Proposed Method For Mechanical Stimulation of the Small Intestine

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4/30/20

Biomaterials
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Introduction:

This project seeks to explore the hypothesis that mechanical stimulation within intestinal tracts stimulates intestinal cell proliferation to provide a treatment for diabetes. This was explored through research of Rhue-En-Y (RNY) bypass procedure, Gastric Electrical stimulation, and other similar weight loss procedures that provided insight into the properties enabling the proliferation of gastrointestinal cells. This research gave us the knowledge to carry out a brainstorming design process where we took performance and design specifications into account. We also discussed testing methods to be able to confirm whether the proposed mechanical stimulation is actually able to meet the hypothesized result.

The gastrointestinal tract is made up of four main components --the esophagus, the stomach, and the small and large intestines. The process of digestion begins with the mechanical and chemical breakdown of food through mastication. Then, through a series of muscle contractions within the esophagus, the food is passed into the stomach where it undergoes further chemical breakdown. The stomach then leads to the opening of the small intestine, known as the duodenum. Once in the small intestine, a series of expansions and contractions work to proliferate GI cells enabling the digestion and absorption of nutrients. Folds within the small and large intestines allow there to be more villi that are used to digest food.

Processes such as the RNY bypass procedure enable a reduction of type 2 diabetes and see healthy blood glucose and hemoglobin levels within a majority of obese patients. A study comparing the effect of duodenal-jejunal bypass on rats suggests that diabetes control results from the increased motility of chyme to the intestine, enabling release of glucagon-like peptide 1 (GLP-1) in the distal bowel. GLP-1 stimulates insulin secretion and causes pancreatic beta cells to proliferate.[1] However, researchers have not been sure whether the increased motility causes weight-loss, or if the weight loss has to do with the nature of bypassing the stomach itself.

It was discovered that Gastric Electrical Stimulation (GES) at certain parameters have different effects on motility. A study conducted by researchers at Duke University suggests that low frequency sinusoidal currents may improve the efficacy of GI pacing.[2] Another study sought to compound the results of Gastric Electrical Stimulation with the above mentioned GLP-1 secretion. On its own, GES has been used as a method to accelerate motility within the stomach and intestines. Researchers with the Veterans Research and Education Foundation found that Intestinal electrical stimulation in rats attenuates hyperglycemia levels in the blood. Results are associated with those of a bypass procedure --with a reduced invasiveness. GLP-1 secretion improves β-cell function, reducing blood-glucose levels and suggesting IES as a potential treatment for diabetes.

Other GI tract procedures were explored to find biocompatible materials that work within the conditions of digestion. Another weight-loss procedure known as the intragastric balloon entails introducing a saline-filled silicone sphere directly to the stomach through a catheter. The balloon is designed to “sit” in the stomach, inducing satiety with less food. The silicone sphere is

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[1] Rubino F,. The mechanism of diabetes control after gastrointestinal bypass surgery reveals a role of the proximal small intestine in the pathophysiology of type 2 diabetes (2006) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1856597/

[2] Barth BB, et al., 2017. Electrical stimulation of gut motility guided by an in silico model. J. Neural Eng.

designed to be left in place for up to 6 months. [3] Other biomaterials that are compatible within the GI tract include synthesized biomaterials (Silicone, Polyvinyl Acetate Phthalate, poly-L-lactic acid, poly glycolic acid (PGA), poly ε-caprolactone, derived hydrogels, etc) and natural biomaterials (collagen scaffolds, small-intestinal submucosa derived scaffolds).[4]

Design:

In making a design. There were two major paths that we had come to. The first one was a purely mechanical solution that would rely on the mechanical properties of the device to push the intestines and mechanically stimulate them. The type of design was one that relied on implanted electromagnets to push a plastic coated metal capsule into one of the walls of the intestines. We decided to move forward with the purely mechanical idea because there would not be any need for charging, no invasive surgery would be required to implant electromagnets, and we were unsure if the magnets would be able to provide enough stimulation to the intestines.

The final design has three separate parts. The central core of the design is a silicone coated spherocylinder that had 8 openings The insides of the core would have a polyurethane shell to contain the high gas pressures within the capsule. These openings were where the base of the second part of the device is inserted, the telescoping arms. The telescoping arms would allow for the exterior pad to extend away from the center of the device to their full length of up to 1.2 inches. The telescoping arms are made from polyurethane for its strength and its relatively low friction. The pressure of the compressed air inside of the core would have to be 438 MPa in order to provide a force of one Newton to the exterior of the arms, which would push on the walls of the intestine. This is a high pressure that could be decreased by increasing the diameter of the telescoping arms. In theory the structure would be able to withstand the high pressures. The exterior pad is made from a hydrogel to be both biocompatible and soft so that it does not damage the intestines.

