Endoscopic Interventions

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Disclosures

• Shelby Sullivan, M.D. has financial interests to disclose.

• Research Support / Grants
  • Aspire Bariatrics, ReShape Medical, GI Dynamics, USGI Medical, Obalon, BAROnova, Elira

• Consulting / Employment
  • USGI Medical, Obalon, Spatz, Elira Therapeutics, Aspire Bariatrics, GI Dynamics
Endoscopic Metabolic and Bariatric Therapy

- Less risk than surgery
- More weight loss than lifestyle therapy or medications
- Indicated for lower BMI patients
- Covered by insurance in limited cases at this time

Ponce J. Surgery for Obesity and Related Diseases. 2015;11(4):874-881
Abu Dayyeh B. Gastrointestinal Endoscopy. 2015;81(5 Suppl):A8147
Sullivan S. Gastroenterology. 2016;150(4) S1267
Endoscopic Bariatric and Metabolic Therapies

Gastric Therapies
- Intragastric Balloons (IGB)
  - ReShape Intragastric Dual Balloon System (ReShape Medical)
  - Orbera Balloon System (Apollo Endosurgery)
  - Obalon Balloon System (Obalon Therapeutics)
  - Elipse Balloon (Allurion Technologies)
  - Spatz III Adjustable Balloon (SPATZ FGIA)
- Suturing and Plication procedures
  - Endoscopic Sleeve Gastroplasty (Overstitch, Apollo Endosurgery)
  - Primary Obesity Surgery Endoluminal (Incisionless Operating Platform, USGI Medical)
- Aspiration Therapy (Aspire Bariatrics)
- Transpyloric Shuttle (BARONova)

Small Bowel Therapies
- Bypass liners
  - Duodenojejunal Bypass Liner: EndoBarrier (GI Dynamix)
  - Gastroduodenojejunal Bypass Liner: ValenTx Endoluminal Bypass (ValenTx Inc)
- Intestinal bypass: Incisionless Anastamosis System (GI Windows)
- Duodenal Mucosal Resurfacing: Revita DMR (Fractyl Laboratories Inc)

Weight loss with metabolic effects dependent on weight loss

Metabolic effects independent of weight loss, but some weight loss may be seen
## FDA Approved Intragastric Balloons

<table>
<thead>
<tr>
<th>Device</th>
<th>Device Image</th>
<th>Characteristics</th>
<th>FDA Status</th>
</tr>
</thead>
</table>
| **ReShape Dual Balloon System**  | ![Device Image](image1) | - Two medical grade silicone spheres joined by a flexible shaft  
- each balloon filled with 375 ml to 450 ml of saline dyed with methylene blue  
- Endoscopically placed and removed after 6 months  | • Approved July 28, 2015  
• BMI 30-40kg/m² with one obesity related comorbidity |
| ReShape Medical, San Clemente, CA | ![Device Image](image2) |                                                                          |                                                                          |
| **Orbera Intragastric Balloon**, Apollo Endosurgery, Austin, TX | ![Device Image](image3) | - Medical grade silicone sphere, filled with 400-700 ml of saline  
- Endoscopically placed and removed | • Approved August 5, 2015  
• BMI 30-40kg/m² |
| **Obalon Balloon System**, Obalon Therapeutics, Carlsbad, CA | ![Device Image](image4) | - Thin polymer ellipse shape  
- filled with 250 ml of a nitrogen mix gas  
- 3 balloons administered over 8 to 12-week period  
- Swallowed and endoscopically removed 6 months after first balloon administration | • Approved September 8, 2016  
• BMI 30-40kg/m² |
## Comparison of Intragastric Balloon Pivotal Trial Data

