Endolumenal Balloon Therapy

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Bariatric Surgical Approaches

Limitations of Surgery

- Relatively expensive
- Skilled surgeons needed
- Patient apprehension

Less Effective

More Effective
Effective Obesity Treatment

More than 1,000,000 U.S. adults now have a BMI >50

- Lifestyle: 3%
- Medications: 1%
- Surgery: 1%
- Unmet Need: 95%
New devices and technologies may be beneficial
  - Less pain / risk / cost
  - Improved acceptance: 1/400 pts now treated
  - Possibly novel applications

If the risk reduction is significant, expected durability and effectiveness may also be reduced
Mean % EWL difference between groups should be at least 15% for primary procedures
Must assure that is still statistically significant
Primary therapy:
25% EWL, less weight loss if lower risk

ASMB/ASGE White Paper: A pathway to endoscopic bariatric therapies

SOARD 2011; 7(6): 672-682
Gastrointest Endosc 2011; 74(5): 943-953
Weight Loss Treatments

% EXCESS WEIGHT LOSS

INVASIVENESS / RISK PROFILE

Endoscopic Procedures

Endosuturing / Sleeves

Balloons

Pharmaceutical

Current treatments

Sleeve Gastrectomy

RYGB

BPD/DS
Gastric Weight Loss Devices: Early Experiences

Intragastrical balloon as an artificial bezoar for treatment of obesity.

Nieben OG. Lancet 1982
Introduction of Garren-Edwards Bubble

- September 1985
- FDA approved Garren-Edwards Bubble
- Cylinder 'tin can' shape with sharp edges
- Elastomer plastic
- Air Filled and only 220ml
- Recommended placement: 3 months
High rate of complications due to its design, small volume and short durability

<table>
<thead>
<tr>
<th>Old Balloons Complications</th>
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<tbody>
<tr>
<td>Gastric Erosion</td>
<td>26%</td>
</tr>
<tr>
<td>Gastric Ulcers</td>
<td>14%</td>
</tr>
<tr>
<td>Small Bowel Obstruction</td>
<td>2%</td>
</tr>
<tr>
<td>Mallory-Weiss Tear</td>
<td>11%</td>
</tr>
<tr>
<td>Oesophageal lacerations</td>
<td>1%</td>
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</table>

Not Effective

Not Safe
Withdrawal of Garren-Edwards Bubble

- 20,000 sold in the first year
- 1986-1988: complications presented and increased in frequency
- 1988: FDA restricted the use to 'investigation trials'
- May 15, 1988 the company withdrew the product from the market
1987: Balloon Consensus Panel

• 1987 Obesity Congress “Tarpon Springs” (Florida, USA): Scientific conference held with 75 international experts from the fields of gastroenterology, surgery, obesity, nutrition and behavior medicine to develop a general consensus on this technology/treatment option.

• Conference Conclusions with respect to a Gastric Volume-Displacing Weight Loss Device:
  - Be effective at promoting weight loss
  - Be filled with liquid (not air)
  - Be capable of adjustment to various sizes
  - Have smooth surface and low potential for causing ulcers and obstructions
  - Contain a radiopaque marker that allows proper follow-up of the device if it deflates
  - Be constructed of durable materials that DO NOT LEAK


1990s Intragastric Balloon

- Spherical
- Silicone
- Smooth surface
- Radiopac
- Durability: 6-9 months
- Saline filled: 400-700 ml
What's Available in the United States?
Status of Balloons in the U.S.

* TWO balloons are currently approved in the U.S.

