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Luminal Advances in Gastroenterology

To review several advances that MAY impact your day-to-day practice in luminal GI in the near future

To understand limitations in these

*I will be discussing off-label and non-approved indications for various instruments/equipment

OBJECTIVES

Disclosures

<table>
<thead>
<tr>
<th>Speaker</th>
<th>Advisory</th>
<th>Research</th>
</tr>
</thead>
<tbody>
<tr>
<td>Janssen</td>
<td>✓</td>
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<tr>
<td>Abbott</td>
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<tr>
<td>Olympus</td>
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<tr>
<td>GIVEN Imaging</td>
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<td>Aptalis</td>
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<td>Roche</td>
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<tr>
<td>Boston Scientific</td>
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<tr>
<td>ConMed</td>
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<td>Shire</td>
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<td>Proctor&amp;Gamble</td>
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<td>Cook</td>
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</table>
1. Hemospray
2. Cyanoacrylate
3. UGI Predictors of Bleeding Scores
4. Capsules
5. Reflux
6. New methods for bacterial eradication
7. Colonoscopy advances


*International Consensus Recommendations on the Management of Patients With Nonvariceal Upper Gastrointestinal Bleeding*

Alan N. Barkun, MD, MSc (Clinical Epidemiology); Marc Bardou, MD, PhD; Ernst J. Kulpers, MD; Joseph Sung, MD; Richard H. Hunt, MD; Myriam Martel, BSc; and Paul Sinclair, MSc, for the International Consensus Upper Gastrointestinal Bleeding Conference Group**
Absorbs water, forms barrier - tamponade results
Concentrates blood cells and clotting factors, physical lattice favoring hemostasis

**What is Hemospray?**
- Hemospray is proprietary material developed specifically for endoscopic hemostasis.
- No human or animal proteins - no known allergens.
- Subjected to biocompatibility testing as outlined per ISO standard 10993-1. This standard is recognized by all agencies that regulate the use of medical device materials for human use.
- Per testing results, Hemospray deemed to be non-toxic, systemically or topically.
- Similar materials have been used by the military for topical battlefield hemostasis applications.
What is Hemospray?

Intended Use: Used for nonvariceal gastrointestinal bleeding

- Available
- Disposable
- Preassembled with CO2 cartridge
- Available with 7 or 10 FR Catheter
  - 220 cm catheter length
  - Packaged with extra catheter
- Contains no human/animal proteins
- No known allergens/non toxic-topically/systemically

Advantages

Hemospray, unlike traditional therapies, is a non-thermal, non-mechanical modality that doesn’t require the precise targeting of other endoscopic devices.

That means:

- **Non-thermal**: No immediate or chronic tissue changes occur as sometimes experienced with thermal modalities.
- **Non-mechanical**: Since no mechanical force is applied, the powder minimizes the risk of tissue trauma as experienced by mechanical modalities.
- **Non-specific targeting**: Powder is sprayed toward the source of the bleed, so it does not require the accuracy needed for conventional modalities.

GLP Animal Study:

**Objective**: To investigate the local and systemic effects of Hemospray in a swine model of gastric bleeding

Hemospray did not:

- Cause any systemic embolic effects
- Cause any bowel obstruction or unexplained bowel effects
- Cause any local or regional paralytic effects
- Cause any systemic vasculopathic effects
- Alter healing of the surgical site
Acute Hemostasis: 19/20 patients ‡
No Recurrent Bleeding: 17/19 patients †
Procedural Adverse Events: None
Device-related SAE: None
Mortality/SAE at 30-day follow-up: None (20 patients)

‡ Subsequently, 3 applications of hemostasis clips and 1 application of 8 mL adrenaline failed to maintain hemostasis. The patient was referred on for arterial embolization and was found to have a pseudoaneurysm.
† No active bleed was observed in two patients who had recurrent bleeding within 72 hours of the study procedure: the observation of recurrent bleeding was based

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**SEAL Product Evaluation:**

Survey to Evaluate the Application of Hemospray™ in the Luminal Tract

**Objective:** To gain clinical experience with Hemospray in Europe and Canada

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of Patients</th>
<th>Hemospray Monotherapy</th>
<th>Hemospray + Additional endoscopic therapy</th>
<th>Standard endoscopic therapy + Hemospray</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastroduodenal ulceration</td>
<td>58% (n=41)</td>
<td>6 (75%)</td>
<td>17 (71%)</td>
<td></td>
</tr>
<tr>
<td>Tumours</td>
<td>7% (n=6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oesophageal ulceration</td>
<td>4% (n=3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dieulafoy lesion</td>
<td>4% (n=3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-EMR</td>
<td>3% (n=2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAVE</td>
<td>3% (n=2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other causes</td>
<td>21% (n=15)</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

