SPATZ
ADJUSTABLE GASTRIC BALLOON

Spatz Adjustable Gastric Balloon White Paper

May 2019

Currently under FDA review and not approved for sale in the US.

Table of Contents

Introduction

Obesity has been increasingly cited as a major health issue in recent decades. The American Heart Association (AHA) noted that in 2010, 60-70% of the US population was either overweight or obese, putting them at risk for heart disease, stroke, high blood pressure and diabetes [1]. Of the 154.7 million Americans who were overweight or obese in 2010, 78.4 million were obese (body mass index [BMI] of 30.0 kg/m_2 and higher). If current trends in the growth of obesity continue, total healthcare costs attributable to obesity could reach $861-$957 billion by 2030, which would account for 16%-18% of U.S. health expenditures [2].

Obesity Treatment Challenges

Treatment options for the obese population in the U.S. include weight loss management programs, pharmaceuticals, bariatric surgeries (gastric bypass, mini bypass, sleeve gastrectomy, and gastric banding) [3], and more recently, intragastric balloons (IGB). Bariatric surgery, which is the only therapeutic method associated with consistently demonstrable sustained weight loss, is expensive and surgeon-specific, and has associated morbidity and mortality rates that have led the medical community to seek non-surgical bariatric solutions.

IGB Limitations

Intragastric balloons for weight loss were introduced in the 1980s with over 300,000 balloons implanted worldwide. The medical literature is robust with clinical studies demonstrating intragastric balloon efficacy [4, 5]. Between 2015 and 2019 FDA approved 4 intragastric balloons for commercial use [6, 7, 8, 9].

There are several shortcomings associated with gastric balloons:

- **Intolerance** - studies report that 10% of patients are intolerant to gastric balloons and require early balloon removal [4 ,5]. FDA studies of Obalon, Orbera, Reshape and the Transpyloric Shuttle (TPS) reveal an early extraction rate of 14%-22% [6,7,8,9]. Unfortunately, there is no medical way of identifying these patients in advance, and they require early removal of the balloon.
- **Transient Balloon effect** – balloon effect decreases significantly within 3-4 months resulting in cessation of weight loss and even weight regain while the balloon is still implanted [10, 11, 12].

Success rates < 50%

FDA trials reveal that successful outcomes were achieved in 24.7%, 38.7%, 46.4% and 48.8% in the 4 FDA tested balloons (Obalon, Transpyloric Shuttle, Reshape and Orbera, respectively) – less than half of patients had a successful outcome [6, 7, 8, 9].

Spatz3 Adjustable Gastric Balloon

The Spatz3 is the only intragastric balloon that enables volume adjustment, which translates into increased success rates. The Spatz3 is placed in the stomach and occupies approximately one-third of the stomach's volume. This causes the stomach to empty very slowly, keeping food in longer than usual. The food builds up over time which produces symptoms that signal the patient that there is an abundance of food in the stomach. Patients thereby learn to eat less.

When gastric balloons cause intolerance or when they lose their effect after several months, we volume-adjust the Spatz3, which translates into increased success rates. The Spatz3 Adjustable balloon is the first and only gastric balloon that addresses these challenges:

- **Intolerance solution** - intolerant patients have their Spatz balloon adjusted downward to alleviate intolerance and thereby prevent early extraction [13, 14, 15]. Alternatively, patients may opt to start with a small balloon (300-350 ml vs 500-550 ml) in order to prevent intolerance, with the aim of enlarging the balloon several months later
- **Transient effect solution** - when balloon effect wears off the Spatz3 can have the balloon volume adjusted upward to prevent weight regain and to give a second round of weight loss. Accordingly, the Spatz3 up adjustment feature helps rejuvenate the weight loss trend and provides an effective-extended treatment. [13,14,15]. With these two interventions the Spatz3 Adjustable Balloon achieved the highest weight loss results and the highest success rates (83.7%) among the 5 FDA tested gastric balloons [15].

These 2 interventions yield the highest success rates of all gastric balloons.