<table>
<thead>
<tr>
<th>Device</th>
<th>Number of subjects</th>
<th>Body Mass Index (kg/m²)</th>
<th>Percent total Body Weight loss</th>
<th>Active Group Responder rate</th>
<th>Serious Adverse Event Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls Group</td>
<td>Active Group</td>
<td>Control Group</td>
<td>Active Group</td>
<td>Control Group</td>
<td>Active Group</td>
</tr>
<tr>
<td>Orbera</td>
<td>130</td>
<td>125</td>
<td>35.4±2.7</td>
<td>35.2±3.2</td>
<td>3.3±5.0%</td>
</tr>
<tr>
<td>Reshape</td>
<td>139</td>
<td>187</td>
<td>35.4±2.6</td>
<td>35.4±2.8</td>
<td>3.3%</td>
</tr>
<tr>
<td>Obalon</td>
<td>189</td>
<td>198</td>
<td>35.4±2.7</td>
<td>35.1±2.7</td>
<td>3.4±5.0%</td>
</tr>
</tbody>
</table>

*Sham-Controlled Trials*
Intragastric Balloon: Higher Effectiveness in Clinical Practice

![Graph showing percent total body weight loss for RESHAPE and ORBERA](image)

- **RESHAPE**
  - N=101
  - FDA Trial
  - US Clinical Case Series

- **ORBERA**
  - N=199
  - FDA Trial
  - US Clinical Case Series

References:
- Ponce J. *Surgery for Obesity and Related Diseases*. 2015;11(4):874-881
- Agnihotri A. *Clinical Gastroenterology and Hepatology* 2018;16:1081–1088
- Vargas EJ. *Clinical Gastroenterology and Hepatology* 2018;16:1073–1080
IGB Long-Term Weight Loss

Percent of Patients Successful and %EWL

Maximizing Weight Loss and Maintenance: Combination Therapy

- Percent excess BMI loss at 12 Months
- Percent of Patients with >10% Total Body Weight Loss

## FDA Approved IGB Non-Serious Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>ReShape (%)</th>
<th>Orbera (%)</th>
<th>Obalon (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>86.7</td>
<td>86.8</td>
<td>17.3</td>
</tr>
<tr>
<td>Nausea</td>
<td>61.0</td>
<td>75.6</td>
<td>56.0</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>54.5</td>
<td>57.5</td>
<td>72.6</td>
</tr>
<tr>
<td>Gastric Ulcer</td>
<td>35.2*</td>
<td>0</td>
<td>0.9</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>17.8</td>
<td>21.3</td>
<td>16.9‡</td>
</tr>
<tr>
<td>Eructation</td>
<td>16.7</td>
<td>24.4</td>
<td>9.2</td>
</tr>
<tr>
<td>Abdominal Discomfort</td>
<td>13.3</td>
<td>6.3</td>
<td>0</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>11.0</td>
<td>17.5</td>
<td>14.6</td>
</tr>
<tr>
<td>Erosive Gastritis</td>
<td>9.1</td>
<td>0.6</td>
<td>7.1†</td>
</tr>
<tr>
<td>GERD</td>
<td>6.8</td>
<td>30.0</td>
<td>(see dyspepsia)</td>
</tr>
<tr>
<td>Erosive Esophagitis</td>
<td>0.4</td>
<td>0.6</td>
<td>1.8</td>
</tr>
<tr>
<td>Constipation</td>
<td>5.3</td>
<td>0</td>
<td>2.7</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3.0</td>
<td>13.1</td>
<td>8.3</td>
</tr>
</tbody>
</table>

*After design modification of the distal tip of the ReShape Balloon, the ulcer rate decreased to 10%.
‡Composite of Dyspepsia and GERD.
UPDATE: Potential Risks with Liquid-filled Intragastric Balloons - Letter to Health Care Providers
June 4, 2018

Additional Information Regarding Death Reports:
The FDA continues to work with the manufacturers to evaluate reports of deaths in patients with liquid-filled intragastric balloon systems used to treat obesity. Since our August 2017 update (https://www.fda.gov/MedicalDevices/Safety/LettersForHealthCareProviders/ucm570787.htm):

- The FDA has received reports of five additional deaths that occurred worldwide since 2016. Four of these deaths (three with the Orbera Intragastric Balloon System manufactured by Apollo Endosurgery, and one with the ReShape Integrated Dual Balloon System manufactured by ReShape Lifesciences) occurred following gastric perforation one day to 3.5 weeks after balloon placement. The fifth death was reported for a patient who had the Orbera Intragastric Balloon System. The report does not mention a perforation event and the manufacturer is still investigating this death.