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**Peptic ulcer outcomes**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Hemospray Monotherapy</th>
<th>Hemospray + Additional endoscopic therapy</th>
<th>Standard endoscopic therapy + Hemospray</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of peptic ulcers</td>
<td>18 (46%)</td>
<td>6 (75%)</td>
<td>17 (71%)</td>
</tr>
<tr>
<td>Proportion Forrest 1a</td>
<td>7/18 (39%)</td>
<td>3/6 (50%)</td>
<td>8/17 (47%)</td>
</tr>
<tr>
<td>Proportion Forrest 1b</td>
<td>9/18 (50%)</td>
<td>3/6 (50%)</td>
<td>8/17 (47%)</td>
</tr>
<tr>
<td>Unclassified ulcer</td>
<td>2/18 (11%)</td>
<td>0</td>
<td>1/17 (6%)</td>
</tr>
</tbody>
</table>
Rebleeding

<table>
<thead>
<tr>
<th></th>
<th>Hemospray Monotherapy</th>
<th>Hemospray + Additional endoscopic therapy</th>
<th>Standard endoscopic therapy + Hemospray</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Rebleed</td>
<td>6</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Forrest 1a Rebleed</td>
<td>3</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Forrest 1b Rebleed</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Unclassified ulcer Rebleed</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Non ulcer Rebleed</td>
<td>3</td>
<td>0</td>
<td>3</td>
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</tbody>
</table>

**Conclusion:** Hemospray, which was recently described in the management of nonmalignant upper GI hemorrhage, may become the method of choice in neoplastic bleeding given its noncontact application, malleable nature, and ability to cover large and multiple areas of bleeding.

Early Clinical Evidence

*Use of the endoscopically applied hemostatic powder TC-325 in cancer-related upper GI hemorrhage: preliminary experience*

**Conclusion:** Hemospray, which was recently described in the management of nonmalignant upper GI hemorrhage, may become the method of choice in neoplastic bleeding given its noncontact application, malleable nature, and ability to cover large and multiple areas of bleeding.

**Principle Investigators:**

Yen-I Chen, MD, Alan N. Barkun, MD, MSc, Constantine Souklias, MD, Serge Mayrand, MD, Peter Ghali, MD

Montreal, Quebec, Canada

**Non-Variceal Bleeding**

- Actively bleeding
  - Massive bleeding
    - Hemostatic powder to achieve control of the bleeding field
  - Unsuccessful use of conventional hemostatic therapies
    - Hemostatic powder to achieve control of the bleeding field
- Low risk of rebleeding
  - Hemostatic powder as sole hemostatic modality
- Malignant bleeding
  - High risk of rebleeding
    - Hemostatic powder as adjuvant hemostatic modality

**Not actively bleeding**

- No role for Hemostatic powder application

Barkun et al GIE 2013
Spraying n-butyl-2-cyanoacrylate (Histoacryl) as a rescue therapy for gastrointestinal malignant tumor bleeding after failed conventional therapy.

Prachayakul V et al.
The Use of Cyanoacrylate Spray in Difficult to Treat Acute Gastrointestinal Bleeding

ACG 2012
Audrey Sachdeva, Donald J. Portocarrero, Sukhpreet Walia, John J. Kim, Terence Lewis*, Van Ziper Medicine/Gastroenterology, Loma Linda University Medical Center, Loma Linda, CA, United States.

Spraying n-butyl-2-cyanoacrylate (Histoacryl) might be a simple and final technique for bleeding gastrointestinal lesions.

Endoscopy 2009
T. Shida, S. Takano, M. Miyazaki Department of General Surgery, Chiba University Graduate School of Medicine, Chiba, Japan

Prospective randomized comparison between axial and lateral viewing capsule endoscopy in patients with obscure digestive bleeding.

(1) Lyon; (2) Nice; (3) Nîmes; (4) Lille.

French society of digestive endoscopy (SFED)
Capsule endoscopy is a major decision-making tool in several clinical situations:

Obscure digestive bleeding

Anemia:
2 milliards people worldwide*
½ iron deficiency
16% obscure bleeding

Capsule: 50-60% diag.
Sensitivity 90%

*UNICEF/UNU/WHO 2004

Capsocam° capsule specificities

- Size: 31 x 11.3 mm
- Frame Rate: 20 fps - 5 fps per camera maximum 20 images/second but filtered by a motion sensor
- 4 cameras with a 360° view
- Lateral viewing
- Long battery life (15 hrs)
Innovative device:
2) No external file transmission
   i.e. no controller / belt
   i.e. capsule retrieval

Telangiectasias
Polyp
Villous atrophy

Aim
To compare the diagnostic yield of Capsocam° and Pillcam SB2° capsule examination in the same patients with obscure digestive bleeding

Major endpoint : K value > 0.60

Patients
→ Objective : 65 consecutive patients with obscure digestive bleeding in 4 french experienced centers (> 200 capsules)
Methods

In each center :
- All patients received the two capsules sequentially (1 hour interval) in randomized order
- Two films red blindly in randomized order by two experienced readers.
- Pathologic images selected and classified as :
  P2 (highly relevant)
  P1 (uncertain relevance)
  P0 (low relevance)

Methods

- Compare crude results :
  Concordant negative cases
  Concordant positive cases (same diagnosis)
  Discordant cases : positive/negative, different diagnosis
- Systematic expert group review of discordant cases, exemple : positive capsule1, negative capsule 2 : new reading of capsule 2.

