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Magnetic Compression Anastomosis (Magnamosis): First-In-Human Trial

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BACKGROUND: Magnetic compression anastomosis (magnamosis) uses a pair of self-centering magnetic Harrison Rings to create an intestinal anastomosis without sutures or staples. We report the first-in-human case series using this unique device.

STUDY DESIGN: We conducted a prospective, single-center, first-in-human pilot trial to evaluate the feasibility and safety of creating an intestinal anastomosis using the Magnamosis device. Adult patients requiring any intestinal anastomosis to restore bowel continuity were eligible for inclusion. For each procedure, 1 Harrison Ring was placed in the lumen of each intestinal segment. The rings were brought together and mated, and left to form a side to side, functional end to end anastomosis. Device movement was monitored with serial x-rays until it was passed in the stool. Patients were monitored for adverse effects with routine clinic appointments, as well as questionnaires.

RESULTS: Five patients have undergone small bowel anastomosis with the Magnamosis device. All 5 patients had severe systemic disease and underwent complex open urinary reconstruction procedures, with the device used to restore small bowel continuity after isolation of an ileal segment. All devices passed without obstruction or pain. No patients have had any complications related to their anastomosis, including anastomotic leaks, bleeding, or stricture at median follow-up of 13 months.

CONCLUSIONS: In this initial case series from the first-in-human trial of the Magnamosis device, the device was successfully placed and effectively formed a side to side, functional end to end small bowel anastomosis in all 5 patients. No patients have had any anastomotic complications at intermediate follow-up. (J Am Coll Surg 2017;225:676–681. © 2017 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

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Intestinal anastomosis is fundamental to surgery. Whether repairing traumatic injury, correcting congenital anomalies, or resecting tumors, surgeons have performed this procedure for centuries. Currently, most anastomoses are either handsewn or made with staplers, but a device that could automatically and consistently produce an optimal anastomosis could reduce morbidity and save considerable operative time and resources. The concept of compression anastomosis was first credited to French physician Felix-Nicholas Denans in the early 19th century.[1,2] Magnetic compression anastomosis (magnamosis) is a modern iteration of this classic idea, which uses the force of magnetic attraction to form an intestinal anastomosis without sutures or staples.

The Magnamosis device (Magnamosis, Inc) is a pair of self-centering, rare earth magnets encased in a specially engineered polycarbonate shell (Fig. 1). To form an anastomosis, a single magnetic Harrison Ring is placed within

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Figure 1. The Magnamosis device. The device consists of a pair of specially engineered magnetic Harrison Rings. One magnetic ring is placed within the lumen of each intestinal segment to be joined. The graded compressive force created by the magnetic casing induces necrosis centrally, and allows for remodeling at the periphery.

the lumen of each segment of intestine where the anastomosis is desired. When the 2 rings are mated, the interposed tissue is compressed, causing necrosis and anastomosis formation. The device passes through the newly formed anastomosis and leaves no foreign bodies. In extensive preclinical testing, including animal trials in more than 90 pigs and 10 monkeys, we have demonstrated the device's ability to consistently create histologically well-formed anastomoses with burst strength comparable with or better than handsewn or stapled anastomoses.[3-8] Here, we report the first-in-human case series using this novel device.

METHODS

Design

This was a prospective, single-center, first-in-human pilot trial to evaluate the feasibility, safety, and therapeutic benefit of creating an intestinal anastomosis using the Magnamosis device. The study was registered with ClinicalTrials.gov (NCT02043392) and approved by the University of California San Francisco Committee on Human Research (IRB# 13-11536).

Participants

Adult patients at our institution requiring any small or large bowel anastomosis to restore bowel continuity were eligible for inclusion. The use of the Magnamosis device does not affect the conduct of the indicated surgical procedure and is simply an alternative to sutures or staples. Though the device can be delivered by open, laparoscopic, or endoscopic techniques, this initial case series focused on open procedures for proof-of-concept testing. Patients who met the inclusion criteria were invited to participate in the study by an attending surgeon. Informed consent was obtained from all study participants.

