

Protocol #: 19-0278

Title: The effect of a gas-filled intragastric balloon or Endoscopic Sleeve Gastroplasty for weight loss compared with a meal replacement weight loss program on gastric emptying, hormonal adaptation to weight loss, and hunger

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SPECIFIC AIMS: The disease obesity continues to be a major health issue in the US with over one third of the population having a mass index $>30 \text{ kg/m}^2$. Obesity is associated with serious cardiometabolic complications including diabetes, hypertension, dyslipidemia and myocardial infarction. Rates of successful obesity treatment with weight loss and weight maintenance remain low. Several endoscopic bariatric therapies and procedures have been approved for use in the United States, including three intragastric balloon systems (2 fluid-filled and one gas-filled) and endoscopic sleeve gastroplasty (ESG), both of which have lower risks than bariatric surgery and do not alter gastrointestinal anatomy. Weight loss with all intragastric balloons and ESG is higher than lifestyle therapy or weight loss medications, but less than bariatric surgery. Unlike weight loss medications where weight loss from the medication is regained within 6-8 months after therapy ends, weight loss maintenance with intragastric balloons remains high with 66-88.5% of the weight loss maintained 6 months after device removal. Data suggests that space occupying devices with a volume of 400 ml or more in the stomach increase feelings of fullness and result in weight loss, but this does not explain the prolonged effect of weight loss maintenance after balloon removal. Although few studies have investigated the mechanism of action of fluid-filled balloons and one study with 4 patients undergoing ESG on weight loss, these data suggest that gastric emptying as well as space occupation contribute to weight loss. However, no studies have investigated the mechanisms of action of gas filled intragastric balloons on weight loss.

Understanding the mechanisms responsible for weight loss with the gas filled intragastric balloon system and eSG as well as any weight loss independent effects on blood glucose control would lay the groundwork for studies evaluating predictors of response to improve patient selection as well as studies understanding the mechanisms behind weight loss maintenance and developing strategies to prolong weight loss maintenance. **Therefore, the purpose of this pilot study is to determine the effects 10% total body weight loss (%TBWL) in patients with obesity treated with the intragastric balloon (GF- IGB) system or ESG compared to patients with obesity treated with a meal replacement program (MRP) on 1) gastric emptying, 2) hormonal adaptation to weight loss and 3) hunger. The following specific aims will be evaluated:**

AIM 1. Gastric emptying measured by technetium 99 gastric emptying study. Hypothesis 1. We hypothesize that treatment with GF-IGB and ESG will result in greater gastric retention of contents at 2 hours compared with patients who are treated with MRP.

AIM 2. Acyl-Ghrelin, glucose and insulin will be measured at multiple times points during a mixed meal test (MMT). Hypothesis 2. We hypothesize that weight loss induced increase in active ghrelin concentrations seen during a mixed meal tolerance test will be lower in patients treated with GF-IGB and ESG compared with patients treated with MRP, but there will be no difference in glucose and insulin concentrations.

Aim 3. Level of hunger will be measured using a visual analog scale. Hypothesis 3. We hypothesize that hunger will increase before and during a MMT after weight loss with MRP but will not change from baseline after weight loss with GF-IGB or ESG treatment.

1. Background and Significance

Obesity is a chronic disease which is associated with and contributes to multiple medical co-morbidities including but not limited to cardiovascular disease, diabetes, nonalcoholic fatty liver disease, and many different cancers. Obesity is also associated with an increased risk of all-cause mortality. Despite these known risks, treatment remains limited. This has contributed to the increase in the prevalence of obesity with 42.4% of adults in the US adults having a body mass index (BMI) >30 kg/m² of¹.