Results : technical issues

73 pts included

Capsocam (11 cases) :
- 5 recording failures
- 5 pts did not send back the capsule
- 1 pt unable to ingest

Pillcam (2) :
- 1 recording failure
- 1 pt unable to ingest

60 pts analyzed
73 patients included
60 patients with both capsule procedures

1. First Reading
36 discordant
16 Concordant -
8 Concordant +

2. Expert group review: 10 C-/P- and 15 C+/P+

3. Final results
26 Concordant -
11 (18.3 %) discordant
5 C+/P-
6 C-/P +
23 Concordant +
43.3 %

Results: main objective
K value:
0.63 per protocol
0.6 intention to treat
Case study 2

Sensitivity: per patient analysis

<table>
<thead>
<tr>
<th></th>
<th>Positive findings P.protocol</th>
<th>Positive findings ITT</th>
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</thead>
<tbody>
<tr>
<td>Capsocam*</td>
<td>46.7</td>
<td>38.4</td>
</tr>
<tr>
<td>Given SB2*</td>
<td>48.3</td>
<td>43.8</td>
</tr>
<tr>
<td>p</td>
<td>1</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Per lesion analysis (only P1 or P2 images)

<table>
<thead>
<tr>
<th></th>
<th>C+/G+</th>
<th>C+/G-</th>
<th>C-/G+</th>
<th>Total nb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Telangiectasia</td>
<td>57</td>
<td>33</td>
<td>8</td>
<td>88</td>
</tr>
<tr>
<td>Tumor/polyp</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>3</td>
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<tr>
<td>Ulcerations</td>
<td>9</td>
<td>2</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>Duodenitis</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>4</td>
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<td>Portal Hypert.</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Bleeding</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>

Capsocam* 108
Given SB2* 85
p 0.001
Conclusion: Comparable efficiency of the Capsovision® and PillCam SB2® capsule system regarding the diagnostic yield and image quality. Circumferential viewing may improve angiectasia viewing.

Gastrointestinal Endoscopy 2013: in press
Rajan et al. Mayo Clinic

Training in Small Bowel Capsule Endoscopy: Assessing and Defining Competency

CE training has been based on expert opinion
1. Weekend hands on training course
2. An interest in small bowel disorders
3. 10 supervised examinations
4. 10 reviewed studies (double read)

More objective data required
Establish structured training in CE during fellowship
Formalized assessment tool to evaluate 06-12
Prospectively analyze competency in CE interpretation
Define metrics
Determine if there is a correlation in CE interpretation with number of other procedures

Objectives

Capsule competency test developed which assesses:
1. Indications, contraindications
2. Complications
3. Identify, interpret and document abn.

All 3rd and 4th yr advanced endoscopy fellows completed CapCT max score 100 points included short videos and one full video
Could do assessment tool after 5 supervised cases

Methods

39 fellows (36 3rd year and 3 4th year)
Only permitted to do it once
8 staff did examination - mean score 91%
Felt that 82% was a pass

Experience | Mean scores:
--- | ---
<10 cases | 79%
11-20 cases | 79%
21-35 cases | 85% NS from staff

No association with endoscopic experience

Results
Over 20 supervised CE studies are required to achieve competency

28% of those <20 capsule experience achieved competency
71% of those >20 capsule experience achieved competency

Conclusion

Blatchford scoring system for identifying patients at high or low risk of rebleeding

- Blatchford risk score identifies patients at low or high risk of needing treatment to manage their bleeding.
- Blatchford Score
  - Blood urea nitrogen (>6.5 mmol / L)
  - SBP (<110 mmHg)
  - HR (>100 bpm)
  - Hb (<130 g / L for men, <120 g / L women)
  - Absence of tachycardia, melena, syncope, comorbidity
  - Endoscopic findings were not considered
  - Blatchford scores ≤2 are associated with <5% risk of rebleeding

Blatchford, Lancet 2000; 356: 1318

Gastrointestinal Endoscopy 2013: in press
Bryant et al. Royal Adelaide Hospital, Australia

Performance of Glasgow-Blatchford Score in predicting clinical outcomes and intervention in Hospitalized Patients
**Blatchford scoring system:**
Admission risk markers and associated score component value

