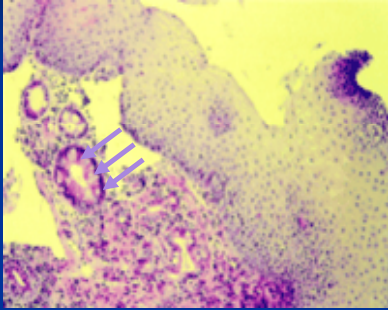


KTP-YAG Laser Therapy



Gastrointest Endosc 1999;49:8-12

Thermal Laser Ablation



Thermal Ablative Therapy

- Mucosal ablation will result in complete ablation in 1/3 pts and partial ablation in 2/3 pts
- Resultant squamous mucosa may regress, as buried glands proliferate
- Esophageal strictures occur in 1/3 of patients
- Anti-reflux therapy must be maintained to minimize repetitive injury and metaplasia
- Endoscopic surveillance with deep biopsies must be continued

Endoscopic Ablative Therapy

Chemical

Photodynamic Therapy



Barrett's Esophagus with cancer

48 hours necrosis mucosal surface

3 months normal GE junction

Complications of PDT



Photosensitivity

Stricture

Subsquamous Barrett's

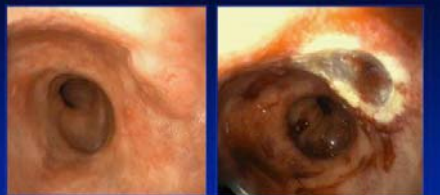
Wang KK, Nijhawan PK. Complications of photodynamic therapy in gastrointestinal disease. *Gastrointest Endosc Clin N Am* 2000; 10:487-95.

PDT Summary

- PDT effective for treatment of Barrett's HGD, but does not uniformly eradicate disease and does not absolve the need for surveillance
- PDT has a high complication rate, especially stricture formation
- PDT and stenting is effective for patients with esophageal obstruction by cancer

Endoscopic Mucosal Resection

Indications for Endoscopic Mucosal Resection

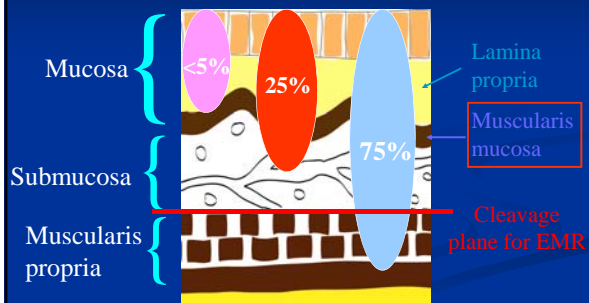


- Raised Lesions
- Focal area of HGD
- CIS (< 2 cm)
- Suspicion of malignancy
- Less 50% circumference
- T1a Cancer

Ell C. Gastroenterology 2000; 118:670-7.

Staging Esophageal Adenocarcinoma

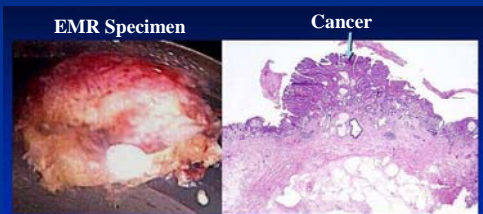
The relationship between depth of invasion and nodal metastases



Endoscopic Mucosal Resection



EMR: Mucosal Cancer



EMR: Complications

- Bleeding
 - Immediate (some series 39%) versus delayed (rare)
 - More common with gastric versus esophageal excision
- Perforation
 - Rare with submucosal saline injection and cap technique
- Stricture
 - BID PPI therapy before and after procedure
 - Limit to 1/2 - 3/4 the circumference of the esophagus
 - Incidence of 25 - 35 %

EMR for High-Grade Dysplasia or Adenocarcinoma

- 35 patients high risk for surgical resection
- 17% had failed PDT
- 60% had long-segment Barrett's
- 9% with only HGD, 91% with intramucosal cancer
- 49 EMRs, complications in 20%, no perforations
- Mean follow-up 12 months
- Local recurrence or metachronous carcinoma developed in 6 (17%)