Endoscopic bariatric therapies are a new class of treatment for obesity which have demonstrated more weight loss than lifestyle therapy alone and fewer complications than bariatric surgery with less weight loss than bariatric surgery²⁻⁵. Four endoscopic devices are currently approved by the FDA for the treatment of obesity, including two intragastric balloons (IGB). One of the balloons systems are fluid filled (FF-IGB) and one is gas filled (GF-IGB). Although the GF-IGB system is swallowed, all the balloon systems require an endoscopist for endoscopic removal. In clinical registry series, these balloons demonstrate similar weight loss at 6 months⁶⁻⁸. Unlike weight loss medications, weight loss maintenance is prolonged after IGB removal, which was demonstrated meta-analysis of studies and case series outside of the US of the single FF-IGB demonstrated weight loss maintenance after balloon removal⁹ and in the US pivotal trials²⁻⁴. While the occupancy of space in the stomach by IGB is known to induce satiation and satiety^{10, 11}, this mechanism is only present with the IGB in place. Therefore, the prolonged effects of weight loss maintenance after IGB removal suggest other mechanisms contributing to weight loss with IGB treatment beyond space occupation. ESG is completed endoscopically with a device that has FDA 510k clearance for tissue apposition in the GI tract. Weight loss with ESG in a recent meta-analysis in 1772 patients demonstrated 16.5% TBWL at 12 months and 17.2% TBWL at 18-245 months¹². **Understanding the mechanisms contributing to weight loss with the GF-IGB system and ESG will lay the groundwork for future studies to enhance the effect of IGBs and ESG on initial weight loss, patient selection, and weight loss maintenance; increasing benefits to patients treated with IGBs or ESG.**

FF-IGB are known to delay gastric emptying^{10, 11}. This is consistent with practice patterns as patients reliably have food left in their stomachs after an overnight fast requiring multiple days of liquid diet prior to endoscopic removal to avoid aspiration. In one study, the FF-IGB delayed gastric emptying compared to both baseline and a control group and the change in gastric emptying was associated with weight loss (12). Gastric emptying has been studied in only 4 patients before and after ESG. In these 4 patients, there was a 90 minute increase to the time for 50% of emptying of solid foods, however the limited number of patients in that study reduce overall certainty of the effect of ESG on gastric emptying¹³. No studies have investigated the effects of the GF-IGB on gastric emptying. **This protocol will clarify the effects of the GF-IGB and ESG on gastric emptying compared with a control group matched on weight loss. This will elucidate the weight loss independent effects of the devices since patients will be studied at baseline and 10% total body weight loss.**

Another possible mechanism by which IGBs and ESG may induce weight loss and weight loss maintenance is through alterations in gut hormones. Ghrelin is a hormone secreted by X/A like cells, which are predominantly in the fundus of the stomach¹⁴. Ghrelin concentrations fluctuate with eating, increasing pre-meals and decreasing in response to food in the stomach. Moreover, infusion of ghrelin stimulates eating in humans and is the only known hormone secreted from the GI tract to stimulate hunger¹⁵. Weight loss with lifestyle therapy alone has been shown to increase fasting and meal test "active" or acyl-ghrelin concentrations, which correlated with increased hunger on visual analogue scale (VAS) testing¹⁶. Acyl-Ghrelin concentrations were still elevated at one year after weight loss despite weight regain of almost 50%, which suggests that acyl-ghrelin plays an important role in weight regain. Studies investigating ghrelin concentrations in the setting of FF-IGBs have been mixed, demonstrating decreased fasting plasma total ghrelin concentrations¹⁷, no change in fasting or meal test ghrelin concentrations in FF-IGB or control groups^{18, 19}, increased fasting plasma ghrelin compared to a control group at months 1 and 6 with decreased ghrelin in the active arm compared to the control arm after removal²⁰ and increased ghrelin concentrations in a single arm²¹. However, these studies measured

total ghrelin not acyl ghrelin. This limits the reliability of the data especially since no change in ghrelin concentrations were seen in control patients with weight loss in which an increase in acyl- ghrelin is expected. Moreover, all the studies were with FF-IGB and none were in the GF-IGB system.

Balloon type may have an effect on acyl-ghrelin concentrations as GF-IGB tend to float in the fundus and body of the stomach, which may affect the IGB's ability to suppress acyl-ghrelin secretion. In one of the aforementioned studies a post-hoc analysis demonstrated that the small number of patients whose FF-IGBs localized to the fundus had greater suppression of ghrelin¹⁹.

Fasting ghrelin has been evaluated in one study with 12 patients pre and post ESG. Fasting ghrelin concentrations did not increase with weight loss, but meal testing was not performed

²²Therefore, this protocol will determine the effects of 10% TBWL from either GF-IGB system treatment or ESG treatment compared to lifestyle and meal replacement therapy on acyl-ghrelin concentrations, the active form of ghrelin which stimulates hunger, and the sensation of hunger with the VAS. This will allow for the detection of effects that are specific to either procedure and independent of weight loss.