<table>
<thead>
<tr>
<th>Admission risk marker</th>
<th>Score component value</th>
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</thead>
<tbody>
<tr>
<td>Blood urea (mmol/L)</td>
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</tr>
<tr>
<td>≤6.5</td>
<td>0</td>
</tr>
<tr>
<td>6.5-8.0</td>
<td>1</td>
</tr>
<tr>
<td>&gt;8.0</td>
<td>2</td>
</tr>
<tr>
<td>≤10.0</td>
<td>3</td>
</tr>
<tr>
<td>&gt;10.0</td>
<td>4</td>
</tr>
<tr>
<td>Haemoglobin (g/L) for men</td>
<td></td>
</tr>
<tr>
<td>≤120</td>
<td>0</td>
</tr>
<tr>
<td>120-130</td>
<td>1</td>
</tr>
<tr>
<td>&gt;130</td>
<td>2</td>
</tr>
<tr>
<td>≤100</td>
<td>3</td>
</tr>
<tr>
<td>&gt;100</td>
<td>4</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
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<td>100-119</td>
<td>0</td>
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<tr>
<td>100</td>
<td>1</td>
</tr>
<tr>
<td>90-99</td>
<td>2</td>
</tr>
<tr>
<td>&lt;90</td>
<td>3</td>
</tr>
<tr>
<td>Other markers</td>
<td></td>
</tr>
<tr>
<td>Pulse &lt;100 (per min)</td>
<td>4</td>
</tr>
<tr>
<td>Presentation with melaena</td>
<td>2</td>
</tr>
<tr>
<td>Presentation with syncope</td>
<td>3</td>
</tr>
<tr>
<td>Hepatic disease</td>
<td>6</td>
</tr>
<tr>
<td>Variable</td>
<td>0 1 2 3</td>
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</table>

Blatchford score of ≤2 are associated with <5% risk of rebleeding.

**Rockall scoring system for severity of acute UGI bleeding**

A score of ≤2 (low risk) is associated with excellent prognosis; score >8 is associated with high risk of death.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Score 0</th>
<th>1</th>
<th>2</th>
<th>3</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>≤60</td>
<td>60–79</td>
<td>80+</td>
<td></td>
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<tr>
<td>Shock</td>
<td>Nil</td>
<td>Hypertension (DBP ≥100)</td>
<td>Rebleed, liver failure, disseminated intravascular coagulation</td>
<td></td>
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<tr>
<td>Co-morbidity</td>
<td>Nil major</td>
<td>Cardiac failure (e.g., MI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnoses (Endoscopy)</td>
<td>M-W lesion, no lesion, no SRH*</td>
<td>All other diagnoses including ulcer etc.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major SRH* (Endoscopy)</td>
<td>None or dark spot</td>
<td>Stigmata of recent hemorrhage</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*SRH=Stigmata of recent hemorrhage

**UGI hemorrhage common**

Scoring systems:
- Rockall designed to predict death
- Pre-endoscopy Rockall not fully validated
- Glasgow-Blatchford Score doesn’t require endoscopy designed to predict need for intervention/validated recently shown to be better at predicting death, XE, surgery
- GBS 0 safe for discharge
- GBS ≤2 managed as outpatients
2010-12 consecutive prospective in-patients with UGI bleeding
Included both variceal and non-variceal
Data collected and analyzed

Methods

Results

GBS pre RS and Post RS all predicted XF, rebleeding repeat endoscopy or death
Only GBS and Post RS predicted surgery
ROC
GBS and Post RS were superior to Pre RS in need for endoscopic Rx
GBS superior in predicting XF and surgery
All three similar in death
Example:
None of 61 pts with GBS<3 needed XF or endoscopic therapy
None of 168 pts with GBS>7 needed surgery
Role of GBS appears appropriate for in and outpatients
Some data suggests that >12 hours better outcomes for very high risk
this may help predict those patients

Limitations: Not compared to AIMS65 Salzman GIE 2011
5 factors present at admission with the best discrimination
albumin less than 3.0 g/dL
international normalized ratio greater than 1.5
altered mental status
systolic blood pressure 90 mm Hg or lower
age older than 65 years
For those with no risk factors, the mortality rate was 0.3% compared
with 31.8% in patients with all 5 (P < .001). Predictive for LOS and costs

Conclusions

Periowave Process
- Sensitizer is applied to the periodontal pockets
- Irrigation irrigates the treatment site
- Illumination illuminates the treatment site
- Eradication targeted bacteria and virulence factors are destroyed
Two types of Photochemical Reactions

*Requirements of a Photochemical Reaction*
- A photosensitizer
  - Must adhere to the cell that is being targeted
  - Presence of oxygen will enhance the reaction
- A light source with these critical features:
  - Specific wavelength that matches the chosen photosensitizer
  - Adequate power to produce enough Oxygen Derived Free Radicals

*Absorption Spectrum is Specific to Photosensitizer*
- Generation of reactive molecules requires both a specific wavelength of light and a photosensitizer that are matched (670nm)
Photodisinfection: Method of Action

- Reactive molecules destroy bacteria by oxidizing the cell membrane
- Causes the cell to rupture

1. Before damage
2. During illumination
3. Aggregation
4. Rupture

Direct Kill Mechanism

- SEM showing the stained cells ruptured after illumination

Untreated P. gingivalis After Illumination

Sensitizer Selective To Bacterial Membranes and Pathogens Remain Sensitive (no resistance)

- No damage to human tissue

Mamalian Cells
- Hydrophobic interactions
- Outer leaflet
- Inner leaflet
- Neutral cholesterol

Bacterial Cells
- Electrostatic and hydrophobic interactions
- Hydrophobic interactions
- Protoctactic plasma membrane of a multicellular animal (erythrocytes)
- Zwitterionic phospholipids
- Acid phospholipids
Pathogens Remain Susceptible to PDT

Unlike antibiotics, pathogens remain susceptible to PDT after repeated exposures.