Eli C, et al. *Gastroenterology*, 2000

EMR ± Ablation for Barrett's with HGD or Intramucosal Adenocarcinoma

- 33 patients, median Barrett's length 5 cm (4 - 8)
- 7 patients referred for esophagectomy after EMR
 - 5 for submucosal invasion, 2 for persistent/recurrent dz
- 26 patients
 - 3 EMR only
 - 23 additional therapy (often combination)
 - Repeat EMR: 13
 - PDT: 19 (5 had recurrent BE, 7 had buried IM)
 - APC: 3
- Median F/U = 19 mo
- 13 no Barrett's, 13 with Barrett's (6 with LGD)

Peters F, et al. *GI Endoscopy*, 2005

EMR Conclusions

- EMR is the only endoscopic technique that provides a pathologic specimen
- Critical to know depth of invasion to assess risk of lymph node metastases
- Factor patient age, co-morbidities, length of Barrett's, esophageal function in treatment plan
- EMR with or without ablation is a viable option in select patients with HGD or intramucosal adenocarcinoma of the esophagus

“Ideal” Treatment Objectives

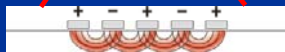
- Per-oral endoscopic approach
- Remove all IM
- Circumferential removal
- Uniform, reproducible, treatment depth
- Target depth...muscularis mucosae
- No injury to submucosa or deeper structures
- Very low risk of complications
- No buried glands
- Quick
- Re-treatment possible if required

Ablation of Barrett’s Esophagus using the HALO³⁶⁰ System and HALO⁹⁰ System

How Ablation with the HALO³⁶⁰ System Works



HALO³⁶⁰
Ablation Catheter



Balloon Based Bipolar Design

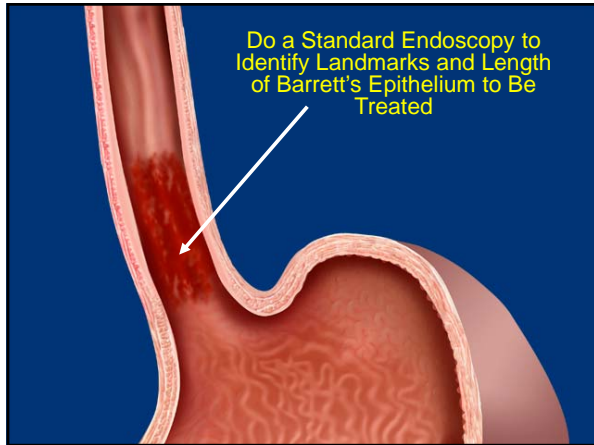
- Allows for 360 Degree Ablation of Targeted Tissue creating an even target -
300 W (10 J/S²) - 300 msec
- Eliminates “Point and Shoot”;
- Energy Density and Ablation Depth Control of less than 1000 um -
prevent strictures or perforations

HALO⁹⁰ System

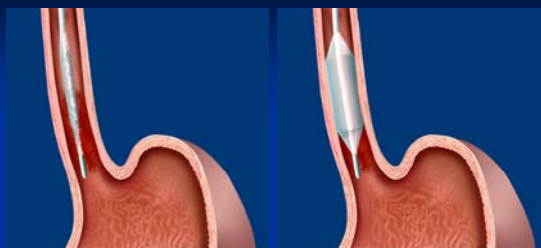
- Scope-mounted endoscopic ablation
- Focal ablative therapy
- Controlled depth
 - Energy density, electrode geometry
- Primary therapy short segment Barrett's
- Touch-up for focal residual disease after ablation or other therapies*