* Allergan completed a pivotal trial in the U.S. in 2009 for a single, spherical balloon
  * Company decided not to pursue FDA approval
  * Apollo Endosurgery recently acquired the Allergan balloon and announced plans to submit the original pivotal study data to FDA in 2014 as they meet the new FDA endpoints
  * Approved August 2015

* ReShape Medical recently completed a pivotal trial in the U.S. for a dual balloon
  * Study successfully met its endpoints, Company submitted study data to the FDA mid-2014
  * Approved July 2015
Apollo Orbera

FDA approved
FDA Approved

Reshape Duo
Mechanism of Action

- Delayed Gastric Emptying
- Gastric Volume Reduction
- Baroreceptor stimulation 'stretch' receptors

- X-Ray of a positioned Balloon

- Volume of 500-700mL = diameter of 11cm

This Product is NOT APPROVED in the U.S.
**Orbera Effectiveness (OUS Results)**

- **Prospective, multicenter study of 323 patient in Europe**
  - Mean Weight Loss: -15.2kg +/- 10.5kg
  - Percent Excess Weight Loss (EWL): 48.3% +/- 28.1%
  - Mean reduction in BMI: -5.3kg/m² +/- 3.4kg/m²

- **Meta-analysis of 3,608 patients**
  - Mean Weight Loss: -14.7kg (12.4 - 17)
  - Percent Excess Weight Loss (EWL): 32.1% (26.9 - 37.4)
  - Mean reduction in BMI: -5.7kg/m² (4.4 – 6.9)

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230+

Peer reviewed publications on Orbera / BIB covering over 8,000 patients
BioEnterics® Intragastric Balloon (BIB®): a short-term, double-blind, randomised, controlled, crossover study on weight reduction in morbidly obese patients

A Genco¹, M Cipriano¹, V Bacci¹, M Cuzzolaro¹, A Materia¹, L Raparelli¹, C Docimo³, M Lorenzo² and N Basso¹

¹Department of Surgery ‘Paride Stefanini’, University ‘La Sapienza’ Medical School, Rome, Italy; ²Italian Group for LapBand & BIB® – GILB, Città della Scienza, Naples, Italy and ³Euroconsult, data elaboration and analysis, Naples, Italy
**Inability to lose weight (40 - 45 BMI patients)**

**Patients selection and enrolling**

**Randomization**

**Group A**
- Upper G.I. endoscopy
- BIB® placement
- Crossover
- BIB® removal
- Sham
- Upper G.I. endoscopy
- BIB® removal
- End of the study

**Group B**
- Upper G.I. endoscopy
- Sham
- BIB®
- Upper G.I. endoscopy
- BIB® removal

**Time**
- Start: 3 months
- Time: 6 months
Figure 2  BMI trend during different times of the study.
CE Marked in EU

FDA approved

Unique dual balloon design concept for:

- **Weight Loss** → 900cc of saline fills more of the stomach, slows gastric emptying
- **Tolerability** → Conforms to the stomach’s natural curvature to improve comfort
- **Safety** → Substantially reduces risk of migration/obstruction
U.S. Pilot IDE Study (n=30) - completed
- Prospective, randomized multi-center trial
  - Duo + diet & exercise vs. diet & exercise alone

U.S. Pivotal IDE Study (n=326) – finished and approved
- Prospective, randomized, sham-controlled multi-center trial
  - Duo + diet & exercise vs. sham procedure + diet & exercise
  - 8 participating U.S. sites; enrollment completed Feb, 2013
- Approved 2015
U.S. Pilot Study Reshape Results (n=21)
32% EWL at removal; 60% maintained at 1 year

Reshape US Pivotal IDE Study

First obesity device to meet its study efficacy endpoints in a randomized, sham-controlled clinical study (326 patients 2:1 ratio)

The REDUCE pivotal trial: a prospective, randomized controlled pivotal trial of a dual intragastric balloon for the treatment of obesity

Jaime Ponce, M.D., George Woodman, M.D., James Swain, M.D., Erik Wilson, M.D., Wayne English, M.D., Sanyed Ikramuddin, M.D., Eric Bour, M.D., Steven Edmundowicz, M.D., Brad Snyder, M.D., Flavia Soto, M.D., Shelby Sullivan, M.D., Richard Holcomb, Ph.D., John Lehmann, M.D. for the REDUCE Pivotal Trial Investigators