* Periowave Oral Photodisinfection System

**Features:**
- Class 1 Laser (No safety glasses required)
- Sterilizable Outer Sheath
- Smooth Switch™ Technology

**Cordless convenience:**
- No power cords, fiber optic cables or footswitches
- Easy to use:
  - Ergonomically designed for weight and balance
  - 60 second treatment cycles are easily interrupted or cancelled using the Smooth Switch™

* Gingivitis

**Patient Profile**
29-year-old female, non-smoker, 7 months pregnant, exhibiting pregnancy gingivopathy (marginal gingivitis) caused by combination of hormonal changes of pregnancy and anticoagulation therapy. Generalized 4-5 mm pockets with heavy bleeding on probing (Fig. 1.1)

**Treatment Protocol**

1. Initial Periowave treatment:
   - Full-mouth SRP and PW treatment was performed along with localized gingivectomy to remove gingival hyperplasia. Cessation of anticoagulant therapy.
   - No BOP present on gingiva.

2. Second Periowave Treatment:
   - 10 months after initial PW treatment following full mouth debridement

**Result**
10 months after initial PW treatment:
- Gingivitis after both 6 months and 1 month after cessation of hormone therapy. Generalized 4-5 mm pockets with no BOP and reduced inflammation (Fig. 1.2)
- 1 month after second Periowave treatment:
  - Only 3 pockets of 4-5 mm on the lingual of teeth 46-47. All other areas healed by physical instrumentation / mechanical debridement.

*Fig. 1.1 Pre-Periowave treatment. PD 4-5 mm, heavy BOP.*
*Fig. 1.2 10 months after initial Periowave treatment. PD 4-5 mm, some BOP.*
*Fig. 1.3 1 month after second Periowave treatment. PD mostly 1-2 mm, no BOP.*
PDT Applications - Disease Prevention & Treatment

Current Indications:
- Nasal decolonization
- Dental
- Oral infections
- Ear infections
- Trach stoma infections

Future:
- Ventilator Associated Pneumonia Prevention - VAP
- Sinusitis
- Oncology

Immediate Pre-Operative Decolonization
Treatment with Intranasal Photodisinfection Therapy and Chlorhexidine Body Wipes
Decreases Surgical Site Infections
3000 patients preoperatively

Other applications: Potential
1. C Diff
2. H P/PUD
3. Biliary infections
4. Esophageal candidiasis
5. IBD/Pouchitis

A Prospective, Randomized Study on the Effect of Band Ligation with or without EMR as a Treatment for GERD: Pilot Study, 12 Month Experience

William Kessler, Gail McNulty, Glen Lehman
Indiana University Health
Objectives

- Background of Endoscopic Treatment of GERD
- Rationale for study
- Present Pilot data
- Future Studies

The Ideal Endoscopic Therapy for GERD

- Would be:
  - Safe
  - Effective
  - User-Independent
  - Economically Viable

- Is judged by:
  - Symptom relief
  - Reduction in PPI Use
  - pH Improvement


Similar Endoluminal Therapies

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<thead>
<tr>
<th>Device</th>
<th>FDA</th>
<th>GERD Sx</th>
<th>Acid Exp.</th>
<th>PPI Use</th>
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<tbody>
<tr>
<td>Stretta (Mederi)</td>
<td>2000</td>
<td>↓</td>
<td>↓</td>
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</tr>
<tr>
<td>EndoCinch (BARD)</td>
<td>2001</td>
<td>↓</td>
<td>N/S</td>
<td>↓</td>
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<tr>
<td>NDO Plicator (NDO-Ethicon)</td>
<td>2003</td>
<td>↓</td>
<td>↓(6 mo)</td>
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<tr>
<td>EsophyX (EGS)</td>
<td>2007</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>SRS (Medigus)</td>
<td>2012</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
</tbody>
</table>

Schwartz MP Gut 2007
Rothstein P Castro 2006
Kessler WR DOW 2011
Abdel AM Surg Endosc 2010
Dughe O Drug Ther Endosc 2011
Testoni PA Surg Endosc 2012
Cadiere GB World J Surg 2008
### Short Comings of Current Options

<table>
<thead>
<tr>
<th>Device</th>
<th>General Anesthesia</th>
<th>Equipment &amp; Training</th>
<th>CPT Code</th>
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<tbody>
<tr>
<td>EndoCinch (BARD)</td>
<td>No</td>
<td>Yes</td>
<td>43499</td>
</tr>
<tr>
<td>NDO Plicator (Ethicon)</td>
<td>No</td>
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<td>43499</td>
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<tr>
<td>SRS (Medigus)</td>
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<td>Yes</td>
<td>43499</td>
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<tr>
<td>Stretta (Mederi)</td>
<td>No</td>
<td>Yes</td>
<td>43257</td>
</tr>
<tr>
<td>EsophyX (EGS)</td>
<td>Yes</td>
<td>Yes</td>
<td>43499</td>
</tr>
</tbody>
</table>

