Radiofrequency Ablation for Barrett’s Esophagus with HGD

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Learning Objectives:

- What is Radiofrequency Ablation?
- What are the indications for use of RFA in Barrett’s?
- What are the clinical results?
- What are the risks and potential limitations?
What is Radiofrequency Ablation?

• Implies destruction and, ultimately, removal of tissue
• Mechanism: thermal energy to promote coagulative necrosis
• Endpoint is irreversible cell injury and death
• Seminal observation: BE, when ablated in an anacidic milieu, regenerates squamous epithelium
RF Electrode Technology

- High power
- Rapid delivery (very short “on” time)
- Energy density control
- Tight electrode spacing
Human Esophagus

Ablation Target

Muscularis mucosa
(Ablation Target Depth)

Submucosa with esophageal glands

Muscularis propria

Controlling ablation depth avoids stricture

EMR Depth

Surgical Depth
Radiofrequency Balloon-Based Ablation Therapy (BARRx)

HALO 360 °

- Uniform circumferential ablation
- 3 cm in length
- Individualized with sizing balloon
- Precise energy delivery in < 1 sec
HALO 360 RFA
HALO$^{90}$ Device
How does RFA compare with other therapies for BE with HGD/ImCa?

- **Ablation**
  - Thermal (MPEC, LASER, APBC)
  - Chryotherapy
  - Cytotoxic (PDT)

- **Resection**
  - Endoscopic Mucosal Resection (EMR)
    - Provides histologic specimen for inspection

- **Reliable, reproducible, broad field, real time, endoscopically directed, immediately observed results, efficiently (time & cost)**
Why Do We Care About BE?

Acid Reflux

Barrett’s

LGD

HGD

EMC

Intervention

Invasive Carcinoma

- AdenoCA Esophagus & EG-J is increasing
- Most, if not all, associated with Barrett’s
- 30 to 125-fold increase cancer risk
- 1% - 5% life-time (0.5% per yr) cancer risk

Goal of surveillance is detection of dysplasia

What is the Fate of BE Dysplasia?

- Inter-observer variability (85% agree HGD)
- 13-43% HGD on Bx have CA at esophagectomy
- 16-60% HGD on Bx develop CA in 5-7 yr
- However: ~ 50% remain stable
  ~ 25% regress to LGD
- Multi-focal >> Uni-focal HGD (56% vs 14%)
- LGD: 62-65% regress; 12-25% persist; 10-28% progress

2001;96:1355; Gastro 2001;120:1630
Selective Clinical Trial and Observational Highlights

- AIM Clinical Trial (n=102)
  - Dosimetry & effectiveness trial, IM 2-6 cm, 1 year f/u
  - Short-term safety and efficacy for non-dysplastic BE
- US HGD Registry
  - HALO 360/90 for HGD indication
  - 142 pt, median f/u 1 yr, 92 pt > 1 BX f/u:
    - CR-HGD 90.2%
    - CR-D 80.4%
    - CR-IM 54.3%
- Combined modality therapy with ER
  - ER followed by RFA in 6 pts.
U.S. multi-center, randomized, single-blind, sham-controlled trial
- 2:1 RFA vs sham
- length stratified (1-4 cm vs 4-8 cm)
- four maximum RFA sessions
- identical biopsy protocols, equal sampling
- 12 mo cross-over to treatment for all
- 127 patients
Patients Screened 574

Pathology Reviews 191

Confirmed on Pathology Review 169

Randomized 127

LGD 64

HGD 63

Randomization

Ablation 42
Sham 22
Ablation 42
Sham 21

383 not eligible
- elected non-trial RFA
- > 8 cm length
- prior PDT/EMR

22 rejected
- Cancer 6
- IND/ND 14
- No IM 2

42 ineligible
- EGD abnormality
- Cohort full
- Refused RCT
## Interim Analysis

### 12 month CR-D (HGD Cohort)

<table>
<thead>
<tr>
<th></th>
<th>RFA</th>
<th>Sham</th>
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<tbody>
<tr>
<td><strong>ITT</strong></td>
<td>67%*</td>
<td>0%</td>
</tr>
<tr>
<td><strong>PP</strong></td>
<td>83%**</td>
<td>0%</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.001
Interim Analysis
12 month CR-D (LGD Cohort)

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<tbody>
<tr>
<td>ITT</td>
<td>96%**</td>
<td>33%</td>
</tr>
<tr>
<td>PP</td>
<td>100%**</td>
<td>36%</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.001
## Interim Analysis

### 12 month CR-IM (all)

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<tr>
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<td>74%**</td>
<td>0%</td>
</tr>
<tr>
<td>PP</td>
<td>83%**</td>
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*p<0.05, **p<0.001
Impact on Cancer Progression?

- **Treatment Group (n=1)**
  - Any dysplasia grade to AdenoCa (n=0, 0.0%)
  - LGD to HGD: (n=1, 1.2%)
- **Sham Group (n=7)**
  - HGD to AdenoCa: (n=4, 19.0%)
    - All 4 removed from trial for treatment
    - Patient #1 had EMR+HALO, now CR-IM at 12 months
    - Patient #2-3: esophagectomy based on pathology findings
    - Patient #4: pending EMR staging
  - LGD to HGD: (n=3, 13.6%)
    - remain in trial, will cross-over to treatment
How about “Buried Barrett’s”? 

Subsquamous IM: 

- **Baseline incidence of SSIM (25%)**  
  - 21% of patients in HGD cohort  
  - 30% of LGD cohort  

- **12 month incidence of SSIM**  
  - 42% of patients in sham group  
  - 2% of patients in RFA group
Adverse Events?

- Chest pain & odynophagia (manageable)
- Transient dysphagia
- Strictures (uncommon ~3%)
  - Circumferential ablation
  - Excess dosing
  - Adjunctive to ELR
  - Respond to dilation
- Bleeding (rare, coagulopathy)
- Perforation (rare, technique dependent)
RFA for BE Conclusions

- Appears to be safe and well tolerated
- Data from non-dysplastic cohorts resolved dosimetry and durability issues
- Data from dysplastic cohorts demonstrate differences in histological outcomes as well as cancer progression outcomes
- Acceptable post ablation pain
- Few strictures
- “Buried Barrett’s” is uncommon
- Nuances to optimize therapy still emerging
- Needs validation & longer follow in BE with HGD
- Application in nondysplastic BE remains unsupported