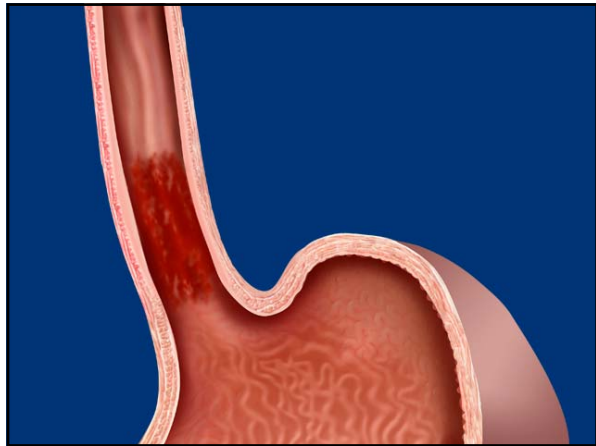
Do a Standard Endoscopy to Identify Landmarks and Length of Barrett's Epithelium to Be Treated

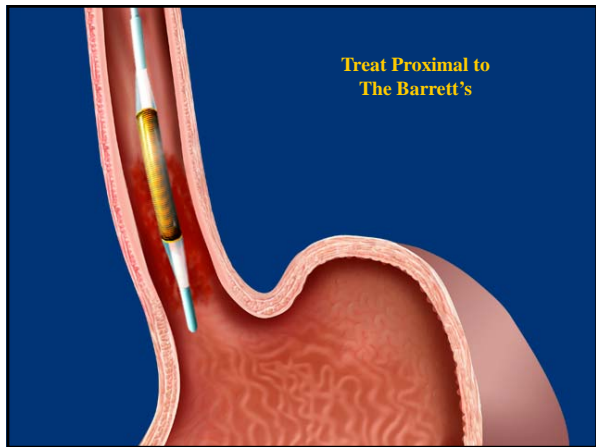


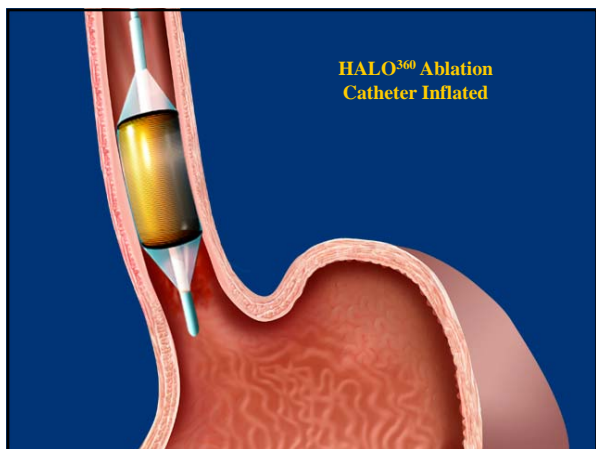
Sizing Balloon

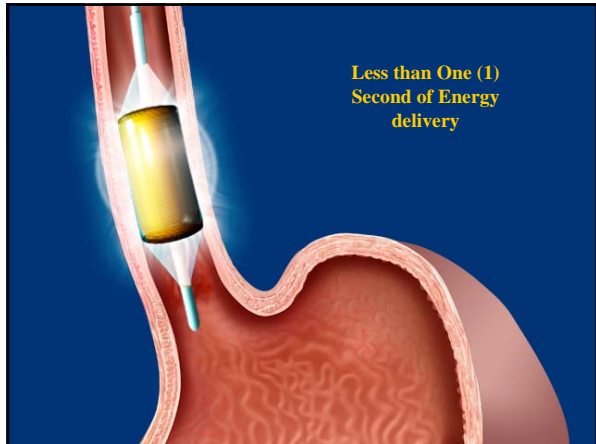


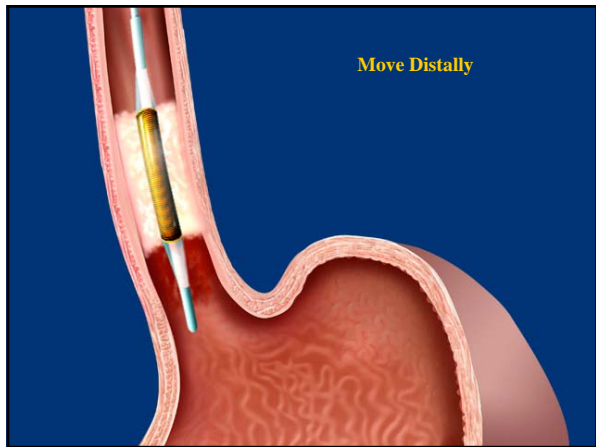
Once inflated, the HALO³⁶⁰ Sizing Balloon Automatically Measures the Inner Diameter of the Esophagus