### Benefit of Band/EMR

<table>
<thead>
<tr>
<th>Device</th>
<th>General Anesthesia</th>
<th>Equipment &amp; Training</th>
<th>CPT Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>EndoCinch (BARD)</td>
<td>No</td>
<td>Yes</td>
<td>43499</td>
</tr>
<tr>
<td>NDO Plicator (Ethicon)</td>
<td>No</td>
<td>Yes</td>
<td>43499</td>
</tr>
<tr>
<td>SRS (Medigus)</td>
<td>Yes</td>
<td>Yes</td>
<td>43499</td>
</tr>
<tr>
<td>Stretta (Mederi)</td>
<td>No</td>
<td>Yes</td>
<td>43257</td>
</tr>
<tr>
<td>EsophyX (EGS)</td>
<td>Yes</td>
<td>Yes</td>
<td>43499</td>
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<tr>
<td>Band/EMR of LES and Cardia</td>
<td>No</td>
<td>No</td>
<td>43205</td>
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</tbody>
</table>

### Concept: Iatrogenic Distal Esophageal Stricture

- Esophageal Variceal Therapy
  - Sclerotherapy
  - Band ligation
- Barrett’s Therapy

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Schmitz RJ Am J Gastroenterol 2001
Masci E Hepato-Gastroenterology 1999

---

Endoscopy 2011;45:E25

---

24
**Stricture Rates with EMR/ESD**

<table>
<thead>
<tr>
<th>Study</th>
<th>% Circum</th>
<th>Stricture Rate (%)</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lewis/ Piraka</td>
<td>50</td>
<td>67</td>
<td>EMR</td>
</tr>
<tr>
<td>Mizuta/Onishi</td>
<td>71</td>
<td>100% S /96% Sp</td>
<td>ESD</td>
</tr>
<tr>
<td>Katada/Yoshida</td>
<td>75</td>
<td>68</td>
<td>EMR</td>
</tr>
<tr>
<td>Pouw/Bergman</td>
<td>100</td>
<td>49.7</td>
<td>EMR</td>
</tr>
</tbody>
</table>

Lewis JJ Gastrointest Endosc 2011
Mizuta H Diseases of the Esophagus 2009
Katada C Gastrointest Endosc 2003
Pouw RE Gut 2010

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**Concept: Multiple Focal Scars**

![Image of SCJ with multiple scars](image)

---

**Aims of Study**

- **Primary**
  - Safety of Banding +/- EMR for GERD
    - Adverse Events (AE)
    - Serious Adverse Events (SAE)
    - Unanticipated Adverse Device Effects (UADE)
  - ≥ 30% Improvement in HRQL (Off PPI)
- **Secondary**
  - Total Acid Exposure on 48 hr pH Study
  - ≥ 30% Reduction in PPI Dose
Patient Selection
• Age ≥ 18
• Typical GERD symptoms, ≥ daily PPI x 6 months
• PPI Responsive (HRQL ≥ 6 greater off than on PPI)
• GERD HRQL ≥ 20 (off PPI)
• Abnormal pH; Wireless 48 Hour study
  • ≥ 24 Hour period
  • Total >4.5%, Supine >2%, DeMeester >14.7

Patient Selection
Exclusion Criteria
• Abnormal Esophageal Body Motility
• BMI > 38
• LA Grade C/D Erosive Esophagitis
• Barrett’s Esophagus
• Hiatal Hernia ≥ 3 cm

Study Design:
Randomized, Single Blind
GERD HRQL, pH testing, Esophageal Manometry, Endoscopy
Banding (5) Band w/EMR (5)
6 months
GERD HRQL PPI Use 48 Hr pH
12 Months
GERD HRQL PPI Use
Sites of Banding with or without EMR

All treatments within 2 mm of SCJ
EMR < 50% Circumference
Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Banding Alone (5)</th>
<th>EMR (5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (m/f)</td>
<td>2:3</td>
<td>2:3</td>
</tr>
<tr>
<td>Mean Age in years (range)</td>
<td>52.2 (39-60)</td>
<td>49.8 (31-66)</td>
</tr>
<tr>
<td>Mean BMI (range)</td>
<td>25.8 (21.6-31.5)</td>
<td>27.3 (23.9-31.6)</td>
</tr>
<tr>
<td>HH: Mean length cm (range)</td>
<td>5/5: 1.4 (1-2)</td>
<td>4/5: 1.0 (0-2)</td>
</tr>
<tr>
<td>EE Present: LA Grade</td>
<td>1/5: B</td>
<td>1/5: B</td>
</tr>
</tbody>
</table>