FDA Trial Result Comparison (5 balloons)

The following table summarizes the FDA trial results from five intragastric balloons:

FDA TRIALS: 5 Intragastric Balloons

Intragastric Balloon	FDA Obalon	FDA Reshape	FDA Orbera	FDA TransPyloric Shuttle	FDA Spatz3
% TBL	6.6%	6.8%	10.2%	9.4%	14.9%
% EWL	24.1%	25.1%	38%	30.2%	52.9%
Weight Loss	14.4 lbs	14.3 lbs	21.8 lbs	20.5 lbs	31.7 lbs
Added wt loss after up adjustment	-	-	-	-	Additional 14.7% EWL
Response Rate (> 10% TBL or > 25%EWL)	24.7%	48.8%	46.4%	38.7%	83.7%

Summary of Spatz3 Results Compared with Non-Adjustable Balloons:

- Higher weight loss results
- Higher Response Rates
- Extra weight loss after Up Adjustment

Presidential Plenary Presentation at DDW 2019

SPATZ3

Spatz FDA Pivotal Clinical Trial

The primary clinical data set in support of this PMA is from the “A randomized, controlled, multi-center study comparing the Spatz3 Adjustable Balloon System plus diet and exercise to diet and exercise alone” study (Spatz3 US Pivotal Study), which is a study of 288 subjects at seven investigational sites in the US.

The study was conducted under IDE G160061, approved on July 29, 2016 and complies with 21 CFR 812. Informed consent was obtained from study subjects in compliance with 21 CFR 50 and IRB approval was obtained in compliance with 21 CFR 56.

The study evaluated the safety and effectiveness of the Spatz3 in adults with a BMI ≥ 30 and < 40 who have failed to achieve and maintain weight-loss with a weight control program.

Subjects were studied in a randomized, controlled, multi-center study. The control group received dietary/exercise counseling for 32 weeks. The treatment group received dietary/exercise counseling plus the Spatz3 balloon for 32 weeks, and then were followed for an additional 24 weeks.

Effectiveness Endpoints

There are two co-primary effectiveness endpoints:

- Percent change in total body weight (%TBL) at 32 weeks; and
- Clinical response, where a responder was defined as a subject with at least a 5% loss in total body weight at 32 weeks.

The following secondary endpoints were pre-specified in the clinical protocol and an observational analysis.

- Maintenance of 40% of the total body weight loss with the balloon six months after the balloon is removed.
- Clinical response, where a responder was defined as a subject with at least a 25% loss in excess body weight at 32 weeks.

Safety Endpoints

The incidence, frequency, and severity of adverse events related to treatment with the device were reported. There were no pre-specified safety endpoints.

- Study subjects were adult patients (22 years of age or above) with a BMI ≥ 30 and < 40 that met the eligibility criteria below.
- All eligibility criteria were met at the time of randomization.
- The primary analysis was based on the intent-to-treat dataset, which included all randomized subjects according to their randomized treatment.

The ITT population included all 288 randomized subjects according to each subject's randomized treatment group.

Efficacy analyses were conducted with the following ITT population datasets:

- Non-imputed dataset of blinded weights at the balloon extraction visit (either week 32 or unscheduled visit)
- Multiply-imputed dataset of blinded weights at week 32.
- Last observation carried forward (LOCF)-imputed dataset of blinded weights at week 32
- Non-imputed dataset of blinded weights at the end of the 6-month post-removal follow-up (i.e., week 56 for subjects whose balloon was removed on week 32).

Spatz FDA Results

The Spatz3 US Pivotal study had two co-primary effectiveness endpoints, both of which were met. These endpoints demonstrated that the Spatz3 Adjustable Balloon System was more effective than a medically supervised diet and exercise program alone for 32 weeks.

The first co-primary endpoint was that the Treatment Group would achieve a mean percent total body loss (%TBL) that exceeded that of the control group by 4.5%. At Week 32 the difference between the balloon and control mean %TBLs predicted by the linear model from the multiply-imputed ITT population dataset was 11.2%, and its 97.5% lower confidence bound was 9.5%.

The second co-primary effectiveness endpoint was that the response rate in the Treatment group would exceed 50%, where a responder is defined as a ≥5% loss in total body weight at 32 weeks. At week 32 the proportion of responders from the multiply-imputed ITT population was 90.7% with an exact 97.5% lower confidence bound of 86.1%.