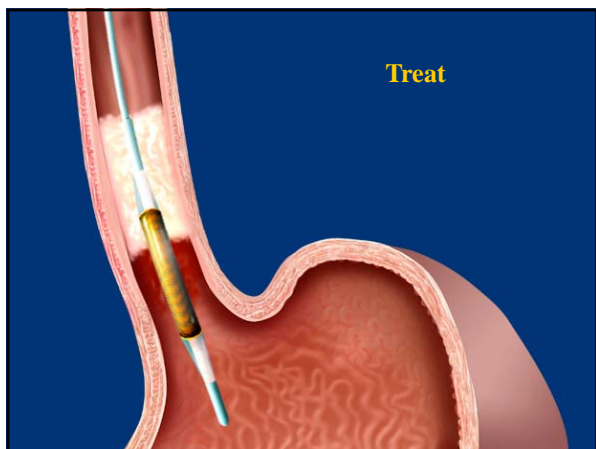


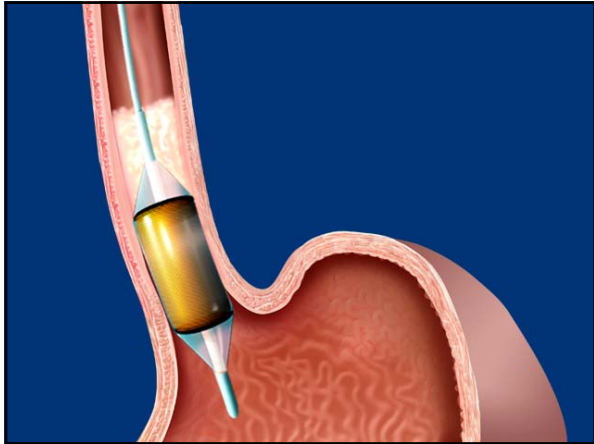


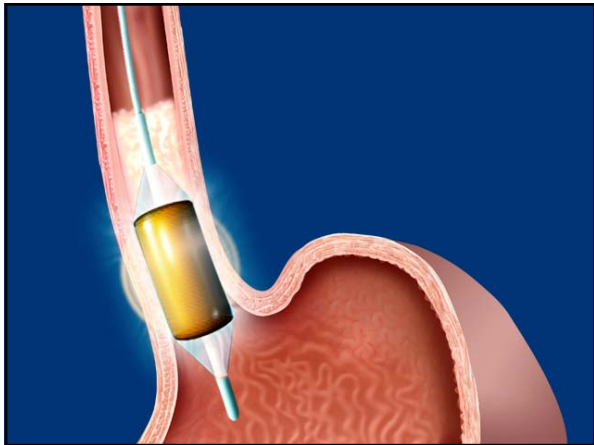












Immediate Endoscopic Effect

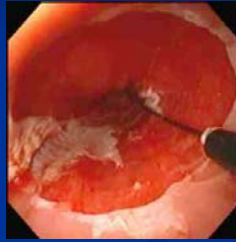
Margin of Treatment View in Treatment Area

Both images are after one application of energy

Endoscopic Appearance



Baseline, 4 cm IM



Immediate Slough

46

Complete Response after HALO³⁶⁰



Clinical Trials

Endoscopic Ablation of Intestinal Metaplasia Containing High-Grade Dysplasia in Esophagectomy Patients Using A Balloon-Based Ablation System (HALO³⁶⁰ System)