Since 2016, the FDA has received reports of a total of 12 deaths that occurred in patients with liquid-filled intragastric balloon systems worldwide. Seven of these 12 deaths were patients in the U.S. (four with the Orbera Intragastric Balloon System, and three with the ReShape Integrated Dual Balloon System).

In collaboration with the manufacturers, the FDA has approved new U.S. labeling for the Orbera and ReShape balloon systems with more information about possible death associated with the use of these devices in the U.S. Please see the statements from each manufacturer (Apollo Endosurgery, https://,r-apolloendosurgery.com/Orbera-Labeling/ and ReShape Lifesciences, https://www reshape-lifesciences.com/unsafe-weight-loss/Orbera/labeling)s for additional details about the new labeling.

The FDA recommends health care providers:

- Instruct patients regarding symptoms of potentially life-threatening complications such as balloon deflation, gastrointestinal obstruction, ulceration, and gastric and esophageal perforation
- Monitor patients closely during the entire term of treatment with liquid-filled intragastric balloon systems for potential complications, including acute pancreatitis and spontaneous hyperinflation as stated in our February 2017 letter (https://www.fda.gov/MedicalDevices/Safety/LettersForHealthCareProviders/ucm540655.html) to health care providers.
- Report any adverse events related to intragastric balloon systems through MedWatch, the FDA Safety Information and Adverse Event Reporting program (https://www.fda.gov/Safety/MedWatch/HowToReport/default.htm).

- Report events that did not occur in the pivotal trials
  - Hyperinflation
  - Pancreatitis
  - Death

- 12 Deaths reported to FDA, 7 from inside the US
- Risk from US Data
  - Orbera: 0.036%
  - ReShape: 0.06%
AspireAssist System (Aspire Bariatrics, King of Prussia, PA)

• Similar in concept to a percutaneous endoscopic gastrostomy tube
• Aspirate gastric contents ~20 minutes after meals 2-3 x/day
• Removes 25-30% of calories consumed at that meal
• Accounts for 50-80% of weight loss – lifestyle and mealtime behaviors reduce overall food intake
• Food choices improve anecdotally
Two Co-Primary Endpoints BMI 35-55 kg/m²

Co-Primary Endpoint #1
Mean %EWL at 52 Weeks of AT Group at least 10% greater than Control Group

Co-Primary Endpoint #2
At least 50% of AT group achieves 25 %EWL or more at 52 Weeks

Thompson CC. Am J Gastroenterol. 2017;112:447-457
<table>
<thead>
<tr>
<th>Adverse events</th>
<th>No. of Subjects (%)</th>
<th>No. of Subjects, Perioperative*</th>
<th>No. of Subject, Postoperative**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peristomal granulation tissue</td>
<td>45 (40.5%)</td>
<td>0</td>
<td>45</td>
</tr>
<tr>
<td>Abdominal pain ≤4 weeks after A-tube placement*</td>
<td>42 (37.8%)</td>
<td>41</td>
<td>1</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>19 (17.1%)</td>
<td>15</td>
<td>4</td>
</tr>
<tr>
<td>Peristomal irritation</td>
<td>19 (17.1%)</td>
<td>2</td>
<td>17</td>
</tr>
<tr>
<td>Intermittent abdominal discomfort</td>
<td>18 (16.2%)</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>Possible or definite peristomal bacterial infection</td>
<td>15 (13.5%)</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>Abdominal pain &gt;4 weeks after A-tube placement*</td>
<td>9 (8.1%)</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Dyspepsia (acid reflux, heartburn, hiccups, belching)</td>
<td>7 (6.3%)</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Peristomal inflammation</td>
<td>6 (5.4%)</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

