Ileal Partial Diversion for Treatment of Type 2 Diabetes with MAGIC™ IPD

Mohammad M. Karimzada MD[1], Lauren L. Evans MD[1], Vamsi Aribindi MD[1], Veeshal Patel MD[1], Vinith Johnson BS[1], Monica Jain MD[2], Craig A. Munroe MD[1], Robert H. Lustig MD[3], Lee Swanstrom MD[4], Cannon Yates[5], Rose Carion[5], Michael R. Harrison MD[1]

1. University of California at San Francisco, Dept of Surgery, San Francisco, CA;2. University of California at San Francisco, Dept of Gastroenterology, San Francisco, CA; 2. Cedars-Sinai Medical Center, Dept of Surgery, Los Angeles, CA; 3. University of California at San Francisco, Dept of Endocrinology, San Francisco, CA; 4. Dept of Surgery, Institutes des Hôpitaux Universitaires (IHU) of the University of Strasbourg, Strasbourg, France; 5. San Jose State University, Dept of Engineering, San Jose, CA

Objective of Device

MAGIC™ IPD is a novel device that allows for creation of partial jejunoileal diversion (also known as ileal partial diversion [IPD]) for minimally invasive treatment of type 2 diabetes (T2DM). T2DM is an epidemic that affects over 10% of Americans and 400 million globally, with increasing incidence across all ages. Current therapies are limited by treatment failure. Experts such as those in the Diabetes Surgery Summit recognize the need to incorporate metabolic surgery in the T2DM treatment algorithm. Typical procedures such as sleeve gastrectomy or gastric bypass involve major reconfiguration of the gastrointestinal tract, requiring significant diet modifications and leaving patients vulnerable to perioperative complications and long-term side effects including but not limited to gastrointestinal bleeding,

In contrast, IPD avoids resection and leaves the gastrointestinal tract in continuity by placing a side-to-side anastomosis between the proximal jejunum and distal ileum to allow for a conduit carrying early chyme content. This partial diversion exploits the hormonal mechanisms of traditional gastric bypass, in particular glucagon-like peptide 1 (GLP-1) augmentation, to improve insulin resistance and induce weight loss. GLP-1 has been widely studied within the context of diabetes and obesity,

MAGIC IPD is a device that can achieve this through minimally invasive delivery via hybrid laparoscopy/endoscopy, with the ability to be completely endoscopic with further development.

Methods

To investigate the efficacy of MAGIC IPD in creating effective ileal partial diversion (IPD), a nonhuman primate model was used. California National Primate Research Center (CNPRC) was selected as the site for study. Total of 12 rhesus monkeys (macaca mulatta) in underwent intervention across two separate studies (5, then 7 monkeys). The location of anastomosis To induce insulin resistance, specimens were fed 500cc per day of a 15% high-fructose corn syrup (HFCS) beverage in addition to high-fat monkey chow diet prior to MAGIC IPD intervention. Specimens underwent open laparotomy under general anesthesia and magnetic modules were placed via proximal intestine enterotomy. Data presented were based on both groups with different intervention times, as indicated. Blood samples were drawn at regular intervals and intravenous glucose tolerance tests were performed after induction of insulin resistance with diabetogenic diet, and after MAGIC IPD intervention. Fig. 1 demonstrates placement of the MAGIC IPD anchors, creating a partial diversion that diverts about 80% of the small intestine (based on observed typical length of 200cm for adult rhesus macaque specimen). Friedmann's test used for statistical analyses.

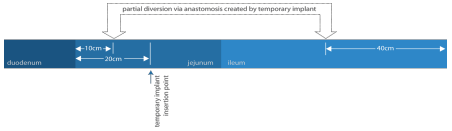


Figure 1. Graphical representation of MAGIC IPD anchors placement within small intestine of adult rhesus macaque.

Technology

MAGIC IPD is an innovative device system that leverages an innovative design for enteroenteral anastomoses through magnetic compression. The design innovation includes anchors with specialized surface geometries designed to facilitate rapid creation of a healthy anastomosis. Anchors are placed in an intraluminal position in opposing bowel segments and the magnetic anchors then "mate" or appose the anchors and intestinal serosa at the desired location. Transmural magnetic compression from the apposed anchors induce controlled central necrosis and peripheral healing (Fig. 2). The mated anchor pair then detaches and passes via the rectum after anastomosis formation is complete.

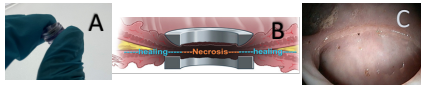


Figure 2. MAGIC IPD anchors (A), animation of mated anchors during anastomosis formation (B), endoscopic image of healed anastomosis (C).

Animal Studies

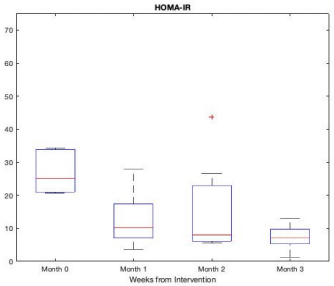


Figure 3. Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) of specimens at time of MAGIC IPD procedure and 3 months later.

	Pre-intervention	Post-intervention	Percent Change
Fasting Insulin	118	39 (3 months)	- 67 %
Fasting Glucose	91.2	73.0 (3 months)	- 20 %
GLP-1 AUC during glucose tolerance test	290	732 (6 weeks)	+ 152%

Table 1. Fasting labs and glucose tolerance testing results before and after intervention. Data from two groups of specimens with different post-intervention survival.

Discussion

MAGIC IPD has undergone rigorous animal testing and demonstrates great potential in translating into a minimally invasive procedural treatment for diabetes. Most recently, monkey studies indicate statistically significant decreases in fasting glucose and insulin after MAGIC IPD intervention, decreasing by 20% and 67%, respectively (Table 1). Accordingly, this led to a significant decrease in HOMA-IR (Fig. 3) of greater than 3.5 fold, signifying substantial improvement in insulin resistance.. The mechanism of this improvement is likely driven by GLP-1 augmentation. Table 1 displays a 152% increase in GLP-1 during glucose tolerance testing after MAGIC IPD. Thought to be central to the hormonal response in bariatric surgeries such as Roux-en-Y gastric bypass, GLP-1 is an incretin that induces insulin secretion, improves insulin resistance, and induces satiety and weight loss. In creating a conduit to divert early intestinal content to the distal ileum via MAGIC IPD, stimulation of GLP-1 secreting L-cells are thought to be optimized.

Work in Progress

In these studies, the MAGIC IPD anchors were placed during open surgery with enterotomy. However, the aim is to work towards an entirely endoscopic approach. In its current and initial iteration, the focus is to develop a combined endoscopic/laparoscopic approach that achieves placement without an enterotomy of any kind. To do so, cadaver studies are in progress using specialized and proprietary endoscopic enhancements such as caps designed to work with commercially available snares and endoscopes (Fig. 4). Nonabrasive, biosafe materials were used.

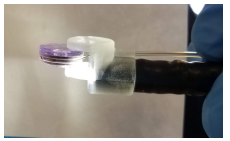


Figure 4. MAGIC Endoscopic Cap with MAGIC IPD anchor secured by commercially available oval snare

Conclusion

MAGIC IPD is an effective technology in improving insulin resistance and has great potential to become a procedural treatment for diabetes. As the development of the procedure continues, it is ready for transition into clinical trial.

UCSF Surgical Innovations
Departments of Surgery and Bioengineering & Therapeutic Sciences