Received: September 30, 2014; Accepted: December 8, 2014; Published Online: December 16, 2014

Results

Mean BMI was 35.4. Both primary endpoints were met. DUO weight loss was over twice that of DIET. DUO patients had significantly greater %EWL at 24 weeks (25.1% intent-to-treat (ITT), 27.9% completed cases (CC, n = 167) compared with DIET patients (11.3% ITT, P = .004, 12.3% CC, n = 126). DUO patients significantly exceeded a 35% response rate (49.1% ITT, P<.001, 54.5% CC) for weight loss dichotomized at 25%EWL. Accommodative symptoms abated rapidly with support and medication. Balloon deflation occurred in 6% without migrations. Early retrieval for nonulcer intolerance occurred in 9%. Gastric ulcers were observed; a minor device change led to significantly reduced ulcer size and frequency (10%).

Conclusion

The DBS was significantly more effective than diet and exercise in causing weight loss with a low adverse event profile.
Who Wants Balloons?

In patient market research with patients eligible for ORBERA™ and surgical weight loss procedures:
- Significantly more interest and willingness to pay for ORBERA™ than surgery.
- Men are more likely than women to indicate preference for ORBERA™.

Percent of Eligible Patients Interested in Procedure

- ORBERA™: 42%
- Surgery: 10%

4x surgical alternatives

Question: Based on what you’ve seen and read, which procedure/option would you prefer? n=297
Summary

- Two Balloons accepted by FDA in 2015
- Safe and attractive to patients NOT candidates or NOT desiring surgery.
- Efficacy in loosing at least 10% of EW
- Best results will likely be in comprehensive programs.
- Continued research to make balloons last longer and also easier to place and manage
- As temporary treatments, we can retreat patients and combine with other techniques
- Will likely open more patients to bariatric procedures
TOGA Stapler

Not FDA Approved
TOGA Barium at 3 months
TOGA Pilot Study Phase II
Weight Loss

%EWL by Site

Follow-up Point:
- TOGA
- 3 Mo.
- 6 Mo.
- 9 Mo.
- 12 Mo.
- 15 Mo.
- 18 Mo.
- 21 Mo.
- 24 Mo.

% Excess Weight Loss:
- 0%
- 10%
- 20%
- 30%
- 40%
- 50%
- 60%

Graphs:
- Phase II AVG
- Belg. Phase II Avg.
- Italy Phase II Avg.
- Mex Phase II Avg.

Not FDA Approved
Hemoglobin A1c (n=42)
TOGA Pivotal FDA Trial

9 National Centers 23000 patient requests
4 high volume centers
Cedars Sinai, Columbia, Wash U, UT Houston
University of Texas is the only center in the South 6400 patient requests
275 blinded patients with 1 year crossover
1/3 Sham
2/3 TOGAs
TOGA Pivotal FDA Trial

<table>
<thead>
<tr>
<th></th>
<th>TOGA</th>
<th>Sham</th>
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</thead>
<tbody>
<tr>
<td>12 Month %EWL</td>
<td>23%</td>
<td>14%</td>
</tr>
<tr>
<td>&gt;25% EWL</td>
<td>44%</td>
<td>20%</td>
</tr>
<tr>
<td>&lt;25% EWL</td>
<td>56%</td>
<td>80%</td>
</tr>
<tr>
<td>Difference from control</td>
<td>23.3%</td>
<td>14.3%</td>
</tr>
<tr>
<td>14.3% confidence interval</td>
<td></td>
<td>12.5%</td>
</tr>
</tbody>
</table>

Adverse Events

- 1% Esophageal perforation
- 1% Gastric perforation
- Mortality 0% All AEs resolved

Both endpoints from EWL and AEs were met
Mean Percent Excess Weight Loss by Study Arm
New devices and technologies may be beneficial
- Less pain / risk / cost
- Improved acceptance: 1/400 pts now treated
- Possibly novel applications