Device

The Magnamosis device is composed of a matched pair of self-centering rare earth neodymium-iron-boron ring magnets encased in medical-grade polycarbonate (Fig. 1).[3,4,8] Each magnet has an external diameter of 23 mm, internal diameter of 9.6 mm, and thickness of 6.6 mm. The device is sterilized by electron beam irradiation and packaged in sets of 2. Once placed within the desired intestinal segments, the 2 rings self-align and self-center, and the mated rings compress the interposed tissue. To promote self-centering, one side of the device has a slightly convex surface, and the other side is slightly concave, allowing for a cup and saucer effect when the 2 magnets are mated. The geometry of the mating surfaces is specially engineered to reduce the risk of anastomotic complications.[3,8] The device produces a gradient of compressive forces on the bowel wall that causes transmural ischemia and necrosis centrally, but allows for remodeling of the intestine at the periphery, to gradually form a full-thickness anastomosis.[3] After extensive testing for biocompatibility, compressive force, and burst performance, the device was approved by the Food and Drug Administration for clinical trial (IDE G130046) to assess safety in a pilot study.

Surgical technique

A full preoperative surgical evaluation was conducted, and patients received preoperative bowel preparation and antibiotics per the surgeon's standard practice. All procedures were performed by a single surgeon, with the Magnamosis Inc research team immediately available in the operating room for consultation. In each case, standard surgical techniques were used to place 1 Harrison Ring in the lumen of each of the 2 segments of intestine (Video 1).[9] The magnets were brought together and mated to form a side to side, functional end to end anastomosis (Fig. 2). Before mating, the serosal surface of the intestine was checked for intervening tissue or debris that would prevent the magnets from mating uniformly. If the surgeon is not satisfied with the geometry or appearance of the intestine after coupling the magnets, the magnets can be disengaged by gentle traction and repositioned. To ensure immediate patency, a hole was created with cautery, under direct vision, between the central portion of the mated rings. Patency was confirmed by inserting a straight angiocatheter and infusing saline through the

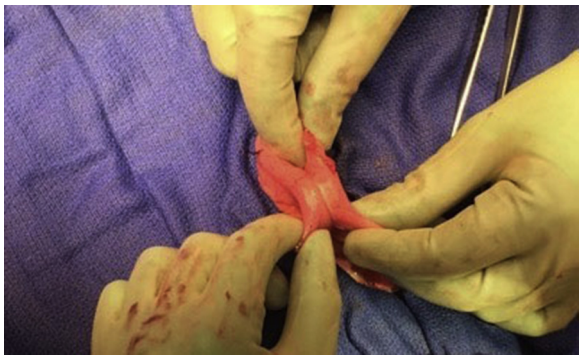

Figure 2. Magnet mating. Magnets within the lumen of each intestinal segment are brought together and mated. Due to properties of the magnets themselves, as well as the design of the outer casing, the 2 parts of the device self-align and self-center to ensure proper configuration.

catheter from the proximal to the distal segment of the joined intestines. Enterotomies were closed transversely with a single stapler fire.

Postoperative management

All patients received routine postoperative management in accordance with their procedures. Time to resumption of feeding was based on the clinical judgement of the surgeon. A plain abdominal x-ray was obtained in the postoperative anesthesia care unit and serially (every few days) thereafter to monitor magnet position and passage (Fig. 3). All patients wore either a dog tag or medical alert bracelet to avoid any MRI until the magnet had passed. As long they met the usual standard hospital discharge criteria, patients were discharged before the magnets passed. Outpatient clinic follow-up was determined by the attending surgeon. In addition, telephone calls were performed by the study team at 3 months, 12 months, and 2 years post procedure.

Data analysis

Variables and outcomes assessed in this pilot trial include the following: the incidence of device-related complications, including anastomotic leaks, bleeding, perforation, and anastomotic stricture (documented by symptoms or imaging within 3 months of the procedure); duration of hospitalization; number of days to passage of the Magnamosis device (found in stool or absent on x-ray); and number of days to the first postoperative bowel movement.