5 SAEs in 4 subjects, all resolved (3.6% SAE rate)

Thompson CC. Am J Gastroenterol. 2017;112:447-457
Eating Behaviors

Subjects assessed for binge-eating, bulimia, & night-eating syndrome

- Eating Behavior Assessment: Questionnaire on Eating and Weight Patterns-Revised and the Eating Disorder Examination
- Assessments at Baseline, Week 14 (AT subjects only), Week 28, and Week 52
- 1 Control subject developed binge-eating syndrome at Week 28 and was removed from study
- No AT subject showed any evidence of worsening eating behaviors

Frequency of aspiration monitored by Connector counts

- No evidence of any subject excessively aspirating

Self–reported eating behaviors:

- 91% of patients reported strongly agreeing/somewhat agreeing to increased chewing
- 78% reported significantly/somewhat decreased calorie consumption

Thompson CC. Am J Gastroenterol. 2017;112:447-457
US and European Studies: Completer Percent Total Body Weight Loss

Month 0  Year 1  Year 2  Year 3  Year 4

Percent

PATHWAY
US Pilot
Sweden Pilot*
Super Obesity
European Registgy

Thompson CC. Am J Gastroenterol. 2017;112:447-457
Noren E. BioMed Central Obesity. 2016;3:56
Machytka E. Gastroenterology 2016;150:S822-S823
Nystrom M. Obesity Surgery. Epub 2-1-18
Endoscopic Sleeve Gastroplasty (ESG)

• Performed with the Apollo Overstitch (Apollo Endosurgery, Austin, Tx)

• Requirements
  • General Anesthesia
  • Argon Plasma Coagulation
  • 90-120 minutes
  • DVT prophylaxis
  • Overtube optional
Multicenter Study of 248 Patients for 24 Months

• 3 centers (2 US, 1 Spain)
• Jan 2013-Nov 2015
• SAE 2%*
  • 2 perigastric fluid collection
  • Splenic laceration
  • PE
  • Pneumoperitoneum and Pneumothorax
• Variable Lifestyle Therapy
• Follow-up
  • 215/248 at 6 months (87%)
  • 57/92 at 24 months (62%)

*Hospitalizations for post-procedure symptoms not counted in SAE rate

Lopez-Nava, G. Obesity Surgery. Epub 4.27.17
## Investigational Intragastric Balloons in the US

<table>
<thead>
<tr>
<th>Device</th>
<th>Device Image</th>
<th>Characteristics</th>
<th>FDA Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spatz III Adjustable Balloon System</td>
<td><img src="image" alt="Spatz III Adjustable Balloon Image" /></td>
<td>• Spherical silicone balloon around a curved catheter which extends outside the balloon to adjust fill volume after implantation,</td>
<td>Pivotal Trial Complete</td>
</tr>
<tr>
<td>Spatz FGIA, Inc, Great Neck, NY</td>
<td></td>
<td>• Filled with saline dyed with methylene blue 300-900 ml</td>
<td></td>
</tr>
<tr>
<td>Elipse Intragastric Balloon Allurion</td>
<td><img src="image" alt="Elipse Intragastric Balloon Image" /></td>
<td>• Spherical balloon made of a film</td>
<td>Pivotal Trial Ongoing</td>
</tr>
<tr>
<td>Allurion Technologies</td>
<td></td>
<td>• Filled with 550 ml of saline</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Swallowed</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Self deflates and passes through GI tract at 4 months</td>
<td></td>
</tr>
</tbody>
</table>
TransPyloric Shuttle (TPS, BARONova, Gloeta, CA)

- Silicone sheath filled with a coiled cord of silicone
- Placed endoscopically through an overtube
- Intermittently blocks the pylorus
- Remains in the stomach for 12 months
- Pivotal trial complete
On the Horizon: Small Bowel Therapies

Intestinal Bypass Liners
- Endobarrier
- ValenTx Endoluminal Bypass

Duodenal Mucosal Resurfacing
- Revita DMR

Endoscopic Intestinal Bypass
- Incisionless Anastomosis System
• 39 subjects completed trial
  • N=11 with short segment ablation <6 cm duodenum
  • N=28 with long segment >9 cm of duodenum
  • N=8 with long segment, baseline HgbA1c between 7.5 and 10%, and on stable medications
• Weight loss <3 kg at week 24
Thank You