The pre-specified secondary endpoints for maintenance of weight loss and %EWL were also both met. The proportion of balloon subjects who, by the end of the 6-month post-removal follow-up, had maintained ≥40% of the weight loss they had achieved by the balloon extraction date ranged from 56.1% to 72.9% (depending on how missing data were handled), which is greater than the pre-specified performance goal of 50%. The proportion of subjects with EWL ≥ 25% calculated from the multiply-imputed ITT population dataset was 83.7%, which is greater than the pre-specified performance goal of 35%.

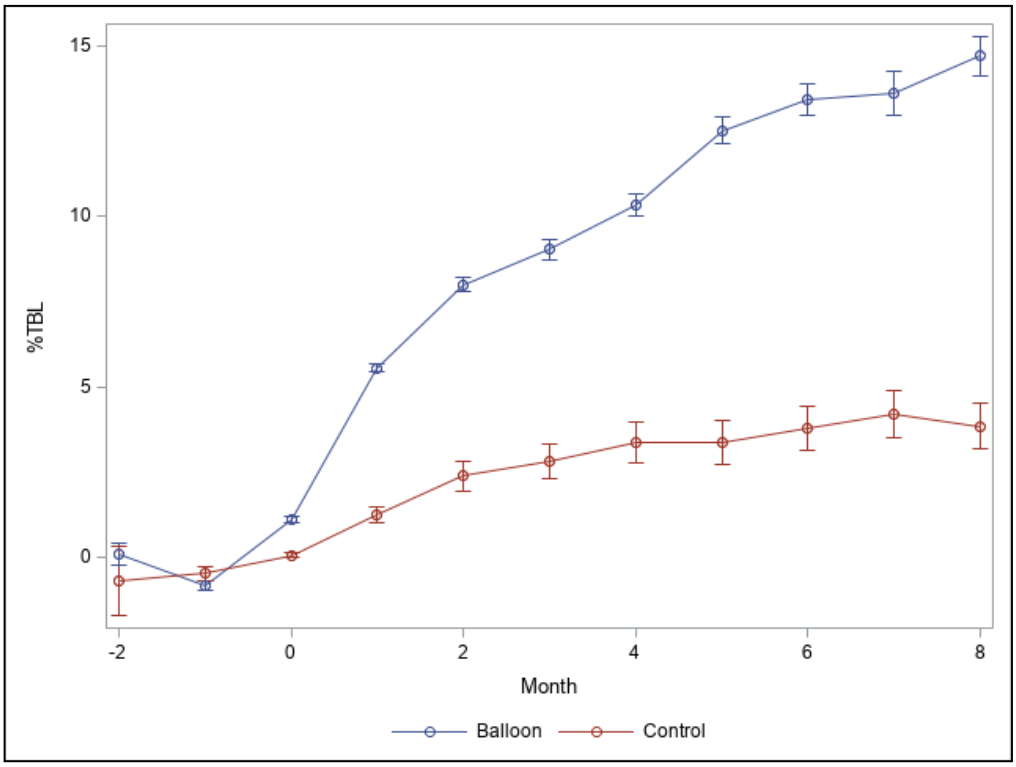
The Spatz3 US Pivotal clinical study did not have a pre-specified safety endpoint. The safety assessment included a complete review of reported serious adverse events (SAEs) and adverse events. There were no balloon deflations with migration into the small intestine or gastrointestinal obstructions reported during the study.

Almost all balloon subjects experienced AEs related to the balloon. However, the most frequent AEs were nausea, vomiting, and the majority of these events were characterized as either mild (71.1%) or moderate (20.3%). Ten (5.3%) balloon subjects experienced 24 serious adverse events (SAE) that were deemed Device-Related, while one control subject (1%) experienced one SAE. All SAEs were anticipated. All Device-Related SAEs were classified to the MeDRA Gastrointestinal disorders and Metabolism and Nutritional Disorders System organ classes, the most frequent being nausea, vomiting, and dehydration.