RESULTS

Patient characteristics

Five patients were recruited from May 2014 to the present. Although the study was open to all surgeons at our institution, the first surgeons with eligible patients to participate were urologists using bowel segments to create uretero-ileal urinary diversion. Three of the five study participants were quadriplegic with neurogenic bladder and recurrent urinary stones, neurogenic bowel, and constipation, and were bedridden. Two patients had end-stage renal disease requiring hemodialysis and were candidates for renal transplantation. Three patients had previous abdominal operations, and all 5 had

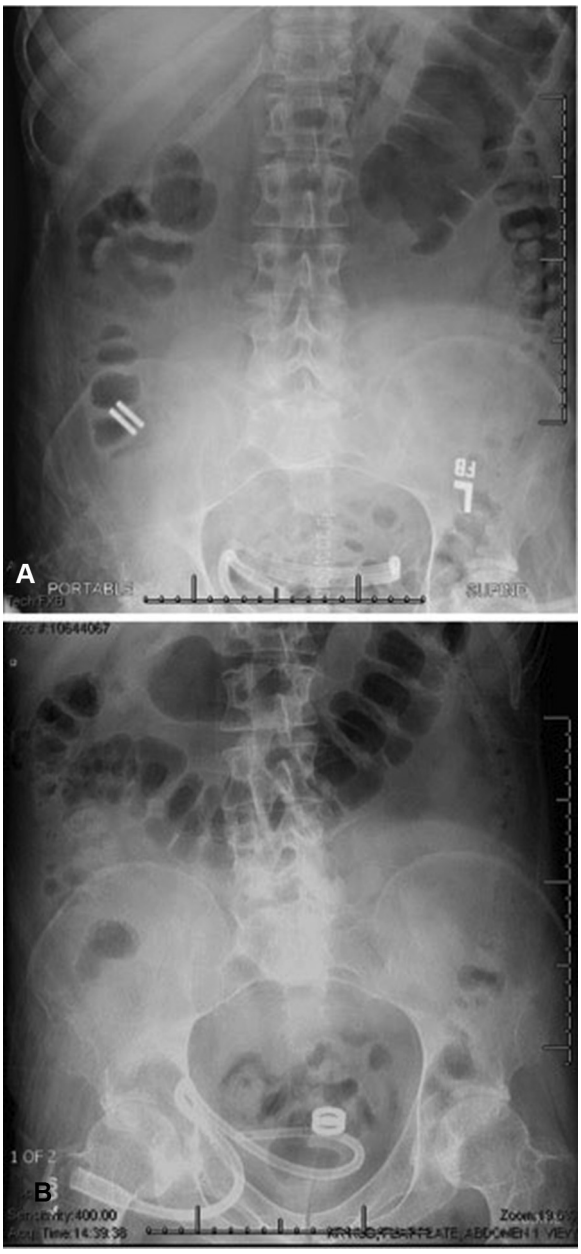

Figure 3. Magnet passage. Mated magnets are visible on abdominal x-ray. (A) First in the right lower quadrant soon after placement, and (B) in the superior rectum 1 day before passage.

undergone multiple previous urologic procedures. See eDocument 1 for additional information about patient characteristics and procedures.

The patients underwent a variety of open urologic procedures, during which the Magnamosis device was used as an alternative to a bowel stapler (eDocument 1). The total operative time ranged from 4 hours, 45 minutes to 7 hours, 27 minutes. The restoration of intestinal continuity with the device took approximately 25 to 35 minutes.

The magnets were found in the stool of the 3 bedridden patients, and on abdominal x-ray (demonstrating lack of magnets) in the 2 other patients, who were unaware that the magnets had already passed. Passage of the device was confirmed at 2 to 8 weeks after the operation (Table 1). Four patients were discharged after documented magnet passage, and 1 patient (patient 5) was discharged with the magnets in situ and followed with abdominal films on postoperative days 54 and 85. The latter film demonstrated absence of the magnets.