2. Innovation and Knowledge to be Gained: This proposal is innovative for several reasons. It will be the first ever study to evaluate any mechanisms of action of the GF-IGB system approved for use in the US and will add important information to the effect of ESG on gastric emptying as only 4 subjects have had gastric emptying measured pre and post ESG. Second, the study will determine a hormonal response to weight loss by procedures compared with diet through measuring the active form of ghrelin, acyl-ghrelin. Third, no other study investigating mechanisms of action of endoscopic bariatric therapies have compared outcomes with patients achieving the same amount of weight loss through diet alone. Weight loss itself has many effects, and the only way to mitigate the confounding effect of weight loss is to compare changes in these mechanism of action parameters in patients who have the same amount of weight loss, but have not undergone these procedures. Fourth, the study population will come from three clinically administered weight loss programs with different weight loss treatments. Although not a randomized control study, the participant populations in this comparative analysis more closely approximate clinical patient populations. The results from this study will lay the groundwork for future studies into additional gut hormone adaptation, optimization of patient selection to those with the highest likelihood of response to treatment with the GF-IGB system or ESG and studies investigating mechanisms of weight loss maintenance. This information will improve patient outcomes with GF-IGB or ESG treatment by endoscopists.

3. Preliminary Data

The research in this proposal involves using a combination of research techniques including imaging, meal testing, and questionnaires to determine the effects of the GF-IGB system and ESG on gastric emptying, hormonal adaptation to weight loss, and hunger which I have used in two previous studies.

In one study 18 subjects with obesity and nonalcoholic fatty liver disease were randomized in a 1:2 ratio to 16 weeks of: 1) no exercise (BMI 40.0 ± 5.4 kg/m², IHTG $21.3 \pm 10.8\%$) or 2) Exercise at 45%-55% of VO₂ max for 30-60 minutes 5 days/week (BMI 37.1 ± 4.0 kg/m², IHTG $20.4 \pm 6.8\%$). One exercise session per week was monitored at our center and subjects were re-fed calories expended during exercise by providing a liquid formula meal if any change in weight occurred to maintain weight stability. IHTG, measured with magnetic resonance spectroscopy, decreased by $10.3 \pm 4.6\%$ in the exercise group, but did not change in the control group, $p=0.044$. Exercise also decreased plasma alanine transaminase (ALT) concentrations by $12.8 \pm 3.1\%$, $p = 0.04$. Exercise did not affect hepatic lipoprotein secretion rates²³.

In a second study, 11 subjects with obesity were studied before and after a 4-week isocaloric diet high in high-fructose corn-syrup (HFCS). All meals were made in a bionutrition kitchen with 25% of total calories from HFCS. Patients were weighed every 3-4 days at meal pick-up and foods were adjusted to maintain weight. No change in weight (98.2 ± 12.8 kg and 97.8 ± 12.6 , $p=0.336$) or IHTG (2.2% [1.6,3.5] and 3.0% [2.1,6.5], $p=0.424$) measured by MRS occurred during the 4-week trial. Meal testing with a liquid mixed

meal (without HFCS at baseline and with 25% of calories as HFCS at end study testing) revealed trends towards increased fasting plasma uric acid concentrations (5.3 ± 0.8 mg/dl baseline and 5.9 ± 1.4 mg/dl end-study, $p=0.062$) and Uric Acid Area Under the Curve (1188 ± 154 baseline and 1343 ± 335 end-study, $p=0.091$). The high HFCS intervention resulted in a $12.8 \pm 7\%$ increase in plasma total cholesterol concentration, $25.4 \pm 31\%$ increase in plasma triglyceride concentration, and a trend towards an increase in very low-density lipoprotein-triglyceride rate of secretion. No changes were seen in glucose kinetics measured by hyperinsulinemic euglycemic clamp testing (manuscript in preparation).