C. Daniel Smith¹, Pablo A. Bejarano², W. Scott Melvin³, Marco G. Patti⁴, Raman Muthusamy⁵, Brian J. Dunkin⁶

1. Emory University School of Medicine, Department of Surgery
2. University of Miami School of Medicine, Department of Pathology
3. The Ohio State University, Center for Minimally Invasive Surgery
4. University of California San Francisco, Department of Surgery
5. University of California San Francisco, Division of Gastroenterology
6. University of Miami School of Medicine, Department of Surgery

Results

Eradication of HGD epithelium

- Ablation zone is sharply demarcated
- Max ablation depth is muscularis mucosae
- Deepest effect occurred at highest dose
 - SM edema
 - 14 J/cm² (4x)
- Complete eradication of HGD in 9 of 10 zones
 - Single failure was focal and occurred at low dose (10 J/cm², 2x) likely due to incomplete overlap
- **Treatment should be with 12J/cm² (2 app)**

Radiofrequency Ablation of Barrett Esophagus Containing High Grade Dysplasia

Bergman, Jacques J.¹; Sondermeijer, Carine¹; Peters, Femke P.¹; Curvers, W.L.¹; ten Kate, Fiebo J.²; Fockens, Paul¹

1. Gastroenterology and Hepatology, Academic Medical Centre Amsterdam, Amsterdam, Netherlands. 2. Pathology, Academic Medical Centre Amsterdam, Amsterdam, Netherlands

Results

- 23 patients, HGD/Cancer (13 previous EMR)
- Ablation procedures
 - Circumferential (mean 1.5 sessions)
 - Focal (mean 2.6 sessions)
- No stricture formation or serious adverse events
- Outcomes
 - CR Dysplasia = 96% (22/23 patients)
 - CR IM = 92% (21/23 patients)
 - No stricture formation or serious adverse events
 - Eradication of genetic markers (FISH and IHC)
 - Preservation of esophageal physiology

AIM Clinical Trial

Sharma VK, Fleischer DE, Wang KK, Overholt B,
Lightdale C, Kimmey M, Reymunde A, Santiago N,
Chuttani R, Pleskow D, Chang K

Results

- 102 patients non-dysplastic IM
- Dosimetry phase: 10 J/cm²
- Effectiveness phase
 - 70% CR at 1 year
 - 85% CR at 2.5 years
- No strictures or buried glands
- Over 6000 biopsy fragments
 - Central pathology lab review
- Final target: 100% CR

Focal Ablation for Treatment of Dysplastic and Non-Dysplastic Barrett's Esophagus: Safety Profile and Initial Experience with the HALO90 Device in 508 Cases

Richard Rothstein, Kenneth Chang, Bergein F Overholt, Jacques Bergman, Nicholas Shaheen

Results

- 508 patients with Barrett's esophagus
 - HGD, LGD, non-dysplastic
 - 182 trial cases, 326 non-trial cases
- Focal ablation using HALO⁹⁰ device
- Results (safety and tolerability)
 - No strictures or serious adverse events
 - 14 day diary scores (post-ablation) show only mild and transient symptoms

Radiofrequency Ablation in Barrett's Esophagus with Dysplasia

Nicholas Shaheen, Prateek Sharma, Bergein Overholt, Herbert Wolfsen, Kenneth Wang, David E Fleischer et al.

NEJM 2009;360:2277-88

Results

- 127 patients with Barrett's esophagus
 - Multicenter study – 19 centers
 - Randomized 2:1 ablation vs sham procedure
 - Stratified length BE < 4 cm > 8 cm; LGD or HGD
- Ablation using HALO³⁶⁰ device (12 J)
 - Omeprazole 40mg BID 12 months
 - Could receive up to 4 treatment sessions at Baseline, 2, 4, and 9 months
- EGD with Bx (4 quad every 1 cm)
 - Every 3 months for HGD
 - At 6 and 12 months for LGD

Results

12 months Follow up

Variable	Ablation	Sham
Low Grade Dysplasia	91%	23%
High Grade Dysplasia	81%	19%
Intestinal Metaplasia	77%	2%
Disease Progression	4%	16%
Cancer	1%	9%

Complications – More chest discomfort, GI bleed (1%), stricture (6%)

Endoscopic Radiofrequency Ablation for Barrett's Esophagus: 5-year Outcomes From a Prospective Multicenter Trial

David E Fleischer, Bergein Overholt, Prateek Sharma, Kenneth Wang, et al.