As clearly stated in the medical literature on intragastric balloons, this modality is associated with gastrointestinal related adverse events in almost all patients at some point in their treatment. With few exceptions, the first week of treatment is associated with the most gastrointestinal symptoms as the stomach accommodates to the foreign body within. This foreign body interferes with gastric emptying, which results in food accumulating in the stomach which in turn causes AEs such as nausea, vomiting, pain and others. As time progresses the symptoms lessen unless the patient overeats. This negative feedback with overeating is part of intragastric balloon therapy.

	Balloon Mean ± SD Median (Range)	**Control** Mean ± SD Median (Range)
Week 32 Weight (lb)	182.9 ± 29.5 180.4 (131.0-269.0)	208.2 ± 28.6 208.0 (140.0-306.0)
Total Body Loss (lb)	31.7 ± 15.5 31.0 (0.0-74.0)	7.6 ± 12.3 5.0 (-15.0-50.0)
Total Body Loss (%)	14.9 ± 7.2 14.5 (0.0-32.6)	3.6 ± 5.8 2.4 (-6.7-21.7)
Excess Weight Loss (%)	52.9 ± 28.1 48.8 (0.0-165.0)	12.3 ± 20.3 8.6 (-24.4-79.0)

Total Body Loss (Mean %TBL± Standard Error) by Group – ITT Population



Response Rate (EWL≥25%) at Week 32 – ITT Population

	All Balloon Subjects		Responders (EWL≥25%)	
	N	Mean %EWL	N	Proportion
Multiple Imputation	187	52.9%	156.6	83.7%

Total Body Loss (%TBL) and Excess Weight Loss (%EWL) Between Week 18 Up-adjustment and Week 32

Timeframe	Up-adjusted on week 18			Not up-adjusted on week 18		
	Subjects (N)	Mean %TBL (% of Week 32 %TBL)	Mean %EWL (% of Week 32 %EWL)	Subjects (N)	Mean %TBL (% of Week 32 %TBL)	Mean %EWL (% of Week 32 %EWL)
Day 0 to Week 18/20	134	11.3% (73%)	41.2% (74%)	53	11.7% (87%)	39.1% (86%)
Week 18/20 to Week 32		4.1% (27%)	14.7% (26%)		1.9% (15%)	6.3% (14%)
Day 0 to Week 32		15.4% (100%)	55.9% (100%)		13.5% (100%)	45.5% (100%)

Volume Adjustment Functions

The following adjustments were offered during the US Pivotal Study:

- **Down Adjustment** - The Spatz3 Adjustable Balloon is unique in that it allows for the adjustment of balloon volume during the implantation period. Downward adjustment may allow subjects who would otherwise request early balloon extraction to continue with the therapy. In the Spatz3 US Pivotal Study, downward adjustments were offered to 50 subjects who requested early balloon removal. Twenty-eight consented to down adjustment and 21/28 (75%) were able to complete the 32 weeks and avoid early extraction. Two of these 7 subjects had the explant more than 100 days after the downward adjustment, therefore the proportion of early explants avoided by the adjustment could be higher (82%) if these are counted as such.
- **Up Adjustment** - In the subset of the multiply-imputed ITT population balloon subjects that received an up-adjustment in week 18 (134 of 187, or 72%), the time under treatment after the up-adjustment accounted for 27% of their Week 32 TBL and 26% of their Week 32 EWL. Among balloon subjects who were not up-adjusted on week 18 (53 of 187), the time on study between weeks 20 and 32 accounted for 15% of their Week 32 TBL and 14% of their Week 32 EWL. Up-adjusted balloon subjects achieved, on average, 14% higher TBLs than non-up-adjusted balloon subjects.

Conclusion

The results of the Spatz3 US Pivotal clinical study provide valid scientific evidence demonstrating that the device is safe and effective. The co-primary endpoint results demonstrate that in a significant portion of the target population the device will provide clinically significant results. The down and up adjustment functions were demonstrated to enhance balloon efficacy, yielding the highest weight loss and the highest success rates of all 5 intragastric balloons tested by the FDA. Although most of the treatment subject experienced adverse events, these were generally mild and generally resolved within 14 days.

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