4. Approach

4.1 Subjects: The study population will consist of 11 patients with a BMI 30-40 kg/m² and age 22-65 years old who are weight stable (defined as <5% weight change in the last 3 months) and initiating clinical treatment with the GF-IGB system, 11 patients with a BMI 30-40 kg/m² and age 22-65 years old who are weight stable (defined as <5% weight change in the last 3 months) and initiating clinical treatment with ESG, and 11 patients with a BMI 30-40 kg/m² and age 22-65 who are weight stable and initiating clinical treatment with a medically supervised MRP (My New Weigh; University of Colorado, Anschutz Health and Wellness Center). After undergoing any required laboratory testing or imaging for the patient's self-chosen treatments, patient will present for screening. The screening visit will consist of a history and physical examination, the Patient Health Questionnaire- 9 (PHQ-9)²⁴, and the Questionnaire on Eating and Weight Patterns – 5²⁵ (Appendix A). Patients with a history of liver disease, uncontrolled thyroid disease, anemia, diabetes, eating disorder, uncontrolled depression defined as a score ≥ 10 PHQ-9, on weight loss medications in the last 3 months, history of gastroparesis, bariatric surgery, or history to allergy or intolerance to any component of the meal used in the gastric emptying study or mixed meal test will be excluded. Women who are pregnant or lactating, prisoners, non-English speakers, and decisionally challenged adults will also be excluded. We anticipate consenting 25 patients in each arm to achieve the required number of patients completing all study testing in each arm for achieve adequate statistical power (See 5.2 Power Calculation). We will attempt to match enrollment based on BMI in categories of BMI 30-34.9 kg/m² and 35-40 kg/m².

4.1 Study Protocol

4.1.a. Overview. All patients will undergo study testing at baseline prior to initiating treatment with the GF-IGB system, ESG, or MRP. Study testing will consist of two separate visits within 7 days of each other at both baseline and at 10% total body weight loss (TBWL). On visit one, patients will undergo a gastric emptying study and on visit two, patients will undergo a mixed meal test and VAS for hunger. All subjects will be called weekly to review weight loss and rate of weight loss in order to appropriately time end study testing.

4.1.b. Treatments (Standard of Care): The three groups will consist of patients undergoing the following clinical treatments as part of their clinical care. These treatments are not affected by study participation.

GF-IGB System Treatment: After the patients meet all clinical GF-IGB system treatment (FDA approved, Appendix B) criteria and pre-placement activities, patients report to the endoscopy lab after an overnight fast for balloon administration at their own expense. The balloon, contained in a hard, cellulose food grade capsule and attached to a thin catheter, is swallowed by the patient in a standing position. Once the two-step verification of balloon passage into the stomach by both fluoroscopy and pressure reading, the balloon is inflated to a volume of 250 ml with a nitrogen-mix gas, additional imaging of the inflated balloon is obtained, the catheter is ejected from the balloon, and the catheter is pulled out through the patient's mouth. The process is repeated at week 2 for the second balloon and between weeks 4-8 for the third balloon based on patient preference. All patients are given an individualized calorie prescription by a registered dietitian for a goal of up to 2 pounds of weight loss per week. The balloons are removed endoscopically 6 months after placement of the first balloon(5). Patients also attend monthly virtual individual diet coaching and monthly virtual group behavior coaching sessions both delivered by a registered dietitian for twelve months focused on long-term behavior change, 6 months while the balloons are in place and six months after the balloons are removed.

ESG Treatment: After the patients meet all clinical ESG treatment criteria, patients report to the endoscopy lab after an overnight fast for the ESG procedure at their own expense. Endoscopic sleeve gastroplasty is a weight loss procedure that uses an FDA 510K cleared endoscopic suturing device known as Overstitch to reduce the size of the gastric body. The procedure is completed with an endoscope, which is a flexible tube with a camera, with the suturing device attached at the distal tip. suturing device attached to it. It is inserted through the mouth, down the esophagus, and into the stomach. Sutures with 8-10 bites 1.5-2 cm apart in a U-shape pattern are placed starting distally 6 cm proximal to the pylorus. When the suture is tightened the greater curve of the stomach is reduced in size. Additional sutures are placed moving proximally up to 2 cm distal to the gastroesophageal junction. An additional row of sutures is then placed again in the distal to proximal stomach to complete the gastroplasty. The final shape of the gastric body is a tube 3-4 cm in diameter. This decreases the amount of food one can consume, which leads to the consumption of fewer calories throughout the day, resulting in weight loss. However, for long-term success and maintenance of weight loss, a healthy diet and exercise are also required with the consumption of smaller portion sizes. All patients are given an individualized calorie prescription by a registered dietitian for a goal of up to 2 pounds of weight loss per week. Patients also attend monthly virtual individual diet coaching and monthly virtual group behavior coaching sessions both delivered by a registered dietitian for twelve months focused on long-term behavior change.