Endoscopy 2010;42;862-3

Results

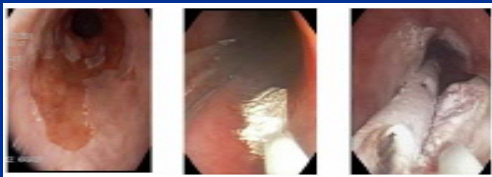
- 50 patients with Barrett's esophagus ND (5 yrs)
 - Multicenter study – 19 centers
 - Randomized 2:1 ablation vs sham procedure
 - Stratified length BE < 6 cm
- Ablation using HALO³⁶⁰ device (12 J)
 - Omeprazole 40mg BID 12 months
 - Could receive up to 4 treatment sessions at Baseline, 2, 4, and 9 months
- EGD with Bx (4 quad every 1 cm) annually
- CR – IM 92%
- Focal NDBE – 8% - ReBarrx – 100% CR-IM
- Median duration of CR-IM 4.2 years

RFA Summary

- RFA effective for treatment of Barrett's HGD and non-dysplastic Barrett's (> 80 – 100%)
- Minimal complications – Stricture rate < 0.1%
- Reproducible and effective treatment
- User friendly application
- Outpatient procedure
- Minimal capital cost
- Long term follow up warranted (> 5 years)

Cold Ablation System

CSA - CryoSpray Ablation



Liquid nitrogen (-196 °C)
4 – 10 sec sprays

The Society of Thoracic Surgeons Practice Guideline Series: Guidelines for the Management of Barrett's Esophagus With High-Grade Dysplasia

Hiran C. Fernando, MD, Sudish C. Murthy, MD, PhD, Wayne Hofstetter, MD, Joseph B. Shrager, MD, Charles Bridges, MD, ScD, John D. Mitchell, MD, Rodney J. Landreneau, MD, Ellen R. Clough, PhD, and Thomas J. Watson, MD

Boston University School of Medicine and Department of Cardiothoracic Surgery, Boston Medical Center, Boston, Massachusetts; Thoracic and Cardiovascular Surgery, Cleveland Clinic, Cleveland, Ohio; Stanford University School of Medicine, Stanford, California; Department of Thoracic and Cardiovascular Surgery, University of Texas MD Anderson Cancer Center, Houston, Texas; Division of Cardiovascular Surgery, University of Pennsylvania Health System, Philadelphia, Pennsylvania; Division of Cardiothoracic Surgery, Department of Surgery, University of Colorado School of Medicine, Denver, Colorado; University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; The Society of Thoracic Surgeons, Chicago, Illinois; Division of Thoracic and Foregut Surgery, Department of Surgery, University of Rochester School of Medicine and Dentistry, Rochester, New York

The management of Barrett's esophagus with high-grade dysplasia is controversial. The standard of care has traditionally been esophagectomy. However, a number of treatment options aimed at esophageal preservation are increasingly being utilized by many centers. These esophageal-sparing approaches include endoscopic surveillance,

mucosal ablation, and endoscopic mucosal resection. In this guideline we review the best evidence supporting these commonly used strategies for high-grade dysplasia to better define management and guide future investigation.

(Ann Thorac Surg 2009;87:1993-2002)
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Current Management of BE Summary

- Individualize patients
- Multidisciplinary approach - Cost
 - GI Medicine
 - Surgery
 - Pathology
 - Preventive Medicine
- Work-up
 - EGD, Motility study, 24 - ph study, EUS
- Patient education - Long-term Follow-up
- Support Group - Swallowing Center