Procedural Results

<table>
<thead>
<tr>
<th>Variable</th>
<th>Banding alone</th>
<th>EMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completed</td>
<td>5/5</td>
<td>5/5</td>
</tr>
<tr>
<td>Mean Duration (min)</td>
<td>21 (19-23)</td>
<td>54 (45-69)</td>
</tr>
<tr>
<td>Mean # of Bands (E/G)</td>
<td>4/4</td>
<td>3.2/3.6</td>
</tr>
<tr>
<td>Major Complications</td>
<td>0/5</td>
<td>0/5</td>
</tr>
<tr>
<td>Lesser Complications</td>
<td>1/5 (chest pain)</td>
<td>1/5 (bleeding)</td>
</tr>
</tbody>
</table>
Results

Adverse Event (AE): Dysphagia
- 1/5 Banded, resolved at 1 month
- 4/5 EMR
  - 1 patient resolved
  - 2 patients Dysphagia Sx < ↓ GERD Sx
  - 1 patient dilated x2

Results

- Aims Banding alone EMR
  - Mean (reduction)
  - Mean (reduction)

Primary
- Safety
  - No Study-Related SAEs/UADEs
  - No Study-Related SAEs/UADEs
- ≥ ↓30% HRQL
  - Pre: 27, Post: 10.6 (↓61%)
  - Pre: 26.2, Post: 7.4 (↓72%)

Secondary
- pH
  - Pre: 8.4, Post: 7.0 (↓17%)
  - Pre: 8.3, Post: 4.7 (↓43%)
- ↓PPI by 30%
  - Pre: 52, Post: 5 (↓90%)
  - Pre: 72, Post: 2 (↓97%)

All Endpoints Met

Summary
- No procedure-related SAEs/UADEs
- At least partially effective
- Dysphagia is common after Band with EMR
Limitations

- Small sample size
- No pH data at 12 months
- Only one treatment session done

Conclusion

- Relative Advantages
  - MAC Sedation
  - Outpatient Setting
  - Relatively Inexpensive
  - Potential Widespread Use
  - Anti-Reflux Surgery Remains an Option

NOVEL COLONOSCOPE:

FULL SPECTRUM ENDOSCOPY

The Fuse™ Study
New Study Shows Traditional Colonoscopy Misses up to 42% of Adenomas\(^1\)

Demonstrated Clinical Need

- Significant numbers of adenomas (up to 42%) are missed with traditional forward-viewing (TFV) colonoscopes\(^1,2,3,4\).
- There is a need for improved technology without "add on" accessories or additional procedure time.
- EndoChoice\(^5\), Atlanta, GA, USA has:
  - $\geq 330^\circ$ Field of View
- The Fuse colonoscope maintains all standard capabilities
  - Flexible, re-useable scope (168cm length, 12.8mm outer diameter)
  - Full tip deflection
  - Working channel (3.8mm)
  - Forward water jet irrigation
  - Air insufflation, suction

Novel Technology

- EndoChoice\(^6\), Atlanta, GA, USA has:
  - $\geq 330^\circ$ Field of View
- The Fuse colonoscope maintains all standard capabilities
  - Flexible, re-useable scope (168cm length, 12.8mm outer diameter)
  - Full tip deflection
  - Working channel (3.8mm)
  - Forward water jet irrigation
  - Air insufflation, suction
Traditional Forward View

Full Spectrum (Fuse™) View

Fuse™ Distal Tip
Fuse™ System - Full Spectrum View
- HD video images presented on 3 monitors
- LED illumination
- Standard scope functionality

Comparing Traditional Forward-Viewing Colonoscopy with “Full Spectrum Endoscopy”: A Randomized, Multicenter Tandem Colonoscopy Study – The FUSE Study

Ian M. Gralnek, Peter D. Siersema, Ori Segel, Alain Suissa, Zamir Halpern, Alan Sloyer, Leon M.G. Moons, Erwin Santo, Sveta Domanov, Ralph D’Agostino Jr., Jay Fenster, Douglas K. Rex

Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Carmel Medical Center and Gilton Hospital, Haifa, Israel; Utrecht University Medical Center, Utrecht, The Netherlands; Tel Aviv Sourasky Medical Center and Tel Aviv University School of Medicine, Tel Aviv, Israel; North Shore Gastroenterology, Great Neck, NY, USA; Wake Forest University, Winston-Salem, NC, USA; South Shore Gastroenterology, Cedarmont, NY, USA; Indiana University, Indianapolis, IN, USA

DDW 2013 – AGA/ASGE Plenary Session
May 18, 2013

Study Aims

1. To determine the additional number of adenomas found using Fuse™ colonoscopy

2. To determine the adenoma miss rates for both TFV colonoscopy and Fuse
Study Design

- Randomized (concealed allocation)
  - Tandem colonoscopy design
  - Same day, back-to-back, by the same endoscopist
  - 170° TFV vs. Fuse 330°
- All polyps removed when identified
  - Except hyperplastic rectal polyps (1mm-2mm)
  - All adenomas and cancers confirmed by pathology
- Multicenter
  - Israel (3) Netherlands (1) USA (2)