MRP: After patients meet all criteria for the medically supervised MRP program and enroll in the program at their own expense, patients are given an individualized calorie prescription by a registered dietitian for a goal of 2 pounds weight loss per week. Patients are seen in a group-based program once a week focused on long-term behavior change and use meal replacements for a nutritionally balanced very low-calorie diet for 20 weeks.

4.1.c. Gastric emptying study (research related). After an overnight fast, patients will report to the radiology suite at the University of Colorado Hospital. Subjects will consume a meal consisting of 118 ml (4 oz) of liquid egg substitute mixed with technetium colloidal sulfur and cooked until firm, two pieces of white bread, and 29 gm of a jam as well as 120 ml of water ingested upright over 10 minutes. Immediately after ingestion, planar static imaging of the anterior and posterior abdomen with the patient in the upright position will be performed. Radiotracer activity in the stomach will be obtained with anterior and posterior regions of interest placed over the stomach, and percent retention calculated using the geometric mean at baseline, 0.5 hour, 1 hour, 2 hours, 3 hours, and 4hours after ingestion. If there is less than 10% food remaining in the stomach at the 3 hour mark the gastric emptying study will stop at 3 hours.

4.1.d. Mixed Meal Test (research related): On a day separate from the gastric emptying study, patients will report to the Clinical Translational Research Center (CTRC) at the University of Colorado School of Medicine after an overnight fast. An intravenous catheter will be inserted into a hand or forearm vein for blood draws. Immediately before and at 15, 30, 60, 90, 120, 150, and 180 minutes after consumptions of a mixed meal, blood will be drawn for measurement of acyl-ghrelin, plasma insulin, and plasma glucose concentrations. The mixed meal will be a mixture of liquids and solids and contain 550 kcal with a macronutrient content of 51% carbohydrate, 33% fat, and 16% protein.

4.1.e. Visual Analogue Scales to assess Hunger (Research Related): A validated questionnaire (The Visual Analogue Scales for measurement of appetite sensations) ²⁶ will be given to patients during the mixed meal test. Subjects will fill out the questionnaire immediately before the mixed meal and at 15, 30, 60, 90, 120, 150, and 180 minutes after consuming the mixed meal.

4.1.f. Follow-up weight at 12 months: patients will report for a follow-up visit at 12 months after initiating therapy for weight.

5. Statistical Analysis.

5.1 Data analysis. The primary analysis will be a group by study-time repeated (baseline-end study) measures analysis of variance which will include an evaluation of statistical contrasts that compare between group differences in changes from baseline to end. Analyses will be performed on the following variables: percent of gastric retention at 2 hours, fasting and Area Under the Curve (AUC) for acyl ghrelin, insulin, glucose, and VAS-hunger. A Student's t-test for paired samples will also be performed on each variable from baseline to end-study testing. All data will be analyzed using SPSS (IBM, Armonk, NY)

5.2 Power calculation. The primary endpoints used for the power calculation in this study are change in gastric emptying at 2 hours, acyl-ghrelin concentrations, and visual analog scale. In assessing statistical power, we will use statistical contrasts of change from baseline between the groups, assuming 11 patients in each group. Based on previous work, a conservative estimate of standard deviation of the change is assumed to be roughly 80% of the amount of change for fasting acyl-ghrelin and VAS Hunger (16) and 60% for percent gastric retention at 2 hours ¹¹. All tests are two-sided and performed at the 0.05 level of significance. GPower 3.1 (Universitat Duesseldorf, Germany) was used for power calculations. The impact of these assumptions is as follows (Table 1):

Table 1. Power Calculations

Variable	Baseline	Response to Weight Loss			Between Group (compared with MRP)	
		MRP	GF-IGB	ESG	GF-IGB	ESG
% Retention at 2 hours	25±14.5%	0	+12.5 (50%)	+12.5 (50%)	96%	96%
Acyl Ghrelin pg/ml	125±100	+50 (40%)	+10 (8%)	+10 (8%)	86%	86%
Visual Analog Scale	32±25	+11 (40%)	0	0	80%	80%

6.0. Study timeline.

Subjects will be recruited over two years from patient populations already at the University of Colorado. Our current practice had 15 GF-IGB patients per year since the start of the program with 80% of the current patient population meeting study criteria. Our current practice also had 18 ESG patients in the last 12 year months with 75% of the current patient population meeting study criteria. The MRP at the University of Colorado enrolls >40 patients per year with >50% meeting study inclusion criteria. Baseline to End-Study Testing is expected to take 16 weeks per patient. Consenting will need to be performed on 25 subjects in each group (total of 75 subjects). Assuming an attrition rate of 20% for patients undergoing baseline testing, all study testing should be completed with 11 subjects in each group within two years. If a participant has not reached 10% TBWL by the end of the clinic program, they will be withdrawn from the study.