The device will enter the gastrointestinal tract through a pill that is ingested orally. The pill is 0.3 inches in diameter and 0.7 inches long, end to end, putting it in the larger end of pill sizes. The coating of the pill is made from polyvinyl acetate phthalate, which acts as an enteric coating. This coating dissolves in fluids with a pH between 7-9. This would allow for the capsule to protect the device in the acidic environment of the stomach. The capsule is then designed to dissolve in the alkaline conditions present within the small intestine. The pill would digest approximately 1-2 hours after ingestion.

Once the coating dissolves in the small intestine, the device is able to expand up to its full size. The fully expanded size of the device is 1.2 inches. The size of the device is meant to be slightly larger than the 1 inch diameter of the small intestine so that the intestinal wall is expanded, which triggers a response in the Enteric Nervous System. The Enteric Nervous System allows the intestines to act independently from the brain. This means that if the intestinal nerves are triggered, the digestion processes can occur without needing confirmation from the

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[3] Mayo Clinic https://www.mayoclinic.org/tests-procedures/intragastric-balloon/about/pac-20394435

[4] Biomaterials science : an introduction to materials in medicine / edited by Buddy D. Ratner ... [et al.].– 2nd ed

brain. Once the Enteric Nervous System senses the stretching of the gastro intestinal walls, the intestines begin to secrete digestive juices and enzymes, as well as begin the distension of the muscles controlling the intestines. This intestinal movement consists of two major types of motion: peristaltic waves, and segmental contraction. The device would ideally activate both, as the intestine would try to break down the device and push it further down the GI tract.

Testing and Validation:

Testing and validation procedure is critical for understanding whether the design is functioning properly, stimulating the GI tract mechanically or not. There has been a very important design which is used to track the movement of internal organs, mainly stomach and intestines. It is used for different purposes, colonoscopy or stomach diseases. However, it is made using advanced technology and experimentally tested. It will be suitable for our purpose and testing our design. The technology that can be used for in vivo tracking is the magnetic sensing technology. There is an endoscopic capsule which produces biomarkers around the GI tract. The GI tract is approximately 9 m long. Fiber optic endoscopes, colonoscopes are around 2.5 m long so they cannot go deeper inside the GI tract and they cannot offer an efficient solution. There are some examples for wireless capsule endoscopes, they offer more efficient solutions however they cannot examine the functional changes inside the GI tract. The solution would be to create biomarkers near the affected spots and trace the response through some clinical methods, e.g breadth testing.[5]

The magnetic tracking system has a magnet inserted inside the capsule. When the capsule is in the body, there are magnetic sensors outside the body which can measure the magnetic field strengths. The magnetic field depends on the distance of the magnet from a specific point and also its orientation. This problem can be solved by placing several magnetic sensors. Magnetic sensors are connected to a magnetic board controller. [6]

It is a tracking system that can show the location of the capsule in real time as it travels through the digestive tract. It is free from the pitfalls that most radio-frequency tracking systems suffer from. Research on magnetic sensory hardware, empirically developed models and experimental results shows that this technique is suitable for in vivo applications.

This magnetic sensor is tested for finding solutions to other stomach-related diseases. Even though no formal testing systems are processed for the RNY bypass procedure, this technology could be applied to this design. The experimental procedure for the magnetic tracking system is made by making a pig swallow the capsule. The tracking system tracked the location of the capsule. Also, while testing, four X-rays were taken to compare the locations at the exact moment when each X-ray was taken. At the end of the trial, the tracking system's comparison time for finding the exact location is measured to be 7.518 ms.

[5] A Real-Time Localization System for an Endoscopic Capsule Using Magnetic Sensors
[6] A Real-Time Localization System for an Endoscopic Capsule Using Magnetic Sensors

Conclusion:

This is a device that is ingested by swallowing a pill. The capsule dissolves once it reaches the intestines then it expands using compressed gas to allow for the external pads to push against the intestinal wall to mechanically stimulate the intestines. The purpose of this stimulation is to promote the proliferation of the intestinal cells, which could be an effective therapy for diabetes. There are multiple ways we would validate the effectiveness of the device, such as using magnetic sensor technology which would allow for the tracking of intestinal movements.

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