Length of follow-up ranges from 6 to 18 months (median 13 months) to date, and is ongoing. No patients reported symptoms related to their intestinal anastomosis, either in clinic appointments or on focused questionnaire. None of the 5 patients have experienced any complications related to the magnet, including anastomotic leak, bleeding, or stricture. Four of the 5 patients experienced surgical complications unrelated to the small intestinal anastomosis. The most significant of these occurred in patient 2, who died 11 months after his procedure, after an extended hospitalization due to aspiration pneumonia. Additionally, patient 4 was admitted 3 months after the operation for abdominal pain, nausea, and emesis. She was diagnosed with closed loop obstruction and underwent exploratory laparotomy, which showed internal herniation of a segment of small intestine through adhesions in the pelvis. The hernia was reduced and adhesions were lysed. The ileal conduit and Magnamosis segment were visualized and were not involved. Other complications included *Clostridium difficile* infection and superficial surgical site infection.

DISCUSSION

In this first case series of the Magnamosis device in humans, we found that despite the complicated medical conditions and comorbidities of the 5 study participants, the device safely and successfully performed in every case. No patient experienced anastomotic leak, bleeding, or stricture formation. Although histologic examination is clearly impossible in a clinical trial, we did have the unexpected opportunity to view the anastomosis 3 months postoperatively in a patient who required surgical exploration for an unrelated adhesive obstruction. The anastomosis was intact, patent, and well-formed.

In swine studies, the device passed into the stool in 7 to 14 days.[3] However, in our patients, it took at least 18 days. This might not be typical, however, as the patient population in this cohort had overall poor baseline functional status; several patients had severe neurologic dysfunction with poor gastrointestinal motility preoperatively. In addition, these patients underwent extensive, lengthy, open reconstructive procedures, and 2 patients had significant postoperative ileus. We would therefore expect a healthier cohort to mobilize and pass the device more quickly. Early postoperative feeding has been shown to decrease postoperative ileus in major abdominal operations, including urologic reconstruction,[10-13] and early feeding might have also hastened resumption of bowel function and magnet passage in these patients. Regardless of how long the magnets take to pass, we do not anticipate any risk to patients from the magnets within the intestine, either from obstruction, or from their magnetic properties. None of the patients experienced obstructive symptoms from the device, and our previous clinical trial demonstrated the safety of an implanted magnetic device for correction of pectus excavatum for up to 2 years.[14-16] In cases of delayed passage, the experience of patient 5 confirmed that patients can be discharged safely home before passing the magnets, and will likely pass them without their knowledge.

The anastomosis was performed in about 30 minutes in each case, generally becoming quicker as the study progressed. The device placement has 2 steps: placing the magnets in the lumen of the intestine and mating them, and creating a hole through the center of the ring for immediate patency. There was some learning curve involved for both steps. Regular surgical instruments, because they are ferromagnetic and attracted to

Table 1. Clinical Course

Duration of event, d	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Time to first bowel movement	4	3	18	17	7
Time to start liquids	13	29	17	17	33
Time to passage of magnet	17	50	22	18	54–85*
Hospital stay	18	51	23	19	42

*Passage occurred sometime between abdominal x-rays on day 54 and day 85.

the device, make manipulation of the Harrison Rings difficult. After the first operation, nonmagnetic, titanium-based instruments were used to introduce the magnets, which significantly improved ease of placement. For the second step, it was initially difficult to create immediate patency by cauterizing the central tissue between the rings under direct vision because of the 90-degree angulation of the target tissue along the bowel wall in relation to the intestinal lumen. This angle became more direct when the enterotomy used to insert the second magnet into the intestine was made closer to where the magnets would be mated. Next-generation devices will incorporate creation of immediate patency into the magnet deployment.