7.0 Recruitment and Consenting:

Study participants in the GF-IGB and ESG group will be recruited from the endoscopic bariatric therapy clinical practice who have passed all clinical pre-procedure testing and are scheduled to undergo device placement. Study participants in the MRP group will be recruited from the My New Weigh meal replacement program who have met all clinical program entry criteria. Medical records will be reviewed for inclusion and exclusion criteria prior to consent and subjects will be asked face to face, or over the phone if they would like to participate in this study. Patients will then be scheduled for consent and screening. The consenting process will be performed by the study coordinator in a face to

face visit. Only the study participant will be allowed to provide consent for the study.

8.0 Potential Risks for Patients

8.1 General: We anticipate no psychological, social or legal risks beyond those of participation in health-related research in general. The potential risks associated with participation in this study are small. They will be explained to all subjects who desire to participate in this research project. In addition, subjects will be informed that there is a possibility of unforeseeable risk, although we consider this unlikely. The research coordinator and/or the PI will ensure understanding of the consent and study procedures, as well as laboratory results; in addition, the research coordinator and/or PI will explain the various procedures and answer any questions the subjects may have before initiating any procedures. Whenever concerns arise, subjects will be informed that they are free to withdraw from the study at any time with no bias or prejudice.

8.2 Confidentiality: All key personnel involved in the design or conduct of the research involving the human subjects will receive the required education on the protection of human research participants prior to the start of this project. All specimens will be obtained solely for research purposes. Study samples and datasheets will be coded with an identification number for each subject. All data will be treated confidentially, and the subjects' names and identities will not be disclosed in any published reports. Clinic records are maintained in EPIC and study related data will be maintained on de-identified case report forms that will be entered into RedCap. A locked excel spreadsheet on a secured server will be used to maintain the key to the identification of study subject ID numbers.

8.3 Questionnaires: Patients could screen positive for moderate or severe depression or an eating disorder. Patients will be notified of these results and referral resources will be given to patients. If the patient wants these results sent to their primary care physicians, a copy of the results and referral resources will be sent to the subject's primary care physician.

8.4 Gastric Emptying Study: This research involves exposure to radiation equivalent to 40 mrems per study from the gastric emptying study. This is equivalent to <13%% of the amount of average radiation exposure adults in the US receive each year. Participants could also have an allergic reaction to the food components of the test. All subjects will be advised of the radiation exposure and will be questioned about food allergies and if they have a known allergy to any component of the test meal, they will be excluded from the study.

8.5 Intravenous catheter insertion: Possible side effects of intravenous catheter insertion are discomfort, bruising, and/or bleeding at the site of needle insertion. Occasionally some people experience dizziness or feel faint. An infection can occur at the site of catheter insertion. Aseptic technique for intravenous catheter insertion will be used to prevent infection, participants will have IV catheter insertion while seated or reclined, and the site will be monitored during the mixed meal test for any signs of intravenous catheter malfunction.

9.0 Data Monitoring:

This the study related procedures in this protocol (questionnaires, visual analog scale, gastric emptying study, and mixed meal tests with blood draws) are low risk. The PI will review any adverse events that occur from study related procedures as they occur. There will not be a formal interim analysis.

10.0 Potential Scientific Problems:

This is an ambitious protocol which will require enough patient volume for adequate enrollment, however we have adequate patient populations to recruit for this study. Detailed follow-up of patients is necessary to ensure testing at 10% TBWL, and I have experience with two other trials that required carefully monitoring weight to eliminate confounding from change in weight. I will employ similar strategies in this study to test patients at the required %TBWL and we have budgeted for an assumed 20% attrition rate after enrollment and baseline testing to have adequate sample to achieve sufficient

power.

11.0 Funding:

Grant funding is currently pending for this study from the American Society for Gastrointestinal Endoscopy, but PI start-up funds are currently available to complete all study testing.

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