If the risk reduction is significant, expected durability and effectiveness may also be reduced
Mean % EWL difference between groups should be at least 15% for primary procedures
Must assure that is still statistically significant
Primary therapy:
25% EWL, less weight loss if lower risk
Early Intervention: Endoluminal Suturing

- Endoluminal Vertical Gastroplasty
  - 64 patients, 12 mo f/u
  - Procedural time 45 min
  - %EWL at 1, 3, 12 mo: 21.1, 39.6, 58.1
  - No complications

<table>
<thead>
<tr>
<th>BMI (Kg/m²)</th>
<th>&lt;35</th>
<th>35-40</th>
<th>&gt;40</th>
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<tbody>
<tr>
<td>% Excess Weight Loss</td>
<td>85.1</td>
<td>56.5</td>
<td>48.9</td>
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POSE procedure
POSE Platform

**Transport**
- Provides access into stomach
- Features:
  - 4-way, lockable steering
  - Instrument locks
- Allows for full visualization during procedure

**grasper**
- Cannulated grasper
- Delivers the Snow-Shoe™ Suture Anchor
- 33mm-jaws allow for large full-thickness bites

**Suture Anchor**
- Expandable anchors prevent pull-through
- 3 year durability data on file

**helix**
- Helical cork screw
- Easy to use tissue manipulator
Fundus appearance after reduction

Procedure goal: invagination of the fundus, under tension

**FIG 1:** Fundus is “bunched” up

**FIG 2:** In antegrade view, fundus is effaced and can be seen sloping down towards greater curve
Distal body appearance before/after reduction

Distal Body Plications to delay complete gastric emptying by slowing antral mill

- Slower total transit of food from the antrum to small bowel
- Prolonged fullness
- Prolonged absence of hunger
POSE evolution: lessons learned

1: US Registry:
- Controlled trial: no
- Device generation: 1st
- Procedure: fundus only
- Patient selection: controlled
- Follow up: variable

2: OUS Registry:
- Controlled trial: no
- Device generation: mixed
- Procedure: variable
- Patient selection: commercial
- Follow up: uncontrolled

3: TEKNON Commercial:
- Controlled trial: No
- Device generation: 2nd (EZ)
- Procedure: standardized
- Patient selection: commercial
- Follow up: standardized

4: MOTIVATE:
- Controlled trial: yes
- Device generation: 2nd (EZ)
- Procedure: fundus + 3 DB variations
- Patient selection: optimized/controlled
- Follow up: optimized/controlled
Overstitch Full Thickness Suturing
Endoluminal Sutured Sleeve
Post-Plication
Clinical Update – Primary Obesity

6 month follow up, N=4

<table>
<thead>
<tr>
<th>Patient</th>
<th>Initial weight (Kg)</th>
<th>Initial BMI (Kg/m²)</th>
<th>Final weight (Kg)</th>
<th>Weight loss (Kg)</th>
<th>% weight loss</th>
<th>Final BMI (Kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>K.Z</td>
<td>89.1</td>
<td>32.0</td>
<td>69.5</td>
<td>19.6</td>
<td>22.47</td>
<td>24.7</td>
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<tr>
<td>V.T</td>
<td>89.0</td>
<td>32.0</td>
<td>75.0</td>
<td>14.0</td>
<td>15.73</td>
<td>26.9</td>
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<tr>
<td>J.S</td>
<td>86.9</td>
<td>32.4</td>
<td>69.1</td>
<td>17.8</td>
<td>20.48</td>
<td>26.0</td>
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<tr>
<td>L.C</td>
<td>95.0</td>
<td>35.0</td>
<td>85.0</td>
<td>10.0</td>
<td>10.53</td>
<td>32.4</td>
</tr>
<tr>
<td>Mean</td>
<td>90.0 Kg</td>
<td>32.85 Kg/m²</td>
<td>74.65 Kg</td>
<td>15.35 Kg</td>
<td>17.3%</td>
<td>27.5 Kg/m²</td>
</tr>
</tbody>
</table>
3 Basic Steps