Although limited foremost by its small sample size, our initial experience with these first human patients yielded several important findings. First, the device works safely in a wide range of ages and even in high-risk patients. Second, patients can be safely discharged from the hospital with the device in place. Third, nonmagnetic instruments improve the surgeon's ability to handle the magnets. Fourth, a mechanism to create immediate patency between the mated magnets would simplify and shorten the procedure. The Magnamosis device's method of slow tissue remodeling without leaving foreign bodies creates a well-formed anastomosis, which can decrease the incidence of anastomotic leaks. In addition, the simplicity of merely "sticking" the 2 segments of intestine together can save substantial operative time. However, open operation is not the best way to showcase the merits of magnamosis. In our subsequent patients, we plan to focus on laparoscopic delivery of the Magnamosis device, which currently can be deployed using laparoscopic, endoscopic, radiographic, or hybrid techniques. In addition, the device can be sized and adapted to a variety of intraluminal anastomoses, including intestinal, urologic, and biliary applications, with wide-reaching implications for the future of surgery.

CONCLUSIONS

This initial case series from the first-in-human trial of the Magnamosis device shows that the device was successfully placed and effectively formed a side to side, functional end to end small bowel anastomosis in all 5 patients studied. None have had any complications related to the anastomosis after up to 18 months of follow-up.

Author Contributions

Study conception and design: Kwiat, Harrison
Acquisition of data: Hsi, Imamura-Ching, Stoller
Analysis and interpreation of data: Graves, Co, Harrison
Drafting of manuscript: Graves, Co
Critical revision: Hsi, Imamura-Ching, Harrison, Stoller

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eDocument 1. Patient Characteristics and Procedures

Patient no.	Diagnosis	ASA	Comorbidities and surgical history	Procedure	Total operative time	Magnamosis, min
1: 28-year-old male	C6–C7 quadriplegia due to spinal cord injury from gunshot wound; neurogenic bladder, bladder stones, meatal hypospadias; s/p cystoscopy, suprapubic tube placement; s/p cystolithotomy and ileal chimney	3	Asthma, autonomic dysreflexia, depression	Open cystolithotomy, continent catheterizable channel with ileum to bladder	4 h, 45 min	35
2: 69-year-old male	C5–C7 quadriplegia due to motor vehicle collision; neurogenic bladder, bladder stones, bilateral nephrolithiasis s/p cystolitholapaxy for bladder stones; s/p bilateral nephrostomy tube placement for acute kidney injury; s/p suprapubic catheter	4	Decubitus coccygeal ulcer, depression, constipation	Supratrigonal cystectomy, ileal conduit, excision suprapubic tube tract	6 h	30
3: 30-year-old male	Quadriplegia due to spinal cord injury from gunshot wound; neurogenic bladder and nephrolithiasis, urethral stricture; s/p suprapubic catheter	3	Deep vein thrombosis with IVC filter; on warfarin; s/p colostomy	Supratrigonal cystectomy, ileal conduit, excision suprapubic tract	6 h	25
4: 44-year-old female	ESRD on hemodialysis with urethral obstruction; s/p multiple dilations; s/p bilateral cutaneous ureterostomies; s/p revision ureterostomy with ureterolysis, right pelvic kidney, poor capacity, and poorly compliant bladder	3	Gastroesophageal reflux hypertension, gout	Left laparoscopic nephro-ureterectomy, right open nephro-ureterectomy, supratrigonal cystectomy, ileal conduit	7 h, 27 min	25
5: 58-year-old male	ESRD on hemodialysis due to congenital anomaly of urinary system with noncompliant, low-capacity bladder, right nonfunctional kidney with cutaneous right ureterostomy; s/p left radical nephrectomy	3	Carotid artery stenosis s/p stroke, coronary artery disease s/p myocardial infarction, alcohol abuse, anemia, gastroesophageal reflux, hypertension, hyperlipidemia; s/p carotid endarterectomy; 3-vessel coronary artery bypass graft	Laparoscopic lysis of adhesions, right laparoscopic nephro-ureterectomy, open excision distal ureteral stump, ileal conduit	6 h	30

ASA, American Society of Anesthesiologists physical status classification; ESRD, end-stage renal disease; s/p, status post.