Inclusion/Exclusion Criteria

- Inclusion
  - Subjects: 18-70 years old
  - Colonoscopy for CRC screening, polyp surveillance, diagnostic evaluation
- Exclusion
  - History of colonic resection, IBD, polyposis, XRT to abdomen/pelvis
  - Suspected colonic bleeding, stricture, diverticulitis, toxic megacolon

Subject Demographics

- Mean age 55.8 ± 9.7 years
- 101 female (54.6%) / 84 male (45.4%)
- Baseline characteristics
  - Age, gender, reason for colonoscopy were similar
- Indications for colonoscopy
  - CRC screening = 103 (55.7%)
  - Polyp surveillance = 38 (19.5%)
  - Diagnostic evaluation = 46 (24.8%)
Procedure Times Comparable

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Time to Cecum (median time)</th>
<th>Withdrawal Time (median time)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TFV Colonoscopy</td>
<td>5.1 minutes</td>
<td>5.6 minutes</td>
</tr>
<tr>
<td>Fuse™ Colonoscopy</td>
<td>4.8 minutes</td>
<td>6.2 minutes</td>
</tr>
</tbody>
</table>

\[p=\text{NS} \quad p<0.0001\]

71% Incremental Adenoma Find Rate* by Fuse™

- N=88 randomized to: TFV followed by Fuse
- At TFV colonoscopy: 28 adenomas found
- At Fuse colonoscopy: 20 additional adenomas found
- 20/28 (71.4%) increase in adenomas found with Fuse

*per lesion analysis

8% Incremental Adenoma Find Rate* by TFV

- N=97 randomized to: Fuse™ followed by TFV
- At Fuse colonoscopy: 59 adenomas, 2 CAs found
- At TFV colonoscopy: 5 additional adenomas found
- 5/61 (8.2%) increase in adenomas found with TFV

*per lesion analysis
Results – TFV Missed Meaningful Adenomas

TFV colonoscopy missed 20 adenomas:
- Morphology = 2 pedunculated, 18 sessile
- Size = 14 (1-5mm), 5 (6-9mm), 1 (≥10mm)
- Adenoma subtype = 18 TA, 1 TVA, 1 villous
- Location = 14 (70.0%) R colon, 6 (30.0%) L colon

Results - Clinical Impact of Adenomas Missed by TFV

TFV missed adenomas in 15 patients:
- Fuse™ changed colonoscopy surveillance in 8/15 (53.3%)
  - 6/15 (40.0%) 5-10 years 3 years
  - 2/15 (13.3%) 10 years 5-10 years
- 8/88 (9.1%) in the TFV 1st arm received a change in colonoscopy surveillance recommendations

Results – Fuse™ Missed Some Adenomas

Fuse colonoscopy missed 5 adenomas
- Morphology = all 5 (100%) sessile
- Size = all 5 (100%) 1-5mm
- Adenoma subtype = all 5 (100%) tubular
- Location = 2 right colon, 3 left colon
Results - Clinical Impact of Adenomas Missed by Fuse™

Fuse missed adenomas in zero unique patients
  - TFV changed colonoscopy surveillance in 0/5 (0%)

Fuse™ Study Conclusions

As compared to Traditional Forward View (TFV):
  - Fuse found an additional 71% more adenomas after TFV
  - Fuse had a significantly lower adenoma miss rate (8%) compared to TFV (42%)
  - Fuse shortened the interval recommendations in 53% of the exams where standard colonoscopy failed to identify all polyps present
Adenoma Detection in Tandem Studies

<table>
<thead>
<tr>
<th>Tandem Studies</th>
<th>Adenoma Miss Rates</th>
<th>Additional Adenomas Detected by 2nd Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rex et al., 1997 Gastro N=183 vs. TFV</td>
<td>24%</td>
<td>2nd Pass 31%</td>
</tr>
<tr>
<td>Siersema et al., 2012 WJG N=349 vs. TFV</td>
<td>31%</td>
<td>TER 46%</td>
</tr>
<tr>
<td>Gralnek et al., 2013 DDW N=185 vs. Fuse™</td>
<td>42%</td>
<td>Fuse™ 71%</td>
</tr>
</tbody>
</table>
## Summary Data

<table>
<thead>
<tr>
<th>Method</th>
<th>Adenomas Missed</th>
<th>Additional Adenomas Detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traditional Forward View(2)</td>
<td>42% p&lt;0.0001</td>
<td>8% p&lt;0.0001</td>
</tr>
<tr>
<td>3rd Eye Retroscope(1)</td>
<td>18%</td>
<td>46%</td>
</tr>
<tr>
<td>Fuse™ (2)</td>
<td>8% p=0.0001</td>
<td>71% p&lt;0.0001</td>
</tr>
</tbody>
</table>

(1) Siersema et al., 2012 WJG 
(2) Gralnek et al., DDW 2013 Plenary Session.