- Endoscopy with APC marking
- Outer row suturing
- Inner row suturing
APC Marking
A = Anterior
P = Posterior
L = Lateral
Suture Technique

- 6 throws
- 6 throws
- 6 throws
- 6 throws
- 6 throws
- 2 throws
- 6 throws
- 5 throws
11 Months Later
PROMISE Trial

- **PRimary Obesity Multicenter Incisionless Suturing Evaluation**
- **Multi-Center**
  - Brigham and Women’s Boston
  - St. Joseph’s New Jersey
  - University of Texas Houston
  - Jackson South Florida
- 20 patients total (5 each) BMI 30-35
- **Primary endpoint**
  - Safety and feasibility of the procedure
- **Secondary endpoint**
  - Efficacy and durability
## PROMISe Follow Up Schedule

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<tbody>
<tr>
<td>Pre-op</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>0-7 days Post-op</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>1 mos. Post-op</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>3 mos. Post-op</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>6 mos. Post-op</td>
<td>✓</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>9 mos. Post-op</td>
<td>✓</td>
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<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>12 mos. Post-op</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>

† Only required if pre-op testing results showed FBG > 100 mg/dl
‡ BDI-II Score ≥20, recommend referral for psychiatric follow-up
PROMISE Trial Data

- 20 Females
- Average Age 36.7 ± 2.3 years
- Starting weight 90.4 ± 2.0 kg (199 ± 4.4 lbs)
- Initial BMI 33.4 ± 0.3 kg/m²
PROMISE Trial Data

- **Initial Adverse Events**
  - Nausea and vomiting in 3 patients
  - Postoperative pain in 2 patients

- **Severe Adverse Events—None**
  - No clinical postoperative bleeding
  - No clinical postoperative infection

- **17 patients followed for a year (3 pregnant)**
## PROMISE Trial Data

<table>
<thead>
<tr>
<th>F/U months</th>
<th>Patient #s</th>
<th>Weight Loss (kg)</th>
<th>BMI Drop</th>
<th>EWL %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>8.2</td>
<td>3.0</td>
<td>28%</td>
</tr>
<tr>
<td>6</td>
<td>17</td>
<td>15.0</td>
<td>5.5</td>
<td>63%</td>
</tr>
<tr>
<td>12</td>
<td>17</td>
<td>15.5</td>
<td>5.8</td>
<td>68%</td>
</tr>
</tbody>
</table>
Mayo Changes in Weight at 3 and 6 Months for all 10 patients

6cm ± 2 decrease in waist circumference
Mayo Weight Trends at 1 Year

Lbs

Patient 1
Patient 2
Patient 3
Patient 4
Patient 5

0 months
3 months
6 months
12 months
How Does It Work?

- Surgical Sleeve Gastrectomy
- Endoscopic Sleeve Gastroplasty
Gastric Scintigraphy

Pre Gastroplasty

180 minute

16% retained

3 Months Post Gastroplasty

180 minute

45% retained

Maximum Tolerated Volume Test

32 minutes at 30mL/min = 960kcal with fullness of 72/100mm VAS

10 minutes at 30mL/min = 300kcal with fullness of 78/100mm VAS
Who Belongs Here?

Patient
Who Belongs Here?

Gastroenterologist

Patient
Who Belongs Here?

Bariatric Surgeon

Patient
Conclusions

* The future is bright for all bariatric procedures

* Advanced flexible endoscopy is becoming a larger part of bariatrics.

* Surgeons should have and grow their advanced use of flexible endoscopy as many more endoluminal procedures are coming.

* Gastroenterologists will learn about all bariatric options and create a bariatric practices.

* Combined comprehensive programs are the future.
Thank You

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Division Chief, Minimally Invasive Surgeons of Texas
University of Texas Health Science Center at Houston